GHANA COLLEGE OF PHYSICIANS AND SURGEONS

FACULTY OF ANAESTHESIA

EFFECT OF PERINEURAL DEXAMETHASONE ON ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK FOR POST CAESAREAN ANALGESIA AT KORLE-BU TEACHING HOSPITAL

SUBMITTED TO THE FACULTY OF ANAESTHESIA, IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE CONFERMENT OF A FELLOW OF THE GHANA COLLEGE OF SURGEONS (FGCS)

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DECLARATION

I declare that this dissertation is my own work produced from research undertaken under supervision at Korle-Bu Teaching Hospital. This dissertation has not been previously submitted in any form to another institution for the award of other degrees or diplomas. Authors and publishers whose works have been utilised in this work have been duly acknowledged in the text and list of references.

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CERTIFICATION BY SUPERVISORS

We certify that this work was carried out by **Dr Daniel Akwanfo Yaw Sottie** at the Korle-Bu Teaching Hospital, Accra under our supervision. We have also supervised the writing of the dissertation.

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DEDICATION

This book is dedicated to God Almighty for the gift of life and blessings, to my family for their support, and to all the patients who participated in the study for making this research possible and allowing the discovery of improved ways of obstetric anaesthetic practice.

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ABSTRACT

INTRODUCTION

Caesarean delivery (CD) is a common surgical procedure with associated significant post-operative pain. Adequate post caesarean analgesia enables the new mother to take care of the new born while preventing the debilitating effects of uncontrolled post-operative pain. The most frequent negative response to caesarean delivery in Ghanaian women is pain. Analgesic options following CD in Korle-Bu Teaching Hospital include the use of intrathecal opioids (fentanyl), parenteral opioids (intramuscular pethidine), intravenous paracetamol and rectal diclofenac. The addition of the bilateral transversus abdominis plane (TAP) block with dexamethasone as an adjunct to the existing pain management modalities will provide adequate post caesarean delivery analgesia and improve patient satisfaction.

AIM

The aim of this study was to assess the effectiveness and safety of perineural dexamethasone in ultrasound guided bilateral TAP block in providing post-operative analgesia in parturients who underwent caesarean delivery under spinal anaesthesia at Korle-Bu Teaching Hospital.

METHODS

This was a prospective, randomized, double blind study of 99 electively booked patients for caesarean delivery under spinal anaesthesia. These were divided into three groups of 33 each after meeting inclusion/exclusion criteria and giving informed consent. Ultrasound guided bilateral TAP block was administered immediately after caesarean delivery under spinal anaesthesia (using either bupivacaine + dexamethasone (group A), only bupivacaine (group B) or only saline (group C)). Time to request for first analgesia, systemic opioid consumption, numerical rating scale (NRS) pain scores, incidence of pruritus, nausea and vomiting and participants' satisfaction were recorded. This was entered into Microsoft Excel spread sheet and Statistical Package for the Social Scientists (SPSS) software version 25 used for data analysis.

RESULTS

The time to first analgesic request was significantly prolonged in the bupivacaine group (327.5 ± 98.69 minutes) compared to the saline group (256.5 ± 72.33 minutes) (p-value = 0.023); with addition of dexamethasone resulting in further prolongation (485.2 ± 143.03 minutes) (p-value < 0.0001) of the time to first rescue analgesic. There was a significantly lower consumption of

systemic opioids in the bupivacaine group (269.1 ± 64.44mg) compared to the saline group (380.6 ± 39.21mg) (*p*-value < 0.0001); with further significant lowering of opioid analgesic requirements (113.6 ± 81.58mg) on addition of dexamethasone (*p*-value < 0.0001). NRS pain scores at rest and on coughing were lower in the intervention groups compared to the control group. Lower NRS pain scores were recorded with addition of dexamethasone although they were not always significant. The incidence of adverse events of pruritus, nausea and vomiting and sedation was not significantly different amongst the three groups. Participants who had dexamethasone + bupivacaine had higher satisfaction scores than participants who had bupivacaine; who in turn had higher satisfaction scores than participants who had saline.

CONCLUSION

Addition of dexamethasone to bupivacaine for a TAP block is safe, has opioid sparing effect and provided better postoperative analgesia after Caesarean delivery compared to control and bupivacaine alone TAP at Korle-Bu Teaching Hospital.

Keywords: Caesarean Delivery; Post-operative analgesia; Bilateral TAP Block

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LIST OF ABBREVIATIONS

ACOG	-	American College of Obstetricians and Gynecologists
ANOVA	-	Analysis of Variance
ASA	-	American Society of Anesthesiologists
ASIS	-	Anterior Superior Iliac Spine
BK	-	Bradykinin
BMI	-	Body Mass Index
BP	-	Blood Pressure
CD	-	Caesarean Delivery
CI	-	Confidence Interval
COX	-	Cyclooxygenase
COX-2	-	Cyclooxygenase-2
CSE	-	Combined Spinal-Epidural
CSF	-	Cerebrospinal Fluid
EOM	-	External Oblique Muscle
FPS-R	-	Faces Pain Scale-Revised
IASP	-	International Association for the Study of Pain
IH	-	Iliohypogastric
II	-	Ilioinguinal
IM	-	Intramuscular
IOM	-	Internal Oblique Muscle
IV	-	Intravenous
KBTH	-	Korle-Bu Teaching Hospital
LAST	-	Local Anaesthetic Systemic Toxicity
LIP	-	Latissimo-Iliac Point
MAP	-	Mean Arterial Pressure
NGF	-	Nerve Growth Factor
NMDA	-	N-Methyl-D-Aspartate
NRS	-	Numerical Rating Scale
NSAID	-	Non-Steroidal Anti-Inflammatory Drug
PACU	-	Post Anaesthesia Care Unit
PCA	-	Patient Controlled Analgesia
PGE2	-	Prostaglandin E2

PONV	-	Post-Operative Nausea and Vomiting
QLM	-	Quadratus Lumborum Muscle
RAM	-	Rectus Abdominis Muscle
RCT	-	Randomised Controlled Trial
TAM	-	Transversus Abdominis Muscle
TAP	-	Transversus Abdominis Plane
US	-	Ultrasound
VAPS	-	Visual Analogue Pain Score
VRS	-	Verbal Rating Scale

CHAPTER 1: INTRODUCTION

1.1 Introduction

Caesarean delivery (CD) is described as the most common surgical procedure in the world.[1] An analysis by Betran et al. demonstrated that caesarean delivery accounts for about 18.6% of births worldwide and up to 11.4% of births in West Africa.[2] They also noted that there was an increasing trend in caesarean delivery rates all over the world. The Ghana Demographic and Health Survey of 2014 reported a national caesarean section rate of 13%.[3] In Korle-Bu Teaching Hospital (KBTH), a study by Gulati and Hjelde on indications for caesarean sections showed that caesarean delivery constituted 34.7% of all deliveries.[4] Gulati and Hjelde noted that the main indications for caesarean sections were previous caesarean section (37.6%), foetal distress (9.1%) and foetal malpresentation including breech (8.6%). They also showed that younger women and nulliparas had significantly more caesarean sections than older women and multiparas.

Caesarean delivery is a major surgery often associated with significant pain in the immediate post-operative period. Dolin and colleagues[5] reviewed studies examining the incidence of pain (Visual Analogue Pain Score (VAPS) score > 3) after major surgery including CD. They found the incidence of moderate-severe pain of 20.9% in patients with epidural analgesia, 35.8% for patient-controlled analgesia (PCA), and 67.2% for intramuscular (IM) analgesia.[5]

Research has also demonstrated an increased risk for persistent pain following caesarean delivery.[6,7] In a 2-yr follow-up of almost 1,000 women for breech delivery by caesarean section, there was a 20% incidence of pain, mostly comprising backache and headache, with approximately 5% with pain in the superficial or deep abdomen.[6] A Danish postal survey showed pain in the surgical area of 19% at 3 months and 12% at 10 months after caesarean delivery, with 50% of these women experiencing daily or near daily pain.[7] Eisenach et al. sought to determine whether caesarean delivery increases the risk of persistent pain after childbirth.[8] They found that the prevalence of severe acute pain within 36 hours postpartum was 10.9%, while chronic pain and depression at 8 weeks postpartum were 9.8% and 11.2%, respectively. They also noted that the severity of acute postpartum pain, but not the mode of delivery, was independently related to the risk of chronic postpartum pain and depression. Women with severe acute postpartum pain had a 2.5-fold higher risk of persistent pain and a 3.0-fold higher risk of postpartum depression compared to those with mild postpartum pain. Their findings indicate that caesarean delivery per se does not increase the risk of persistent

pain and postpartum depression. However, the severity of the acute pain response to delivery predicts persistent morbidity, signifying the need to more carefully address pain management in the days following delivery.

Achieving adequate analgesia early following CD enables the new mother to assume the duties of care of the new born without contending with the debilitating effects of severe post-operative pain. Options for pain relief after CD may include the use of intrathecal opioids, systemic opioids or a combination of intrathecal and systemic opioids. These are usually combined with other analgesic modalities as part of the multimodal approach to analgesia.[9] These other analgesic modalities include non-steroidal anti-inflammatory drugs, paracetamol, tramadol and novel analgesics such as ketamine, clonidine and gabapentin. In addition, local anaesthetic techniques such as wound infiltration, epidural analgesia and peripheral nerve blocks are also employed. Nonpharmacological options such as acupuncture, relaxation, music therapy, hypnosis and transcutaneous electrical nerve stimulation as adjuvants to conventional analgesia to achieve effective perioperative pain management are also available.[9]

While opioids remain a major component of the acute pain management repertoire of clinicians, they are often associated with adverse effects irrespective of the route of administration. These adverse effects include nausea, pruritus, sedation and respiratory depression (in both the mother and new-born).[10] According to Pyati and Gan,[9] in a paper on perioperative pain management, the ideal postoperative analgesic regimen would provide effective pain relief, reduce opioid-related adverse effects and the surgical stress response, and improve clinical outcome, e.g. morbidity, mortality and duration of hospital stay.

Perineural analgesic techniques have assumed an increasing and important role in the management of perioperative pain in recent years.[11] The transversus abdominis plane (TAP) block is one such technique employed for pain relief after lower abdominal surgery.[12,13] The TAP block involves the deposition of local anaesthetic solution with or without adjuncts in the plane between the internal oblique muscle (IOM) and transversus abdominis muscles (TAM). This aims to block the thoracolumbar spinal nerves supplying sensation to the anterolateral abdominal wall.[12]

1.2 Problem Statement

Effective management of postoperative acute pain is an important aspect of the care of the surgical patient. Suboptimal pain control, apart from not being humane, may result in increased morbidity or mortality.[14,15] Research evidence has revealed that surgery suppresses the immune system and that this suppression is proportionate to the invasiveness of the surgery.[16,17] Good analgesia can reduce this harmful effect.[18]

Post-operative pain management in the general surgical unit of the Korle-Bu Teaching Hospital has been demonstrated to be less than satisfactory.[19] In the study by Clegg-Lamptey and Hodasi,[19] they note that 24% of patients had significant pain at rest on the first postoperative day while 46% had significant pain on movement on the first postoperative day. They explained that doctors did not prescribe effective analgesia or prescribed analgesics with infrequent dosing intervals. They further explained that doctors and nurses were reluctant to prescribe and administer opiates like morphine due to the fear of respiratory depression and addiction. Danso and colleagues in a study on the preference of Ghanaian women for vaginal or caesarean delivery postpartum also demonstrated that pain is the most frequent negative response to caesarean delivery in the two biggest teaching hospitals in Ghana.[20] In the study, one of the main reasons why respondents preferred vaginal delivery over caesarean delivery was due to their perception of the absence of long term pain (23% of respondents). The above demonstrate that current pain management practices do not meet the expectations of Ghanaian patients for good pain relief after caesarean delivery.

The analgesia regimen currently practiced at the obstetric unit of Korle-Bu Teaching hospital for caesarean delivery is described in this paragraph. Where there are no contraindications to performance of a subarachnoid block, intrathecal administration of 15-25mcg fentanyl is performed in addition to the 10mg of intrathecal bupivacaine administered for the sub-arachnoid block. Where a central neuraxial block is contraindicated or cannot be performed for anaesthesia, a general anaesthetic is performed where morphine is administered as the main intraoperative analgesic at a dose of up to 0.1mg/kg. All patients receive intravenous paracetamol 1000mg intraoperatively and administration is continued postoperatively at 6 hourly intervals. Intramuscular pethidine is also administered at a dose of 1.5mg/kg up to a maximum of 100mg in the immediate postoperative period and same continued at 6 hourly intervals. Rectal diclofenac 100mg is administered prior to exit from the operating theatre if no contraindication and this is continued at 12 hourly intervals.

There are a number of problems with the above analgesic regimen. First, while administration of subarachnoid or epidural opioids to parturients, offers several advantages when recovering from CD including excellent postoperative analgesia with a decrease in total dose of opioid required, a low level of sedation, minimal accumulation of the drug in breast milk and facilitation of early ambulation, studies that measure 24-hour opioid consumption confirm the limitations of single shot neuraxial fentanyl for adequate postoperative analgesia.[21] This is because, fentanyl, being highly lipid soluble has better direct diffusion into neural tissue as well as greater delivery to the dorsal horn by spinal segmental arteries. This enables fentanyl to have a relatively rapid uptake into the lipid-rich dorsal horn and consequently have a rapid onset of action but a short duration. On the other hand, morphine, which is lipid insoluble is retained in the cerebrospinal fluid (CSF), providing a longer supply to the spinal cord and consequently a slower onset, but longer duration of analgesia after the administration of a single dose.[22] However, because morphine resides for a longer period of time in the CSF it may spread rostrally, from which complications such as respiratory depression may arise.[23] This dreaded complication of delayed respiratory depression prevents the regular use of intrathecal morphine in the obstetric unit of Korle-Bu Teaching Hospital. In addition, preservative free morphine suitable for intrathecal administration, is not readily available in Korle-Bu Teaching Hospital. Secondly, in situations where a general anaesthetic is performed, patients do not even get the benefit of the excellent albeit short duration analgesic effect of intrathecal fentanyl. These patients rely on intravenous morphine 0.1mg/kg, a dose which, anecdotally, is not achieved on a regular basis. Thirdly, in the postoperative period, although, intramuscular pethidine is prescribed to be administered at 6 hourly intervals (rather than the recommended 4 hourly intervals[24]) there are frequent missed doses due to a general uneasiness of health personnel (nurses) in the administration of opioid analgesics and the high workload of the nurses. Furthermore, rectal diclofenac administration is often not applicable to all patients. This is because, the two major causes of morbidity and mortality remain complications related to hypertensive disorders of pregnancy and complications associated with obstetric haemorrhage. Diclofenac with its negative effect on the kidneys, especially in the setting of kidney injury, as well as its propensity to interfere with coagulation makes it unsuitable for use in the obstetric patient with hypertensive disorder or with haemorrhage. From the foregoing, the main problem with pre-existing pain management protocols is inadequate analgesia with reliance on systemic opioids such as pethidine. Afferent neural blockade (e.g. TAP block) with local anaesthetics is

the most effective analgesic technique,[18] but this is rarely performed post caesarean delivery at KBTH.

1.3 Justification/Relevance

Adequate post-operative analgesia apart from being humane helps to prevent the deleterious effects of poor post-operative pain control. These deleterious effects include increased catabolism, increased cardiorespiratory demand and work, immunosuppression, coagulation disturbances and prolonged recovery and discharge times.[9] Consequently, these result in poor patient satisfaction, impair quality of recovery from surgery and increase the financial burden of healthcare.

The advantages of effective post-operative pain control include patient comfort and therefore satisfaction, earlier mobilisation, fewer cardiopulmonary ill effects, a lesser risk of deep vein thrombosis, earlier recovery with less probability of the development of chronic neuropathic pain, and reduced financial burden of patient care.[18]

Analgesic options following CD in Korle-Bu Teaching Hospital most commonly include the use of intrathecal opioids (fentanyl), parenteral opioids (intramuscular pethidine), intravenous paracetamol and rectal diclofenac if not contraindicated. Some patients receive local anaesthetic infiltration of the wound when a general anaesthetic is performed in situations when spinal anaesthesia is contraindicated or cannot be performed. To provide truly multimodal analgesia, the modalities enumerated above need to be administered simultaneously. This, however, is not the case at all times as some of the modalities may be contraindicated in certain patient groups excluding them from optimal post-operative analgesia.

This study sought to expand the repertoire of post-operative analgesic options available to parturients who undergo caesarean delivery at Korle-Bu Teaching Hospital. This will ensure almost universal inclusion of all patient groups for optimal postoperative pain relief and also improve the satisfaction of patients. It will also help to reduce the dependence on opioids for post-operative analgesia and avoid the adverse effects associated with the use of opioids.

1.4 Aim of the Study

The aim of this study was to assess the effectiveness and safety of perineural dexamethasone in ultrasound guided bilateral TAP block in providing post-operative analgesia in parturients who underwent caesarean delivery under spinal anaesthesia at Korle-Bu Teaching Hospital.

1.5 Specific Objectives

To compare among all study groups the following:

1. The time to first request for rescue analgesia.
2. At rest and on coughing numerical rating scale (NRS) pain scores at the time of TAP block performance (0 hours) and at 2, 6, 12 and 24 hours after surgery.
3. The total amount of systemic opioid required during the first 24 hours after caesarean delivery.
4. The incidence and severity of nausea, vomiting, pruritus and sedation during the first 24 hours after caesarean delivery

1.6 Hypothesis/Research Question

H_o: There will be no difference in pain scores in patients who undergo caesarean delivery at Korle-Bu Teaching Hospital under spinal anaesthesia when they receive either a TAP block with bupivacaine only, a TAP block with bupivacaine and dexamethasone or a TAP block with saline.

H_1: There will be a difference in pain scores in patients who undergo caesarean delivery at Korle-Bu Teaching Hospital under spinal anaesthesia when they receive either a TAP block with bupivacaine only, a TAP block with bupivacaine and dexamethasone or a TAP block with saline.

Where H_o = Null hypothesis

H_1 = Alternate hypothesis

CHAPTER 2: LITERATURE REVIEW

2.1 Pain following caesarean delivery

The International Association for the Study of Pain (IASP) defines pain as "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."[25] When pain is experienced immediately, and for a short duration after a definite tissue injury such as surgery for caesarean delivery, it is termed as "acute", with the anticipation that after a given duration of time the tissue heals and the pain resolves. Pain failing to resolve can then be categorised as chronic. The exact time of transition from acute pain to chronic pain is not agreed on by authors. Kainu et al.[26] and Macrae et al.[27] suggest the change of classification from acute to chronic pain at the 2 month mark after surgery. However, Landau, Bollag and Ortner[28] suggest a period of 2-3 months. Generally, pain is regarded as chronic when it lasts or recurs for more than 3 to 6 months.[29] Pain may vary in intensity (mild, moderate, or severe), quality (sharp, burning, or dull), duration (transient, intermittent, or persistent), and referral (superficial or deep, localised or diffuse).[30]

Pregnancy is associated with increased excitability of mechanosensitive afferent nerve fibres which innervate the uterine cervix and lower uterine corpus.[31] The change in sensitivity of the nerve fibres is thought to be due to elevated oestrogen levels during pregnancy.[32]

Postoperative pain results from direct trauma to tissue and subsequent inflammation. Local and systemic inflammatory cytokines act to sensitize the peripheral nerves and enhance pain perception.[30] According to Woolf, in peripheral sensitization, inflammatory mediators, such as prostaglandin E2 (PGE2), bradykinin (BK), and nerve growth factor (NGF), activate intracellular kinases in the peripheral terminal that phosphorylate transducer channels to reduce their threshold or phosphorylate sodium channels to increase excitability.

Pain following caesarean delivery has two components.[33] Somatic pain arising from cutaneous and deep nociceptors within the abdominal wound are transmitted within the anterior divisions of the spinal segmental nerves (T10-L1), which run laterally in the abdominal wall between the layers of the transversus abdominis and internal oblique muscles. Visceral uterine nociceptive stimuli from uterine contractions ascend via afferent nerve fibres that ascend through the inferior hypogastric plexus and enter the spinal cord via the T10–L1 spinal nerves.[34,35] According to Lavand'homme,[33] diverse mechanisms underlie somatic and visceral pain transmission, at spinal and supraspinal levels, supporting different sensitivity to analgesics.

Postoperative pain after caesarean delivery at rest is usually well managed by systemic parenteral opioids, while pain induced by movement, for example coughing or moving about, is less responsive, requiring higher opioid doses. The higher incidence of side effects of parenteral opioids limits the dose increment required for the management of dynamic pain following caesarean delivery. Common observations show incomplete pain relief with opioids alone, particularly on day 2 after caesarean delivery when parturients start to mobilize and take care of their newborns.[36]

2.2 Analgesia after Caesarean Delivery

Keating et al.[34] describe the ideal post-caesarean analgesic regimen to be one that was cost-effective, simple to implement and with minimal impact on staff workload. It should also provide consistent and high-quality pain relief while catering for wide interpatient variability but have a low incidence of side-effects and complications. Furthermore, it should not interfere with the maternal care of the neonate or with the commencement and or establishment of breastfeeding and there should be minimal drug transfer into breast milk with no adverse effects on the neonate.

Providing good quality postoperative analgesia is imperative not only as a humanitarian intervention. There is ample evidence in literature that optimal pain relief following any kind of surgery leads to earlier mobilization, less frequent pulmonary and cardiac complications, a lesser risk of deep vein thrombosis, an earlier return of gastrointestinal function, and quicker recovery from the surgery.[37]

In specific reference to mothers after CD there are additional positive effects of good postoperative analgesia. Poor analgesia can inhibit the ability of the mother to take care of the newborn infant and pain and/or anxiety can impair effective breastfeeding. Furthermore inadequate treatment of acute pain has been demonstrated to lead to chronic pain.[27] In a multicentre, prospective study of 1288 women hospitalized after CD or vaginal delivery, 10.9% experienced severe pain. It was further shown that the women with severe acute postdelivery pain had a 2.5-fold increased risk of persistent pain and a 3.0-fold increased risk of depression 2 months after delivery.[8]

In addition to the advantages of good pain relief for new nursing mothers, there is the increasing need for anaesthetists to respond to maternal demands and expectations. Carvalho and colleagues[38] investigated patient preferences for anaesthesia outcomes associated with caesarean delivery. They used written questionnaires to request patients to rank various anaesthetic outcomes and showed that pain during and after CD were the two most dreaded

outcomes with minor side effects such as shivering and itching thought to be of only moderate concern.

Achieving the goals of excellent post-operative pain relief while meeting the expectations of mothers after caesarean delivery requires a multimodal approach.[33,39] This is because, it is unlikely that utilization of one method alone will be effective in pain management and so the concept of multimodal analgesia is now well established in clinical practice. Approaches as part of the multimodal regimen can be divided into opioid-based techniques using intrathecal, epidural, or systemic routes. These may then be combined with adjuvant agents. Local anaesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs), paracetamol, gabapentin, and epidural clonidine have been demonstrated to be efficacious adjuvants to opioid analgesia after caesarean delivery.[40–42]

Multimodal therapy has long been advocated for postoperative analgesia in non-obstetric patients, and it clearly provides benefit to obstetric patients.[39] Multimodal analgesia is a technique intended to improve analgesia and to reduce the incidence of unpleasant opioid-related side effects. It is achieved by combining analgesics which work by different mechanisms and at different sites in the nervous system (Figure 2.1) and results in an additive or even synergistic effect whilst at the same time reducing side effects.

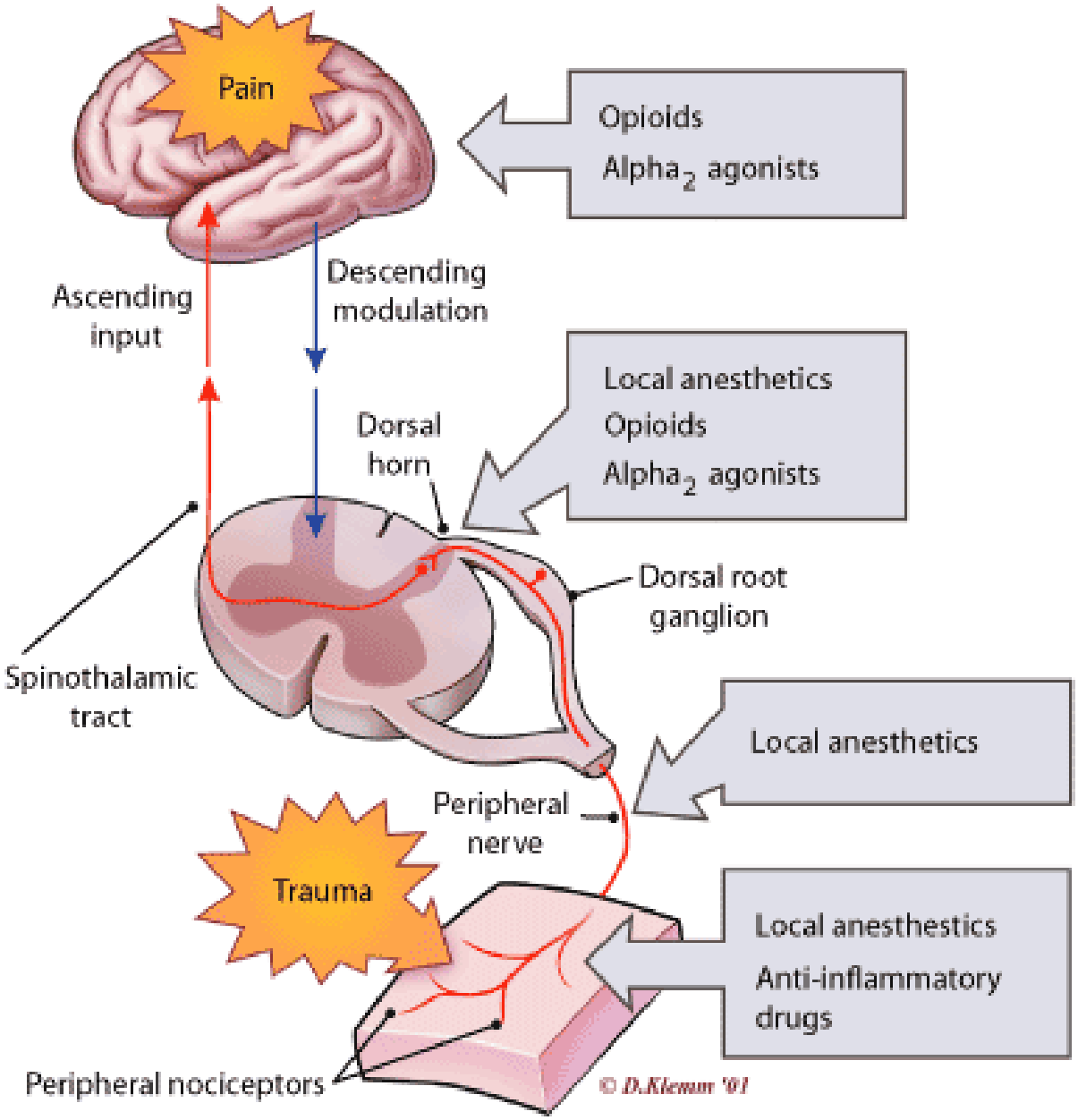

Figure 2.1: Pain pathways and intervention points for multimodal analgesia

Source: Gottschalk & Smith[43]

2.2.1 Neuraxial Opioid Analgesia

The majority of caesarean deliveries are performed using spinal, epidural, or combined spinal–epidural (CSE) anaesthesia techniques.[44] The safety benefits of neuraxial anaesthesia over general anaesthesia in the pregnant patient are well documented.[45] Neuraxial opioid administration augments intraoperative anaesthesia and optimizes postoperative analgesia.[46] Administration of subarachnoid or epidural opioids to parturients also offers several advantages when recovering from CD. These include excellent postoperative analgesia with a decrease in

total dose of opioid required, a low level of sedation, minimal accumulation of the drug in breast milk and facilitation of early ambulation.

Neuraxial analgesic techniques seem more likely to decrease perioperative morbidity in high-risk obstetric patients than systemic analgesic techniques. The benefits include a lower rate of perioperative cardiovascular complications, a lowered incidence of pulmonary infections and pulmonary embolism, a faster return of gastrointestinal function, fewer coagulation disturbances, and reduction in inflammatory and stress responses to surgery.[47] Neuraxial opioids may be administered as a single shot or continuous technique employing indwelling catheters. The single shot technique is usually employed for intrathecal administration whereas the catheter-based technique is largely reserved for the epidural route. Continuous postoperative neuraxial analgesia techniques have some disadvantages, including decreased mobilisation because of infusion pumps, more complicated management of postoperative thromboprophylaxis, and increased nursing workload.[48]

Potency, onset, duration of action, and side effects vary depending on the opioid used and the route of its administration with pruritus, nausea, and vomiting being the most common side effects of these agents, resulting in a decrease in maternal satisfaction. Opioids that may be administered via the neuraxial route commonly include morphine, diamorphine and fentanyl. Other less commonly used neuraxial opioids include pethidine, buprenorphine, hydromorphone, sufentanil and nalbuphine.

Despite the administration of neuraxial opioid analgesia, the quality and duration of analgesia after caesarean delivery is most times not optimal. Therefore, neuraxial opioid analgesia is seldom the sole analgesic technique used for post-caesarean analgesia. Instead, neuraxial opioids should be regarded as part of a multimodal analgesic strategy for the management of post-caesarean pain.[33,39,41]

2.2.1.1 Neuraxial Morphine

Morphine is highly ionized and hydrophilic and does not penetrate lipid-rich tissues as rapidly as fentanyl. Morphine requires 45–60 minutes to achieve a peak effect, and the duration of analgesia is 14-36 hours depending on the dose administered.[23,49]

A number of intrathecal morphine doses have been researched. Uchiyama et al.[50] performed a dose response trial with intrathecal morphine 0mg, 0.05mg, 0.1mg, and 0.2mg. They observed that 0.1mg and 0.2mg provided comparable and effective post-caesarean analgesia for 28 hours. The 0.05mg dose was less effective, and the incidence of side effects was greater with the 0.2mg dose. The authors concluded that intrathecal morphine 0.1mg is the

optimal dose for post-caesarean analgesia. Palmer et al. reported a ceiling effect with doses greater than 75 mcg, as measured by patient-controlled IV morphine consumption with no clear dose–response relationship demonstrated using doses greater than 100 mcg.[51] Higher doses conferred no additional analgesic benefit but caused a dose-dependent increase in side effects, particularly pruritus. Yang et al. administered 100 or 250 mcg of morphine as a component of spinal anaesthesia to 60 women undergoing elective CD. Participants also received 20 mcg of intrathecal fentanyl and perioperative and postoperative NSAIDs as standard. There was no statistically significant difference between the small and larger-dose morphine groups in pain score, as measured by a VAPS.[52] In a systematic review of intrathecal opioid usage in patients undergoing CD, Dahl et al.[23] demonstrated a median time to initial analgesic request of 27 hours (range 11–29 hours) and suggested an intrathecal dose of 100 mcg. A 2016 meta-analysis comparing low-dose (0.05 to 0.1 mg) and high-dose (>0.1 to 0.25 mg) intrathecal morphine found mean time to first analgesic request was longer (mean difference, 4.5 hours; 95% CI, 1.8 to 7.1; $P = 0.0008$) for the high-dose group compared with the low-dose group.[49]

Side effects of intrathecal morphine reported in literature include pruritus, nausea and vomiting, urinary retention, and early or delayed respiratory depression. The most common adverse effect, pruritus, was shown to be more severe as morphine doses increased. If a morphine dose of 100 mcg is used, Dahl et al. estimated that 43% of parturients will experience pruritus, and 12% will experience nausea and vomiting.[23]

Epidural morphine is usually administered as a single bolus dose. Because of its low lipid solubility, it has a relatively slow onset of action with its peak analgesic effect occurring after 60–90 minutes. However, its duration of action has been shown to provide pain relief for approximately 24 hours.[53] A 2010 systematic review of ten studies by Bonnet et al.[46] comparing analgesia efficacy and/or adverse effects of a single bolus dose of epidural morphine versus systemic opioids after elective CD demonstrated that a single bolus of epidural morphine provides superior analgesia than parenteral opioids but with an effect limited to the first postoperative day after CD and with an increase in side effects. A range of doses have been investigated by researchers. Palmer et al.[54] performed a dose–response study looking at varying doses of epidural morphine between 0 and 5 mg for post-CD pain and found a ceiling effect in terms of analgesia. They found no difference in cumulative systemic morphine use above 3.75 mg used epidurally while 3 mg of morphine epidurally appeared equivalent to 100mcg intrathecally[51] and was found to provide analgesia for 12–24 hours. Based on this study and a systematic review, the general practice is to use 3 mg of preservative-free morphine in the

epidural space.[46] Due to its prolonged analgesic effects, epidural morphine can be administered as an intermittent bolus or as a continuous infusion. The quality of analgesia seems to be superior when utilizing continuous epidural infusions compared with an intermittent bolus. A study in the non-obstetric population evaluating the quality of analgesia produced by epidural morphine administered either as bolus doses or via continuous infusion showed that participants who were randomised to receive continuous infusion of epidural morphine reported a higher quality of analgesia than those who received intermittent bolus injections.[55] Based on apparent greater clinical analgesic efficacy and a lower rate of respiratory depression it would appear that patients would derive a greater benefit from receiving epidural morphine as a continuous infusion.

A number of studies have compared the analgesic efficacy of epidural and intrathecal administration of opioids. Sarvela et al.[56] performed a double-blinded, randomized controlled trial comparing 3 mg epidural morphine with either 100 mcg or 200 mcg intrathecal morphine and found no significant differences in pain scores. They noted, however, that rescue analgesia was demanded more often in the 100mcg group suggesting this dose was less efficacious for post-CD analgesia and unsurprisingly the 100mcg group were shown to have decreased incidence of pruritus. Duale et al.[57] noted modest improvements in pain scores and lower intravenous patient controlled analgesia (PCA) morphine usage with epidural morphine 2mg than with intrathecal morphine 0.075mg. In both studies,[56,57] the incidence of side effects (e.g., sedation, pruritus, nausea and vomiting) was not different between the epidural and intrathecal routes. A meta-analysis by Ng et al. in 2004 concluded that both epidural and intrathecal techniques provide effective post-caesarean analgesia; neither technique is superior in terms of analgesic efficacy.[58] However, intrathecal administration results in less systemic drug exposure and less potential foetal drug exposure and has a faster onset of action than epidural administration of morphine. If a CSE anaesthetic is anticipated, intrathecal delivery of the opioid may be preferable. Profound sedation and respiratory depression requiring opioid reversal and intensive care monitoring has been reported after unintentional subdural or intrathecal administration of a dose intended for epidural administration.[59]

Bloor et al. compared intrathecal diamorphine 0.3 mg with 3.0 mg epidural diamorphine where they established that the duration and quality of analgesia was similar in the two groups but the incidence of pruritus was higher and more severe in the intrathecal group.[60] In contrast, Hallworth et al.[61] showed a high incidence of pruritus in both groups but more nausea and vomiting in the epidural group when comparing intrathecal diamorphine 0.25mg with

diamorphine 5mg epidurally. Duration and quality of analgesia were similar as demonstrated in other studies. While it seems that in terms of analgesic effect the two routes are at par, it is worth noting that both intrathecal and epidural opioids may result in significant levels of pruritus with larger epidural opioid doses producing more nausea and vomiting.

2.2.1.2 Neuraxial Fentanyl

Fentanyl is debatably one of the most commonly administered intrathecal opioids worldwide. Its relatively high lipid solubility results in a greater restriction of segmental activity and rapid onset of action when compared to morphine. Although intrathecal fentanyl offers a relatively short duration of analgesia, it is shown to improve intraoperative analgesia, especially during uterine exteriorization, and enables the patient to have a better postoperative transition to other analgesic regimens during recovery from intrathecal anaesthesia.[21,62,63] The short duration of action of fentanyl generally makes it an unsuitable singular choice intraoperatively to provide post-CD analgesia but Siddik-Sayyid et al.[63] report that intrathecal fentanyl may offer a longer-term analgesic effect when co-administered with a local anaesthetic at the time of CD. Considering the neuraxial pharmacological profile of fentanyl and morphine previously discussed, intrathecal fentanyl may be combined with intrathecal preservative-free morphine to achieve better intraoperative analgesia in addition to the benefits of analgesia lasting well into the second postoperative day. In contrast to morphine, intrathecal fentanyl does not appear to increase the patient's risk of nausea and vomiting following CD and produces less severe pruritus and respiratory depression.[23]

Fentanyl, which is highly lipid soluble when compared to morphine, seems to undergo preferential vascular absorption instead of meningeal penetration following epidural administration. In fact, the value of utilizing fentanyl for epidural analgesia is controversial. Ellis et al.[64] in a randomized double-blind comparison of epidural versus intravenous fentanyl infusion for analgesia after caesarean section demonstrated that the quality of analgesia, the incidence of side effects, daily fentanyl utilization, and plasma levels after 24 hours of infusion are similar between patients receiving either epidural or IV therapy. Sevarino et al.[65] performed a double-blinded randomized study on 40 participants undergoing elective CD under lidocaine epidural anaesthesia who received after delivery either saline or 100 mcg fentanyl through the epidural catheter. All patients were provided with an IV pethidine PCA postoperatively and it was noted that no differences in PCA use were recorded between the groups. The researchers concluded that a single bolus of epidural fentanyl does not provide an advantage for postoperative analgesia in this patient population.

2.2.1.3 Patient Controlled Epidural Analgesia

The use of continuous epidural analgesia is a prevalent method of managing postoperative pain in patients undergoing thoracic or upper abdominal surgery. Better static and dynamic analgesia has been reported in reviews of studies that compared epidural analgesia with intravenous PCA after non-obstetric surgery.[5] However, in the obstetric population, continuous epidural techniques are less commonly used for post-caesarean analgesia. The reasons include diminished maternal satisfaction due to local anaesthetic–induced motor block in lower limbs and the lack of physical independence from infusion devices in the postpartum period. Continuous epidural techniques have been demonstrated to increase cost with a potential increase in the risk for catheter-related complications such as haematoma and infection in comparison with single-dose administration of neuraxial morphine.[44,66]

2.2.2 Non-Opioid Adjuvants for Neuraxial Analgesia

The addition of neuraxial non-opioid adjuvants to local anaesthetic agents has the potential to improve the quality of both intra-operative anaesthesia and post-caesarean analgesia. Non-opioid neuraxial adjuvants have different sites and mechanisms of action, and interactions between neuraxial opioids and non-opioid adjuvants may be additive or synergistic.[67] Potential benefits of neuraxial drug combinations comprise a reduction in dose of individual drugs (with subsequent reductions in dose dependent side effects), and specifically a reduction in postoperative opioid requirements and opioid-related side effects.[67]

Agents that have been successfully investigated include alpha-2 adrenergic receptor agonists such as clonidine, dexmedetomidine and adrenaline. Clonidine has been demonstrated to potentiate sensory and motor blockade when administered with epidural local anaesthetics and acts additively or synergistically with intraspinal opioids.[67] In combination with an intrathecal local anaesthetic, intrathecal clonidine may also prolong the regression of sensory block, improve postoperative analgesia, and decrease intraoperative pain.[68] However, combining intrathecal clonidine and local anaesthetic may also increase the risk for hypotension in a non–dose-dependent manner.[68] Qi et al.[69] compared bupivacaine 10 mg, bupivacaine 10mg combined with dexmedetomidine 5mcg, and bupivacaine 10 mg combined with morphine 0.1mg. Sensory blockade was longer in the dexmedetomidine groups than in other groups. Intrathecal dexmedetomidine provided similar analgesia and less pruritus and shivering compared with morphine.[69] A combined intrathecal regimen of adrenaline 200mcg with morphine 0.2mg improved intra- and postoperative analgesia compared with intrathecal morphine 0.2mg alone.[70]

Neostigmine, ketamine and magnesium are agents which are still under investigation for use in neuraxial anaesthesia and analgesia.

2.2.3 Systemic Opioid Analgesia

In Korle-Bu Teaching hospital, most women receive neuraxial opioids usually fentanyl for post-operative pain relief after caesarean delivery. This follows trends in the developed world because majority of caesarean delivery operations in the world are performed under neuraxial anaesthesia. Performance of neuraxial anaesthesia provides an avenue to administer the neuraxial opioids at the time of performance of the neuraxial anaesthetic for the surgical procedure. Many patients, however, require additional systemic analgesics to further improve pain relief and to limit side effects.[23,71] This is because neuraxial opioids administered as a single shot technique do not last long enough to cover the entire postoperative period. Furthermore, patients who receive general anaesthesia usually require systemic analgesics.

2.2.3.1 Choice of Opioid for Systemic Analgesia

Where availability of opioid analgesics is not a concern, considerations that affect the choice of opioid analgesic for systemic use include the speed of onset, duration of action, overall efficacy, which side effects they produce and how frequently the side effects occur. The patient's choice as a result of the effect of their past experience and the level of analgesia the patient desires is also taken into account. For example, a patient may prefer tramadol to morphine due to previous severe nausea and vomiting associated with morphine.

Pethidine is an opioid analgesic which is relied on heavily for systemic opioid analgesia in Korle-Bu Teaching Hospital for postoperative analgesia. The American Pain Society[72] and the American College of Obstetricians and Gynecologists (ACOG),[73] however, do not support the use of pethidine in obstetric patients due to the accumulation of norpethidine in the neonate and its consequent effect on neurobehavioral scores.

2.2.3.2 Parenteral Opioid Analgesia

Parenteral opioids may be administered intravenously, intramuscularly or subcutaneously as boluses or as continuous infusions. Intramuscular and subcutaneous opioids are relatively cheap, easy to administer, and associated with a long history of safety but are not commonly used in the developed countries due to the need for recurring painful injections, delayed and occasionally variable absorption of drug, and an unpredictable analgesic response

caused by variation in plasma opioid concentration. The current practice for the administration of parenteral opioids after caesarean delivery in Korle-Bu Teaching Hospital involves the use of 1.5mg/kg of intramuscular pethidine up to a maximum dose of 100mg at 6 hourly intervals or intravenous morphine setup to run at a continuous rate of 1-2mg/hr via a syringe driver.

Intravenous patient-controlled analgesia (PCA) enables patients to regulate their own pain management by self-administering small doses of intravenous opioids at frequent intervals. McNicol, Ferguson and Hudcova[74] performed a meta-analysis on forty-nine studies involving 3412 participants on PCA versus non-patient controlled opioid analgesia for postoperative pain. They demonstrated that participants receiving PCA had lower VAS pain intensity scores compared to those receiving non-patient controlled analgesia over most time intervals. They also found that participants were more satisfied with PCA and consumed higher amounts of opioids than controls. The higher opioid consumption amount in PCA compared to non-PCA may be due to the relatively higher immediate availability of opioid medication (literally at the press of a button) to patients receiving PCA compared to patients not receiving PCA. Patients not receiving PCA would first have to alert health personnel about their pain and request for analgesia. The health personnel would then have to look up the prescribed opioids in the patient's notes and subsequently go through a number of steps to make the opioid medication available to the patient as a result of the controlled nature of opioid medications. McNicol et al.[74] also observed that those receiving PCA had a higher incidence of pruritus but similar incidence of other adverse events. They found no difference in the length of hospital stay.

The American Society of Anesthesiologists (ASA) Task Force for Acute Pain Management in the Perioperative Setting recommended that epidural or intrathecal opioids, systemic opioid PCA, and peripheral regional techniques should be used in preference to intramuscular opioids ordered 'as needed.'[75] The American Pain Society has recommended the use of intravenous opioid PCA whenever parenteral delivery of analgesics is necessary and the oral route is not available.[76]

However, when neuraxial opioids are used, research has revealed that intravenous PCA is not usually required. Graham and Russell[77] in a double-blind assessment of the analgesic sparing effect of intrathecal diamorphine (0.3mg) with spinal anaesthesia for elective caesarean section concluded that the results of this study indicate that the addition of diamorphine 0.3 mg to 0.5% hyperbaric bupivacaine for spinal anaesthesia for elective caesarean section significantly extends the time to first PCA demand for morphine, reduces total morphine

requirements postoperatively and, in addition, results in 32% of patients (6/19) requiring no postoperative parenteral morphine. The morphine PCA system delivered an on-demand bolus of morphine 2mg with a lock-out time of 3 minutes and no background infusion. A similar study by Husaini and Russell[78] comparing intrathecal diamorphine 0.2mg with intrathecal morphine 0.2mg for postoperative analgesia after caesarean section under spinal anaesthesia demonstrated that pain scores equivalent to mild to moderate pain are obtained using an average of only 5 mg PCA morphine in 24 hours and 15% of patients required no morphine at all when intrathecal diamorphine was used. The PCA system in their study delivered an on-demand bolus of morphine 1mg with a lock-out time of 3 minutes and no background infusion. Overall Husaini and Russell concluded that there was no difference between the diamorphine group and the morphine group with respect to the 24-hour PCA morphine demands (diamorphine patients 5.5mg, morphine patients 5.0mg) and the static and dynamic VAS for pain.

However, for those patients who receive no neuraxial opioids such as in CD under general anaesthesia and in whom effective analgesia via the IV route is required, different opioids can be delivered utilizing a PCA pump, including fentanyl, morphine, and hydromorphone.

The goal of opioid administration is to achieve effective pain relief with minimal side effects. It is imperative to frequently monitor the respiratory rate, continuous pulse oximetry and sedation level before giving an additional dose or adjusting the PCA bolus dose. Patients with comorbidities such as hepatic or renal dysfunction (e.g., occurring with severe preeclampsia), morbid obesity, and/or obstructive sleep apnoea are especially vulnerable to the respiratory depressant effects of opioids. This category of patients may need special modifications to pain management, especially the use of multimodal analgesia. There is variability between studies in the criteria used for defining respiratory depression: indicators employed may include respiratory rate, oxygen saturation, sedation levels, intervention with naloxone or hypercapnoea. Cashman and Dolin[79] in a metanalysis demonstrated that for PCA, the mean reported incidence of respiratory depression varied between 1.2% and 11.5%, using hypoventilation and oxygen desaturation, respectively, as indicators whereas for epidural analgesia, the mean reported incidence of respiratory depression varied between 1.1% and 15.1%, using hypoventilation and oxygen desaturation, respectively, as indicators. McCormack et al.[80] demonstrated significantly higher transcutaneous carbon dioxide levels in patients who received PCA morphine (1mg bolus of morphine with a 5 minute lockout period and no

continuous background infusion) compared to patients who received epidural opioid (0.1% bupivacaine with 2 mcg/ml fentanyl titrated to analgesic needs and block level).

2.2.3.3 Oral Opioid Analgesia

Opioid oral analgesics are seldom employed for post-caesarean analgesia in Korle-Bu Teaching Hospital. Where there is the need to use oral opioids, for example, for persistent pain beyond the first post-operative day or in special patient groups such as in sickle cell disease patients, options available include oral morphine formulations (tablets or syrup), tramadol alone or in combination with paracetamol and combination of codeine phosphate and paracetamol.

However, some researchers have promoted the use of oral analgesics rather than intravenous PCA as there is rarely a requirement for a prolonged fasting period after caesarean delivery.[81] This is not likely to be feasible in Korle-Bu Teaching Hospital as patients after caesarean delivery still undergo prolonged fasting and oral intake established mostly on the day after surgery.

Research outcomes suggests that intravenous administration of opioids is not superior to oral opioids for postoperative analgesia.[76] Davis et al.[81] conducted a study among 96 participants to determine whether oral analgesia with oxycodone- acetaminophen or a patient-controlled analgesia device with morphine provided superior analgesia after caesarean delivery. They reported that patients randomized to oral oxycodone experienced less pain, nausea, and drowsiness 6 hours after caesarean delivery compared with those who received intravenous PCA morphine. They recommended that consideration should be given to expanding the use of oral analgesia in patients immediately after caesarean delivery. Dieterich et al.[82] in a comparative study of oral oxycodone and intravenous PCA piritramide involving 239 participants found intravenous PCA and oral opioids provided similar degrees of satisfaction and pain scores after caesarean delivery. Another study by Jakobi et al. assessed patient satisfaction with oral analgesia following CD and found that it provided satisfactory pain relief, was easily administered and was substantially less expensive compared to IV methods of analgesia.[83]

Hence, when tolerated, oral administration of opioids may be the favoured route of administration. Advantages of this approach are cost savings, facilitation of early mobility, and, possibly, greater patient satisfaction. Long-acting oral opioids are not recommended in the immediate postoperative period because there is the need to titrate doses and also there is not enough evidence that show superiority of long-acting opioids over short-acting oral opioids.[76]

However, in patients who receive long-acting opioids before surgery, an exception may be made to continue their long-acting opioid therapy in the immediate post-operative period.[76]

2.2.4 Systemic Non-Opioid Analgesia

2.2.4.1 Paracetamol

Paracetamol inhibits cyclooxygenase-2 (COX-2) resulting in decreased production of prostaglandin E2 and the activation of descending serotonergic pathways. In the general surgical patients, a meta-analysis by Remy, Marret and Bonnet[84] and a subsequent systematic review by Maund et al.[85] has demonstrated paracetamol to have a useful opioid-sparing effect of up to 20% by reducing postoperative IV PCA morphine consumption.

A 2012 meta-analysis identified four randomized controlled trials evaluating acetaminophen and its effect on opioid consumption after major surgery; only one study included obstetric patients.[86] The meta-analysis showed that acetaminophen was less effective than NSAIDs for decreasing opioid consumption and postoperative nausea and vomiting (PONV).[86] In study participants receiving PCA morphine after CD, Alhashemi and colleagues[87] compared the effects of IV paracetamol with those of oral ibuprofen with respect to pain control and morphine requirements. They measured both VAPS scores and patient satisfaction. VAPS scores were found to decrease similarly in both groups over time; however, there were no differences between groups at any time. Patient satisfaction was high in both groups. They concluded that IV paracetamol was a reasonable adjunct to IV PCA morphine.

There have been few trials looking at paracetamol alone after CD. The combination of NSAIDs and acetaminophen has been shown to be synergistic in human experimental pain studies.[88] Munishankar et al.[89] compared oral paracetamol, diclofenac, and the combination of these for pain relief after CD in a double-blind randomized controlled trial of paracetamol. Study participants given the combination of diclofenac and paracetamol required 38% less morphine than participants given paracetamol alone. Morphine use in participants given diclofenac alone was not significantly different from morphine use in the other two groups. Nauta et al.[90] performed a systematic review of randomized trials comparing a combination of codeine–paracetamol versus NSAIDs in the treatment of postoperative abdominal pain. They demonstrated that none of the studies showed the codeine–paracetamol combination to be superior to NSAIDs in controlling post-laparotomy pain and that fewer adverse effects were reported in the NSAID group. Valentine et al.[91] performed a retrospective medical record review of women who underwent caesarean delivery before and after a change in clinical practice at their institution. All patients in their study received spinal anaesthesia containing

intrathecal morphine 0.2 mg and scheduled NSAIDs for 48 hours postoperatively. Prior to the change in clinical practice, women received combination oral opioid- acetaminophen (paracetamol) analgesics as needed for breakthrough pain. After the change, the women received oral acetaminophen 650mg every 6 hours for 48 hours postoperatively with oral oxycodone administered as needed for breakthrough pain.[91] The scheduled acetaminophen cohort used less opioid than the historical as-needed cohort in the first 48 hours.

Intravenous acetaminophen has gained popularity, with earlier and higher plasma and cerebrospinal fluid levels compared with more slowly absorbed oral acetaminophen.[92] However, in patients with a functioning gastrointestinal system, there is no documented analgesic advantage of intravenous versus oral administration.

2.2.4.2 Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDS) are a class of analgesics that inhibit inflammation by inhibition of the cyclooxygenase (COX) enzymes, which convert arachidonic acid to prostaglandins and thromboxane. NSAIDS are an important constituent of multimodal analgesia. They are effective for perineal pain after vaginal delivery and post caesarean abdominal pain; when administered simultaneously with opioids, they produce up to 50% opioid-sparing effect[93] that can decrease opioid-related side effects.[94] A 2016 systematic review and meta-analysis by Zeng, Nami, Wu and Murphy on the analgesic efficacy of nonsteroidal anti-inflammatory agents (NSAIDs) in patients undergoing caesarean deliveries demonstrated that the use of NSAIDs resulted in lower pain scores up to 24 hours postoperatively, less opioid consumption, and less sedation after caesarean delivery.[95] Jakobi et al. in a study to evaluate patient satisfaction for oral analgesia for post caesarean pain management showed that fixed-interval dosing of NSAIDs provides more effective analgesia and results in better patient satisfaction than on-demand dosing.[96] NSAIDS are linked with adverse effects such as increased risk of bleeding, kidney impairment, gastrointestinal bleeding, and acute bronchospasm and should be used with caution in at-risk patients.

2.2.4.2.1 Diclofenac Sodium

Diclofenac has also been extensively studied in literature. As well as inhibiting COX there is some evidence that diclofenac inhibits lipoxygenase pathways, thus decreasing leukotriene formation and may also inhibit phospholipase A2. These actions may explain the high potency of diclofenac—it has a wide variety of effects including anti-inflammatory, antipyretic, and analgesic actions.[97]

Diclofenac has been shown in a number of studies to have a significant opioid sparing effect. When given in the recommended dose of 150 mg daily, opioid consumption can be reduced by up to 40%.[98] Mitra et al. compared a diclofenac-paracetamol combination with a diclofenac–tramadol combination when considering pain relief after CD in a randomized double-blinded parallel-group controlled trial involving 204 participants.[99] They found both combinations to provide satisfactory postoperative pain relief after CD. The study also revealed that the diclofenac–tramadol combination was overall more efficacious but associated with a higher incidence of postoperative nausea.

Dahl et al.[100] investigated high-dose diclofenac for postoperative analgesia after elective caesarean section in regional anaesthesia. They demonstrated that rectal suppositories (100mg twice a day) decreased morphine consumption (14mg versus 22mg in 32 hours) compared with placebo after caesarean delivery without an increase in side effects.[100] This regimen is currently practiced at Korle-Bu Teaching Hospital due to its simplicity of administration. Dennis et al. demonstrated that single rectal dose of diclofenac 100mg prolonged the mean time to first analgesic administration by more than 5 hours in patients who received intrathecal morphine.[101] Cardoso et al. evaluated small doses of intrathecal morphine combined with systemic diclofenac for postoperative pain control after caesarean delivery.[102] They noted that participants who received intrathecal morphine doses as small as 0.025mg required no rescue analgesic when intramuscular diclofenac 75mg was administered every 8 hours. Munishankar et al.[89] randomized patients who received spinal anaesthesia with bupivacaine and fentanyl to receive one of three analgesics: paracetamol, diclofenac, or diclofenac and paracetamol. They demonstrated that participants who received both diclofenac and paracetamol required less morphine than those who received paracetamol alone.

Baigent et al.[103] in a meta-analysis demonstrated that the cardiovascular risk with diclofenac is similar to that of the selective COX-2 inhibitors and as a result is now contraindicated in those with ischaemic heart disease, peripheral arterial disease, cerebrovascular disease, or established congestive heart failure (New York Heart Association classification II–IV) and this applies to all systemic formulations including suppositories.

2.2.4.2.2 Ibuprofen

Ibuprofen is one of the most widely used NSAIDs that is available without prescription. Because it non-selectively inhibits COX-1 and COX-2 isoenzymes, in addition to its anti-inflammatory, analgesic, and antipyretic properties, ibuprofen also inhibits platelet adhesion and causes renal artery vasoconstriction and gastrointestinal irritation. In a small study 12

patients who ingested oral ibuprofen 400mg every 6 hours for 24 hours), less than 1 mg of ibuprofen was excreted in breast milk in a 36-hour period.[104] Ibuprofen is approved as a therapeutic analgesic and antipyretic for children and therefore is considered compatible with breast-feeding.[94]

2.2.4.2.3 Ketorolac

Ketorolac has been evaluated as a perioperative analgesic, as it appears to have greater potency (similar to opioids) than other NSAIDs and an opioid-sparing effect. El-Tahan et al. studied the effect of preoperative ketorolac for CD, randomly assigning 90 patients to receive either IV ketorolac bolus at 15 mg prior to induction followed by infusion at 7.5mg/h, or saline placebo.[105] Both the IV ketorolac and the saline infusions were stopped at the end of surgery after the last skin stitch was placed. The results showed, in part, that 15.6% of patients in the ketorolac group requested postoperative tramadol for analgesia, compared with 31.1% in the control group. The conclusion was that prophylactic ketorolac improved analgesia after CD.

A randomized, controlled trial by Lowder et al. compared ketorolac with placebo after CD in 44 patients.[106] The ketorolac group was found to have significantly decreased pain scores at 2, 3, 4, 6, 12 and 24 hours and reduced morphine IV PCA requirements at 24 hours compared to the control group. The authors concluded that ketorolac reduced opioid usage and postoperative pain. Another study was performed by Tzeng and Mok[107] to determine the analgesic effect from a combination of ketorolac and low-dose epidural morphine after CD. Ninety patients were enrolled in the study and randomized to three groups to receive postoperatively either (a) epidural morphine 2mg and IV placebo, (b) epidural morphine 2mg and IM ketorolac 30mg, or (c) epidural saline placebo and IM ketorolac 30mg. Group (b) had significant superior pain relief compared to the other two groups. The addition of ketorolac was thought to enhance the analgesic effect of low-dose epidural morphine.

2.2.4.3 Cyclooxygenase-2 Selective Inhibitors

These drugs work by selectively inhibiting the COX-2 enzyme, which is involved in prostaglandin synthesis as part of the inflammatory response pathway. COX-2-specific inhibition both reduces the risk of gastrointestinal adverse events and lacks effect on platelet aggregation, in comparison to non-selective COX inhibitors (that block both the COX-1 and COX-2 enzyme), such as naproxen or ibuprofen. COX-2–selective inhibitors have a potential benefit compared with traditional nonselective NSAIDs in that they have minimal effects on

platelet adhesion and thus are less likely to interfere with blood clot formation and contribute to haemorrhage.

This category of NSAIDs has similar analgesic effectiveness and opioid dose-sparing to traditional NSAIDs in non-obstetric settings.[108] Celecoxib has been used in the perioperatively as an adjuvant analgesic and a Cochrane review assessed the efficacy of a single dose of oral celecoxib for postoperative pain.[109] Eight trials were included in the review. A 200mg dose of celecoxib was as effective as 600/650mg of aspirin and 1000mg of paracetamol for controlling postoperative pain. A dose of 400mg was as effective as 400mg of ibuprofen. The rates of adverse events were similar with celecoxib and placebo. The conclusion of the study was that a single dose of celecoxib was effective for postoperative analgesia. Hence, a 400mg dose was suggested for acute pain.

However, in the setting of caesarean delivery, COX-2 selective inhibitor analgesics do not appear to be as effective as NSAIDs.[110] Lee et al.[110] evaluated a 200mg oral dose of celecoxib compared to placebo and reported no analgesic benefit whilst Fong et al.[111] demonstrated some analgesic benefit after CD with a 400mg dose of celecoxib. Carvalho et al.[112] randomized patients undergoing CD under spinal anaesthesia with intrathecal morphine 0.1mg into two groups to receive either valdecoxib 20mg or placebo. They could not demonstrate any significant analgesic effect of valdecoxib.[112]

The poor analgesic effect and additionally, concerns about the potential to increase the risk for cardiovascular and thrombotic events,[103] combined with the baseline elevated risk for these (cardiovascular and thrombotic) events during pregnancy and postpartum, have prevented COX-2 inhibitors from playing a major role in postpartum analgesia.

2.2.4.4 Alpha2-Adrenergic Receptor Agonists

Alpha2-adrenergic receptor agonists include clonidine and the newer agent dexmedetomidine. They have been used for the management of acute and chronic pain in non-obstetric population[113]. Intravenous dexmedetomidine has been used as an adjunct to opioids as a component of general anaesthesia for caesarean delivery.[114] Dexmedetomidine is excreted in breast milk in extremely small amounts.[115] Neuraxial clonidine has been used for labour analgesia but is not routinely used for post-caesarean analgesia. The epidural formulation of clonidine carries a warning from the FDA not recommending it for obstetric, post-partum, or perioperative pain management due to the risk of haemodynamic instability, especially hypotension and bradycardia at higher intrathecal doses.[116]

2.2.4.5 Magnesium Sulphate

Peripartum magnesium sulphate therapy is used for tocolysis for preterm labour, seizure prophylaxis in women with pre-eclampsia, and foetal neuroprotection in women at risk for preterm delivery.[117] A 2013 meta-analysis of trials of intravenous magnesium for the treatment of acute postoperative pain after non-obstetric surgery done under general anaesthesia concluded that magnesium sulphate use resulted in a small reduction in postoperative pain scores and a significant decrease in opioid use. However, the rate of nausea and vomiting was not reduced.[118]

2.2.4.6 Gabapentin

Gabapentin is an anticonvulsant that has pain relieving effects, especially with respect to neuropathic pain. Hah et al.[119] demonstrated in a randomized clinical trial on the effect of perioperative gabapentin on postoperative pain resolution and opioid cessation in a mixed surgical cohort. They reported the usefulness of gabapentin in the treatment of persistent pain and for postoperative analgesia where it facilitates a quicker withdrawal of opioids.[119] However, its role in opioid-naïve patients after caesarean delivery is not well defined. As a component of a multimodal analgesic regimen in participants undergoing caesarean delivery, a preoperative dose of oral gabapentin 600mg was associated with lower dynamic and static pain scores; however, the incidence of sedation was greater in the gabapentin group than in the placebo group.[42] In a follow-up trial,[120] two doses of gabapentin (300mg and 600mg) were compared with placebo in anticipation of discovering an effective dose without significant sedation. The follow-up trial did not demonstrate efficacy for either dose of gabapentin. These results were confirmed by Monks et al.[121] in a randomized trial comparing perioperative gabapentin (600mg preoperatively followed by 200mg every 8 hours for 2 days) with placebo when added to a multimodal post-caesarean analgesic regimen. Gabapentin produced a clinically insignificant improvement in analgesia after caesarean delivery but was associated with an increased incidence of sedation. From the foregone, gabapentin may therefore be helpful when used for post-caesarean analgesia in patients with persistent pain and those with opioid tolerance.

2.2.4.7 Ketamine

Ketamine, an *N*-methyl-d-aspartate (NMDA) antagonist, has analgesic effects and may useful in the management of acute postoperative pain and prevention or reversal of central sensitization.[122] Low-dose ketamine was assessed for post-caesarean analgesia by comparing

intravenous ketamine 0.15mg/kg, intrathecal fentanyl 10mcg and placebo.[123] The authors reported an increased duration of analgesia in both the fentanyl and ketamine groups compared with the placebo group (time to first analgesic request 145 minutes in the placebo group, 165 minutes in the fentanyl group, 199 minutes in the ketamine group). Ketamine was better than fentanyl and placebo for decreasing pain scores at 90 and 180 minutes, and decreasing analgesic requirements in the first 24 hours, but not in the second 24 hours, after caesarean delivery.[123] In a study in 2012 at Lagos University Teaching Hospital, when intrathecal opioids were not available, the administration of intravenous ketamine 0.15mg/kg immediately following bupivacaine spinal anaesthesia resulted in better postoperative analgesia and reduced analgesic requirements compared with saline-placebo.[124] In contrast, in another study in which women undergoing caesarean delivery were randomized to receive intravenous ketamine 10 mg or placebo shortly after delivery as part of a multimodal regimen of intrathecal morphine and regular NSAIDs, the results failed to show a difference in breakthrough pain, time to first analgesic request, or cumulative rescue analgesic requirements.[125] However, pain scores were lower in the ketamine group 2 weeks after the surgery.

A 2015 systematic literature review and meta-analysis included seven studies of ketamine use during spinal anaesthesia and five during general anesthesia.[126] Intravenous ketamine in the setting of spinal anaesthesia delayed the time to first opioid request and reduced pain after caesarean delivery with no differences in the incidence of nausea, vomiting, pruritus, and psychomimetic effects.[126] Perhaps intravenous ketamine use as part of the multimodal analgesic regimen for caesarean delivery under spinal anaesthesia at Korle-Bu Teaching Hospital should be given more attention than is currently practiced.

2.3 Transversus abdominis plane block

2.3.1 History and background

Rafi first brought the transversus abdominis plane block into the limelight in 2001 when he described it as an abdominal field block with an approach via the lumbar triangle.[127] Since its first description by Rafi, the TAP block has had increased prominence in clinical practice over recent years. It has been the subject of much study for the provision of post-operative analgesia for a wide range of abdominal procedures. A meta-analysis by Brogi and co-workers in 2016 identified the use of TAP blocks in Caesarean delivery, gynaecological procedures, cholecystectomy, appendicectomy, inguinal herniorrhaphy, bariatric surgery, liver resection, gastrectomy, urological surgery and bowel resection.[128]

2.3.2 Anatomy of the Abdominal Wall

The abdominal wall is a continuous cylindrical musculo-aponeurotic structure that attaches to the thoracic cage superiorly, the pelvic girdle inferiorly, and the spinal column posteriorly. Although the abdominal wall is continuous, it is subdivided into the anterior wall, right and left lateral walls, and posterior wall for descriptive purposes (Figure 2.2). The abdominal wall is musculo-aponeurotic, except for the posterior wall, which comprises the lumbar aspect of the vertebral column. The demarcation between the anterior and lateral walls is not well defined; hence, the nomenclature anterolateral abdominal wall is frequently used.[129]

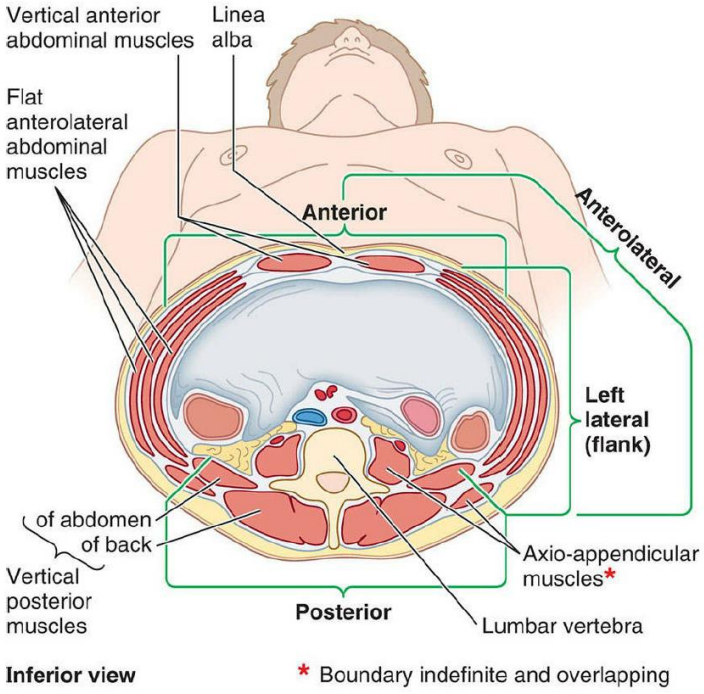

Figure 2.2: Anatomy of the abdominal wall

Source: Keith Moore (Clinically Oriented Anatomy)[129]

2.3.2.1 Anterolateral Abdominal Wall

The anterolateral abdominal wall extends between the posterior axillary lines on either side. The superior limits are the costal margin of the 7th to 10th ribs and xiphoid process of the sternum, and the inferior limits are the iliac crests, inguinal ligament, pubic crest, and symphysis pubis (Figure 2.3). The layers of the abdominal wall are (from superficial to deep) skin and subcutaneous tissue, the abdominal muscles and associated aponeuroses, transversalis fascia, extraperitoneal fat, and parietal peritoneum (Figure 2.4).

The anterolateral abdominal wall has 3 flat muscles (external oblique, internal oblique, transversus abdominis) arranged in concentric layers and 2 paired vertical muscles in the midline (rectus abdominis and pyramidalis).[129] The pyramidalis muscle, which functions to draw down the linea alba is of little clinical significance.[129] All 3 flat muscles taper off into aponeuroses as they near the midline.

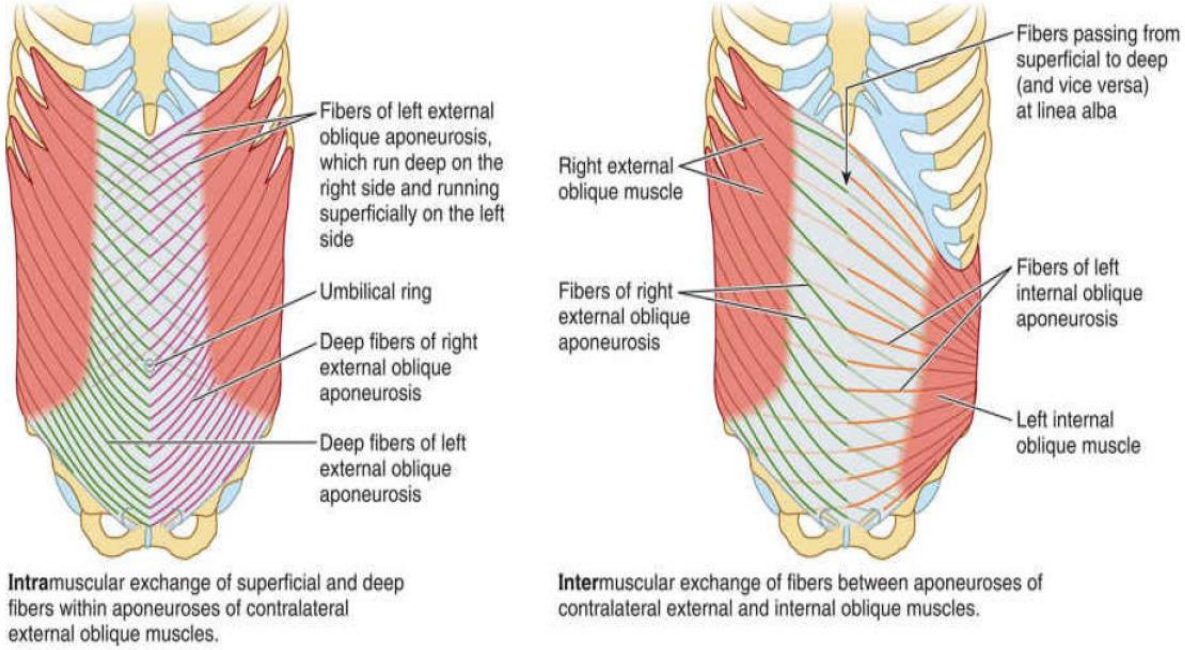

Figure 2.3: External oblique muscles fibres and aponeurosis

Source: Keith Moore (Clinically Oriented Anatomy)[129]

The aponeuroses create the tendinous rectus sheath that invests the rectus abdominis and pyramidalis muscles.

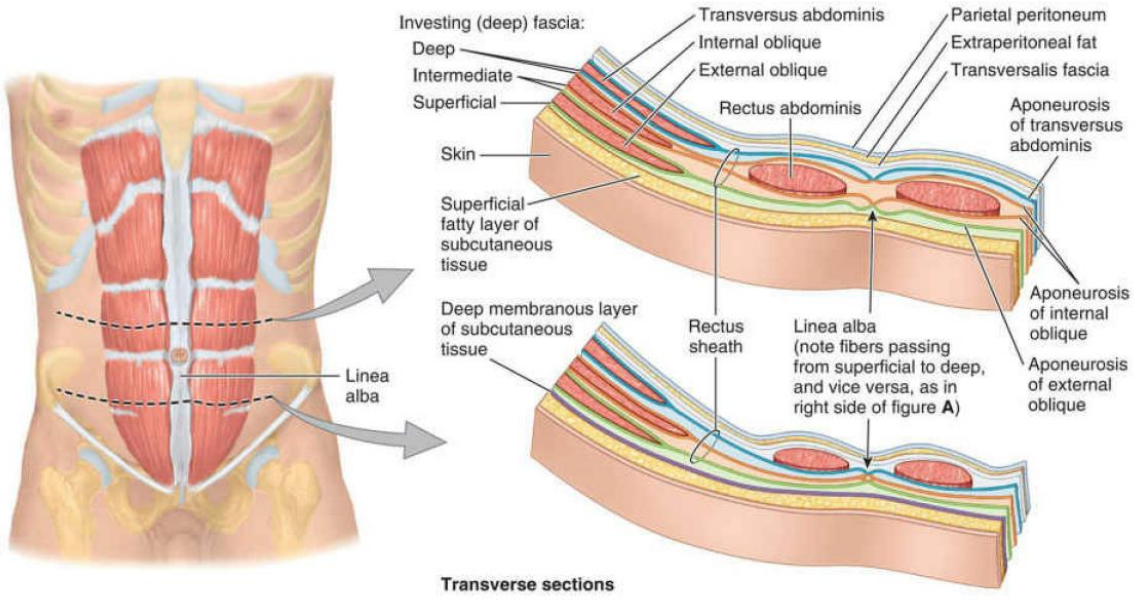

Figure 2.4: Rectus abdominis muscles

Source: Keith Moore (Clinically Oriented Anatomy)[129]

They merge in the midline with the aponeuroses of the contralateral side to form the linea alba. The decussation and interweaving of the aponeurotic fibres here is not only between right and left sides but also between superficial and intermediate and intermediate and deep layers.[129] The specifics of how the muscles and their aponeuroses relate to each other, as well as the various points of reference on the abdominal wall (e.g., midaxillary line, anterior axillary line, midclavicular line), determine the layers visible on ultrasound (US) at different transducer locations (Figure 2.5).[130]

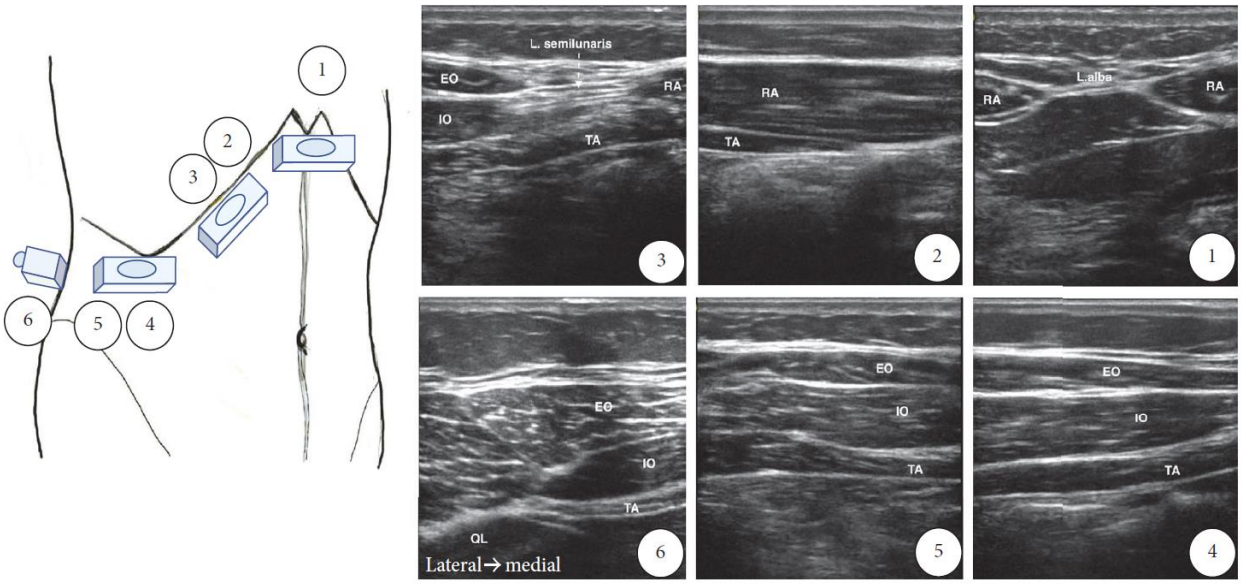

Figure 2.5: Ultrasound identification of the transversus abdominis plane.

Key: RA: rectus abdominis; TA: transversus abdominis; IO: internal oblique muscle; EO: external oblique muscle; QL: quadratus lumborum; L. alba: linea alba; L. semilunaris: linea semilunaris.

Source: Tsai et al.[131]

The external oblique muscle (EOM) originates on the external aspect of the 5th to 12th ribs, and its fibres descend in an inferomedial direction to insert on the anterior iliac crest, linea alba, and pubic tubercle (Figure 2.6).

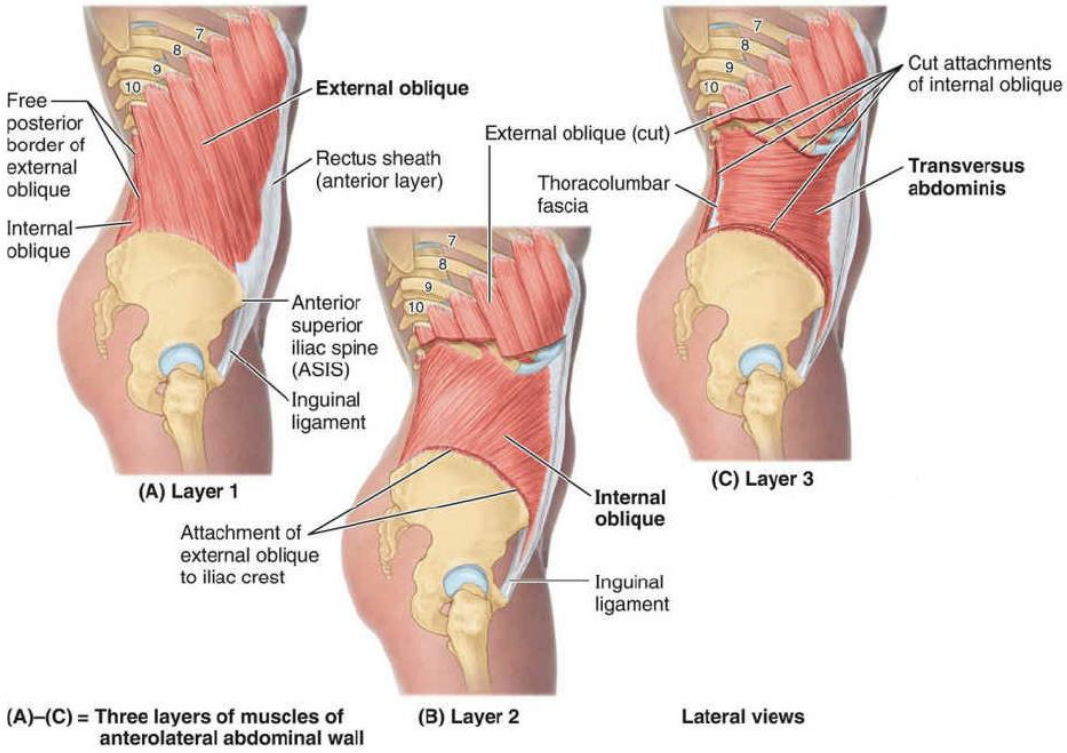

Figure 2.6: The three layers of the anterolateral abdominal wall

Source: Keith Moore (Clinically Oriented Anatomy) [129]

Anteriorly, the EOM tapers off into an extensive aponeurosis medial to the midclavicular line and inferior to a line half-way between the anterior superior iliac spine (ASIS) and the umbilicus; thus, below this line, only 2 muscle layers, internal oblique muscle (IOM) and transversus abdominis muscle (TAM), are apparent on US imaging. The lowermost margin of the EOM aponeurosis forms the inguinal ligament; its medial edge margin merges with the aponeurosis of IOM to form the anterior rectus sheath.[130]

The IOM originates from the iliac crest inferiorly and the thoracolumbar fascia posteriorly, and its fibres ascend in a superior-medial direction (perpendicular to those of the EOM) to insert on the inferior borders of the 10th to 12th ribs and the linea alba. It is a fleshy muscle that on US imaging often appears as the thickest of the 3 flat muscle layers (Figure 2.7).

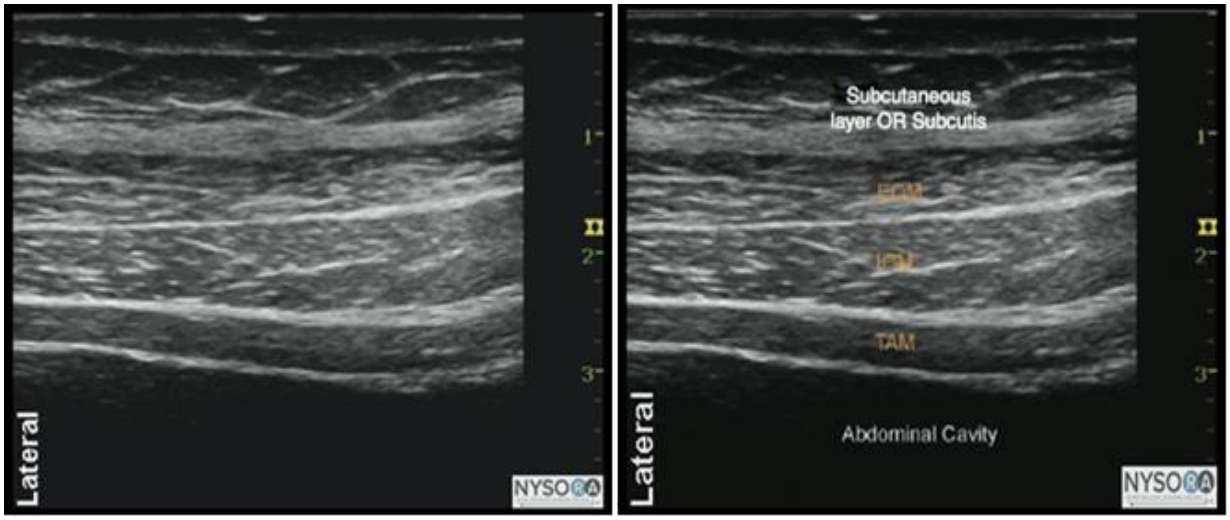

Figure 2.7: Ultrasound anatomy of the anterolateral abdominal wall

Source: NYSORA (Truncal and Cutaneous Nerve Blocks)[132]

Medial to the midclavicular line, the IOM tapers off into its aponeurosis and contributes to the formation of the rectus sheath (Figure 2.6B).

The TAM beings on the inner parts of the 7th to 12th costal cartilages, the thoracolumbar fascia, and iliac crest. The fibres run transversely to insert on the linea alba and pubic tubercle. Similar to the EOM and IOM, it tapers off medially into an aponeurosis that merges with the others to form the rectus sheath (Figure 2.6C). The transition from muscle into aponeurosis occurs along a crescent-shaped line, and thus just inferior to the costal margin, TAM runs deep to rectus abdominis for a short distance before tapering off into its aponeurosis).

The rectus abdominis muscle (RAM) is a paired muscle that originates on the pubic crest and symphysis and ascends vertically to insert on the xiphoid process and 5th to 7th costal cartilages (Figure 2.4A, Figure 2.8).

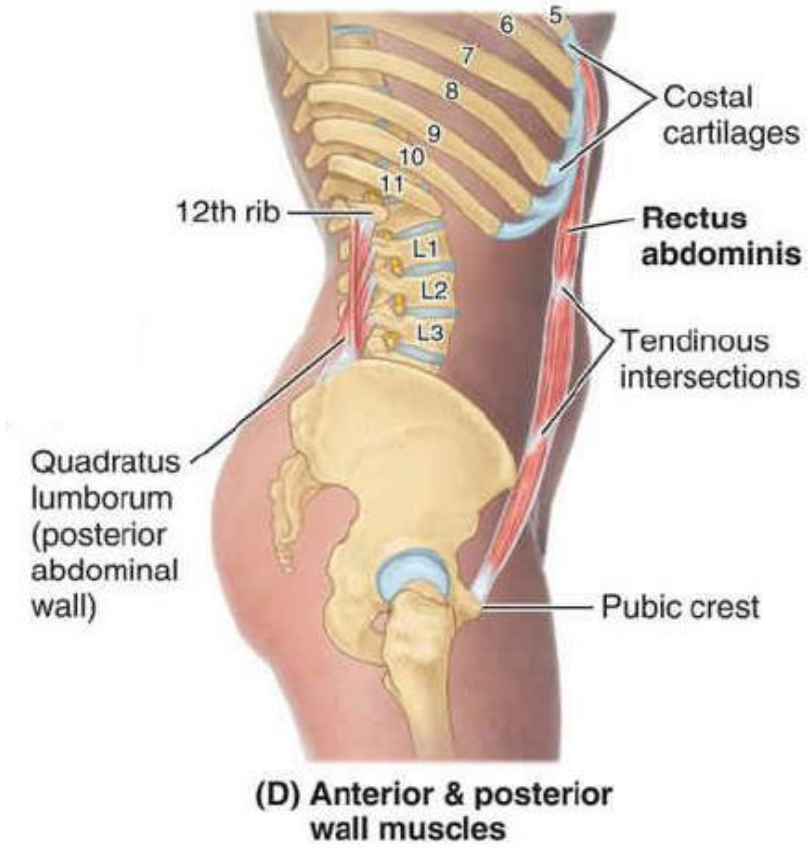

Figure 2.8: Anterior and posterior abdominal wall muscles

Source: Keith Moore (Clinically Oriented Anatomy)[129]

It is invested within the rectus sheath and is attached to the anterior aspect of the rectus sheath by 3 or 4 transverse tendinous insertions. These insertions divide the anterior rectus sheath compartment into separate sub-compartments, giving the RAM its "6-pack" appearance in slender muscular individuals and resultant obstruction craniocaudal spread of injectate. The posterior rectus sheath compartment, in contrast, is unsegmented and is thus a more reasonable location for local anaesthetic injection.[130]

The rectus sheath is formed by the combination of aponeuroses from the EOM, IOM, and TAM. In the superior 75% of the RAM, the anterior layer of the rectus sheath is formed by the EOM and IOM aponeuroses. The IOM aponeurosis divides into 2 layers and also contributes to the posterior layer of the rectus sheath together with the TAM aponeurosis. However, inferior to the level of the ASIS (at the arcuate line), all 3 aponeuroses travel anterior to the RAM generating the anterior layer of the rectus sheath. The inferior 25% of the RAM is therefore lined on its posterior aspect only by its epimysium and the transversalis fascia.[129]

2.3.2.2 Innervation of the Anterior Abdominal Wall

The anterior abdominal wall is innervated by the thoracoabdominal nerves and the ilioinguinal and iliohypogastric nerves (Figure 2.9). The thoracoabdominal nerves originate from the anterior rami of the lower 7 thoracic spinal nerves (T6-T12) and are the continuation of the respective intercostal nerves. The T12 nerve is frequently also known as the subcostal nerve. Each of the nerves give off a lateral cutaneous branch in the midaxillary line, which ascends to enter the subcutaneous tissues along the anterior axillary line and supplies the lateral abdominal wall.[130] The anterior branches of the thoracoabdominal nerves subsequently emerge from the costal margin and travel in the neurovascular TAP between IOM and TAM. The upper segmental nerves T6- T9 only enter the TAP medial to the anterior axillary line (T6 enters it just lateral to the linea alba) and that the other nerves enter it progressively more laterally (Figure 2.9).[133] This has implications for the pattern of nerve involvement that can be expected by injection at different locations in the TAP. Within the TAP, the lower segmental nerves (T9-L1) give off numerous communicating branches to form a longitudinal TAP plexus, from which the terminal anterior branches arise.[133]

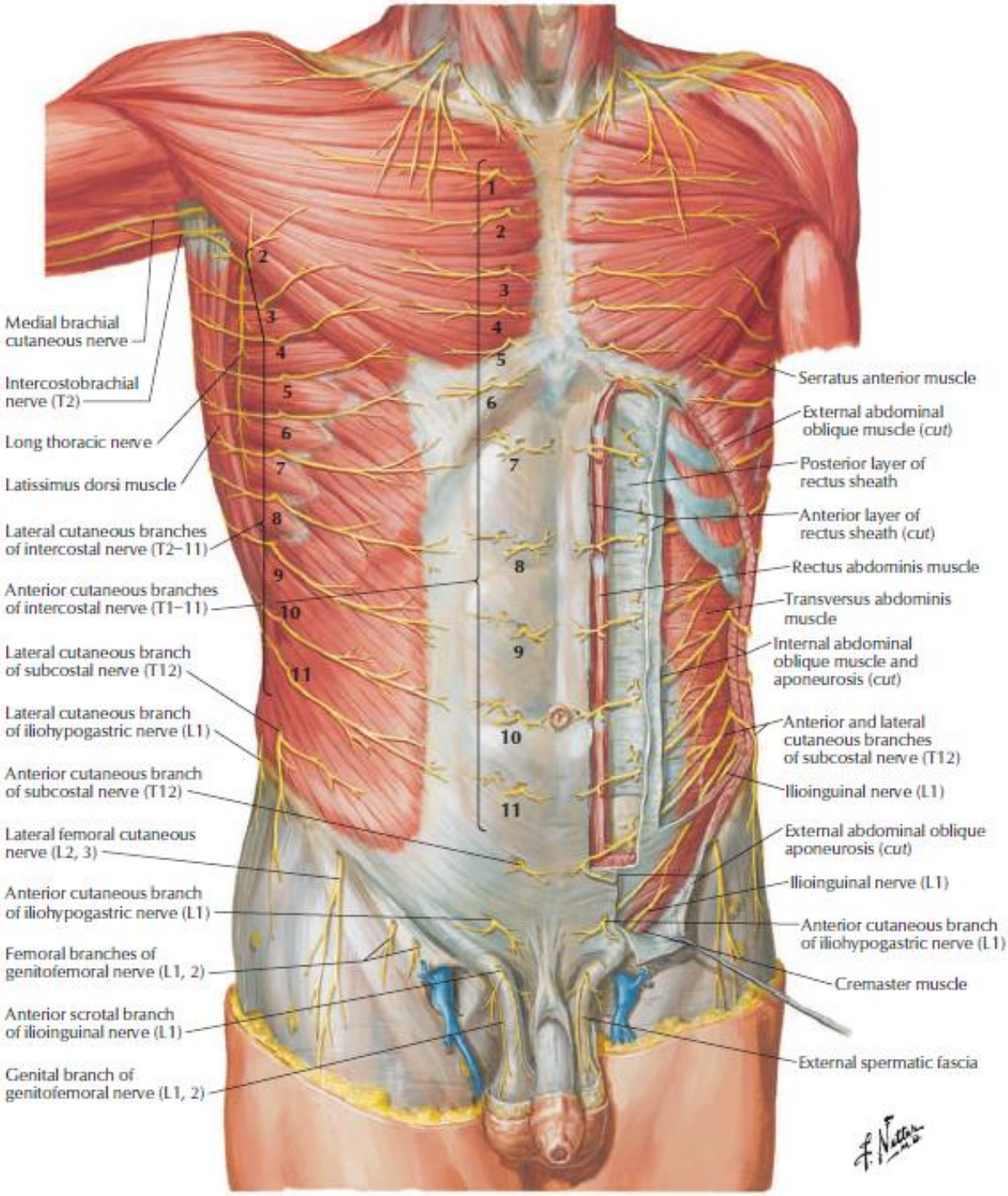

Figure 2.9: Nerves of the anterolateral abdominal wall

Source: Netter's Atlas of Human Anatomy[134]

The terminal anterior cutaneous branches of the thoraco-abdominal nerves enter the rectus sheath at its lateral margin (the linea semilunaris). In the vast majority of cases (89%), the nerves run deep to the posterior surface of RAM before ascending to pierce it 1.6 to 2.6 cm from its lateral margin.[135] However, these nerves sometimes directly pierce the lateral margin

of the RAM and hence may be unaffected by a rectus sheath block. The nerves branch and communicate to generate a longitudinal rectus sheath plexus, prior to entering the subcutaneous tissue of the anterior abdominal wall.[133]

The presence of TAP and rectus sheath plexuses indicates that individual terminal nerves have multiple segmental origins and that the standard portrayal of the cutaneous innervation of the abdominal wall in terms of well-defined dermatomes is not completely true.[136] This may be a reason for the differences between radiographically visualized spread of injectate in the TAP, apparent extent of clinical analgesia, and the cutaneous sensory block reported in research.[137–139]

The ilioinguinal (II) and iliohypogastric (IH) nerves are traditionally described as terminal branches of the anterior ramus of the L1 spinal nerve with sporadic contribution from T12. There is noteworthy variation, with up to 20% having origins from the L2 and L3 nerve roots.[140–142] Both nerves emerge at the lateral margin of the psoas major muscle and run inferolaterally on the ventral surface of the quadratus lumborum muscle (QLM) and TAM, just superior and parallel to the iliac crest. The nerves pierce the TAM and enter the TAP at variable points, but is frequently in the vicinity of the anterior 1/3 of the iliac crest instead of more posteriorly.[140,143,144] The iliohypogastric nerve passes into the TAP earlier in its path than the ilioinguinal nerve, and in a substantial number of individuals, the ilioinguinal nerve only enters the TAP very near to the ASIS (medial to the anterior axillary line).[133] Both nerves continue to ascend through the IOM and EOM to supply the abdominal wall in the inguinal and pubic regions. They pierce the IOM at a variable point medial to the ASIS superior to the inguinal ligament in adults.[140] The anatomic variation in the path of the ilioinguinal and iliohypogastric nerves contributes to the high incidence of unsuccessful blockade of these nerves with the TAP block[145,146] and the landmark-guided techniques of II-IH block.[147,148]

2.3.2.3 Vasculature of the Anterior Abdominal Wall

There is a rich network of arteries and veins within the TAP, which feed and drain the anterior abdominal wall and enables the absorption of local anaesthetic injected in this plane. The major arteries are extensions of the lower thoracic intercostal arteries and the deep circumflex iliac arteries (Figure 2.10). Within the rectus sheath, bilateral superior epigastric arteries (continuations of the internal thoracic arteries) anastomose with the deep inferior epigastric arteries (which originate from the external iliac arteries) and are at risk of accidental puncture during rectus sheath block.[130]

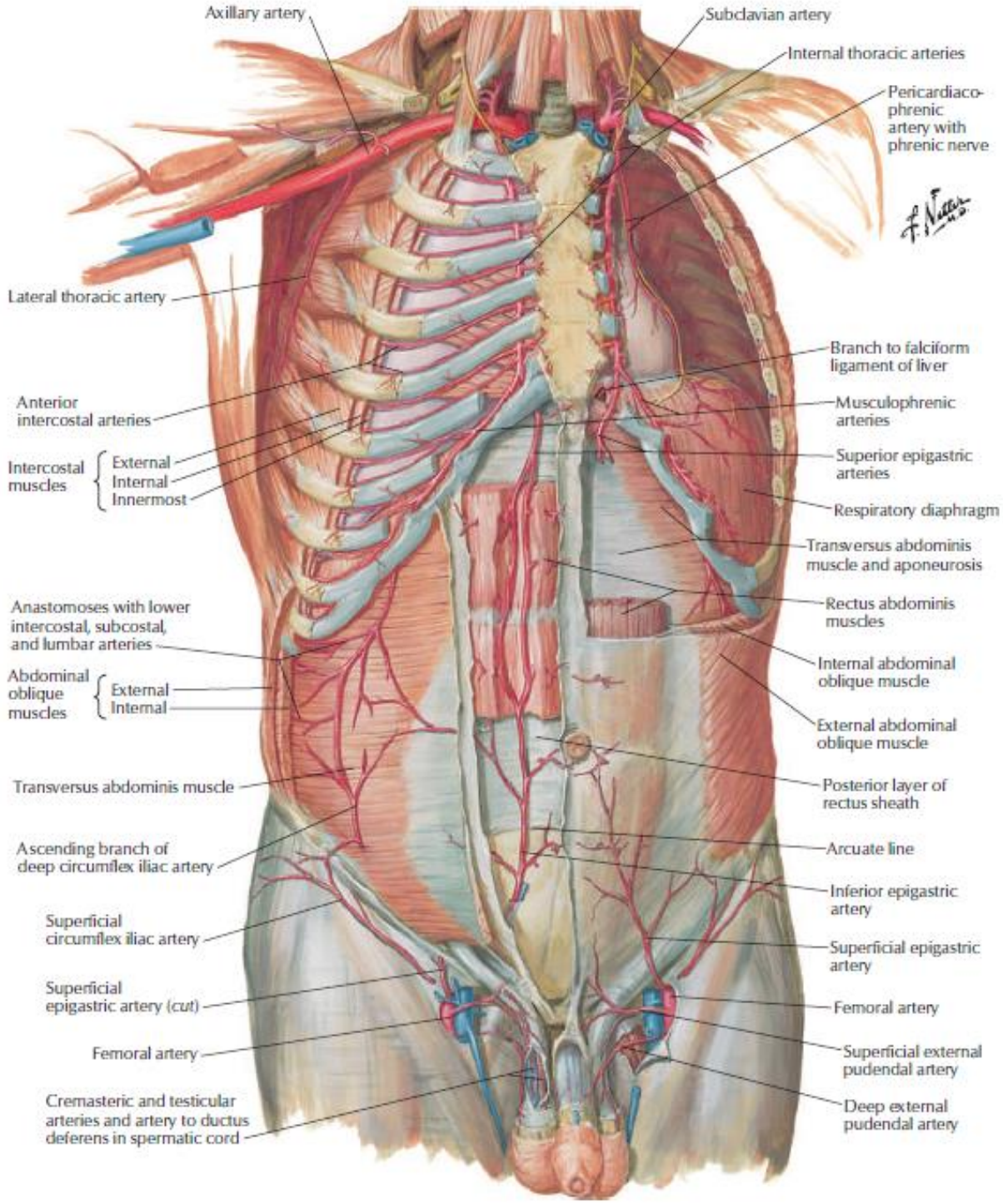

Figure 2.10: Vessels of the anterior abdominal wall

Source: Netter's Atlas of Human Anatomy[134]

2.3.3 Ultrasound Anatomy of the Anterolateral Abdominal Wall

Imaging of the abdominal wall between the costal margin and the iliac crest shows three muscle layers, separated by a hyperechoic fascia: the outermost external oblique (EOM), the internal oblique (IOM), and the transversus abdominis muscles (TAM) (Figure 2.7). Immediately beneath this last muscle is the transversalis fascia, followed by the peritoneum and the bowel beneath, which can be identified as moving bodies due to peristalsis. The nerves of the abdominal wall are not visible reliably, even though this is not essential to achieve a nerve block.

2.3.4 Performance of the TAP Block

The landmark-guided TAP block was first described by Rafi in 2001[127] and has since been modified multiple times. The "TAP block" no matter the approach is aimed to deliver local anaesthetic into the neurovascular fascial plane superficial to the TAM. The objective in all scenarios is to block some or all of the lower 6 thoracic spinal nerves (T7-T12) and the iliohypogastric and ilioinguinal nerves (L1). The approaches differ primarily in the site of needle insertion and injection, which, due to the complicated course of the lower thoracoabdominal nerves and interplay between muscular and fascial layers of the abdominal wall at various points, results subsequently, to differences in the distribution of local anaesthetic and scope of analgesia. Tsai et al.[131] developed a classification system for the various approaches for TAP blocks as outlined in Table 2.1 on the next page.

Table 2.1: Classification of ultrasound-guided TAP blocks and corresponding supply areas

Source: Tsai et al.[131]

Approach	**The main segmental thoracolumbar nerves**		**Supplied area**
Subcostal	T6-9	Anterior cutaneous branches	Upper abdomen just below the xiphoid and parallel to the costal margin
Lateral	T10-12	Anterior cutaneous branches	Anterior abdominal wall at the infraumbilical area, from midline to midclavicular line
Posterior	T9-12	Anterior cutaneous branches (possibly lateral cutaneous branches)	Anterior abdominal wall at the infraumbilical area and possibly lateral abdominal wall between costal margin and iliac crest
Oblique subcostal	T6-L1	Anterior cutaneous branches	Upper and lower abdomen

2.3.4.1 Landmark Guided TAP Block

Technique

The landmark guided TAP block was initially described by Rafi[127] and subsequently by McDonnell et al.[137] Both researchers describe the chief surface landmark as the insertion of the latissimus dorsi on the iliac crest. The point of needle insertion is directly anterior to this "latissimo-iliac point (LIP)"[149] and just above the iliac crest, in the triangle of Petit. The triangle of Petit has been suggested to be variable in terms of its existence and extent.[150,151] Therefore it may be more reasonable to regard the LIP as a more accurate and reliable landmark. McDonnell et al.[137] advises seeking a "double-pop" as the end point for needle insertion, the first pop representing penetration of the EOM fascia and the second pop the deep fascia of IOM. Rafi,[149] in comparison, suggests achieving a single pop (piercing of the deep fascia of IOM) by contacting the external lip of the iliac crest and "walking" the needle tip over. Irrespective of the method employed, the subjective nature of tactile pops as end points for needle introduction may be a factor leading to failure of the landmark based technique, especially in inexperienced hands.[152]

Block Distribution of Landmark Guided TAP Block

When 20 to 40 mL of local anaesthetic is injected using the landmark guided TAP approach, it spreads within the TAP from the iliac crest superiorly to the costal margin, anteriorly to the midaxillary line, and posteriorly to the lateral border of quadratus lumborum muscle[137,153] This TAP spread was thought to be responsible for block efficacy (hence the name) and has been the principle upon which subsequent modifications have been based. Carney et al. have also demonstrated posterior spread of injectate into the plane between transversalis fascia and the ventral surface of quadratus lumborum muscle, and subsequently superiorly into the thoracic paravertebral space.[153] The range of cutaneous sensory block that can be accomplished is not well defined. McDonnell et al.[137] reported attaining a sensory block of the anterior abdominal wall from T7 to L1 although the actual points of sensory evaluation were not indicated. Carney et al.[153] charted the range of sensory loss in 8 blocks and noted variation with patchy and incomplete blockade on the anterior abdominal wall. Regions that were reliably blocked were the region of injection, groin, and upper lateral thigh. Perhaps the variations in sensory deficit achieved with the landmark based TAP block may be due to incorrect needle placement as demonstrated by McDermott et al.[152] with correct needle placement occurring in less than 25% of cases.

2.3.4.2 Ultrasound Guided Lateral TAP Block

Technique

The US-guided lateral TAP block was initially demonstrated in 2007 separately by Hebbard et al.[154] and Shibata et al.[155] Ultrasonography enables direct visualization of the abdominal wall layers, needle position, and local anaesthetic distribution in the TAP. The US probe is positioned in a transverse direction midway between the costal margin and iliac crest and centred on the midaxillary line.[132] The needle is inserted in the anterior axillary line in-plane to the transducer and enters the TAP in the midaxillary line. In contrast to the landmark based technique, the point at which the needle enters into the TAP is anterior and superior to the LIP and triangle of Petit, which results in a different pattern of local anaesthetic distribution.[130]

Block Distribution of Ultrasound Guided TAP Block

The US-guided lateral TAP results in distribution of injectate limited to a region about the midaxillary line which covers only as far as the costal margin, the iliac crest, and the anterior axillary line in majority of scenarios.[153] Posterior coverage past the midaxillary line is

restricted in comparison to the landmark based TAP block.[156] The thoracoabdominal nerves that are reliably blocked include T10, T11, T12, and, to a lesser degree, L1.[145] The nerves superior to T8 are seldom affected due to their entry into the TAP medial to the anterior axillary line. Therefore, US-guided lateral TAP reliably produces blockade of the T11-T12 dermatomes, which is the region of interest following a Pfannenstiel incision for caesarean delivery, and, in the most situations, the T10 dermatome as well.[139,145] The T9 and L1 dermatomes are involved less than half of cases as demonstrated by Lee et al.[145] In the lateral direction, the block frequently fails to go farther than the midclavicular or anterior axillary line,[139,145] Borglum et al.[139] and Carney et al.[153] failed to observe a significant increase in the degree of spread when they increased the volume of injectate.

The results above were obtained from point testing employing dermatomal maps and surface landmarks. However, when cutaneous sensory loss is methodically charted, significant variation in distribution occurs with a non-dermatomal spread which fails to extensively affect the anterior abdominal wall.[138,153] Støving et al.[138] demonstrated a higher fraction of sensory deficit lateral to the line traversing the ASIS instead of medial to it. Craniocaudal spread of sensory loss was limited to the region below the umbilicus as demonstrated in other studies. The non-dermatomal distribution may be attributable to the presence of a TAP plexus and overlapping involvement of multiple spinal nerves to individual terminal divisions.[133]

2.3.5 Pharmacological Agents used in Transversus Abdominis Plane Block

Long-acting local anaesthetic agents including bupivacaine, ropivacaine, and levobupivacaine are most frequently used for TAP blocks. There is significant variation in the doses employed in clinical settings in both the adult and paediatric population, with reported total doses ranging between 2 and 3.5 mg/kg of ropivacaine and 1 and 2.5 mg/kg of bupivacaine.[157–159] Given that the analgesic effect of TAP blocks is dependent on the degree of distribution of local anaesthetic, it is plausible to conclude that the volume administered is a major factor. Research, however, has demonstrated that using volumes greater than 15 to 20mL in adults confers no advantage.[139,153,160] The concentration of local anaesthetic solutions should therefore be subsequently chosen to ensure that maximum recommended doses are not exceeded. Research has demonstrated that doses at the high end of the recommended ranges frequently cause potentially toxic local anaesthetic plasma levels.[161] Griffiths et al.[161] recommend that calculations should use lean instead of actual body weight of patients. Other

researchers have shown that using dilute concentrations of local anaesthetics is feasible without adverse effect on the efficacy of the block.[162]

Two RCTs investigated the effect of adding dexamethasone[163] and dexmedetomidine[164] to the local anaesthetic solution when undertaking TAP blocks for abdominal hysterectomy. Both papers reported an increased time to first analgesic request and lower opioid consumption in the group that received the adjuvant drug in comparison to control participants. Research on clonidine as an adjunct for TAP blocks in participants undergoing caesarean delivery was disappointing.[165]

Recent investigation exposes the potential benefit of liposomal bupivacaine in TAP blocks in prolonging the limited analgesic duration of the single-shot TAP block while simultaneously maintaining the simplicity of the technique.[166]

2.3.6 Analgesia after Transversus Plane Block

McDonnell and colleagues in 2008 investigated the analgesic efficacy of TAP block after caesarean delivery performed through a Pfannenstiel incision in a randomised controlled, double-blind clinical trial involving 50 participants.[167] They randomised the participants to either receive a bilateral landmark-based TAP block using 1.5mg/kg ropivacaine 0.75% (up to a maximum of 150mg) per side or bilateral landmark-based TAP block with saline. They found that the TAP block with ropivacaine compared with placebo reduced postoperative visual analogue scale pain scores, mean total morphine requirements in the first 48 postoperative hours, as well as the incidence of sedation. They did not find any complications attributable to the TAP block. They concluded that the TAP block, as a component of a multimodal analgesic regimen, provided superior analgesia when compared with placebo block up to 48 postoperative hours after elective caesarean delivery.

Baaj et al.[168] in a double-blind, placebo-controlled, randomized study found that TAP block reduced morphine consumption by more than 60% with better patient's satisfaction and less nausea and vomiting. They randomised 40 participants to receive bilateral ultrasound guided TAP block with either 0.25% bupivacaine or saline following a caesarean delivery under spinal anaesthesia using bupivacaine and fentanyl. They concluded that ultrasound guided TAP block improved postoperative analgesia, reduced morphine consumption and improved patient's satisfaction regarding analgesia after caesarean delivery.

The studies of McDonnell et al.[167] and Baaj et al.[168] are similar with respect to anaesthesia for caesarean delivery (spinal anaesthesia using bupivacaine and fentanyl) and postoperative analgesia (IV PCA morphine). However, McDonnell et al. used a landmark approach for the

TAP block with ropivacaine as the intervention drug whereas Baaj et al. used an ultrasound guided approach with bupivacaine. These did not result in different outcomes for the two studies. This may be as a result of the similar analgesic profile of ropivacaine and bupivacaine.[169] Secondly, although ultrasound technology allows easy identification of the different layers of the abdominal wall in real time and may be expected to result in better outcomes compared to landmark-based approach, the efficacy may not be comparable due to varying patterns of spread of local anaesthetic into the TAP dependent of injection site. Both of these studies are however limited by being conducted in a single centre which somewhat limits the generalisability of their results.

Eslamian et al.[170] in a single centre, randomised control, double blind study of 50 participants scheduled to have elective caesarean delivery under general anaesthesia randomly allocated the women to receive either bilateral landmark-based TAP block using 15ml 0.25% bupivacaine on each side or no block prior to emergence from the general anaesthesia. Participants were then given intravenous tramadol 50mg for postoperative analgesia at minimum of 4 hourly intervals on request. The results indicated that parturients who received the bilateral TAP block had significantly lower visual analogue scale (VAS) pain scores at rest and during coughing and consumed significantly less tramadol than parturients who did not receive the TAP block. There was also a significantly longer time to the first request for analgesic in the TAP block group. Although the TAP block was performed under general anaesthesia, careful examination of the block site may reveal evidence of the TAP block in the intervention group whereas the no TAP group may not have such evidence. Further information in the paper to confirm adequate blinding of participants or investigators is not available in the report by Eslamian et al. The single centre design coupled with the inadequacy of blinding warrants caution when interpreting or generalising the results of their study.

The significantly longer time to first analgesic request was also demonstrated by Alemnew and Lemma in Ethiopia.[171] In a single centre prospective cohort study participants scheduled for elective caesarean delivery under spinal anaesthesia were systematically randomised to receive after the caesarean delivery either bilateral TAP block using 20ml 0.25% bupivacaine on each side or wound infiltration with 20ml 0.25% bupivacaine on each side of the incision. This outcome may be due to a more rapid systemic absorption of the bupivacaine infiltrated into the wound compared to the bupivacaine deposited into the TAP. Their study however has some limitations. It was a single centre study without any information on blinding of participants or study personnel. Furthermore, information on the components of

the spinal anaesthetic was not provided. Also, the approach for the performance of the TAP block (landmark or ultrasound guided) was not indicated. In addition, while their postoperative analgesic regimen was reported as tramadol and diclofenac, the dose, route, frequency and triggers for administration of these were not provided in their paper.

Tan et al.[172] in a single centre, randomised double-blind controlled trial investigated the analgesic efficacy of bilateral ultrasound guided TAP block after caesarean delivery under general anaesthesia. Forty (40) participants were randomised to receive TAP block with 20ml 0.25% levobupivacaine on each side or no TAP block while the patient was still under general anaesthesia. They reported that parturients in the intervention group received significantly less morphine in 24 hours than those in the no TAP group. The TAP group had higher satisfaction scores although there were no differences between the groups in the VAS pain scores, sedation level, incidence of nausea and vomiting or the use of antiemetics. In contrast to the study by Eslamian et al., Tan et al. described in detail how blinding was conducted.

In sub-Saharan Africa, Kagwa et al.[173] (Uganda) and Kahsay et al.[174] (Eritrea) demonstrated the analgesic benefits of TAP block after caesarean delivery. While Kagwa et al. performed the block under ultrasound guidance, Kahsay et al. used the landmark approach. The study population in the study by Kagwa et al included heterogenous group of parturients with respect to urgency of caesarean delivery (elective, urgent and emergency caesarean delivery). Participants may have experienced varying degrees of labour pain before enrolment in the study by Kagwa et al. This has the potential to affect the study results since Aksoy et al.[175] demonstrated that experience of labour pain correlated positively with post-partum pain perception. It may be prudent to be careful when one interpreting and or generalising the results of the study by Kagwa et al. The TAP block group in the study by Kahsay et al. received 0.3ml/kg body weight 0.25% isobaric bupivacaine on each side whereas the TAP block group in the study by Kagwa et al.[173] received 20-25ml 0.25% bupivacaine (with 1:400000 adrenaline). The addition of adrenaline to nerve blocks is known to prolong the effect of the block which may have contributed to the analgesic benefit of the TAP block in the study by Kagwa et al.

2.3.7 TAP Block versus Intrathecal Morphine

McMorrow and colleagues in 2011 sought to find out the efficacy of TAP block, to compare ultrasound guided TAP block to intrathecal morphine, and to find out whether any

incremental benefit was obtained from their combination in patients undergoing Caesarean section.[176] They found that pain scores and analgesia requirements were lowest in those receiving 100mcg spinal morphine. They did not observe any additional analgesic benefit when TAP and intrathecal morphine were given together. They observed that while patient satisfaction was similar amongst all the study groups, those who received intrathecal morphine had a higher incidence of pruritus. They concluded that with respect to analgesic benefit, TAP block as described in their study was of no therapeutic value for patients whether administered alone or in combination with spinal morphine. The researchers, however, performed the TAP block using the landmark technique. This does not guarantee correct placement of the injectate leading to a proportion of the blocks failing or being inadequate. All the participants in the study by McMorrow et al.[176] received intravenous PCA morphine (1mg morphine bolus, 5 minutes lockout, no background infusion) which may have implications on the outcome of the study. The immediate access to opioid analgesic and control over pain management that intravenous PCA provides is likely to lead to high satisfaction scores amongst all participants irrespective of their randomised study group. In this situation, the study may not be adequately powered to detect differences between the groups with respect to participant satisfaction as much higher numbers of participants may be required to detect small differences in satisfaction levels amongst the study groups.

Ayedi et al.[177] performed a similar study to that performed by McMorrow et al.[176] In a prospective double-blind study, they randomised participants into two groups to receive either intrathecal morphine 0.1mg or TAP block with 20ml 0.25% bupivacaine on either side. They determined that the mean visual analogue scale pain scores at rest and on movement up to 48 postoperative hours, the median time to first analgesic request and the median intravenous nefopam dose for rescue analgesia were not different between the two groups. These findings contrast with that of McMorrow et al.[176] who found that TAP blocks were inferior to spinal morphine for the provision of postoperative analgesia after caesarean delivery. It is possible that the TAP blocks performed in the study by McMorrow et al. were ineffective. This is because they used a landmark technique which does not guarantee proper placement of the TAP block with increased probability of failed or inadequate blocks.

The studies by Ayedi et al. and McMorrow et al. were, however, concordant on the incidence of complications associated with spinal morphine. Both studies reported increased incidence of pruritus while that of Ayedi et al. also reported an increased incidence of nausea and vomiting associated with the use of spinal morphine. Ayedi et al. concluded that the TAP

block provided equivalent analgesic efficacy compared to spinal morphine up to 48 hours after caesarean delivery with fewer side effects.

Loane et al.[178] in a randomized controlled trial determined that the TAP block was associated with greater supplemental morphine requirements and higher pain scores than subarachnoid morphine but fewer opioid-related side effects. They concluded that the TAP block may be a rational alternative when subarachnoid morphine is contraindicated or not appropriate. Kanazi et al.[179] had similar findings to that of McMorrow et al.[176] and Loane et al.[178]

Champaneria et al.[180] in their meta-analysis on the clinical effectiveness of TAP blocks for pain relief after caesarean section made a number of observations. They noted that TAP block is at least as effective as intrathecal opioids for post-operative analgesia after Caesarean delivery. They reported that TAP block was effective in reducing post-operative opioid consumption and that the greatest analgesic effect was observed in women who had TAP block in the absence of intrathecal morphine. They further noted that there was no difference between TAP block and intrathecal morphine with regards to opioid consumption at 2, 6 and 10 hours postoperatively although intrathecal morphine was superior at 24 hours. TAP block was better at reducing the incidence of PONV when compared to intrathecal morphine. With regards to patient satisfaction, women were more satisfied with TAP block than control. However, when TAP block was compared with intrathecal morphine, a greater number of women preferred intrathecal morphine.

Intrathecal morphine for post caesarean delivery analgesia is not routinely practiced at Korle-Bu Teaching Hospital. The main reason is the risk of delayed respiratory depression with potentially fatal consequences due to challenges with staff numbers and their ability to properly monitor and identify respiratory depression should it occur. Other reasons include the increased incidence of undesirable side effects such as pruritus, nausea and vomiting.

2.3.8 Dexamethasone as an Adjunct

Dexamethasone is a glucocorticoid whose analgesic effects have been established by several studies.[181–183] De Oliveira et al.[183] in their meta-analysis concluded that dexamethasone given preoperatively significantly reduces postoperative pain and opioid consumption after surgery. The biological action of a glucocorticoid occurs 1 – 2 hours after administration.[182] The physiological effect of dexamethasone is thought to be due to its action with the glucocorticoid receptor.[184] Other suggested mechanisms for the antiemetic effect of dexamethasone include: (1) anti-inflammatory effect; (2) interaction with the neurotransmitter

serotonin, and receptor proteins neurokinin-1 and neurokinin-2, and alpha-adrenaline; (3) regulation of the hypothalamic-pituitary-adrenal axis; and (4) reducing pain and the concomitant use of opioids, which in turn reduces opioid-related nausea and vomiting.[185]

Concerns have been raised regarding the effect of dexamethasone on blood glucose concentrations and the incidence of wound infections postoperatively. Hans et al.[186] in their prospective open non-randomized study comparing blood glucose concentration profile after perioperative dexamethasone in 63 non-diabetic and type 2 diabetic patients undergoing abdominal surgery concluded that, after 10mg dexamethasone blood glucose concentrations increased in both patient subsets. In addition, poorly controlled diabetes and severe obesity could increase the development of hyperglycaemia. Their findings have been validated by other studies which showed that the use of dexamethasone may slightly increase blood glucose concentrations within 24 hours.[187] A retrospective study conducted by Bolac et al.[188] which reviewed the medical records of women who underwent laparotomy for endometrial cancer between 2002 and 2007, found no association between single dose dexamethasone for prophylaxis of PONV and wound complications in this patient subset. Their study was limited by its retrospective nature and single centre design. In addition, inferences from this study cannot be generalized as the study was limited to only women undergoing a single surgical procedure. A systematic review and meta-analysis by Waldron et al.[189] looking at 45 studies involving 5796 patients showed that perioperative single-dose dexamethasone was associated with small but statistically significant reductions in postoperative pain, postoperative opioid consumption, need for rescue analgesia, post anaesthetic care unit (PACU) stays, and a longer time to first analgesic dose. Another systematic review by Ho et al.[190] of studies evaluating postoperative infection after antiemetic doses of dexamethasone was unable to show whether a low dose of dexamethasone alone leads to any increase in postoperative wound infections. Gomez-Hernandez et al.[181] in their study in Mexico concluded that 8mg dexamethasone given preoperatively reduces nausea, vomiting and pain as well as the analgesic and antiemetic requirements of women after breast surgery for cancer without apparent side effects. The results of their study were validated by a meta-analysis by De Oliveira et al.[183] in 2011 which concluded that the preoperative administration of the intermediate (0.11 – 0.2mg/kg) doses of dexamethasone was associated with less variability in analgesic effectiveness. This meta-analysis also concluded that low dose (<0.1mg/kg) dexamethasone had no opioid sparing effect. In addition, high dose (>0.2mg/kg) dexamethasone did not seem to be advantageous

compared to intermediate doses. The metanalysis was limited by the fact that there was no uniform postoperative analgesia regimen among the studies analysed.

The use of dexamethasone as an adjunct in peripheral nerve blocks has also come under scrutiny in recent years with clear benefits demonstrated. In a meta-analysis studying the effects of perineural versus intravenous dexamethasone in peripheral nerve blocks, Zorrilla-Vaca and Li[191] reported that perineural dexamethasone was statistically more effective in prolonging the duration of analgesia and sensory block as compared with intravenous dexamethasone. They also noted that perineural dexamethasone tends to be of benefit on other variables such as duration of motor block, pain scores at 24 hours, opioid consumption and PONV. Their review was limited by the fact that most of the studies were performed in brachial plexus blocks, with little representation from lower extremity blocks and no representation from truncal blocks such as TAP block. Albrecht, Kern and Kirkham in a previous systematic review and meta-analysis[192] also had similar findings of prolonged duration of analgesia and motor blockade, lower pain scores at rest and on movement, reduced cumulative morphine consumption and incidence of PONV. They further noted that the safety profile of perineural dexamethasone is promising. Zhao and colleagues[193] and Hussain et al.,[194] however, did not find any difference in effect between perineural and systemic dexamethasone. A Cochrane review by Pehora et al.[195] found a statistically significant lower pain scores at 24 hours for perineural dexamethasone but this was not clinically significant.

In caesarean sections specifically, studies by Sachdeva and Sinha[196] and Akkaya et al.[197] both demonstrated that dexamethasone as an adjunct in TAP block for analgesia after caesarean delivery resulted in significantly prolonged analgesia with lower pain scores as compared to TAP block without dexamethasone. Zemedkun et al.[198] and Aga et al.[199] also demonstrated that dexamethasone resulted in a significantly longer time to first analgesic request. The study by Aga et al.[199] however, was not a randomised controlled study.

Kirkham and colleagues[200] demonstrated that a 4mg dose of perineural dexamethasone represents a ceiling dose and prolongs analgesia when combined with local anaesthetics with higher doses failing to provide additional analgesic duration.

2.3.9 Complications of Transversus Abdominis Plane Block

Research reporting complications of this block are rare.[158] Chin et al. categorised the complications into 3 main categories: needle or mechanical trauma, maldistribution of local anaesthetic, and local anaesthetic systemic toxicity (LAST).

2.3.9.1 Mechanical Trauma

The main concern with abdominal wall blocks, especially the landmark-based techniques where passage of the needle into the right tissue plane is directed solely by subjective tactile pops, is excessively deep needle penetration. Administration of injectate into the peritoneal cavity is relatively harmless aside from failure of the block. However, injury to abdominal viscera have been reported including liver trauma.[201,202] The use of US guidance should greatly reduce this risk, but visceral trauma may still happen if needle tip visualization is inadequate as was the case reported by Lancaster et al.[202] There have been no documentation of neurological injury related to the performance of TAP block to date, and this can be due to the fact that tissue planes, instead of nerves, are aimed for and that any nerves in the region of interest are small and thus less probable to be directly affected by needle trauma. Hence, it is normally acknowledged that truncal blocks including TAP block may be done under general or neuraxial anaesthesia.[203]

2.3.9.2 Maldistribution of Injectate

Unintentional femoral nerve block has been reported with TAP block.[204,205] As with traumatic complications, the probability maldistribution of injectate is higher with the landmark based techniques as the mechanism is extremely deep injection of local anaesthetic into the plane between transversus abdominis and transversalis fascia, which then travels inferiorly beneath the iliopsoas fascia to the femoral nerve and lumbar plexus.[206] All patients receiving truncal blocks (including TAP block but with the exclusion of rectus sheath block) should be alerted to the likelihood of short-lived quadriceps weakness and suitable precautions taken when mobilizing after surgery.[203]

2.3.9.3 Local Anaesthetic Systemic Toxicity

Abdominal wall blocks have substantial potential for LAST because the intermuscular tissue plane offers a high well-vascularized surface for local anaesthetic absorption. Contributory factors comprise the use of comparatively large injection volumes to ensure acceptable distribution and bilateral blocks to cover midline incisions. In obstetric patients, this is especially important since the physiological changes of pregnancy may increase the risk of LAST in parturients.[207] A number of interventions and precautions may assist in reducing the risk of LAST and these should be employed at every opportunity. Addition of adrenaline to the local anaesthetic solution, with its effect on vasoconstriction, reduces peak local anaesthetic

plasma concentration as reported by Covetto et al.[208] and Kitayama et al.[209] Where available, local anaesthetics with less cardiotoxic effects such as ropivacaine and levobupivacaine are preferred to racemic bupivacaine. The use of ultrasound reduces the doses of local anaesthetics used and therefore plasma concentrations.[148] In addition, using more dilute concentrations enable comparable analgesic effect with reduced risk of toxicity.[162] Where patients have a high body mass index, lean body-weight dosing is recommended,[161] and maximum suggested doses of local anaesthetics must always adhered to. Patients should also be meticulously observed for a minimum of 30 to 45 minutes as research indicates this to be mean time to peak plasma concentration following truncal blocks.[148,209]

2.4 Pain Assessment Tools

Ferreira-Valente[210] et al. compared the validity of four pain rating scales namely visual analogue scale (VAS), numerical rating scale (NRS), verbal rating scale (VRS) and faces pain scale-revised (FPS-R) in healthy volunteers and found all four scales to be valid. Their results indicated that all things being equal, any of the four scales could be used for detecting changes in pain, although the VAS and NRS might be considered first when particularly sensitive and responsive measures of pain intensity are needed. The study demonstrated the NRS to be most responsive and able to detect sex differences in pain intensity. This is consistent with other studies which showed a similar sensitivity between the NRS and VAS or a marginal pre-eminence of the NRS over the VAS.[211] Their results provided evidence to back the choice of the NRS over the VAS by some clinicians due to its relative simplicity and ease of administration. Their findings also suggested that the NRS may be slightly more sensitive than the other measures (i.e., VAS, VRS and FPS-R).

The NRS is commonly used in clinical and research settings to assess pain severity[212] and its scores can provide data for parametric analysis.[210] The NRS is an 11-point scale consisting of integers from 0 through 10; 0 representing “No pain” and 10 representing “Worst imaginable pain”. It has been demonstrated to be as sensitive as the VAS whether a 0 – 10 scale or a 0 – 100 scale is used.[211]

CHAPTER 3: MATERIALS AND METHODS

3.1 Study Design

The study was a prospective, randomized, double blind study.

3.2 Study Site/Setting

The study was conducted at the Obstetrics Department of the Korle Bu Teaching Hospital (KBTH). KBTH has approximately 2000 beds and 23 theatres. The obstetrics department has approximately 350 beds, 3 operating theatres and a total of 7 recovery beds (4 beds are in the main recovery room and 3 beds in the recovery room annex). The department has a total annual delivery of 10000-12000 with annual caesarean sections of 3600-4200.

3.3 Study Population

Healthy pregnant women at term scheduled for elective caesarean section were reviewed at the Anaesthesia Clinic and recruited into the study.

3.4 Inclusion and Exclusion Criteria

3.4.1 Inclusion criteria:

1. ASA 2 pregnant women at term presenting for elective caesarean section
2. Ages 18-40 years

3.4.2 Exclusion criteria:

1. Incisions other than Pfannenstiel
2. Documented adverse reaction to local anaesthetics or glucocorticoids
3. Pregnant women with diabetes mellitus
4. Pregnant women with cardiovascular disease
5. Body weight <60kg (so as not to exceed the maximum safe dose)
6. Body mass index >35kg/m^2
7. Presence of foetal pathology
8. Presence of coagulation disorders
9. Premedication with opioid or non-opioid analgesics, corticosteroids or NSAIDs
10. Patients in whom NSAIDs are contraindicated
11. History of postoperative nausea and vomiting
12. Spinal anaesthesia contraindicated
13. Inability to understand and use the numerical rating scale for pain assessment

14. Patients who have an inadequate spinal anaesthetic requiring a repeat subarachnoid block or conversion to general anaesthetic
15. Patients who receive other analgesics outside of the standard analgesic regimen

3.5 Sampling and Sample Size Determination

The sample size required for the study was determined using the formula[213]:

$$N = \left(\frac{r+1}{r}\right)\left(\frac{SD^2\left(Z_\beta + Z_{\alpha/2}\right)^2}{d^2}\right)$$

Where N is the sample size of the single study group, r is the ratio of controls to cases, SD is the assumed standard deviation for the study, Z_β is the standard normal variate for power, $Z_{\alpha/2}$ is the standard normal variate for level of significance and d is the difference in mean.

The above formula was recommended by Charan and Biswas[213] for use when calculating sample size of studies that test hypotheses in clinical trials or clinical interventional studies. This enables the researcher to determine the effect of an intervention; in the case of this study, the effect of perineural dexamethasone on duration of analgesia of TAP block.

From the study by Akkaya et al.[197], mean ± standard deviation for duration of analgesia (time to first analgesia request) after an ultrasound guided bilateral TAP block was 13 ± 7.8 hours when dexamethasone was added to the local anaesthetic and 6.1 ± 4.8 hours without dexamethasone. At a confidence level of 95% ($Z_{\alpha/2}$ = 1.96) and statistical power of 90% (Z_β = 1.28), mean difference d = 6.9, with 1:1:1 matched intervention groups and control group, the sample size is estimated as 27 participants per each group. Adjusting for 10% response failure, the number required for each group is rounded up to 30. Therefore, a total of 90 participants was required for the study. The target was to include at least 99 participants in the study.

3.6 Study Period

The study was conducted over a period of 5 months (June 2021 – October 2021) in order to recruit 99 participants for the study.

Preparation for the study took 4 weeks. In the first two weeks, the principal investigator underwent a two-week self-audit in the performance of TAP blocks to ensure block safety and efficacy. The second two weeks were used for pretesting and training to strengthen the research tools and methods. This involved the principal investigator, the pain assessment nurse, the research assistant and the supervisor.

3.7 Procedures used

3.7.1 Recruitment and Randomisation

Patients scheduled for elective CD under spinal anaesthesia were recruited into the study. A pre-operative assessment consisting of history, physical examination and investigations was conducted on all prospective participants to ensure that study criteria are met. This was also in fulfilment of standard procedure of pre-anaesthetic assessment of all pregnant women scheduled for elective caesarean delivery. The pre-anaesthetic assessment was performed between one and two weeks before the scheduled date of surgery. Potential study participants had the purpose of the study explained to them after the pre-anaesthetic assessment at the anaesthesia clinic. They were given the opportunity and time to ponder their decision to participate in the study. Their decision to participate was obtained during the pre-anaesthetic visit the day before the procedure, when they came into hospital for admission for the surgery. Written consent to take part in the study was obtained on admission prior to the administration of a self-designed questionnaire. The age, weight, height, parity and educational level of all the participants were obtained using the questionnaire.

Patients were randomly assigned to one of three groups – group A, group B and group C. A simple randomization technique was used. Placement into the groups was by simple balloting without replacement. Thirty-three ballots were labelled A, another 33 ballots were labelled B and a further 33 ballots labelled C. All the ballot papers were folded and mixed together in an opaque envelope. The principal investigator then asked patients who met the inclusion criteria to pick a ballot from the opaque envelope to determine which group (A, B or C) the patient had been randomized to. Whichever ballot was picked by the patient was discarded. Subsequent patients who qualified for the study were taken through the same steps until all the ballot papers were exhausted.

3.7.2 Blinding

This was a double-blinded study. The principal investigator and the patients were both blinded to the interventions. Each of the three study groups were given a code (A, B and C) by one of the supervisors: Group A (TAP block using plain bupivacaine with dexamethasone), Group B (TAP block using plain bupivacaine) and Group C (TAP block using saline). Apart from the supervisor who assigned the code to the groups, no other person knew which of the study groups was assigned to which code. This code (A, B or C) was used by the principal investigator and other study personnel for collection of data without they knowing the identity of the groups behind the code. Upon completion of data collection, the identity of the code was

revealed as Group A - the first intervention group (TAP block using plain bupivacaine with dexamethasone), group B - the second intervention group (TAP block using plain bupivacaine) and group C - the control group (TAP block using saline).

All groups underwent an ultrasound-guided bilateral TAP block using the Butterfly iQ® Ultrasound-on-Chip™ (Butterfly Network Inc. USA) portable ultrasound probe[214] paired with a Samsung® Galaxy S10+ Android® mobile phone (Appendix 5). The Butterfly iQ® is a novel subscription-based hand-carried ultrasound system which uses a single, multifrequency, capacitive micromachined ultrasonic transducer (1-9 megahertz [MHz]) to image areas of the body (lung, heart, abdomen, superficial structures). Butterfly iQ comprises three components, namely compatible Apple® or Android® mobile devices, the Butterfly iQ application on the compatible device, and a probe that facilitates connection with the mobile device to generate and receive ultrasound signals. The device has minimum and maximum scan depths of 1cm and 30cm respectively. It is capable of the following scanning modes: M-mode, B-mode, colour doppler, power doppler and pulsed wave doppler depending on the region of the world it is being used. It has 22 scanning presents which automatically optimise the image depending on the part of the body being scanned. The "Musculoskeletal" present was employed during the performance of the TAP block in this study. It was developed with a focus on contrast resolution to highlight crisp borders between structures, and needles with "pop". It is suitable for performing interventions, as well as for diagnostic procedures requiring crisp border detection (such as in TAP block). The preset penetrates from a minimum depth of 1cm to a maximum of 12cm, and automatically translates from linear to trapezoidal format (4cm), and then to curvilinear (8cm).[214]

3.7.3 Conduct of Anaesthesia

On arrival in the pre-anaesthetic area, vascular access of participants was achieved with gauge 18 peripheral intravenous cannula. Participants were preloaded with 1000ml of Ringer lactate solution after which they were transferred to the operating theatre bed and positioned supine with a 15^{o} left lateral tilt. Non-invasive blood pressure, continuous electrocardiogram, pulse oximetry and temperature monitoring were then established. Patients were assisted to sit on the theatre bed with their feet resting on a padded footstool and positioned for the spinal anaesthetic with their backs exposed.

The anaesthesia provider with a head cap and facemask donned, performed a surgical hand scrub and wore sterile gloves. The anaesthetist then prepared drugs and other logistics required for the performance of the spinal anaesthetic in a sterile manner on a sterile trolley.

An assistant helped with setting up the sterile trolley with provision of drapes, 2ml and 5ml syringes, a G25 Whitacre spinal needle, 2% lidocaine, fentanyl 50mcg/ml ampoule and 0.5% heavy bupivacaine. A total amount of 2.5mls consisting of 2ml 0.5% heavy bupivacaine and 0.5ml of 50mcg/ml fentanyl for intrathecal injection was then prepared by the anaesthesia provider into a 5ml syringe and 2mls of 2% plain lidocaine for skin infiltration was also drawn into a 2ml syringe.

The back of the participant was cleaned with antiseptic solution which began at the area of intended injection and moved outwards. This step was repeated and then followed by cleaning with 70% alcohol solution and allowed to dry. Sterile drapes were applied to the back which left the intended site of injection exposed. The L3/L4 lumbar space was identified for the spinal anaesthesia using the intercristal line (Tuffier's line).

The skin at the L3/L4 lumbar space was infiltrated with 2ml of 2% plain lidocaine. A spinal needle introducer was anchored into the interspinous ligament and the gauge 25 pencil point Whitacre spinal needle was introduced through the introducer needle. The spinal needle was advanced until a "pop" was felt as it passed through the dura mater. The stylet of the spinal needle was then removed and placement of the spinal needle in the subarachnoid space confirmed by the free flow of cerebrospinal fluid into the hub of the spinal needle.

The spinal and introducer needles were simultaneously steadied with the dorsum of the non-dominant hand against the patient's back. The 5ml syringe containing the intrathecal local anaesthetic solution was attached to the spinal needle in the subarachnoid space, and gentle aspiration of some clear CSF into the syringe further confirmed the accurate position of the spinal needle in the subarachnoid space. A total of 2.5mls of solution containing 10mg bupivacaine and 25mcg fentanyl was then injected into the subarachnoid space. The patient was placed supine with a 15^{o} left lateral tilt immediately after performance of the spinal anaesthetic.

The blood pressure was checked before and immediately after administration of the sub-arachnoid block. It was then checked every minute for the first 5 minutes, then every 3 minutes for the next 15 minutes and every 5 minutes until the end of the surgery. Sensory level was assessed using cold perception from one dermatome to the other. A minimum sensory level of T6 was considered adequate prior to commencement of surgery.

All patients received 1g intravenous paracetamol intra-operatively and 100mg rectal diclofenac at the end of surgery in accordance with standard practice at the study site. Intravenous paracetamol was continued at 6 hourly intervals in the post-operative period and

rectal diclofenac was also continued 12-hourly in the post-operative period according to current local practice. All other management proceeded as per standard local practice.

3.7.4 Performance of TAP Block

At the end of the Caesarean delivery procedure in the theatre, patients had an ultrasound-guided bilateral TAP block performed using the blinded solution handed over to the principal investigator by the supervisor. A single-injection ultrasound-guided TAP block was performed as described below in all patients using the Butterfly iQ ultrasound probe and BBraun Stimuplex® A 100mm nerve block needle (B. Braun Melsungen AG, 34209 Melsungen, Germany). Lidocaine 2ml 2% is infiltrated at the site of block needle insertion prior to performance of the TAP block. This was done to prevent pain during performance of the TAP block in case the block height of the spinal anaesthetic had regressed. The time the block is performed was noted.

The lateral approach to the TAP block was performed with patient in the supine position by placing the ultrasound probe in the axial plane on the midaxillary line between the subcostal margin and the iliac crest. The three layers of abdominal wall muscles are identified as well as the fascial plane between the internal oblique and the transversus abdominis muscles. The needle is inserted in the anterior axillary line, in plane and directly under the ultrasound probe in an anterior to posterior, lateral to medial direction. The needle tip is advanced until it reaches the fascial plane between the internal oblique and transversus abdominis muscles roughly in the midaxillary line. On negative aspiration of blood, the chosen injectate is delivered in aliquots of 5ml with regular aspiration between aliquots until the total amount of block injectate is administered. This was performed with real time monitoring of injectate spread which appeared as a hypoechoic expansion of the TAP under ultrasound guidance. The TAP block is then performed on the opposite side, using the same technique and the same injectate.

Participants randomised to group A received 20ml 0.25% bupivacaine + 4mg dexamethasone on each side. Participants randomised to group B received 20ml 0.25% bupivacaine on each side whereas the participants randomised to group C received 20ml of 0.9% saline on each side.

The capillary random blood sugar level was checked (using OneTouch Select Plus Flex™ Blood Glucose Monitoring System, LifeScan Europe GmbH, Gubelstrasse 34, 6300 Zug, Switzerland) immediately prior to performance of the TAP block and also at 8 and 24 hours after performance of the block. The pulp of a finger was cleaned with an alcohol-free cleaning

solution. A sterile stylet was then used to stab the finger pulp to obtain a drop of blood, which was then applied onto the test strip to obtain a reading.

The volume and concentration of bupivacaine chosen (20ml of 0.25%) was to ensure that at the minimum exclusion weight of 60kg for participants, the maximum safe dose of bupivacaine (2mg/kg) was not exceeded.

After completion of the surgery and performance of the TAP block, the participant was admitted to the recovery ward where monitoring was continued. Electrocardiogram including heart rate and pulse oximetry is monitored continuously throughout the patient's stay in the recovery ward. Respiratory rate, non-invasive blood pressure and temperature is monitored on arrival in recovery and every 15 minutes thereafter until patient is discharged from the recovery. Fluid input and urine output is monitored and recorded on arrival and at hourly intervals. Random blood sugar is checked on arrival in the recovery and any observed derangement is corrected as needed. The participant was subsequently discharged to the general ward after 3 hours to 4 hours after satisfying existing discharge criteria.

3.7.5 Postoperative pain management and monitoring of participants

The static and dynamic pain score was checked by a trained nurse in the post anaesthesia recovery unit and the general ward using the numerical rating scale (NRS). The static pain score was assessed with the patient lying supine and still with normal tidal breathing (at rest). The participant was then asked to rate the severity of their pain on an 11-point scale ranging from 0 (no pain) to 10 (worst pain imaginable). The dynamic pain score was also assessed by asking the patient to cough and determining how painful it was (on coughing) using the 11-point scale described earlier. The pain scores were checked immediately on arrival in the recovery ward and repeated at 2, 6, 12 and 24 hours after performance of the TAP block. Other parameters that were checked at these time points were non-invasive blood pressure including mean arterial pressure and SpO_2 values. The time elapsed following performance of the TAP block to the first analgesic request was also noted. The random blood sugar was also checked immediately prior to block performance and subsequently at 8 and 24 hours after block performance. The nurse was not privy to which study group the patient belonged.

Participants were instructed to request additional medication in case of breakthrough postoperative pain. Breakthrough postoperative pain was managed using intramuscular pethidine of 1.5mg/kg up to a maximum of 100mg at 4 hourly intervals as needed in the post anaesthesia care unit and on discharge to the ward. The static NRS pain score at the time of

analgesic request was noted. The total amount of pethidine administered in the first 24-hour period after surgery was recorded.

Nausea and vomiting was assessed, and patient was given a score according to the nausea and vomiting score described by McDonnell et al.[215] (none=0; mild= 1; moderate=2; severe=3). Intravenous granisetron 1mg was planned to be used as a rescue antiemetic for any patient who complained of nausea or vomiting.

The incidence of pruritus was assessed and recorded employing the method as described by Horta et al.[216] The level of sedation of participants was assessed at the timepoints for pain assessment. Sedation scores was assigned using the sedation scale described by McDonnell et al.[167] (awake and alert = 0; quietly awake = 1; asleep but easily roused = 2; deep sleep = 3).

Patient satisfaction regarding pain relief was assessed at the end of 24 hours using a 5-point scale[217] (very satisfied, somewhat satisfied, neither satisfied or dissatisfied, somewhat dissatisfied, very dissatisfied).

The site of the TAP block was monitored immediately after performance of the TAP block and at 2, 6, 12 and 24 hours for bleeding and haematoma formation.

3.8 Data Storage and Management

A data collection sheet (Appendix 2) was used to collect the relevant data for the study. All members of the research team treated all data with strict confidentiality. Data was entered into Microsoft® Excel version 2016 (Microsoft Corporation, One Microsoft Way, Redmond Washington, 98052-6399, United States of America) for cleaning and storage. The data was then exported to Statistical Package for the Social Sciences (SPSS) software version 25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corporation) for analysis. To ensure data security, the following strategies were employed:

1) Confidentiality was maintained by using unique serial numbers.
2) Patient identifiers (name, date of birth and contact information) were decoupled from the rest of the data. This data was password protected. Only the principal investigator and supervisors had access to the database and password.
3) Hard copies of personally identifying data and codebook were kept securely locked away at all times when not in use.
4) The rest of the data (anonymized) was entered in a separate Microsoft® Excel file (and exported into SPSS for analysis). All data files (MS Excel and SPSS) were password protected. Anonymized data was assessable only to the PI, supervisors, and statistician.

5) Hard copies of patient's data (questionnaires and physical examination forms) were kept physically restricted in a locked cabinet in the research supervisor's office. The keys to the cabinet remained on the persons of the research supervisor and research candidate at all times.
6) Logical security techniques were ensured when working on the internet. These include the use of antispyware and virus-detection programs on our research computers.
7) Data were backed up daily to external drives during the period of data entry.

3.9 Statistical Data Analysis

Data was analysed by using the SPSS 25 software package. Age, weight and BMI were summarized as mean and standard deviation. Data on previous caesarean delivery, grade of anaesthesia provider and educational status were presented as frequencies and percentages in tables and charts.

One way Analysis of Variance (ANOVA) was used to compare between the three groups the mean time to request for first analgesic, the mean NRS pain score at the time to request for first analgesic and the mean amount of opioid (pethidine) consumed in the first 24 hours. The one-way ANOVA is a statistical test used to determine whether there are any statistically significant differences between the means of three or more independent (unrelated) groups. The one-way ANOVA determines that at least the means of two of the independent groups significantly differ from each other. It does not however determine which pair(s) of means significantly differ. To determine which specific groups differed from each other, a post hoc test is required.

Repeated measures ANOVA was employed to compare all three groups with respect to the static and dynamic NRS pain scores, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, oxygen saturation and random blood sugar. The repeated measures ANOVA compares means across one or more variables that are based on repeated observations. In this study parameters that were repeatedly measured over multiple time points were pain scores, blood sugar readings, blood pressure readings and peripheral oxygen saturation. The repeated measures ANOVA is referred to as "an analysis of dependencies" because it is a test to prove an assumed cause-effect relationship between the independent variable(s), if any, and the dependent variable(s).

Tukey's Honest Significant Difference (HSD) test and Bonferroni test were employed as post hoc tests where necessary for the one-way ANOVA and repeated measures ANOVA respectively. The Tukey HSD and Bonferroni tests are multiple comparison tests employed

after an ANOVA test returns significant results to find out which specific group's means (compared with each other) are different. The test compares all possible pairs of means.

Chi squared test was used to assess differences between the study groups with respect to PONV, pruritus, sedation and participant satisfaction. The Chi-squared test for independence compares two or more variables in a contingency table to see if they are related. It tests to see whether distributions of categorical variables differ from each another. In this study, severity of PONV, pruritus, sedation scores and participant satisfaction scores were categorical variables allowing the use of the Chi squared test for their comparison amongst the three study groups.

Strength of association of factors was expressed at the 95% confidence interval. Statistical significance was defined as p-value <0.05.

3.10 Ethical and Legal Considerations

Approval for the study was sought from the Korle-Bu Teaching Hospital Ethics and Protocol Review Committee (Appendix 4) as well as the dissertation review committee of the Ghana College of Physicians and Surgeons.

Participation in the study was absolutely voluntary. Study participants were adequately informed of the purpose, nature, procedures and potential risks of the study. Points that were emphasized included anonymity, confidentiality and the freedom to decline to participate or withdraw from the study at any time without penalty. Refusal to participate did not affect the conduct of anaesthesia or clinical management of the patient in any way. A signed or thumb-printed informed consent was obtained from patients before enrolment into the study (Appendix 1).

CHAPTER 4: RESULTS

4.1 Participant Demographic Information

Ninety-nine (99) participants were successfully recruited into the study. These were divided into 3 groups with each group comprising 33 participants. Five (5) participants who were approached to participate in the study initially agreed but later declined to participate prior to commencement of anaesthesia and subsequent performance of the TAP block and thus were not included in the final analysis of results. No participant for whom the TAP block was performed withdrew their consent to participate in the study after performance of the block. There were no participant dropouts for any reason from the time of block performance until their final review 24 hours after block performance.

The age distribution of the study participants is shown in Figure 4.1 below. Majority of the participants were in the 25 – 29 years age group (37.4%).

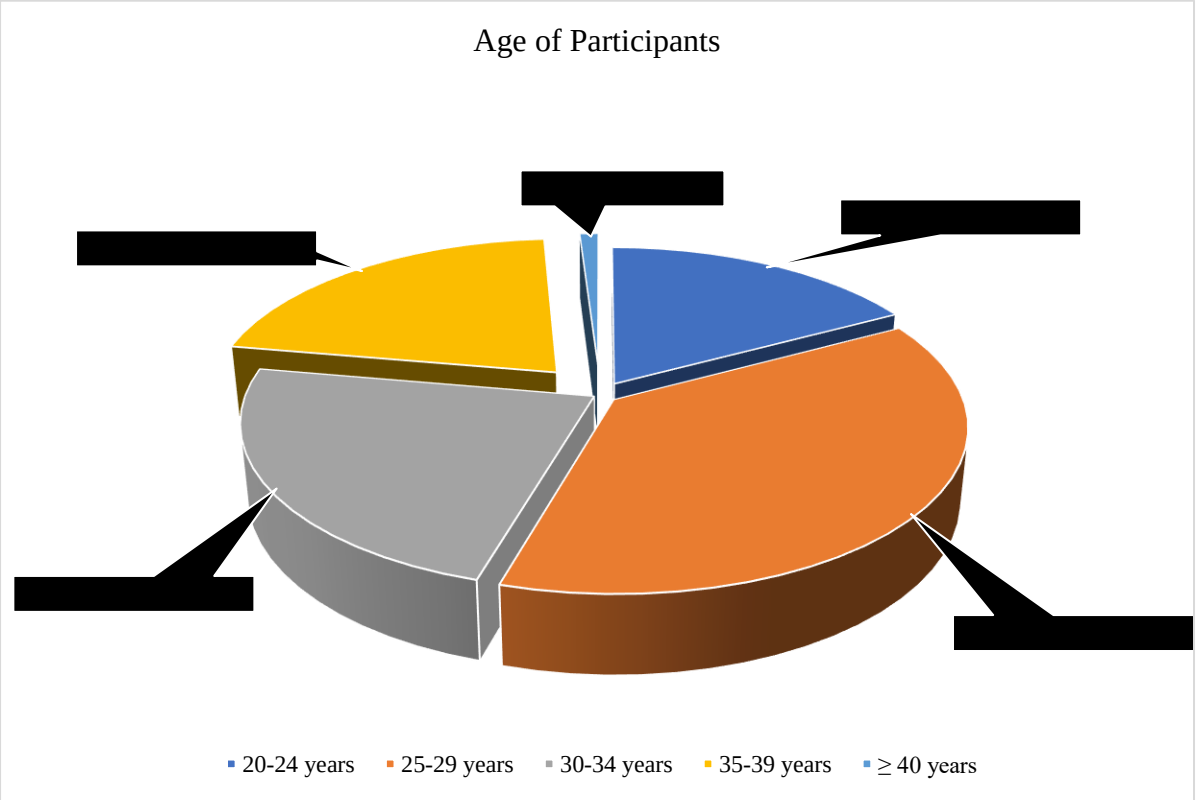

Figure 4.1: Age distribution of study participants

The mean age of participants was 29.8 ± 4.9 years and ranged between 21 and 40 years (Table 4.1).

Table 4.1: Association of demographic characteristics between study groups

Demographic Parameter	Group	N	Mean ± Standard Deviation	Minimum	Maximum	*F*-test	*p*-value
Age (years)	**Group A**	33	30.9 ± 5.1	21	40	1.184	0.310
	Group B	33	29.3 ± 4.8	22	37		
	Group C	33	29.2 ± 4.8	22	39		
	Total	99	29.8 ± 4.9	21	40		
Weight (kg)	**Group A**	33	74.88 ± 9.04	60.0	94.8	0.288	0.751
	Group B	33	73.58 ± 6.53	62.0	87.0		
	Group C	33	73.82 ± 6.39	60.0	84.0		
	Total	99	74.09 ± 7.37	60.0	94.8		
Height (m)	**Group A**	33	1.608 ±0.061	1.45	1.70	0.285	0.752
	Group B	33	1.611 ±0.051	1.50	1.71		
	Group C	33	1.618 ±0.054	1.51	1.70		
	Total	99	1.612 ±0.055	1.45	1.71		
Body Mass Index (kg/m^2)	**Group A**	33	28.93 ± 2.81	22.9	34.4	1.185	0.310
	Group B	33	28.31 ± 1.40	25.2	31.2		
	Group C	33	28.19 ± 1.89	25.0	34.1		
	Total	99	28.48 ± 2.12	22.9	34.4		
Parity	**Group A**	33	1.5 ± 0.87	0	4	0.367	0.694
	Group B	33	1.3 ± 0.78	0	3		
	Group C	33	1.3 ± 0.98	0	3		
	Total	99	1.4 ± 0.87	0	4		
Duration of Surgery (minutes)	**Group A**	33	62.0 ± 9.76	43	80	1.800	0.171
	Group B	33	59.4 ± 9.21	40	82		
	Group C	33	57.2 ± 11.75	40	88		
	Total	99	59.5 ± 10.35	40	88		
Booking Systolic Blood Pressure (mmHg)	**Group A**	33	108.9 ± 8.69	90	124	2.124	0.125
	Group B	33	113.6 ± 9.22	91	130		
	Group C	33	111.2 ± 9.66	96	131		
	Total	99	111.3 ± 9.30	90	131		
Booking Diastolic Blood Pressure (mmHg)	**Group A**	33	67.7 ± 7.77	50	83	0.713	0.493
	Group B	33	68.8 ± 5.97	53	83		
	Group C	33	69.6 ± 6.01	59	82		
	Total	99	68.7 ± 6.62	50	83		

Key: kg – kilograms; m – metres; kg/m^2 – kilogram per square metre, mmHg – millimetres of mercury

As demonstrated in Table 4.1, there was no statistically significant difference between the three study groups with respect to age, weight, body mass index, height, parity, booking blood pressure (systolic and diastolic) and duration of surgery.

Majority of participants were overweight comprising 74.7% (Figure 4.2).

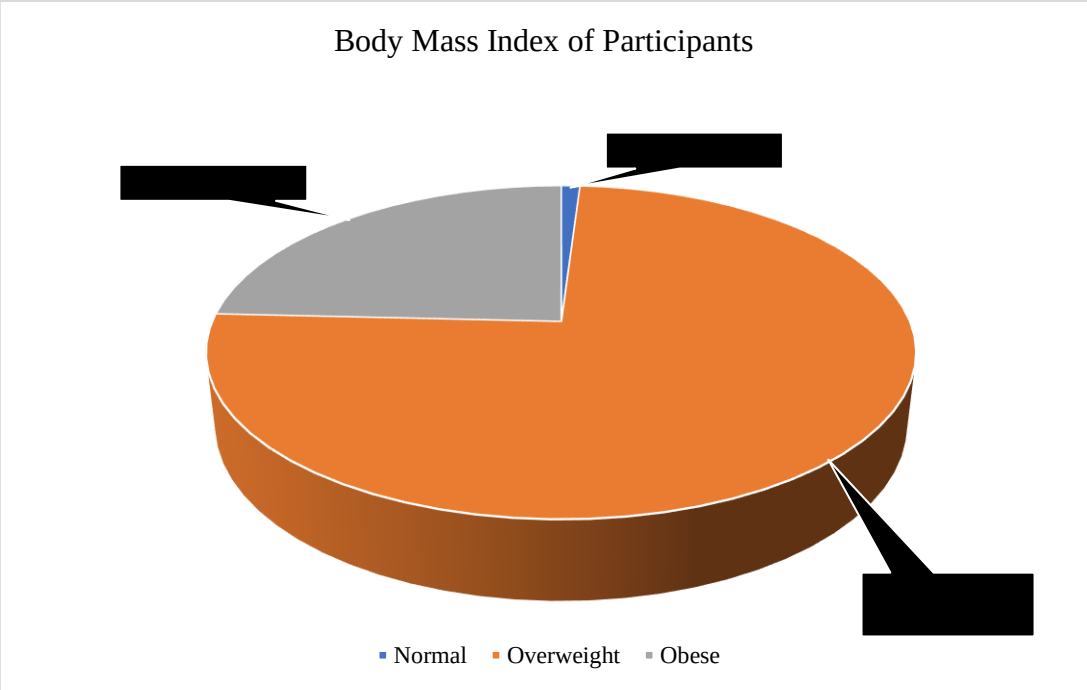

Figure 4.2: Distribution of body mass index of study participants

Study participants weighed between 60.0kg and 94.8kg with a mean weight of 74.09 ± 7.37 kg (Table 4.1).

About 85.9% of participants had received a minimum of secondary education. Four percent (4%) of participants had had no formal education (Figure 4.3).

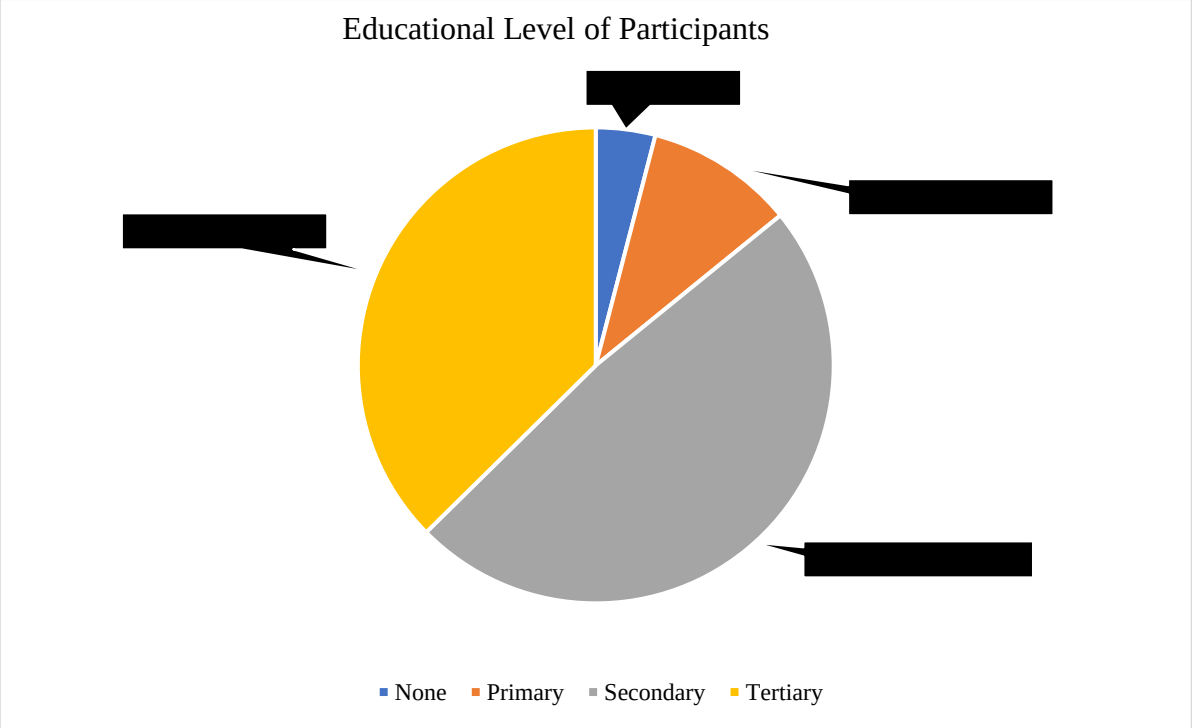

Figure 4.3: Educational level of participants

There was no statistically significant difference between the study groups with respect to the educational level of participants (*p*-value = 0.146) (Table 4.2).

Table 4.2: Study groups in relation to educational level of participants

Educational Level	Group A	Group B	Group C	Total	Pearson $\chi 2$ value (df)	*p*-value
	Count (% within group)					
None	3 (9.1)	0 (0.0)	1 (3.0)	4 (4.0)	9.529 (6)	0.146
Primary	0 (0.0)	4 (12.1)	6 (18.2)	10 (10.1)		
Secondary	17 (51.5)	17 (51.5)	14 (42.4)	48 (48.5)		
Tertiary	13 (39.4)	12 (36.4)	12 (36.4)	37 (37.4)		
Total	33 (100.0)	33 (100.0)	33 (100.0)	99 (100.0)		

About 60.6% of participants had a previous caesarean delivery prior to their involvement in the study. There was no difference between the groups with regard to previous caesarean section of participants (*p*-value = 0.090) (Table 4.3).

Table 4.3: Comparison of study groups with respect to previous caesarean section

Previous Caesarean Section	Group A	Group B	Group C	Total	Pearson χ2 value (df)	*p*-value
	Count (% within group)					
No	11 (33.3)	18 (54.5)	10 (30.3)	39 (39.4)	4.823 (2)	0.090
Yes	22 (66.7)	15 (45.5)	23 (69.7)	60 (60.6)		
Total	33 (100.0)	33 (100.0)	33 (100.0)	99 (100.0)		

The mean parity of participants prior to enrolment in the study was 1.35 ± 0.87 per parturient with a range between 0 and 4 (Table 4.1). Majority of participants (44.4%) had a parity of 1 (Figure 4.4).

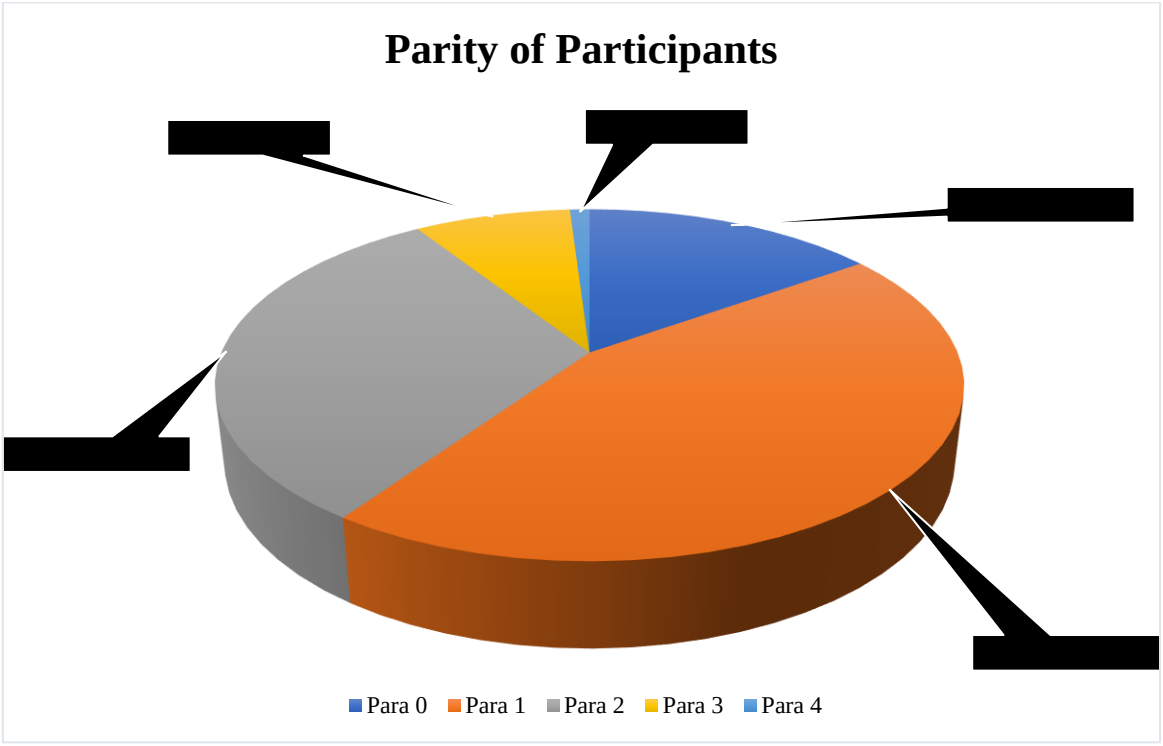

Figure 4.4: Parity of study participants

The mean duration of surgery for caesarean delivery amongst the study participants was 59.5 ± 10.35 minutes (Table 4.1). The shortest and longest duration of surgery was 40 minutes and 88 minutes respectively.

The mean systolic blood pressure at booking visit for antenatal care was 111.3 ± 9.30 mmHg with a range between 90 mmHg and 131 mmHg (Table 4.1). The mean diastolic blood

pressure at the antenatal booking visit was also 68.7 ± 6.62 mmHg with a range between 50 mmHg and 83 mmHg (Table 4.1).

Majority of the anaesthesia for the caesarean deliveries was provided by Certified Registered Anaesthetists (CRA) comprising 37.4% of all the anaesthetics conducted (Figure 4.5).

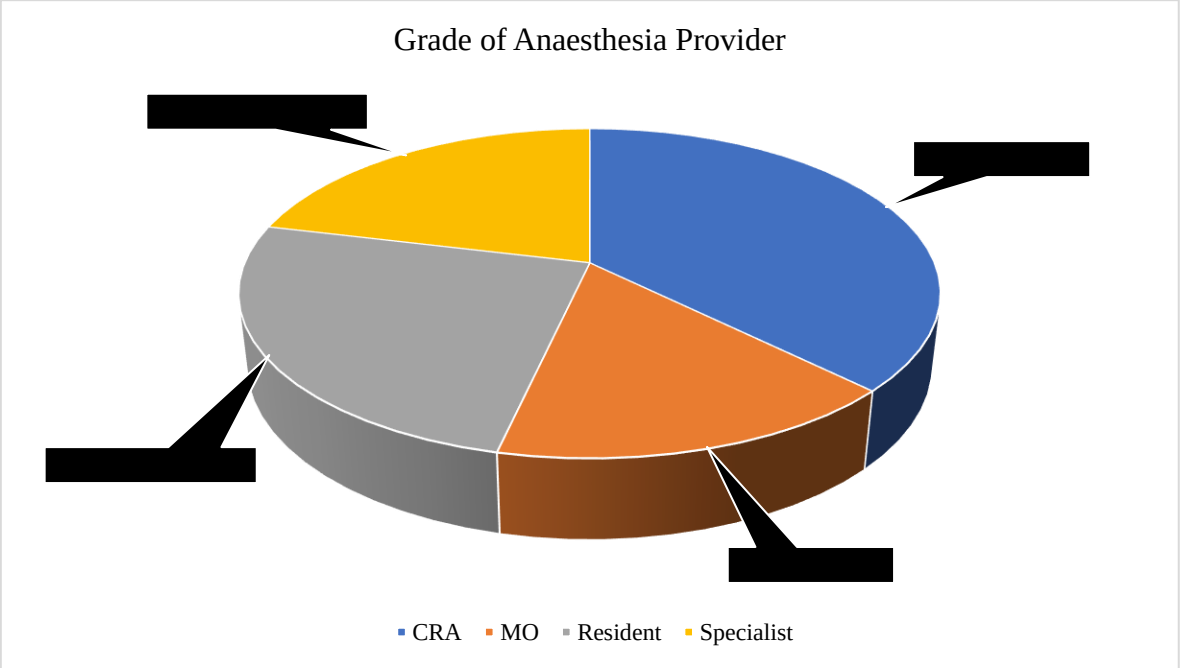

Figure 4.5: Grade of anaesthesia provider for caesarean delivery

There was no statistically significant difference between the three study groups with respect to the grade of the anaesthesia provider for the caesarean delivery (*p*-value = 0.163) (Table 4.4).

Table 4.4: Study groups in relation to anaesthesia provider

Anaesthesia Provider Grade	**Group A**	**Group B**	**Group C**	**Total**	**Pearson χ2 value (df)**	***p*-value**
	Count (% within Group)					
CRA	12 (36.4)	8 (24.2)	17 (51.5)	37 (37.4)		
MO	7 (21.2)	7 (21.2)	2 (6.1)	16 (16.2)		
Resident	7 (21.2)	12 (36.4)	6 (18.2)	25 (25.3)	9.188 (6)	0.163
Specialist	7 (21.2)	6 (18.2)	8 (24.2)	21 (21.2)		
Total	33 (100)	33 (100)	33 (100)	99 (100)		

4.2 Time to Request for First Analgesic

From Table 4.5, there was a statistically significant difference between the mean time to first analgesic request of the three study groups (*p*-value < 0.0001). It took a shorter time for group C patients to request for first analgesia, followed by group B patients and group A patients.

Table 4.5: Mean time to request for first analgesic

	N	Mean ± Standard Deviation (minutes)	Minimum (minutes)	Maximum (minutes)	*F*-test	*p*-value
Group A	27	485.2 ± 143.03	300	870		
Group B	32	327.5 ± 98.69	125	670	35.458	<0.0001
Group C	33	256.5 ± 72.33	135	395		
Total	92	348.3 ± 140.60	125	870		

Multiple comparison post-hoc analysis revealed a statistically significant difference between the mean time to first analgesic request between each of the study groups as demonstrated in Table 4.6 below.

Table 4.6: Post hoc multiple comparison testing for mean time to request for first analgesic

Group Comparison	Mean Difference	95% Confidence Interval for Difference		*p*-value
		Lower Bound	Upper Bound	
Group A v Group B	157.685	91.62	223.75	<0.0001
Group A v Group C	228.670	163.07	294.27	<0.0001
Group B v Group C	70.985	8.26	133.71	0.023

The mean NRS score at the time of first analgesic request was 5.2 ± 1.31, 5.1 ± 1.32 and 5.1 ± 0.99 for groups A, B and C respectively (Table 4.7). There was no statistically significant difference in pain scores at the time of first opioid analgesic intervention (*p*-value = 0.879).

Table 4.7: NRS pain score at time of opioid analgesic intervention

	N	Mean ± Standard Deviation	Minimum	Maximum	*F*-test	*p*-value
Group A	27	5.2 ± 1.31	4	8		
Group B	32	5.1 ± 1.32	3	8	0.129	0.879
Group C	33	5.1 ± 0.99	4	7		
Total	92	5.1 ± 1.20	3	8		

4.3 Pain Scores

4.3.1 NRS Pain Scores at Rest

The NRS pain scores at rest for study participants over the study period are demonstrated in Figure 4.6 and Table 4.9 below. All participants did not report static pain at the time of block performance. The difference in mean static NRS pain scores between the study groups at 2 hours, 6 hours and 12 hours was statistically significant with the 24-hour static NRS pain scores being statistically not significant (Table 4.8).

Table 4.8: NRS pain scores at rest at observation time points

Time point	Group	N	Mean ± Standard Deviation	Minimum	Maximum	*F*-test	*p*-value
0 hours	**Group A**	33	0.0 ± 0.00	0	0	-	-
	Group B	33	0.0 ± 0.00	0	0		
	Group C	33	0.0 ± 0.00	0	0		
	Total	99	0.0 ± 0.00	0	0		
2 hours	**Group A**	33	1.1 ± 0.81	0	3	3.119	0.049
	Group B	33	1.2 ± 1.02	0	3		
	Group C	33	1.7 ± 1.11	0	3		
	Total	99	1.3 ± 1.01	0	3		
6 hours	**Group A**	33	3.4 ± 1.23	0	6	10.330	<0.0001
	Group B	33	3.6 ± 1.15	2	6		
	Group C	33	4.9 ± 1.85	2	8		
	Total	99	4.0 ± 1.58	0	8		
12 hours	**Group A**	33	2.6 ± 1.19	1	6	32.349	<0.0001
	Group B	33	3.4 ± 1.30	1	6		
	Group C	33	4.9 ± 0.98	3	6		
	Total	99	3.7 ± 1.49	1	6		
24 hours	**Group A**	33	1.9 ± 1.30	0	4	1.818	0.168
	Group B	33	2.2 ± 1.17	0	4		
	Group C	33	2.4 ± 1.12	0	4		
	Total	99	2.2 ± 1.21	0	4		

The mean NRS pain score at rest for the 24 hours observation period was 1.8 ± 1.56, 2.1 ± 1.69 and 2.8 ± 2.22 for group A, B and C respectively. The difference in the means was statistically significant (*p*-value < 0.0001) (Table 4.9).

Table 4.9: Mean 24-hour NRS pain score at rest

Groups	Mean ± SD	Standard Error	N	95% Confidence Interval		*F*-test	*p*-value
				Lower Bound	Upper Bound		
Group A	1.8 ± 1.56	0.09	33	1.620	1.980		
Group B	2.1 ± 1.69	0.09	33	1.905	2.264	30.347	<0.0001
Group C	2.8 ± 2.22	0.09	33	2.590	2.949		

Key: SD – Standard Deviation

Comparing the NRS pain scores at rest of the study groups across all the observation time points revealed a statistically significant difference between each of the intervention groups and the control group (*p*-value <0.0001; *p*-value < 0.0001) but not between the two intervention groups (*p*-value = 0.085) (Table 4.10).

Table 4.10: Pairwise comparisons of mean 24-hour NRS pain score

Group Comparison	Mean Difference	95% Confidence Interval for Difference		*p*-value
		Lower Bound	Upper Bound	
Group A v Group B	-0.285	-0.597	0.027	0.085
Group A v Group C	-0.970	-1.281	-0.658	<0.0001
Group B v Group C	-0.685	-0.997	-0.373	<0.0001

Post hoc pairwise analysis demonstrates no statistically significant difference of static NRS pain scores between any of the study groups at the 2-hour observation point (Table 4.11). However, at the 6-hour point, there was a statistically significant difference between each of the intervention groups and the control group but not between the two intervention groups. At the 12-hour mark, there was a statistically significant difference between all the three study groups (Table 4.11).

Table 4.11: Multiple comparisons post hoc analysis of NRS pain scores at rest

Time Point	Group Comparison	Mean Difference	95% Confidence Interval for Difference		*p*-value
			Lower Bound	Upper Bound	
2 hours	Group A v Group B	-0.121	-0.713	0.471	1.000
	Group A v Group C	-0.576	-1.168	0.016	0.060
	Group B v Group C	-0.455	-1.047	0.138	0.194
6 hours	Group A v Group B	-0.121	-0.987	0.744	1.000
	Group A v Group C	-1.455	-2.320	-0.589	<0.0001
	Group B v Group C	-1.333	-2.199	-0.468	0.001
12 hours	Group A v Group B	-0.788	-1.487	-0.089	0.022
	Group A v Group C	-2.273	-2.972	-1.574	<0.0001
	Group B v Group C	-1.485	-2.184	-0.786	<0.0001

The progression of the mean NRS pain scores at rest for each study group at 0 hours, 2 hours, 6 hours, 12 hours and 24 hours is illustrated in Figure 4.6. The NRS pain scores at rest for all observation time points aside the time of block performance was in the order Group A < Group B < Group C. The pain scores of the control group is observed to plateau between the 6 and 12 hour observation points before declining. The two intervention groups also have a peaking of the NRS pain scores at rest but at a lower level before declining to the 24-hour observation point.

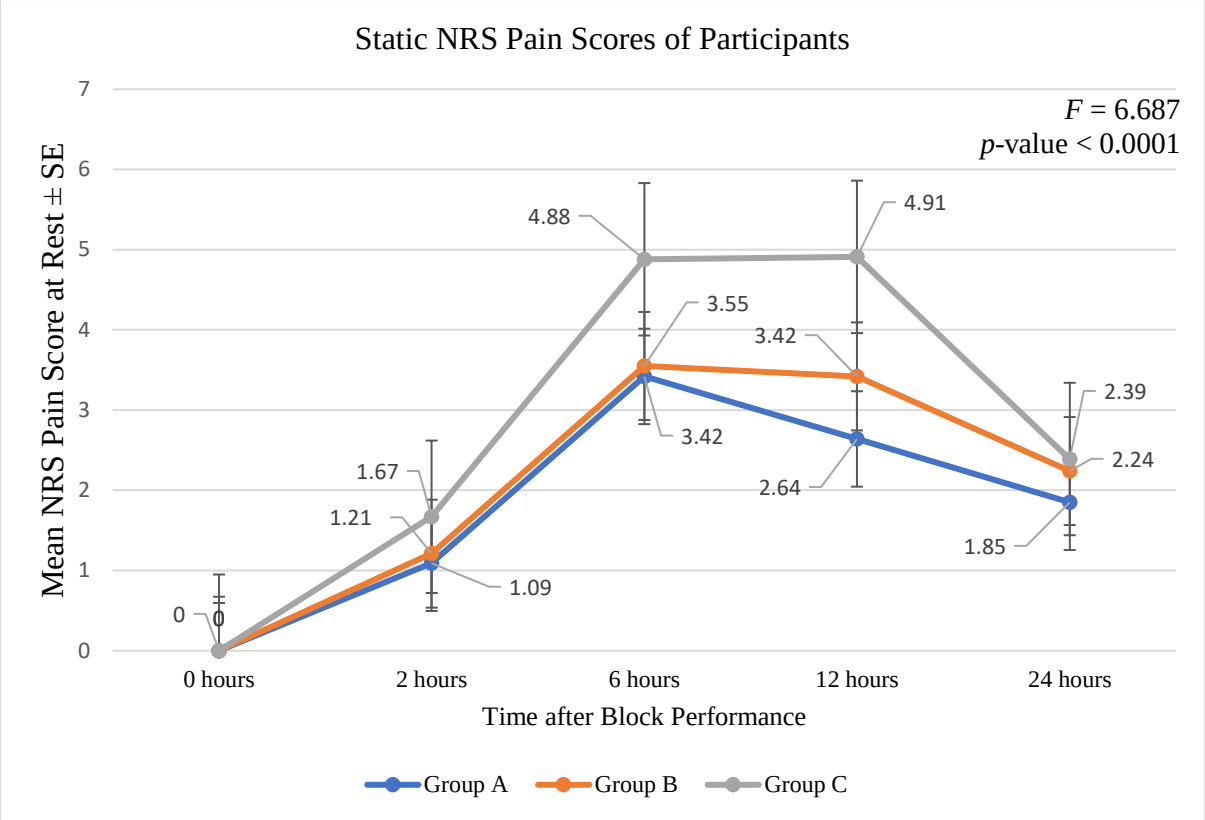

Figure 4.6: NRS pain scores at rest over time

4.3.2 NRS Pain Scores on Coughing

All participants did not report pain on coughing at the time of block performance. The difference in mean NRS pain scores on coughing between the study groups at 2 hours, 6 hours, 12 hours and 24 hours was statistically significant (Table 4.12).

Table 4.12: Mean NRS pain scores on coughing at observation time points

Time point	Group	N	Mean ± Standard Deviation	Minimum	Maximum	*F*-test	*p*-value
0 hours	**Group A**	33	0.0 ± 0.00	0	0	-	-
	Group B	33	0.0 ± 0.00	0	0		
	Group C	33	0.0 ± 0.00	0	0		
	Total	99	0.0 ± 0.00	0	0		
2 hours	**Group A**	33	2.6 ± 1.69	0	5	5.129	0.008
	Group B	33	2.5 ± 1.20	0	5		
	Group C	33	3.5 ± 0.97	2	5		
	Total	99	2.9 ± 1.38	0	5		
6 hours	**Group A**	33	4.3 ± 1.86	1	7	7.145	0.001
	Group B	33	4.6 ± 1.06	2	6		
	Group C	33	5.7 ± 1.79	2	8		
	Total	99	4.9 ± 1.71	1	8		
12 hours	**Group A**	33	3.6 ± 1.35	1	6	8.476	<0.0001
	Group B	33	4.0 ± 1.20	1	7		
	Group C	33	4.8 ± 1.17	2	7		
	Total	99	4.1 ± 1.33	1	7		
24 hours	**Group A**	33	3.3 ± 1.73	1	6	0.401	0.671
	Group B	33	3.6 ± 1.95	1	7		
	Group C	33	3.8 ± 2.15	1	8		
	Total	99	3.6 ± 1.94	1	8		

The mean NRS pain scores on coughing over the study period is demonstrated in Table 4.13 and Figure 4.7.

Table 4.13: Mean 24-hour NRS pain scores on coughing

Groups	Mean ± SD	Standard Error	N	95% Confidence Interval		*F*-test	*p*-value
				Lower Bound	Upper Bound		
Group A	2.8 ± 2.08	0.111	33	2.538	2.977		
Group B	2.9 ± 2.03	0.111	33	2.714	3.153	13.768	<0.0001
Group C	3.5 ± 2.39	0.111	33	3.320	3.759		

Key: SD – Standard Deviation

Aggregation of NRS pain scores on coughing over all time points and pairwise comparison of each of the study groups reveals as statistically significant difference between each of the two intervention groups and the control group but not between the two intervention groups (Table 4.14).

Table 4.14: Pairwise comparison of NRS pain scores on coughing over all time points

Group Comparison	Mean Difference	95% Confidence Interval for Difference		*p*-value
		Lower Bound	Upper Bound	
Group A v Group B	-0.220	-0.696	0.256	0.791
Group A v Group C	-0.977	-1.453	-0.501	<0.0001
Group B v Group C	-0.758	-1.234	-0.281	0.001

Post hoc analysis demonstrates a statistically significant difference between each of the intervention groups and the control group but not between the two intervention groups at the 2-hour, 6-hour and 12-hour observation points for NRS pain scores on coughing (Table 4.15). Thus, the mean NRS pain scores on coughing for each of the study groups were similar at the 24-hour observation point.

Table 4.15: Multiple pairwise comparison of mean NRS pain scores on coughing

Time	Group Pairing	Mean Difference	95% Confidence Interval		*p*-value
			Lower Bound	Upper Bound	
2 hours	**Group A v Group B**	0.152	-0.62	0.93	0.888
	Group A v Group C	-0.818	-1.59	-0.04	0.036
	Group B v Group C	-0.970	-1.75	-0.19	0.010
6 hours	**Group A v Group B**	-0.303	-1.25	0.64	0.726
	Group A v Group C	-1.424	-2.37	-0.48	0.002
	Group B v Group C	-1.121	-2.07	-0.18	0.016
12 hours	**Group A v Group B**	-0.455	-1.18	0.27	0.301
	Group A v Group C	-1.242	-1.97	-0.52	< 0.0001
	Group B v Group C	-0.788	-1.51	-0.06	0.030

The progression of the mean NRS pain scores on coughing for each study group at 0 hours, 2 hours, 6 hours, 12 hours and 24 hours is illustrated in Figure 4.7. The pain scores of the control group are observed to peak at the 6-hour observation point before declining to the 24-hour observation point. The two intervention groups also have a peaking of the mean NRS pain scores on coughing but at a lower level (compared to the NRS pain scores of the control group) before declining to the 24-hour observation point. There was no statistically significant difference at each time point within the groups.

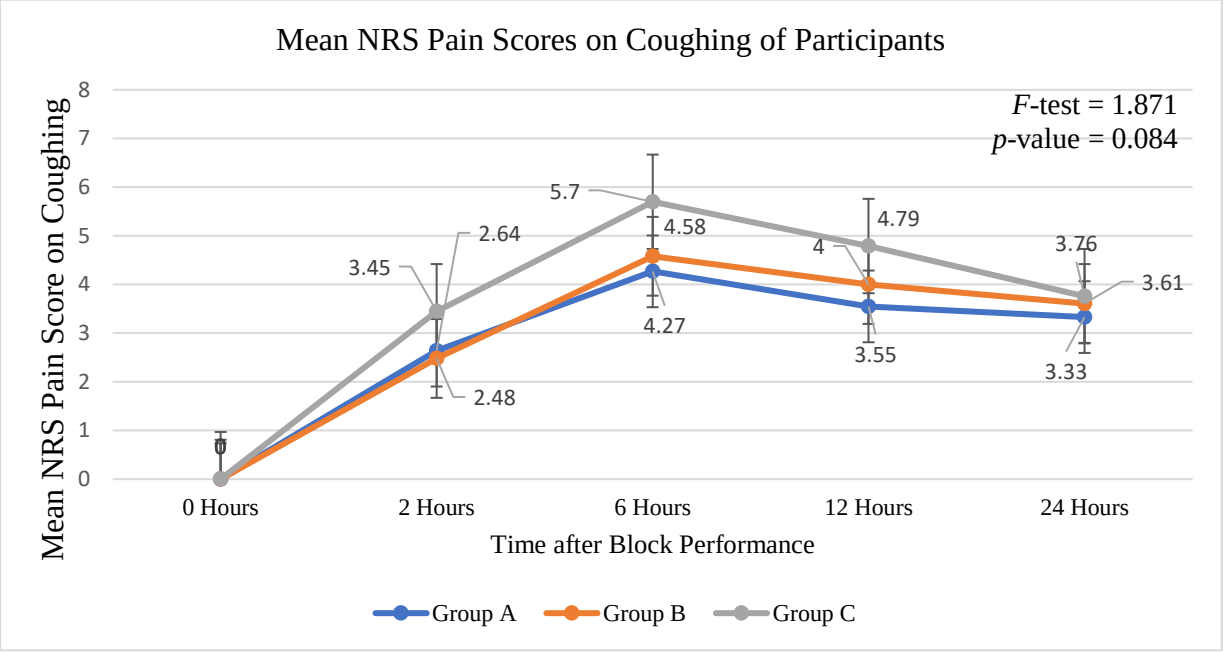

Figure 4.7: Mean NRS pain scores on coughing over time

4.4 Systemic Opioid Requirements

The total mean amount of opioid analgesic (pethidine) administered to study participants during the 24 hours following the performance of the TAP block was 254.4 ± 127.04 mg. Participants required more pethidine as one moves from groups A to C with a statistically significant difference between the mean amount of pethidine required by the three study groups (*p*-value < 0.0001) (Table 4.16).

Table 4.16: Mean 24-hour pethidine consumption of study participants

Group	N	Mean ± Standard Deviation (mg)	Minimum (mg)	Maximum (mg)	*F*-test	*p*-value
Group A	33	113.6 ± 81.58	0	300		
Group B	33	269.1 ± 64.44	0	300	144.188	<0.0001
Group C	33	380.6 ± 39.21	300	400		
Total	99	254.4 ± 127.04	0	400		

Key: mg - milligrams

Pairwise comparison of the mean amount of pethidine consumed by each of the study groups demonstrates a statistically significant difference amongst each of the groups (Table 4.17).

Table 4.17: Pairwise comparison of pethidine consumption

Group Comparison	Mean Difference	95% Confidence Interval for Difference		*p*-value
		Lower Bound	Upper Bound	
Group A v Group B	-155.45	-193.049	-117.860	<0.0001
Group A v Group C	-266.97	-304.564	-229.375	<0.0001
Group B v Group C	-111.52	-149.109	-73.921	<0.0001

4.5 Nausea and Vomiting, Pruritus and Sedation Assessment

4.5.1 Nausea and Vomiting

No participant reported nausea and or vomiting during the study period.

4.5.2 Pruritus

One (1) participant in Group A reported mild pruritus at 0 hours, 2 hours and 6 hours following performance of the TAP block. No other participant reported pruritus. The reported pruritus was not statistically significant between or within the groups at the various time points (Table 4.18).

Table 4.18: Pruritus amongst study participants

Time Point	Severity	Group A	Group B	Group C	Total	Pearson	*p*-value
		Count (% within group)				χ2 value (df)	
At 0 hours	Absent	32 (97)	33 (100)	33 (100)	98 (99)	2.020 (2)	0.364
	Mild	1 (3)	0 (0)	0 (0)	1 (1)		
	Total	33 (100)	33 (100)	33 (100)	99 (100)		
At 2 hours	Absent	32 (97)	33 (100)	33 (100)	98 (99)	2.020 (2)	0.364
	Mild	1 (3)	0 (0)	0 (0)	1 (1)		
	Total	33 (100)	33 (100)	33 (100)	99 (100)		
At 6 hours	Absent	32 (97)	33 (100)	33 (100)	98 (99)	2.020 (2)	0.364
	Mild	1 (3)	0 (0)	0 (0)	1 (1)		
	Total	33 (100)	33 (100)	33 (100)	99 (100)		
At 12 hours	Absent	33 (100)	33 (100)	33 (100)	99 (100)	-	-
	Total	33 (100)	33 (100)	33 (100)	99 (100)		
At 24 hours	Absent	33 (100)	33 (100)	33 (100)	99 (100)	-	-
	Total	33 (100)	33 (100)	33 (100)	99 (100)		
Over 24 hours	Absent	162 (98.2)	165 (100)	165 (100)	492 (99.4)	6.037 (2)	0.050
	Mild	**3 (1.8)**	**0 (0)**	**0 (0)**	**3 (0.6)**		
	Grand Total	165 (100	165 (100)	165 (100)	495 (100)		

4.5.3 Sedation

Majority of participants were most sedated at the 12-hour time point with the maximum sedation being asleep but easily roused. No participant experienced deep sleep (unrousable sedation). The occurrence of sedation at the various time points and amongst study groups was not significantly different (Table 4.19).

Table 4.19: Sedation amongst study participants

Time Point	Sedation Score	Group A	Group B	Group C	Total	Pearson χ2 value (df)	*p*-value
		Count (% within group)					
At 0 Hours	**0**	30 (90.9)	33 (100)	33 (100)	96 (97.0)	6.188 (4)	0.186
	1	1 (3.0)	0 (0)	0 (0)	1 (1.0)		
	2	2 (6.1)	0 (0)	0 (0)	2 (2.0)		
	3	0 (0)	0 (0)	0 (0)	0 (0)		
Total		33 (100)	33 (100)	33 (100)	99 (100)		
At 2 Hours	**0**	23 (69.7)	22 (66.7)	21 (63.6)	66 (66.7)	0.900 (4)	0.925
	1	4 (12.1)	3 (9.1)	3 (9.1)	10 (10.1)		
	2	6 (18.2)	8 (24.2)	9 (27.3)	23 (23.2)		
	3	0 (0)	0 (0)	0 (0)	0 (0)		
Total		33 (100)	33 (100)	33 (100)	99 (100)		
At 6 Hours	**0**	26 (78.8)	28 (84.8)	28 (84.8)	82 (82.8)	0.583 (4)	0.965
	1	4 (12.1)	3 (9.1)	3 (9.1)	10 (10.1)		
	2	3 (9.1)	2 (6.1)	2 (6.1)	7 (7.1)		
	3	0 (0)	0 (0)	0 (0)	0 (0)		
Total		33 (100)	33 (100)	33 (100)	99 (100)		
At 12 Hours	**0**	0 (0)	0 (0)	0 (0)	0 (0)	0.733 (2)	0.693
	1	4 (12.1)	3 (9.1)	2 (6.1)	9 (9.1)		
	2	29 (87.9)	30 (90.9)	31 (93.9)	90 (90.9)		
	3	0 (0)	0 (0)	0 (0)	0 (0)		
Total		33 (100)	33 (100)	33 (100)	99 (100)		
At 24 Hours	**0**	30 (90.9)	31 (93.9)	31 (93.9)	92 (92.9)	0.307 (2)	0.858
	1	3 (9.1)	2 (6.1)	2 (6.1)	7 (7.1)		
	2	0 (0)	0 (0)	0 (0)	0 (0)		
	3	0 (0)	0 (0)	0 (0)	0 (0)		
Total		33 (100)	33 (100)	33 (100)	99 (100)		
Over 24 hours	**0**	109 (66.1)	114 (69.1)	113 (68.5)	336 (67.9)	1.866	0.760
	1	16 (9.7)	11 (6.7)	10 (6.0)	37 (7.5)		
	2	40 (24.2)	40 (24.2)	42 (25.5)	122 (24.6)		
	3	0 (0)	0 (0)	0 (0)	0 (0)		
Grand Total		165 (100)	165 (100)	165 (100)	495 (100)		

*Key: Sedation Score: – **0** - Awake and alert; **1** - Quietly Awake; **2** - Asleep (easily roused); **3** – Deep Sleep*

4.6 Blood Glucose, Blood Pressure and Oxygen Saturation Changes

4.6.1 Blood Glucose Changes

The mean blood glucose at 0 hours, 8 hours and 24 hours after block performance is 4.83 ± 1.099 mmol/L, 6.42 ± 1.753 mmol/L and 5.80 ± 1.461 mmol/L as demonstrated in Table 4.22 and Figure 4.8. There was a statistically significant difference in the mean blood glucose readings between the study groups at the 24-hour time point (*p*-value = 0.028) but not at the 0-hour or 8-hour time point (Table 4.20).

Table 4.20: Blood glucose of study participants at observation time points

Time point	Group	N	Mean ± Standard Deviation (mmol/L)	Minimum (mmol/L)	Maximum (mmol/L)	*F*-test	*p*-value
0 hours	**Group A**	33	4.82 ± 1.266	3.0	7.5	0.061	0.941
	Group B	33	4.79 ± 0.998	3.2	7.6		
	Group C	33	4.88 ± 1.046	3.3	7.7		
	Total	99	4.83 ± 1.099	3.0	7.7		
8 hours	**Group A**	33	6.38 ± 1.992	4.0	10.4	0.479	0.621
	Group B	33	6.24 ± 1.652	3.6	9.2		
	Group C	33	6.66 ± 1.618	3.6	9.8		
	Total	99	6.42 ± 1.753	3.6	10.4		
24 hours	**Group A**	33	5.31 ± 1.250	3.5	7.7	3.729	0.028
	Group B	33	5.82 ± 1.368	3.7	9.0		
	Group C	33	6.26 ± 1.621	3.9	10.1		
	Total	99	5.80 ± 1.461	3.5	10.1		

Key: mmol/L – millimole per litre

Post hoc analysis of the blood glucose at the 24-hour observation point revealed a significant difference in the blood glucose of group A compared to group C (*p*-value = 0.021) (Table 4.21).

Table 4.21: Post hoc pairwise comparison of blood glucose at 24 hours

Group Comparison	Mean Difference	95% Confidence Interval		*p*-value
		Lower Bound	Upper Bound	
Group A v Group B	-0.5182	-1.351	0.315	0.305
Group A v Group C	-0.9545	-1.788	-0.121	0.021
Group B v Group C	-0.4364	-1.269	0.397	0.429

Blood glucose readings of participants over the whole study period did not demonstrate any significant difference amongst the study groups (*p*-value = 0.144) (Table 4.22).

Table 4.22: Mean 24-hour blood glucose readings of study participants

Groups	Mean ± SD (mmol/L)	Standard Error	N	95% Confidence Interval		F-test	*p*-value
				Lower Bound	Upper Bound		
Group A	5.50 ± 1.653	0.158	33	5.188	5.816		
Group B	5.62 ± 1.477	0.158	33	5.301	5.929	1.975	0.144
Group C	5.93 ± 1.621	0.158	33	5.617	6.246		

Key: mmol/L – millimole per litre

The progression of the mean blood glucose for each study group at 0 hours, 8 hours and 24 hours is illustrated in Figure 4.8. The mean random blood sugar for all groups is observed to peak at 8 hours before declining.

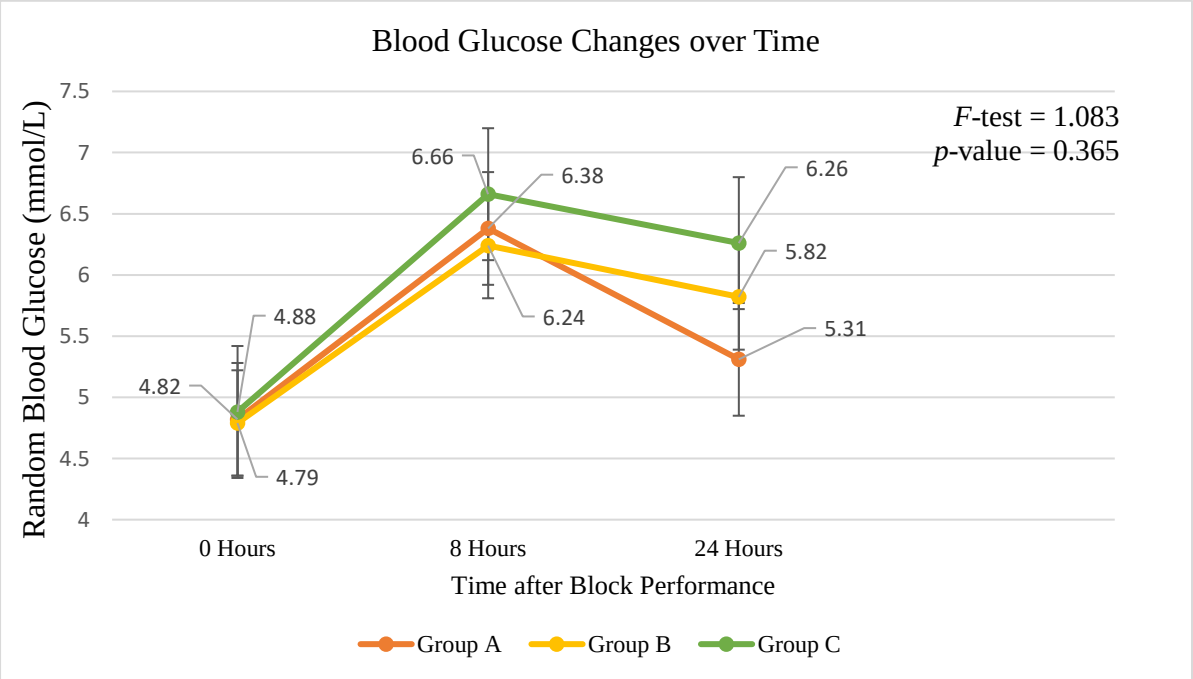

Figure 4.8: Blood glucose readings over time

4.6.2 Blood Pressure Changes

4.6.2.1 Systolic Blood Pressure Changes

The mean systolic BP for study participants at 0 hours, 2 hours, 6 hours, 12 hours and 24 hours are 115.0 ± 13.26 mmHg, 117.2 ± 16.00 mmHg, 120.8 ± 16.53 mmHg, 123.8 ± 13.17 mmHg and 117.9 ± 13.29 mmHg respectively (Table 4.23, Figure 4.9).

Table 4.23: Systolic blood pressure at observation time points

Time Point	Group	N	Mean ± Standard Deviation (mmHg)	Minimum (mmHg)	Maximum (mmHg)	*F*-test	*p*-value
0 hours	**Group A**	33	115.7 ± 15.05	90	149	1.504	0.227
	Group B	33	111.9 ± 12.30	91	154		
	Group C	33	117.4 ± 12.02	90	142		
	Total	99	115.0 ± 13.26	90	154		
2 hours	**Group A**	33	115.5 ± 17.16	89	163	0.315	0.731
	Group B	33	118.6 ± 16.99	90	144		
	Group C	33	117.4 ± 14.00	92	144		
	Total	99	117.2 ± 16.00	89	163		
6 hours	**Group A**	33	124.1 ± 19.16	90	173	1.021	0.364
	Group B	33	118.5 ± 14.56	90	152		
	Group C	33	119.9 ± 15.51	90	149		
	Total	99	120.8 ± 16.53	90	173		
12 hours	**Group A**	33	121.9 ± 13.39	95	146	0.884	0.417
	Group B	33	126.2 ± 13.91	96	150		
	Group C	33	123.5 ± 12.22	92	154		
	Total	99	123.9 ± 13.17	92	154		
24 hours	**Group A**	33	116.1 ± 14.45	89	151	0.506	0.605
	Group B	33	118.3 ± 11.37	93	137		
	Group C	33	119.4 ± 14.04	91	144		
	Total	99	117.9 ± 13.29	89	151		

Key: mmHg – millimetres of mercury

The difference in mean systolic BP between the study groups over the study period was not statistically significant (*p*-value = 0.884) (Table 4.24).

Table 4.24: Comparison of mean 24-hour systolic blood pressure of groups

Groups	Mean ± SD (mmHg)	Standard Error	N	95% Confidence Interval		*F*-test	*p*-value
				Lower Bound	Upper Bound		
Group A	118.7 ± 16.13	1.352	33	115.971	121.338		
Group B	118.7 ± 14.47	1.352	33	116.001	121.368	0.123	0.884
Group C	119.5 ± 13.60	1.352	33	116.807	121.175		

Key: mmHg – millimetres of mercury

Figure 4.9 illustrates the changes in the mean systolic blood pressure of the participants in the study groups over the observation time points.

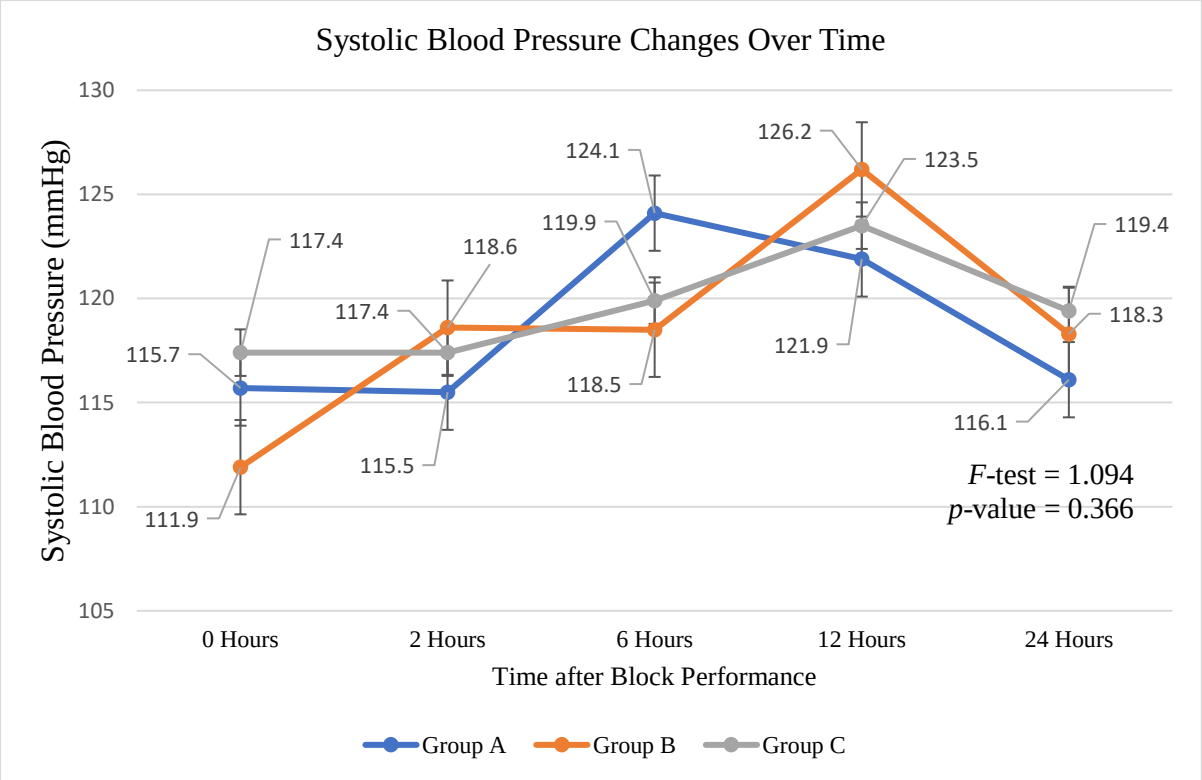

Figure 4.9: Mean systolic blood pressure changes over time

4.6.2.2 Diastolic Blood Pressure Changes

The mean diastolic BP for study participants at 0 hours, 2 hours, 6 hours, 12 hours and 24 hours are 69.6 ± 8.81 mmHg, 69.9 ± 8.92 mmHg, 73.1 ± 10.71 mmHg, 73.8 ± 10.28 mmHg and 70.7 ± 9.90 mmHg respectively (Table 4.25, Figure 4.10).

Table 4.25: Diastolic blood pressure at observation time points

Time Point	Group	N	Mean ± Standard Deviation (mmHg)	Minimum (mmHg)	Maximum (mmHg)	*F*-test	*p*-value
0 hours	**Group A**	33	69.4 ± 8.53	50	91	1.220	0.300
	Group B	33	68.0 ± 8.33	56	86		
	Group C	33	71.4 ± 9.47	56	91		
	Total	99	69.6 ± 8.81	50	91		
2 hours	**Group A**	33	72.7 ± 10.32	51	99	2.918	0.059
	Group B	33	69.5 ± 6.85	59	84		
	Group C	33	67.6 ± 8.74	52	88		
	Total	99	69.9 ± 8.92	51	99		
6 hours	**Group A**	33	72.9 ± 10.43	54	97	0.915	0.404
	Group B	33	71.5 ± 10.69	56	92		
	Group C	33	75.0 ± 11.01	52	95		
	Total	99	73.1 ± 10.71	52	97		
12 hours	**Group A**	33	72.8 ± 10.84	50	93	1.153	0.320
	Group B	33	76.0 ± 11.76	52	99		
	Group C	33	72.6 ± 7.78	57	88		
	Total	99	73.8 ± 10.28	50	99		
24 hours	**Group A**	33	69.8 ± 10.36	50	92	0.635	0.532
	Group B	33	70.0 ± 9.90	56	89		
	Group C	33	72.3 ± 9.52	54	92		
	Total	99	70.7 ± 9.90	50	92		

Key: mmHg – millimetres of mercury

The difference in mean diastolic BP between the study groups over the observation period was not statistically significant (*p*-value = 0.820) (Table 4.26).

Table 4.26: Comparison of mean 24-hour diastolic blood pressure of groups

Groups	Mean ± SD (mmHg)	Standard Error	N	95% Confidence Interval		*F*-test	*p*-value
				Lower Bound	Upper Bound		
Group A	71.5 ± 10.10	0.875	33	69.779	73.251		
Group B	71.0 ± 9.90	0.875	33	69.258	72.730	0.199	0.820
Group C	71.8 ± 9.53	0.875	33	70.021	73.494		

Key: SD – Standard Deviation, mmHg – millimetres of mercury

Figure 4.10 illustrates the changes in the mean diastolic blood pressure of the participants in the study groups over the observation time points.

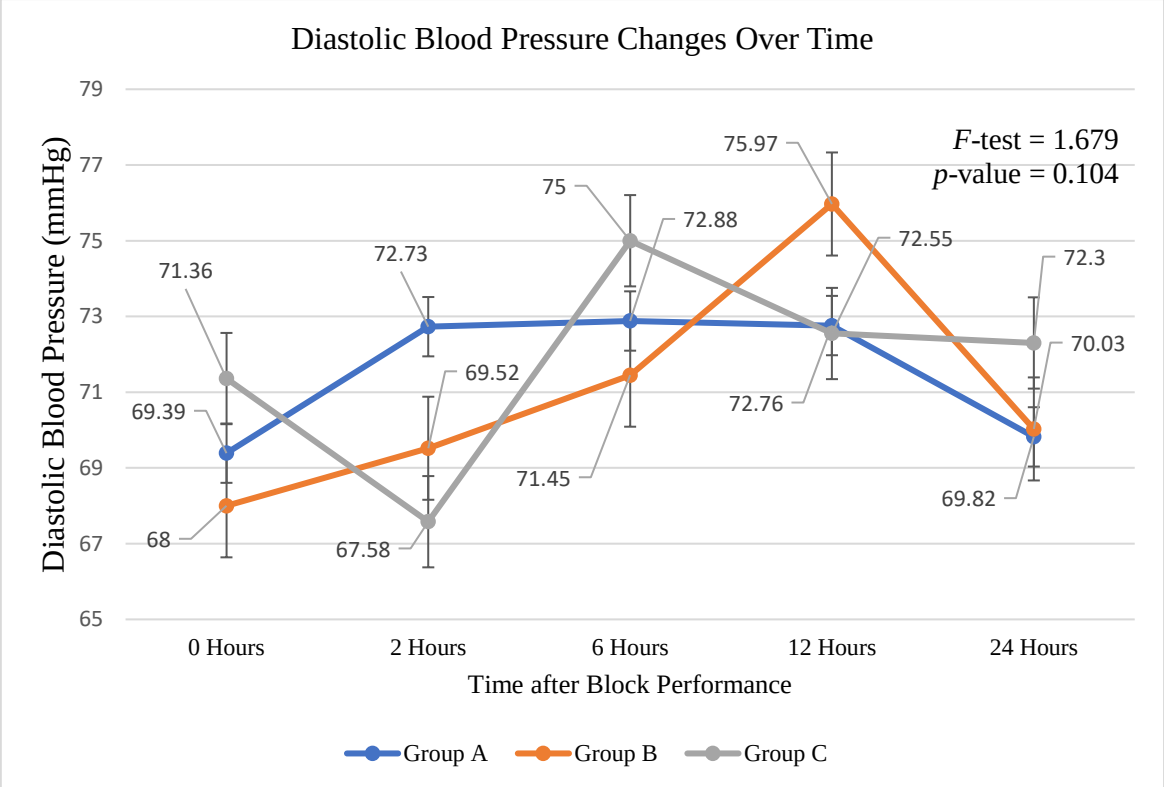

Figure 4.10: Diastolic blood pressure changes over time

4.6.2.3 Mean Arterial Pressure Changes

The mean arterial BP for study participants at 0 hours, 2 hours, 6 hours, 12 hours and 24 hours are 84.7 ± 8.32 mmHg, 85.7 ± 8.48 mmHg, 89.0 ± 10.02 mmHg, 90.5 ± 9.37 mmHg and 86.5 ± 9.20 mmHg respectively (Table 4.27, Figure 4.11).

Table 4.27: Mean arterial blood pressure at observation points

Time point	Group	N	Mean ± Standard Deviation (mmHg)	Minimum (mmHg)	Maximum (mmHg)	*F*-test	*p*-value
0 hours	**Group A**	33	84.8 ± 9.28	63.3	110.3	2.023	0.138
	Group B	33	82.6 ± 7.55	70.7	98.7		
	Group C	33	86.7 ± 7.75	75.0	103.3		
	Total	99	84.7 ± 8.32	63.3	110.3		
2 hours	**Group A**	33	87.0 ± 10.63	64.0	115.7	0.909	0.406
	Group B	33	85.9 ± 6.81	73.7	98.7		
	Group C	33	84.2 ± 7.55	66.7	103.3		
	Total	99	85.7 ± 8.48	64.0	115.7		
6 hours	**Group A**	33	89.9 ± 11.61	66.7	112.3	0.864	0.425
	Group B	33	87.1 ± 9.42	70.7	105.7		
	Group C	33	89.9 ± 8.88	70.7	110.3		
	Total	99	89.0 ± 10.02	66.7	112.3		
12 hours	**Group A**	33	89.1 ± 9.58	66.7	104.3	1.448	0.240
	Group B	33	92.7 ± 10.63	72.7	112.7		
	Group C	33	89.5 ± 7.50	77.0	105.7		
	Total	99	90.5 ± 9.37	66.7	112.7		
24 hours	**Group A**	33	85.3 ± 10.00	66.7	107.0	0.760	0.471
	Group B	33	86.1 ± 8.60	71.7	100.3		
	Group C	33	88.0 ± 9.00	71.0	102.0		
	Total	99	86.5 ± 9.20	66.7	107.0		

Key: mmHg – millimetres of mercury

The difference in mean diastolic BP between the study groups over the observation period was not statistically significant (Table 4.28).

Table 4.28: Comparison of mean 24-hour mean arterial pressure of groups

Group	Mean ± SD (mmHg)	Standard Error	N	95% Confidence Interval		F-test	*p*-value
				Lower Bound	Upper Bound		
Group A	87.2 ± 10.30	0.880	33	85.482	88.974		
Group B	86.9 ± 9.18	0.880	33	85.145	88.637	0.197	0.822
Group C	87.7 ± 8.31	0.880	33	85.923	89.415		

Key: SD – Standard Deviation; mmHg – millimetres of mercury

Figure 4.11 illustrates the changes in the mean arterial blood pressure of the participants in the study groups over the observation time points.

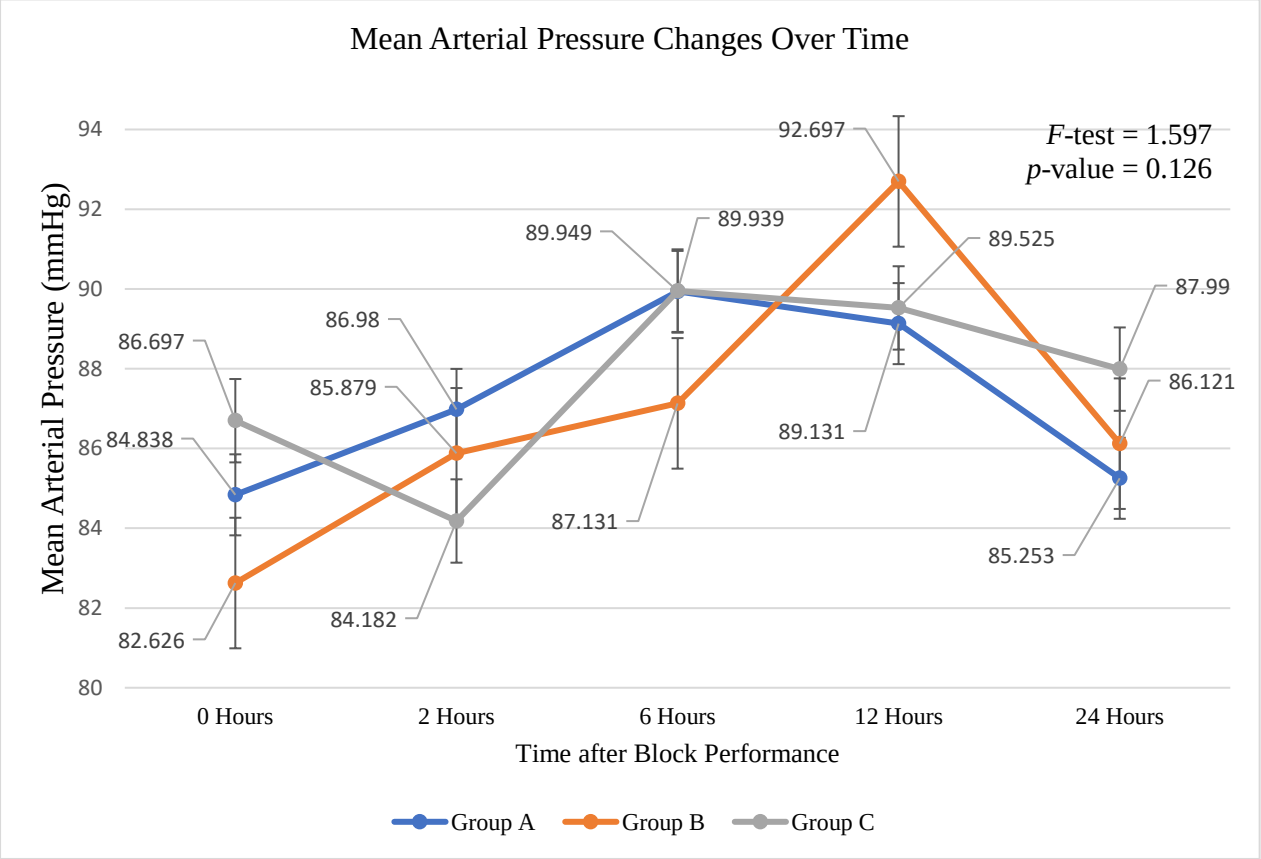

Figure 4.11: Mean arterial pressure changes over time

4.6.3 Oxygen Saturation Changes

The mean oxygen saturation for study participants at 0 hours, 2 hours, 6 hours, 12 hours and 24 hours are 98.99 ± 0.101 %, 98.92 ± 0.274 %, 98.91 ± 0.289 %, 98.89 ± 0.316 % and 98.98 ± 0.141 % respectively (Table 4.29, Figure 4.12).

Table 4.29: Oxygen saturation at observation time points

Time Point	Groups	N	Mean ± Standard Deviation (%)	Minimum	Maximum	*F*-test	*p*-value
0 hours	**Group A**	33	98.97 ± 0.174	98	99	1.000	0.372
	Group B	33	99.00 ± 0.000	99	99		
	Group C	33	99.00 ± 0.000	99	99		
	Total	99	98.99 ± 0.101	98	99		
2 hours	**Group A**	33	98.91 ± 0.292	98	99	0.132	0.876
	Group B	33	98.91 ± 0.292	98	99		
	Group C	33	98.94 ± 0.242	98	99		
	Total	99	98.92 ± 0.274	98	99		
6 hours	**Group A**	33	98.88 ± 0.331	98	99	0.358	0.700
	Group B	33	98.94 ± 0.242	98	99		
	Group C	33	98.91 ± 0.292	98	99		
	Total	99	98.91 ± 0.289	98	99		
12 hours	**Group A**	33	98.85 ± 0.364	98	99	0.704	0.497
	Group B	33	98.94 ± 0.242	98	99		
	Group C	33	98.88 ± 0.331	98	99		
	Total	99	98.89 ± 0.316	98	99		
24 hours	**Group A**	33	98.94 ± 0.242	98	99	2.065	0.132
	Group B	33	99.00 ± 0.000	99	99		
	Group C	33	99.00 ± 0.000	99	99		
	Total	99	98.98 ± 0.141	98	99		

The difference in mean oxygen saturation between the study groups over the study period was not statistically significant (*p*-value = 0.215) (Table 4.30).

Table 4.30: Oxygen saturation of participants

Group	Mean ± SD (%)	Standard Error	N	95% Confidence Interval		*F*-test	*p*-value
				Lower Bound	Upper Bound		
Group A	98.91 ± 0.287	0.020	33	98.869	98.949		
Group B	98.96 ± 0.202	0.020	33	98.918	99.998	1.564	0.215
Group C	98.95 ± 0.227	0.020	33	98.905	98.986		

Key: SD – Standard Deviation

Figure 4.12 below shows the trend of the oxygen saturation readings over the observation time points.

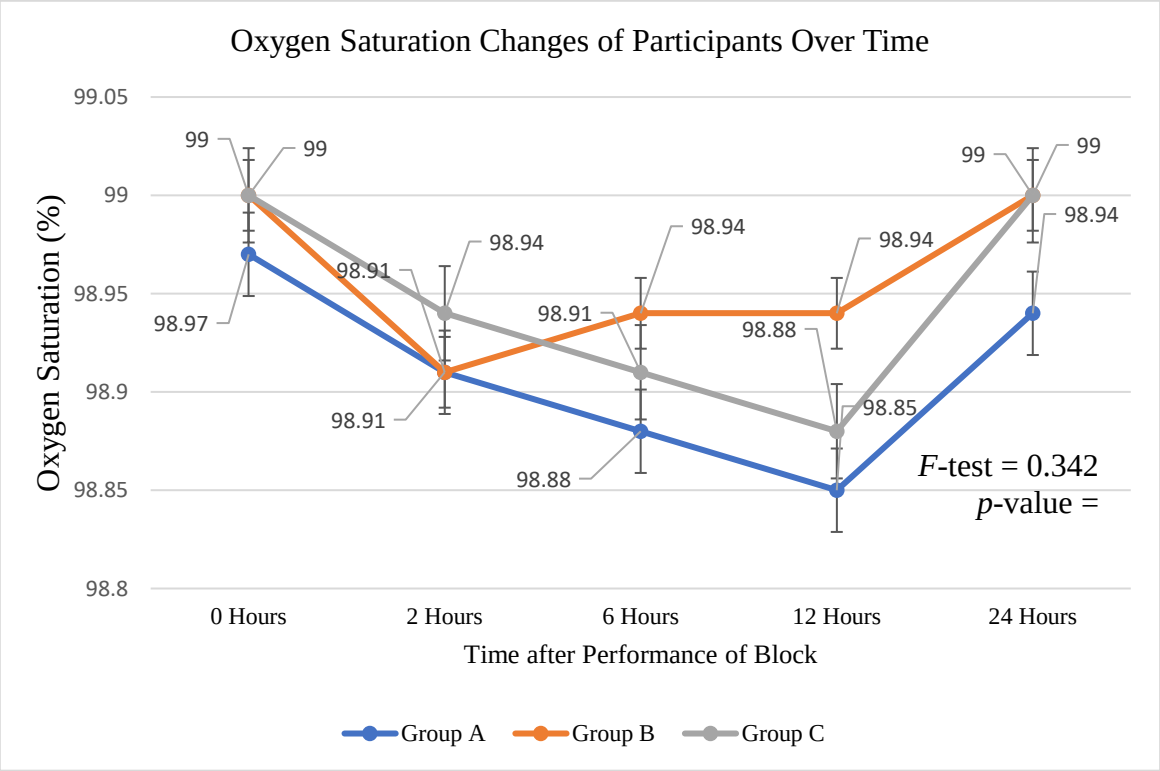

Figure 4.12: Oxygen saturation trend

4.7 Participant Satisfaction

There were no participants that expressed dissatisfaction with the analgesia after the caesarean delivery. A greater fraction of participants in the first intervention group (bupivacaine + dexamethasone) expressed that they were very satisfied (63.6%) compared to the other study groups (Table 4.31). The levels of satisfaction between groups were statistically significant (*p*-value = 0.048).

Table 4.31: Participant satisfaction and group crosstabulation

Satisfaction Level	Group A	Group B	Group C	Total	Pearson $\chi 2$ value (df)	*p*-value
	Count (% within Group)					
Neutral	6 (18.2)	8 (24.2)	16 (48.5)	30 (30.3)	9.582 (4)	0.048
Somewhat Satisfied	6 (18.2)	9 (27.3)	6 (18.2)	21 (21.2)		
Very Satisfied	21 (63.6)	16 (48.5)	11 (33.3)	48 (48.5)		
Total	33 (100.0)	33 (100.0)	33 (100.0)	99 (100.0)		

CHAPTER 5: DISCUSSION

5.1 Demographic and Preoperative Participant Characteristics

There were no statistically significant differences found between the three participant study groups with respect to the demographic characteristics (age, weight, height, BMI, parity and booking blood pressure) as depicted by their respective *p*-values greater than 0.05 (Table 4.1). The educational level of participants, the rate of previous caesarean delivery, grade of anaesthesia provider and the participants' estimated duration of surgery for caesarean delivery were also comparable (*p*-value > 0.05) between the three study groups.

The three study groups were, therefore, comparable. The similarities in participant characteristics and perioperative events allowed for a meaningful comparative study of outcome variables and deductions between the three participant study groups.

5.2 Time to First Analgesic Request

From this study, the mean time to request for first analgesic was significantly prolonged in the intervention groups compared to the control group (Table 4.5 and Table 4.6). Between the two intervention groups, the time to request for first analgesic was also significantly prolonged in the Bupivacaine + Dexamethasone group (group A) compared to the Bupivacaine only group (group B) (*p*-value < 0.0001) (Table 4.6).

The prolonged time to request for analgesia in the intervention groups is similar to the results obtained by Jadon et al.[218] and Eslamian et al.[170] The two studies had two study groups; one intervention group and one control group, whereas the present study consisted of three study groups (two intervention groups and one control group) with a different postoperative analgesic regimen. Eslamian et al.[170] in addition to performing the TAP block using landmark technique, used a reduced total amount of injectate (total of 30ml of 0.25% bupivacaine; 15ml on each side compared to total 40ml of 0.25% bupivacaine; 20ml on each side in the present study) in the intervention group, and also they did not perform a TAP block in the control group at all. The participants in the study by Eslamian et al.[170] had the caesarean delivery conducted under general anaesthesia compared to the spinal anaesthesia employed in the current study. Jadon et al.[218] used 0.375% ropivacaine in the TAP block rather than 0.25% bupivacaine used in the present study. Alemnew and Lemma[171] found similar results of prolonged time to first analgesic request although their study compared bilateral TAP block to wound infiltration. McDonnell et al.[215] also reported prolonged time to first analgesic request in general surgical

patients who received a bilateral TAP block after undergoing large bowel resection compared to patients who did not receive the TAP block.

The TAP block by its nature may seem to be dependent on the degree of spread of the injectate in the interfascial plane with as much involvement of nerve fibres as possible to exert its effect. This means that the volume of injectate is likely to play a significant role with higher volumes likely to result in better outcome. This theoretical reasoning has not been demonstrated in the literature. On the contrary, studies have demonstrated that employing injectate volumes greater than 15 to 20 ml in adult patients do not offer additional advantages.[139,153,160] This may explain why the different comparator studies resulted in similar outcomes although the volumes of injectate were different. Overall, the required minimum volume of 15ml of injectate on each side of the bilateral TAP block was achieved in the studies examined.

Local anaesthetic concentration has been shown to not have an effect on TAP block efficacy[157] while the efficacy of ropivacaine has been shown to be similar to that of bupivacaine for peripheral nerve blocks.[169] These may further account for the similar outcomes obtained by Jadon et al.[218] to the current study.

While a prolongation to first analgesic request has been demonstrated in the current study, the actual length of time is different from the comparator studies. This may be due to differences in anaesthetic technique for caesarean delivery (spinal anaesthesia with varying adjuvants vs general anaesthesia), TAP block technique (operator experience versus landmark-based versus ultrasound guided), postoperative rescue analgesic regimen or population characteristics.

The effect of dexamethasone was demonstrated in similar studies conducted by Aga et al.,[199] Zemedkun et al.,[198] Sachdeva and Sinha,[196] and Akkaya et al.[197] as well as in a metanalysis by Chen et al.[219] The study by Aga et al.[199] is similar to the present study in terms of the type, volume and concentration of local anaesthetic used in the two comparator groups with the only difference being the postoperative analgesic regimen. Sachdeva and Sinha, however, used 40ml 0.2% ropivacaine with 8mg dexamethasone for the intervention group and 40ml 0.2% ropivacaine with 2ml of saline for the control group. Akkaya et al.[197] also used a higher total volume of bupivacaine (60ml 0.25% bupivacaine; 30ml on each side) and higher total amount of dexamethasone (16mg; 8mg on each side) than the present study. The higher dose of dexamethasone employed is unlikely to exaggerate any difference observed between

the two groups since Kirkham et al.[200] demonstrated a ceiling dose of 4mg of perineural dexamethasone for prolongation of duration of analgesia in brachial plexus blocks.

5.3 Comparison of postoperative numeric pain rating scale at rest and coughing

All study participants did not report any pain (at rest or coughing) at the time of block performance (Table 4.8, Table 4.12). This is an expected outcome due to the following reasons. Belzarena et al.[21] reported duration of action of subarachnoid block with fentanyl as an adjunct lasting between 120minutes and 240 minutes. With the mean duration of surgery in this current study lasting approximately 60minutes, the time at which the TAP block was performed was within the effective duration of spinal anaesthesia performed with intrathecal fentanyl as an adjunct.

The mean NRS pain scores at rest and on coughing were significantly higher (Table 4.8, Table 4.12) over the 2-hour to 12-hour observation points in the control group compared to the two intervention groups (Table 4.11, Table 4.15). There were marginally non-significant lower pain scores recorded in the bupivacaine + dexamethasone group compared to the bupivacaine only group (Table 4.8, Table 4.11, Table 4.12 and Table 4.15, Figure 4.6 and Figure 4.7). The finding of lower pain scores in the TAP block intervention groups compared to the control group was also demonstrated by McDonnell et al.,[167] Eslamian et al.,[170] Kagwa et al.[173] and Kahsay et al.[174] Tan et al.[172] did not find a significant difference in the pain scores of their two study groups (TAP block using 20ml 0.25% levobupivacaine versus no TAP block) although the TAP block group used significantly less morphine in 24 hours. They postulated that their inability to find significant differences in the pain scores may be due to the two study groups both receiving PCA morphine for postoperative analgesia and hence self-administering it when they experience pain. They also attributed this difference to the lower power of their study to detect differences in VAS scores.

An examination of the trend of the pain scores over the observation period in this study revealed a rise in the pain scores at rest up to a peak of 6-hour observation point for all study groups (A, B and C) (Figure 4.6). On coughing, there was a rise in pain scores up to a peak of 6-hour observation point for groups A and B, and a peak 12-hour observation point for group C (Figure 4.7). Thereafter there was a downward trend in the pain scores for all the groups at rest and on coughing down to the 24-hour observation point. At the 6-hour observation point the NRS pain score at rest was significantly higher among the control group compared to both interventional groups. (Group A: p-value < 0.0001; Group B: p-value = 0.001). There was however no statistically significant difference in the NRS score at rest between the two

intervention groups at the 6-hour observation point (*p*-value = 1.000). The NRS pain score on coughing at both 6 hours and 12-hour observation points were both statistically significant in the control group compared to the intervention groups (Group A, 6-hour: *p*-value = 0.002; Group A, 12-hour: *p*-value < 0.0001 | Group B, 6-hour: *p*-value = 0.016; Group B, 12-hour: *p*-value = 0.030). There was however no significant difference between the intervention groups (6-hour: *p*-value = 0.726; 12-hour: *p*-value = 0.301)

The trend in NRS scores noted above was also described by McDonnell et al.[167] and Eslamian et al.[170] even though their study designs were different. Patients in the study by McDonnell et al. had spinal anaesthesia, a TAP block and PCA morphine whilst patients in the study by Eslamian et al. had general anaesthesia, a TAP block and intermittent analgesia using tramadol and diclofenac. Kahsay et al.[174] on the other hand demonstrated a steady decline of pain scores from 2 hours postoperatively down to 24 hour observation point, whereas Tan et al. found a decline of pain scores down to a nadir at the 6-12 hour time points for the control group before rising to the 24 hour time point. Patients involved in the study by Kahsay et al. had spinal anaesthesia, a TAP block and intermittent analgesics using paracetamol, diclofenac and morphine injection whereas the patients in the study by Tan et al. had general anaesthesia, a TAP block and PCA morphine for postoperative analgesia. It appears that there is no consistency as to the trend of the NRS scores post TAP. While some studies are finding a gradual increase in pain score until it peaks, others are finding a gradual decrease in pain scores over a 24-hour period. The differences in findings may lie in the different study designs, differences in type, frequency and dosages of analgesics used in addition to TAP block. There were also differences in the medications used for the TAP blocks in these studies. The differences in findings may also be attributed to patient differences.

There was a statistically significant better NRS pain scores at rest in the intervention groups than the control group at the 6- and 12-hour observation points. This is clinically significant since at these time points, the analgesia provided by the spinal anaesthetic would have worn off resulting in increased pain. The pain scores on coughing in the intervention groups were better at all time points but were statistically significant only at the 2-, 6-, and 12-hour observation points. The significantly lower pain scores on coughing recorded in the intervention groups is also clinically significant because it is at this time period after caesarean delivery that patients are expected to mobilise out of bed and undertake caring activities for the new born. The performance of a TAP block especially with the addition of dexamethasone as

part of a multimodal analgesic regimen after Caesarean delivery holds potential in improving care not only to the mother but to the new born as well.

The addition of dexamethasone as an adjunct to TAP block in the present study resulted in lower (statistically not significant) NRS pain scores at rest and on coughing when compared to TAP block without dexamethasone. This finding is in contrast to those of Zemedkun et al.[198] and Aga et al.[199] Findings of other studies such as those by Wegner et al.[220] and Huang et al.[221] also did not demonstrate any significant effect of perineural dexamethasone although these studies did not utilise TAP for post-caesarean analgesia. A number of factors including the dose and route of administration of dexamethasone may have influenced the results, as the actual mechanism of dexamethasone as an analgesic is still under investigation. Secondly, different approaches to the performance of TAP block employed by the different studies may lead to the blockade of different groups of somatic nerves and dermatomes. This may have accounted for the differences in analgesic effect and findings.

From the present study there was a reduction in pain scores with addition of dexamethasone to perineural block. Even though this reduction was not significant, considering the low cost and low risk of injury for the addition of dexamethasone to a block injectate, there still exists some clinical benefit in patient comfort for adding dexamethasone to standard block solutions, especially when early mobilisation after caesarean delivery is to be encouraged.

5.4 Systemic Opioid Consumption

A number of studies have demonstrated the parenteral opioid sparing effect of TAP blocks when used as an analgesic modality following caesarean delivery.[167,170,172,196–199] This is irrespective of the type of opioid or how the parenteral opioid was administered. Some studies[170,196–199] used intermittent intravenous tramadol injections of 50mg or 100mg, others[167,172] used intravenous morphine PCA or intermittent intravenous injections of 0.1mg/kg morphine every 4 hours for breakthrough pain.[174] The present study used intermittent intramuscular injections of 1.5mg/kg of pethidine up to a maximum of 100mg at 4 hourly intervals as needed. The difference in the mean amount of pethidine consumed by each of the study groups over 24 hours was statistically significant (p-value < 0.0001) and demonstrate the parenteral opioid sparing effect of TAP block when utilised as part of the multimodal analgesic regimen. Pairwise analysis of the results shows a statistically significant reduction (p-value < 0.0001) in opioid consumption between groups A and C, a significant reduction in opioid consumption (p-value < 0.0001) between groups B and C, and a significant reduction in opioid consumption (p-value < 0.0001) between groups A and B.

This study clearly demonstrates the opioid sparing effect of perineural dexamethasone in TAP block for post caesarean analgesia. The opioid sparing effect of dexamethasone may be due to its local and or systemic effects once it is absorbed from the injection site. Hussain et al.[194] in a systematic review and metanalysis supported this outcome.

5.5 Incidence of Adverse Effects

5.5.1 Nausea and Vomiting

None of the participants reported nausea and or vomiting during the 24-hour observation period of the present study. It is therefore difficult to demonstrate an antiemetic effect of dexamethasone in the current study.

Belzarena et al. in their study of intrathecal fentanyl as an adjunct to bupivacaine in caesarean delivery found that the incidence of nausea and vomiting was not significantly different with or without fentanyl. They also reported an incidence rate of 6-7% which for PONV.[21]

Sachdeva et al.[196] also reported a low incidence of nausea in their study; 8.57% patients experienced nausea in the control group (TAP with ropivacaine alone) compared to 2.86% in the experimental group (TAP with ropivacaine + dexamethasone) which was not statistically significant. Kahsay et al.[174] reported low (7.7%) incidence of vomiting in the no-TAP group compared to 0% in the TAP group which was not statistically significant. Furthermore, the 5.8% incidence of nausea in their no-TAP group was also not statistically significant from the 1.9% incidence in the TAP group. Aga et al.[199] demonstrated a 27.5% incidence of postoperative nausea and vomiting with a statistically significant lower incidence in the TAP group that received dexamethasone. Zemedkun et al.[198] also demonstrated a lower incidence of nausea in the dexamethasone group compared to the non-dexamethasone group. Both Aga et al. and Zemedkun et al. did not report the use of opioids as adjuncts in the spinal anaesthetic.[198,199]

Overall, the incidence of nausea and vomiting post intrathecal fentanyl is very low. Also, the reduction of nausea and vomiting secondary to perineural dexamethasone is non-significant. Postoperative nausea and vomiting (PONV) is one of the most common complications after caesarean section (CS), with a reported incidence as high as 60–80%.[222,223] This is partly due to the increased use of spinal opioids, which provide effective analgesia during and after CS, but commonly result in nausea and vomiting.[224,225] The obstetric patient is also prone to nausea and vomiting due to the physiological changes of pregnancy.[226] Risk factors for nausea and vomiting in obstetric patients presenting for caesarean delivery varies.

These risk factors are usually stratified. In this current study, the various factors contributing to nausea and vomiting in the selected patients were not studied. It is therefore likely that the patients recruited in this study could be patients with already low risk factors for PONV. Even though Amponsah[227] in 2007 demonstrated a 34% incidence of postoperative nausea and vomiting in Korle-Bu Teaching Hospital, her study did not include obstetric patients, therefore making comparisons and inferences difficult. It will therefore be worthwhile to study the incidence as well as the risk factors for both intraoperative and postoperative nausea and vomiting in obstetric patients at Korle-Bu Teaching Hospital in general.

5.5.2 Pruritus

One participant in the whole of the present study reported mild short-lived (6 hours) pruritus which did not require administration of antipruritic agents. The incidence of mild pruritus was 1.8% in the dexamethasone group and 0.6% overall over the 24-hour period and this was not statistically significant. This is in contrast to the study of Belzarena et al.[21] who found a statistically significant increase in the incidence of pruritus with the addition of fentanyl to the spinal anaesthetic. Kahsay et al.,[174] however, demonstrated a very low incidence of mild pruritus (1.9%) in the no-TAP group compared to 0% in the TAP group with the difference not being statistically significant. It is possible that differences in population may be responsible for this observed difference between the present study and other studies.

5.5.3 Sedation

The differences in the incidence of sedation were not statistically significant amongst the three groups across the observation time points. In contrast, Kahsay et al.[174] reported a significantly higher sedation scale score 1 of 32.7% in the no-TAP group compared to 11.5% in the TAP group and non-statistically significant higher sedation scale score 2 of 1.9% in the no-TAP group compared to 0% in the TAP group. McDonnell et al.[167] demonstrated that TAP block significantly reduced the incidence of sedation, from 36% in the no-TAP group to zero in the TAP block group. They also found that postoperative sedation scores were reduced in patients who received the TAP block at 6 h postoperatively, but not at the other time points. However, McDonnell et al.[167] used intravenous morphine PCA for postoperative analgesia which was likely to contribute to excessive sedation in the no-TAP group.

5.6 Effects on Blood Pressure, Oxygen Saturation and Blood Glucose

5.6.1 Blood Pressure Effects

The present study did not demonstrate any significant differences in blood pressure changes (systolic, diastolic and mean arterial pressure) amongst the study groups over the observation time points. Most of the studies reviewed have not reported any significant effects of TAP block on haemodynamic parameters. The minimal effect of TAP block on haemodynamic parameters is of clinical significance especially in the study setting since practitioners may be able to perform TAP blocks without the need to worry about perturbations in haemodynamic parameters when the patients are discharged to the general ward with infrequent haemodynamic monitoring.

5.6.2 Oxygen Saturation

The present study did not demonstrate a statistically significant difference between the oxygen saturations amongst the study participants (Table 4.29 and Table 4.30). Kahsay et al.[174] categorised absence of respiratory depression as oxygen saturation > 94% on room air and/or respiratory rate of 12-20 breaths per minute. Therefore, although respiratory rate of participants was not measured in the current study, on the basis of oxygen saturation, no respiratory depression occurred amongst the study participants in the current study since all oxygen saturations measured were well above 94% for all participants at all observation time points. This means that in the study setting, TAP blocks may be performed and patients safely transferred to the general ward at the scheduled time of discharge from the recovery ward without concerns of respiratory depression or oxygen desaturation on the ward.

5.6.3 Blood Glucose

In the present study, a significantly lower blood sugar of the dexamethasone group (group A) compared to the saline group (group C) at the 24-hour observation point (p-value = 0.021) was observed. This outcome was not expected since participants in the group A were rather expected to have higher mean blood sugar than participants in group C due to the hyperglycaemic effect of dexamethasone. Greisen et al.[228] demonstrated that acute pain induces insulin resistance in humans. It is plausible that the higher pain scores experienced by the participants in group C at 24 hours may have induced a state of insulin resistance contributing to the comparatively high blood sugar measurements. Secondly, at 24 hours, oral intake of participants would have been fully established. Differences in glycaemic indices of meals taken at this time point between the groups may also contribute to the observed results.

For all participants, there was a non-significant increase in blood sugar levels with a peak at the 8-hour observation point before declining to the 24-hour observation point. Hans et al.[186] in 2006 demonstrated a significant rise in blood glucose with a peak at 2 hours for both diabetic and non-diabetic patients undergoing abdominal surgery and receiving 10mg intravenous dexamethasone.

The statistically non-significant increase in blood glucose levels and the delayed peak in blood glucose levels noted in this current study may be as a result of the slower absorption of dexamethasone when administered as part of TAP block or the lower total dose of dexamethasone used in this study (8mg compared to 10mg in the study by Hans et al.[186]). Secondly, at the 8-hour time point, participants are expected to resume oral intake which may contribute to increased blood sugar levels. However, it is worth noting that blood glucose measurements were measured at infrequent intervals (before the block, 8 hours and 24 hours). This may have masked the true trend in variation of the blood glucose over time.

5.7 Participant Satisfaction

Participants in this study reported good levels of satisfaction for their postoperative analgesia. Maternal satisfaction after caesarean delivery is usually the outcome of a complex interplay of analgesic quality and absence of side effects such as nausea, vomiting and pruritus. In the present study, 63.6% of the dexamethasone group were very satisfied with the postoperative analgesia compared to 48.5% in the bupivacaine only group and 33.3% in the control group. These differences were statistically significant (Table 4.31). While some participants reported neutral satisfaction, no participant reported dissatisfaction with the postoperative analgesia. The findings in this study is similar to the findings of Sachdeva et al.[196]

This finding demonstrates that the performance of the TAP block and the addition of dexamethasone to the injectate has the potential to improve the postoperative analgesia satisfaction scores of parturients after caesarean delivery.

5.8 Study Limitations

The limitations of the study include:

1. Caesarean deliveries in this study were performed by different surgeons with respect to their grade and or experience; each with their own unique surgical technique. Apart from the Pfannenstiel incision, no other aspect of the surgical care was standardised. This has the potential to affect the degree of post-operative pain experienced by participants and hence the results of the study.

2. High risk patients (with ASA physical status III and above) and patients who are likely to benefit from TAP block (patients who have caesarean delivery under general anaesthesia) were excluded from this study. This may affect generalization of the results of the study.

3. The antiemetic effect of dexamethasone could not be demonstrated from the results of this study as no participant reported nausea and or vomiting. There was also paucity of data on the incidence of post operative nausea and vomiting in the obstetric population at the study site to make meaningful inferences from the results obtained.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATION

6.1 Conclusions

From the results of the study, it can be concluded that in Ghanaian parturients who undergo elective caesarean delivery under spinal anaesthesia using 2ml of 0.5% bupivacaine and 25mcg fentanyl:

1. Bilateral TAP block using 0.25% plain bupivacaine significantly prolongs the time to request for first rescue analgesia compared to control (bilateral TAP block with saline). Addition of 8mg of dexamethasone to 0.25% bupivacaine further significantly prolongs the time to request for first rescue analgesia.

2. Bilateral TAP block with 0.25% plain bupivacaine results in lower NRS pain scores at rest and on coughing when compared to control (bilateral TAP block with saline). TAP block with dexamethasone resulted in lower NRS pain scores compared with TAP block without dexamethasone.

3. Bilateral TAP block using 0.25% plain bupivacaine significantly reduces the amount of systemic opioid consumed for postoperative analgesia compared to control (bilateral TAP block with saline). Addition of 8mg of dexamethasone to 0.25% bupivacaine further significantly reduces the postoperative systemic opioid consumption.

4. Bilateral TAP block using 0.25% plain bupivacaine with or without dexamethasone had no significant effect on the incidence of pruritus, nausea and vomiting and sedation.

5. Bilateral TAP block using 0.25% plain bupivacaine results in high participant satisfaction with analgesia compared to control (bilateral TAP block with saline). Addition of 8mg of dexamethasone to 0.25% bupivacaine further increases the participant satisfaction.

6.2 Recommendations

1. TAP blocks should be considered as part of the multimodal analgesic regimen after caesarean delivery at Korle-Bu Teaching Hospital. Placement of a high-resolution ultrasound machine at the obstetric theatre suite will facilitate the performance of the TAP blocks.

2. Where TAP blocks (or any perineural analgesic techniques) are to be performed in Korle-Bu Teaching Hospital, consideration should be given to the routine addition of dexamethasone to the injectate where contraindications do not exist. It is a safe and cheap way of prolonging the duration of analgesia without significantly increasing the risk of untoward side-effects.

3. Further studies are required to investigate the analgesic and anti-emetic effects of dexamethasone as an adjunct in nerve blocks.

4. Further studies are required in high risk (ASA III and IV) patient populations to elucidate the safety profile of bilateral TAP blocks in this patient population.

5. A study to investigate the incidence and associated risk factors of postoperative nausea and vomiting at Korle-Bu Teaching Hospital is required.

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APPENDIX

Appendix 1 - Informed Consent Form

Dr. Daniel Sottie
Department of Anaesthesia
Korle-Bu Teaching Hospital
P.O. Box KB77
Korle-Bu
Email: dsottie@gmail.com
Tel: 0242137396

I am Dr Daniel Sottie, a Senior Resident and Specialist Anaesthetist with the Department of Anaesthesia, Korle-Bu Teaching Hospital. I am conducting research into the efficacy of regional nerve blockade to improve pain relief after elective caesarean delivery.
You are being asked to volunteer as a participant in this research study. This form is designed to provide you with information about this study and to answer any of your questions. After going through this form, you may refuse to participate in the study. This will not affect your management in any way.

Title of Project

Effect of perineural dexamethasone on ultrasound guided transversus abdominis plane block for post caesarean analgesia at Korle-Bu teaching hospital.

Purpose of Study

The aim of this study is to compare the effectiveness and safety of performing an ultrasound guided bilateral TAP block using placebo (normal saline); using only bupivacaine; and using bupivacaine with dexamethasone in providing post-operative analgesia in parturients who undergo caesarean delivery under spinal anaesthesia at Korle-Bu Teaching Hospital.

Procedures

If you agree to participate in the study, you will have your caesarean delivery done under spinal anaesthesia. If there is a need to conduct your procedure under general anaesthesia, we will not recruit you for the study. You will be assessed at the anaesthetic clinic as per our practice for all elective cases. Relevant investigations will be requested and adequate preparations will be made for the procedure. An injection will be given (with the aid of an ultrasound device) on either side of your abdomen just above your waist with the aim of blocking nerves that carry

the sensation of pain. This procedure will be performed immediately after your caesarean surgery while the spinal anaesthetic is still working. Your demographic characteristics (age, weight, height) and other relevant clinical history will be taken and the details recorded in a questionnaire. After the operation the amount of pain you feel will be assessed and further pain relief administered to ensure that you are comfortable.

Benefits

Administration of local anaesthetic in this manner is expected to reduce post-operative opioid analgesic requirements and the accompanying untoward effects of opioids. Patient satisfaction relating to post-operative pain management is expected to be better after this procedure.

Risks

Nerve blocks provide superior pain relief. However, there is a tiny risk of damage to nerves, blood vessels and injection into the peritoneum. The nerves targeted during these blocks are located in a space which is easily identifiable under ultrasound guidance hence access to them is relatively easy with the aid of ultrasound. Damage to blood vessels would be minor and is extremely rare. You might experience minor bruising at the site of injection. The procedure will be discontinued if the patient experiences any adverse reaction to injection of the local anaesthetic.

Confidentiality

All data collected during the course of the study will be kept confidential. Should the results of the study be published, you will be referred to only as a number.

Participant Rights

Any questions you have involving the research and your rights may be addressed to **Dr. Daniel Sottie**. Your participation in this study is voluntary and you are free to withdraw without penalty at any time. Your surgical management will not be affected. Kindly consent if you are satisfied with this information and will like to participate in this study.

My supervisors are:

Dr Robert Djagbletey
Consultant Anaesthetist/Lecturer
Department of Anaesthesia
School of Medicine and Dentistry
University of Ghana

And

Dr Ebenezer Owusu Darkwa
Consultant Anaesthetist/Lecturer
School of Medicine and Dentistry
University of Ghana

Signature/Thumbprint of participant: ..... Date: .....

Witnessed by : ..... Position: ..... Date:.....

Investigator : .....

Date : .....

Appendix 2 - Data Collection Sheet

EFFECT OF PERINEURAL DEXAMETHASONE ON ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK FOR POST CAESAREAN ANALGESIA AT KORLE-BU TEACHING HOSPITAL

DATA COLLECTION FORM

Date:	Patient Identification Number:
Age (years):	Educational Status: None [ ] Primary [ ] Secondary [ ] Tertiary [ ]
Weight (kg):	Booking Blood Pressure (mmHg): Previous CS: Yes [ ] No [ ]
Height (cm):	Anaesthetist Grade: CRA [ ] MO [ ] Resident [ ] Specialist [ ] Cons. [ ]
BMI (kg/m^2):	Duration of surgery:
Parity:	Time of block performance:
RBS (mmol/L):	Before Block: 8 Hours: 24 Hours:

Pain, PONV, Pruritus and Sedation Assessment

Date	Time	Time after TAP block	NRS [0-10] (Static)	NRS [0-10] (Coughing)	BP (mmHg)	MAP (mmHg)	SpO_2 (%)	PONV [0=none; 1=mild; 2=moderate; 3=severe]	Pruritus [0-Absent; 1-Mild; 2-Moderate; 3-Severe]	Sedation Score [0=awake and alert; 1=quietly awake; 2=asleep (easily roused); 3= deep sleep]
		0 hour								
		2 hours								
		6 hours								
		12 hours								
		24 hours								

INTERVENTIONS

Date	Time	NRS	PONV score	Intervention	
				IM Pethidine (mg)	Antiemetic (drug/dose)

Patient Satisfaction (tick): [ ]Very Satisfied [ ]Somewhat Satisfied [ ]Neither Satisfied Nor Dissatisfied [ ]Somewhat Dissatisfied [ ]Very Dissatisfied

Appendix 3 – Korle-Bu Teaching Hospital Institutional Approval Letter

In case of reply the number
And the date of this
Letter should be quoted

My Ref. No. KBTH/MS/CG3/21

Your Ref. No......

KORLE BU TEACHING HOSPITAL
P. O. BOX KB 77,
KORLE BU, ACCRA.

Tel: +233 302 667759/673034-6
Fax: +233 302 667759
Email: Info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

30th May, 2021

DR DANIEL AKWANFO YAW SOTTIE
DEPARTMENT OF ANAESTHESIA
KORLE-BU TEACHING HOSPITAL
KORLE BU

INSTITUTIONAL APPROVAL: KORLE BU TEACHING HOSPITAL-SCIENTIFIC AND TECHNICAL COMMITTEE/INSTITUTIONAL REVIEW BOARD (KBTH-STC/IRB/00001/2020

Following approval of your study entitled "Effect of Perineural Dexamethasone on Ultrasound Guided Transversus Abdominis Plane Block for Post Caesarean Analgesia at Korle-Bu Teaching Hospital" by the Korle Bu Teaching Hospital-Scientific and Technical Committee/Institutional Review Board.

I am pleased to inform you that institutional approval has been granted for the conduct of your study in Korle Bu Teaching Hospital.

Please contact the Heads of Departments to discuss the commencement date of the study.

Please note that, this institutional approval is rendered invalid if the terms of the Institutional Reviewed Board/Scientific and Technical Committee approval are violated.

Sincere regards,

Dr. Ali Samba
Director of Medical Affairs
For: Chief Executive

Appendix 4 – Korle-Bu Teaching Hospital Institutional Review Board Approval

In case of reply the number
And the date of this
Letter should be quoted
My Ref. No. KBTH/MD/RG3/21
Your Ref. No......

KORLE BU TEACHING HOSPITAL
P. O. BOX KB 77,
KORLE BU, ACCRA.

Tel: +233 302 667759/673034-6
Fax: +233 302 667759
Email: Info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

29th May, 2021

DR DANIEL AKWANFO YAW SOTTIE
DEPARTMENT OF ANAESTHESIA
KORLE-BU TEACHING HOSPITAL
KORLE BU

EFFECT OF PERINEURAL DEXAMETHASONE ON ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK FOR POST CAESAREAN ANALGESIA AT KORLE-BU TEACHING HOSPITAL

KBTH-IRB /0001/2020

Investigator: Dr Daniel Akwanfo Yaw Sottie

The Korle Bu Teaching Hospital Institutional Review Board (KBTH IRB) reviewed and granted approval to the study entitled: Effect of Perineural Dexamethasone on Ultrasound Guided Transversus Abdominis Plane Block for Post Caesarean Analgesia at Korle-Bu Teaching Hospital"

Please note that the Board requires you to submit a final review report on completion of this study to the KBTH-IRB.

Kindly, note that, any modification/amendment to the approved study protocol without approval from KBTH-IRB renders this certificate invalid.

Please report all serious adverse events related to this study to KBTH-IRB within seven days verbally and fourteen days in writing.

This IRB approval is valid till 31st October, 2022. You are to submit annual report for continuing review.

Sincere regards,

DR. DANIEL ANKRAH
VICE CHAIR (KBTH-IRB)
FOR: CHAIR (KBTH-IRB

Cc: The Chief Executive Officer, KBTH
The Director of Medical Affairs, KBTH

Appendix 5 – Butterfly iQ® Ultrasound Probe Connected to Samsung® Galaxy S10+ mobile device