

https://dspace.org/

Comparison between two epidural analgesia maintenance techniques at a regional hospital

Sehlapelo, Mathabe

2020
https://hdl.handle.net/10539/29967

Downloaded from a DSpace repository. https://dspace.org/

Comparison between two epidural analgesia maintenance techniques at a regional hospital

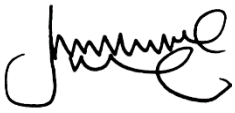
Mathabe Sehlapelo

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Anaesthesiology.

Johannesburg, 2019

Declaration

I, Mathabe Sehlapelo declare that this research report is my own unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



05 June 2020

Abstract

Background

Maintaining a labour epidural with programmed intermittent epidural bolus (PIEB) with patient controlled epidural analgesia (PCEA) using automated pumps has been shown to be beneficial compared to continuous epidural infusion (CEI) with intermittent epidural bolus (IEB). The aim of the study was to compare these two techniques for labour analgesia with regards to haemodynamics, drug consumption, motor blockade, mode of delivery and to describe patient satisfaction and adverse effects.

Methods

A prospective, contextual and comparative study was used. One hundred and twenty patients in the active phase of labour were recruited. Participants were randomly assigned to either the CEI with IEB (Group A, $n = 60$) or PIEB with PCEA (Group B, $n = 60$). The labour epidural was activated and maintained with bupivacaine 0.0625% and fentanyl 2 ug/ml. Achieving a bilateral T10 sensory level and a visual analogue score less than 30 mm was considered as Time Zero (T0), this timing was continued until delivery.

Results

There were no significant differences in participants' characteristics between the groups. A higher percentage of satisfaction was recorded in Group B. Hypotension occurred significantly more often in Group A ($p = 0.002$). Group B had less drug consumption ($p < 0.01$), rescue boluses ($p < 0.01$) and motor blockade ($p = 0.02$). Group A had more assisted deliveries ($p = 0.01$). Adverse effects occurred similarly in both groups.

Conclusion

PIEB with PCEA for maintenance of labour epidural analgesia results in better participant satisfaction, more cardiovascular stability, less drug consumption and less motor blockade with more unassisted deliveries. Labour epidural analgesia techniques using algorithms are proving to be superior to other maintenance techniques. Although more costly, PIEB with PCEA appears to convey benefits.

Acknowledgements

I would like to thank my supervisors Helen Perrie, Juan Scribante, and Janine Wagner for their patience, assistance and guidance.

Dr. Thomas Kleyenstuber the head of the Anaesthesiology department at Rahima Moosa Mother and Child Hospital: thank you for the research hours granted, for mobilising the obstetrics department and labour ward staff to assist.

To the labour ward staff, thank you for bearing with me for the five months of data collection. You made the process very bearable.

Table of contents

Declaration ii

Abstract iii

Acknowledgements iv

Abbreviations x

Statement xi

Section 1: Review of the literature 1

1.1 Introduction 1

1.2 Labour pain 1

1.2.1 Physiology of labour pain 1

1.2.2 The management of labour pain 2

1.3 Effects of poorly managed pain 3

1.4 Management of labour pain 4

1.5 Labour epidural analgesia 6

1.5.1 History of labour epidural analgesia 6

1.5.2 Anatomy 6

1.5.3 The procedure of labour epidural placement 7

1.5.4 The pharmacology of labour epidural 9

1.5.5 Advantages of labour epidural 10

1.5.6 Major and minor side effects 12

1.6 Labour epidural maintenance techniques 16

1.6.1 Intermittent epidural bolus 16
1.6.2 Continuous epidural infusion 16
1.6.3 Patient controlled epidural analgesia 17
1.6.4 Programmed intermittent epidural bolus 19
1.7 Summary 22
1.8 References 23
Section 2: Author's guidelines 32
Section 3: Draft article 39
Section 4: Proposal 57
4.1 Introduction and problem statement 58
4.2 Aim and objectives 59
4.2.1 Aim 59
4.2.2 Objectives 59
4.3 Research assumptions 60
4.4 Demarcation of study field 61
4.5 Ethical considerations 61
4.6 Research methodology 61
4.6.1 Research design 61
4.6.2 Study population 62
4.6.3 Study sample 62
4.6.4 Data collection 63

4.6.5 Data analysis 65
4.7 Significance of the study 65
4.8 Validity and reliability of the study 66
4.9 Potential limitations 66
4.10 Project outline 67
4.10.1 Time frame 67
4.10.2 Budget 67
4.11 References 69
4.12 Appendices 72
Section 5: Annexures 82
5.1 Ethics approval 82
5.2 Graduate studies approval 83
5.3 Hospital CEO approval 84
5.4 Head of department approval 85
5.5 Turnitin report 86

List of figures

Figure 1- Drop in MAP censored due to delivery 47

Figure 2 – Motor block censored due to delivery 48

List of tables

Table I - Participants' characteristics 45

Table II - Participants' satisfaction at different time intervals 46

Table III - Drug consumption 47

Table IV - Mode of delivery 48

Table V - Incidence of adverse effect 49

Abbreviations

ASA	American Society of Anaesthesiologists
CEI	Continuous Epidural Infusion
COMET	Comparative Obstetric Mobile Epidural Trial
IEB	Intermittent Epidural Bolus
MAP	Mean Arterial Pressure
PCEA	Patient Controlled Epidural Analgesia
PDPH	Post Dural Puncture Headache
PIEB	Programmed Intermittent Epidural Bolus
RMMCH	Rahima Moosa Mother and Child Hospital
SASA	South African Society of Anaesthesiologists
VAS	Visual Analogue Scale

Statement

The Research Report consists of a literature review, draft article, study proposal and appendices. The study proposal is included for background reference and is not for examination.

The formatting of this Research Report complies with the University of the Witwatersrand's Style Guide for Theses, Dissertations and Research Reports. The formatting of the draft article is in keeping with the rest of the research report thus may not comply with the author guidelines of the Southern African Journal of Anaesthesia, the journal to which it is intended to be submitted.

Section 1: Review of the literature

1.1 Introduction

The purpose of this literature review is to discuss the maintenance techniques employed after activation of a labour epidural. As an introduction to these techniques, labour pain, the physiology and effects of labour pain, as well as labour analgesia options (with a focus on the labour epidural) will be explored.

1.2 Labour pain

The experience of labour pain is a dynamic process that is this unpleasant, subjective, emotional and complex experience (1, 2). The perception of pain and its severity can be affected by various factors including psychological preparation, emotional support, past experiences and patient expectations (3).

1.2.1 Physiology of labour pain

Labour pain has both peripheral and central mechanisms. Labour is divided into three stages; the first stage begins from the onset of regular contractions and continues up until the cervix is 10 cm dilated. The second stage starts with a fully dilated cervix and ends with the delivery of the foetus and the third stage of labour results in the delivery of the placenta (3-5).

Pain in the first stage of labour is visceral, poorly localised and due to cervical dilatation and distention of the lower segment of the uterus as opposed to the somatic, well-localised pain experienced during the second stage of labour that is due to distention of the pelvic floor muscles, the vagina and perineum. The pain in the first stage of labour is transmitted through the visceral and slow C fibres, enters the spinal cord at T10 − L1 to synapse in the dorsal horn. Associated chemical mediators are bradykinin, leukotrienes, prostaglandins, serotonin and substance P. Pain in the second stage of labour is transmitted through the A delta fibres and enters at S2 – S4 (5).

1.2.2 The management of labour pain

Various scoring systems are used to assess labour pain. They are either electronic (6) , graphical or verbal tools used to measure the intensity of pain (7). They are unidimensional in that they only rate the intensity of pain and not its entire complexity. Labour pain is multidimensional and progressive in nature and using a unidimensional tool will not capture the complexity. The scales commonly used to rate labour pain are the visual analogue scale, numeric rating scale and the verbal rating scale (7).

The visual analogue scale is a 100 mm line represented on paper with the left side being no pain and the right side being the worst pain ever with no numbers represented on the line. The patient marks on the line where they think their pain lies and the physician then takes a 100 mm rule to check how many millimetres it is (7). The visual analogue scale has to be copied to scale to prevent errors. Population demographics, levels of patient literacy and understanding may affect the results obtained (7). In the western world a horizontal scale is used, and in the Chinese population a vertical scale is preferred (8).

The numeric rating scale is an 11, 21 or 101-point rating scale. The numbers are present on the scale for the patient to view, with the left side being no pain and right side representing the worst pain ever. The patient can mark on the paper or verbalise pain intensity using the scale numbering (7).

The verbal rating scale uses words to measure the intensity of pain. The words are adjectives such as no pain, mild pain, moderate pain and severe pain. For research purposes these words are given the numbers 1 − 4 to represent each adjective (7).

The rating scales need to be sensitive, as their sensitivity affects their ability to detect changes in pain intensity. The numeric and visual analogue scales are more sensitive than the verbal rating scale, as the verbal rating scale underestimates small changes in pain intensity (6, 9).

1.3 Effects of poorly managed pain

Pain has been described as a symptom manifesting physically, however, it may cause both physiological and psychological impairment. Severe uncontrolled labour pain is associated with numerous maternal and foetal psychological and physiological adverse effects (10, 11).

Labour pain, when uncontrolled, activates the maternal stress response, this in turn adversely affects the maternal cardiovascular, respiratory, gastrointestinal, haematological, endocrine and metabolic systems (10, 11).

There is an increase in catecholamine release with mediation of sympathetic activity resulting in a rise in heart rate and maternal oxygen demand thus limiting the oxygen supply to the foetus. Constriction of the uterine arteries impedes uterine perfusion and result in a decline in the foetal oxygen supply. Maternal peripheral vascular resistance may increase and blood pressure can rise by up to 15 mmHg (3, 4). There is an increase in tidal volume and respiratory rate with a resultant respiratory alkalosis which causes the haemoglobin dissociation curve to shift to the left with decrease in offloading of oxygen by the maternal haemoglobin to the foetus (3, 4). Pain reduces the motility of the gastrointestinal system and gastric emptying may be decreased, therefore increasing the risk of aspiration of gastric contents (3, 4).

Pain may cause an increase in white cell count which can be misinterpreted as a sign of maternal infection. Pain may also result in an increase in maternal core temperature. Due to an increase in respiratory rate, muscle activity and poor oral intake, patients hydration may be compromised (3, 4).

With the increase in maternal sympathetic drive there are increased plasma levels of adrenaline, noradrenaline, adrenocorticotrophic hormone and cortisol which lead to uncoordinated uterine activity, reduction in perfusion and prolongation of labour (3, 4, 10, 11).

In the postpartum period, women who have experienced uncontrolled severe pain may be at increased risk for the development of postpartum depression, post-traumatic stress disorder and chronic pain syndromes (12-15).

Uteroplacental compromise from uncoordinated uterine contractions leads to foetal distress and subsequently poor Apgar scores at birth (3, 10, 11).

1.4 Management of labour pain

The American College of Obstetricians and Gynaecologists' Committee on Practice Bulletins (16) state that "There is no other circumstance where it is considered acceptable for an individual to experience untreated severe pain, amenable to safe intervention, while under a physician's care. In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labour".

The updated guidelines for labour analgesia, as proposed by the American Society of Anaesthesiologists (ASA) Task Force and Committee on Standards and Practice Parameters (17) in 2016 recommend that "the choice of analgesic technique depends on the medical status of the patient, anaesthetic risk factors, obstetric risk factors, patient preferences, progress of labour and resources at the facility" (17).

Neuraxial techniques have been recognised as the gold-standard for providing labour analgesia (11, 18). Neuraxial analgesic techniques should be offered among the analgesic options for labour pain with the primary goal of providing adequate, safe, reliable, and reproducible maternal analgesia with a minimal motor block achieved with the administration of local anaesthetics at low concentrations with or without opioids (19, 20).

Offering labour analgesia to women intrapartum in a facility allows for respect of ethical pillars, constitutional and statutory obligation (21). Providing neuraxial analgesia reflects the standard of obstetric and anaesthetic care at an institution (22). Guidelines advocate the use of dilute concentrations of local anaesthetics with opioids to produce as little motor block as possible (17).

The characteristics of an ideal labour analgesic include a method that is safe for both the mother and foetus, provides satisfactory pain control and has minimal effects on labour progression and outcome (19, 23).

Different techniques are employed to alleviate the pain of labour. These are classed as pharmacological and non-pharmacological methods.

Non-pharmacological methods are easy to administer and include the following techniques: massage, transcutaneous electrical nerve stimulation, acupuncture, hypnosis, water birth, doula or partner support, mobilisation and Lamaze (3, 5, 20).

Pharmacological techniques include the use of inhalational agents, systemic analgesia and regional techniques.

Inhalational analgesic techniques have been offered to women in labour since the 1800s, in the form of oxygen and nitrous oxide. Entonox, a gas mixture of 50% oxygen and 50% nitrous oxide, is still recommended by South African Society of Anaesthesiologist (SASA) (24). Entonox's solubility allows it to be rapidly taken up by the lungs and absorbed into the blood stream and then exhaled with minimal accumulation in the maternal circulation (25, 26). The use of sevoflurane requires the presence of an anaesthetist. A mixture of sevoflurane, air and oxygen at a concentration of 2 – 4% before contractions is administered to reach an end tidal concentration of 1 – 1.5%. This results in a marked reduction in pain and is safe for the foetus (25, 27).

Systemic analgesia can be offered to labouring woman by either intramuscular, intravenous, patient controlled intravenous opioids or a combination of these techniques (3, 4, 20). Morphine 4 – 5 mg intramuscularly given 4 hourly is recommend by SASA (24). Remifentanil, an agonist at the u-1 opioid receptor, has a fast onset of action 30 – 60 seconds, shorter duration of action than fentanyl and morphine as it has been broken down by plasma and tissue esterase, and has a short context sensitive half-life and no accumulation. No poor labour and foetal outcomes (28-33).

Regional techniques are divided into peripheral nerve blocks and neuraxial techniques. Peripheral nerve blocks employed may be either a pudendal nerve or para-cervical ganglion block. Neuraxial techniques may be either single shot spinal, combined spinal epidural or epidural analgesic techniques (3, 20). Labour epidural analgesia is the current gold-standard for labour analgesia (18, 34, 35).

For the purposes of this literature review only labour epidural analgesia will be discussed as a regional technique.

1.5 Labour epidural analgesia

1.5.1 History of labour epidural analgesia

The epidural space was accidentally infiltrated with 111 mg of cocaine in 1885 by James Corning who was trying to perform a subarachnoid puncture (36). In 1900, Oscar Kreis performed intrathecal injections of cocaine into six labouring women, however, there were toxic effects associated with its use. Procaine was introduced in 1909, and Walter Stoekel described the caudal labour epidural using it. Fidel Mirave developed the single shot lumbar epidural in 1921. Edward Touhy developed the Tuohy needle after experimenting with the Barker spinal needle, threading a ureteric silk catheter into the subarachnoid space. In 1947 Manuel Curbelo described the placement of a lumbar epidural catheter. Flowers performed a continuous epidural block for labour, delivery and caesarean section in 1949. To decrease trauma during insertion, an epidural catheter with a closed tip and lateral hole was developed in 1962. Opiate receptors were discovered by Goldsteine in1971 and morphine was introduced into the epidural space in 1979. The maintenance of epidural analgesia through the patient-controlled method was introduced in1988 (19, 36).

1.5.2 Anatomy

The lumbar area is described as the area running from the upper vertebral body of the first lumbar vertebra to the upper vertebral body of the first sacral vertebra. Through these vertebral bodies, the spinal nerves exit the central nervous system. The spinal support structure is comprised of the longitudinal ligament in the front and the ligamentum flavum, interspinous and supraspinous ligaments behind. The spinal cord is covered by the meninges: the pia mater, arachnoid and dura mater. The cerebrospinal fluid lies between the pia and arachnoid mater. The epidural space is a potential space between the dura mater and ligamentum flavum. The epidural space is a potential space that has to be opened using either saline or air to confirm correct placement (3, 4, 23).

With the midline approach, the needle travels through the skin, fatty subcutaneous tissue, supraspinous and interspinous ligaments and the ligamentum flavum into the epidural space (3, 4).

1.5.3 The procedure of labour epidural placement

The South African Society of Anaesthesiologists, in 2016 (23), published regional anaesthesia guidelines. Although not specific to labour epidurals, these guidelines state that the medical doctors or anaesthetists placing the epidural catheter are responsible for the placement, maintenance and subsequent complications arising from the placement of the labour epidural. Monitoring of the labour epidural can be handed over to a competent junior medical doctor, nurse or midwife who will then assume the responsibility of monitoring the patient during the maintenance period (23).

Before placement of an epidural, contraindications to the procedure must be excluded, informed consent must be attained, adequate intravenous access must be established, adequate maternal and foetal monitoring must be available and resuscitation equipment must be available, checked and functioning. A record of the events of the procedure should also be kept (23).

The placement of the epidural catheter can be done with the labouring patient in the sitting or lateral lying position. The ASA recommends that maternal blood pressure, heart rate, saturation and electrocardiography be monitored (17). Monitoring of maternal temperature is recommended due to the high risk of developing maternal pyrexia (37). There is also a need for foetal monitoring using cardiotocography (17).

The placement of the epidural in the sitting position is easier than in the lateral position as being upright aids with identification of the lumbar spine and interspinous spaces, especially in obese patients (4). Labour epidural catheter placement is performed in an aseptic manner adhering to strict infection control measures (23, 36). The patency of the epidural catheter and filter is tested before use. A loss of resistance syringe can be prefilled with air or normal saline. Loss of resistance to saline is the preferred technique because if accidental puncture of dura is performed with air technique this carries the risk of pneumocephalus,

spinal cord compression, retroperitoneal air, subcutaneous emphysema and a reduction in analgesia offered (4, 38).

The iliac crests are palpated to locate the fourth lumbar interspace. The line that can be drawn from the iliac crests through the L4 – L5 interspace is known as Tuffier's line. Alternately the L3 – L4 interspace can be used to achieve analgesia between T10 – S5 (4, 23). The area is prepared by injecting a local anaesthetic mixture of 5 ml lignocaine 2%. There is also an increased risk of patchiness with air if used as a loss of resistance technique (38, 39). The Tuohy needle is advanced until a point is reached where loss of resistance is encountered. The loss of resistance technique used to find the epidural space was described by Achille Dogliotti (19). This technique is used preferentially to the hanging drop technique (40). The epidural catheter is then threaded through the Tuohy needle, and is advanced 5 – 6 cm further than the point where loss of resistance is encountered (3, 4).

Correct placement of the catheter is then tested by visualising the meniscus of the fluid in the catheter. The fluid meniscus is observed and a drop in the fluid column confirms correct placement (4, 23). The catheter is then strapped securely in place. A test dose usually of lignocaine with adrenaline is bloused. If there are no signs of intravascular or intrathecal placement, then the anaesthetists will proceed to activate or "load" the epidural. An injection of local anaesthetic mixture is administered in increments to the patient with the patient lying supine (4). The volume used to activate the epidural differs between patients but commonly between 8 and 16 ml are used to establish a T10 dermatomal level as assessed using an ice pack (4).

Labour epidurals can also be placed under ultrasound guidance, but this requires training and expertise. Ultrasound guidance helps identify the midline especially in patients who have had previous spine surgery or have spine pathology for example scoliosis. It helps to identify the epidural space, skin to epidural distance and decreases unintended dural puncture (41). Syringes like the Episure® and Epimatic® have been developed to identify the epidural space through visual confirmation (42, 43).

1.5.4 The pharmacology of labour epidural

The epidural liquid mixture is made up of a local anaesthetic agent at a chosen concentration with or without an adjuvant, commonly an opioid (3, 4, 19, 22, 36). For the purposes of this literature review only local anaesthetic agents and opioids will be discussed.

1.5.4..1 Local Anaesthetic agents

Local anaesthetic agents provide reversible reduction or complete alleviation of the pain sensation. They are the agents of choice for use in an epidural and are usually combined with adjuvants. Their mechanism of action is mediated through the blockade of sodium channels through which the transmission of nervous impulses is halted. These agents are available as esters and amides. These chemical classes offer a better understanding in terms of pharmacokinetic principles. The amides: lignocaine, bupivacaine, levobupivacaine and ropivacaine are used in epidural anaesthesia. Lignocaine has a shorter duration of action compared to the other three agents. Lignocaine results in a denser motor blockade and provides less adequate analgesia compared to the longer acting amides (3, 4). Bupivacaine, levobupivacaine and ropivacaine do not have the same quality of motor blockade (44, 45).

The pKa of a drug is the pH at which the drug will be 50% ionised. The pKa for bupivacaine is 8.5, which means that at maternal physiological pH it is highly ionised. As a result of the pKa and due to 95% of the drug being protein bound, there is a decreased placental transfer. Bupivacaine still carries a poor safety profile if injected into the maternal vascular system, with cardiovascular embarrassment requiring resuscitation using advanced life support principles together with the use of an intralipid emulsion. Resuscitation associated with toxicity relating to the use of bupivacaine is usually more difficult to treat, as compared to other agents (3, 4, 23). Bupivacaine is used at concentrations of 0.0625 − 0.1% as these doses best preserve motor functions, good analgesia and patient satisfaction, and less risk of needing an assisted delivery (46).

At these doses patients are be able to ambulate, the benefits of which are a reduction in the risk of labour prolongation, the incidence of malpresentation and assisted deliveries and an increase in patient satisfaction (47).

1.5.4..2 Opioids

Opioids are the most commonly used adjuvants in intrathecal and epidural anaesthesia and are sometimes used as sole agents. The mechanism of action is through the opioid receptors mu, kappa and delta. Opiates directly block the ascending transmission of pain from the dorsal horn of the spinal cord and they activate pain control circuits that descend from the midbrain. Receptors are also found in the substantia gelatinosa which releases substance P which mediates pain. In the epidural space, the opioids will diffuse through the meninges to reach the spinal cord. Highly lipophilic fentanyl will be absorbed in the fatty connective tissue resulting in a sustained release of the drug. In order to act on the spinal cord dorsal horn, the lipophilic agents must be absorbed by the meninges into the epidural space, which can reduce their efficacy when they are placed in the intrathecal space. Commonly used agents are fentanyl, morphine and sufentanil. Morphine is long acting and poorly lipid soluble and therefore it accumulates in the cerebrospinal fluid and spread to the brain with resultant respiratory depression is more common as opposed to fentanyl which is more highly lipid soluble. The side effect profile of these agents is dose dependant. Itching is the most common side effect, other effects are nausea and vomiting, retention of urine, respiratory depression and constipation (3, 4, 23). Anaesthetists in the United States of America prefer to use sufentanil, while in the United Kingdom anaesthetists preferentially use fentanyl. Sufentanil is 4 − 5 times more potent than fentanyl with a longer duration of action. Epidural dosages of fentanyl are 1 − 2 mcg/ml and sufentanil dosages are 0,5 − 1 mcg/ml (46).

1.5.5 Advantages of labour epidural

A labour epidural result in a decrease in the maternal sympathetic drive during labour. Cardiopulmonary benefits are as follows: systemic vascular resistance; stroke work and work of breathing are reduced. Hyperventilation is prevented, with a decrease in the risk of developing foetal acidosis. Reduction in maternal

catecholamines may result in the re-establishment of coordinated uterine activity and placental and uterine perfusion may be improved. These effects will result in better foetal Apgar scores (11, 48).

The use of an epidural also allows the parturient to rest in labour, especially important if labour is prolonged. It allows for active maternal participation, and in case of a caesarean section, the labouring woman can focus on the informed consent and can make an informed decision and ask appropriate questions. Labour epidurals also result in increased patient satisfaction, reduce maternal irritability, and allow for a more positive experience, with a reduction in the rate of episiotomies, and better maternal foetal bonding with early breastfeeding (48). Labour epidurals can be easily converted to provide surgical anaesthesia for caesarean sections and may be associated with an improvement in theatre efficiency (49).

Hu et al. (48), in China, investigated the relationship between labour epidural analgesia and mode of delivery. The team demonstrated that the introduction of epidural analgesia reduced the frequency of caesarean delivery, which improved obstetric and neonatal outcomes with a reduction in the rate of episiotomies, post-partum blood transfusions and non-medically indicated caesarean sections (48).

Fyneface-Ogan et al. (50), found that the duration of the first and second stages of labour were shorter in the epidural group as compared to non-epidural. More women in the epidural group required augmentation of labour with oxytocin than the non-epidural group, and less women with epidurals required emergency caesarean sections. There were no differences in post-delivery events between groups; the women had similar rates of retained placentae, episiotomies and blood loss. The Apgar scores in the epidural group were higher, although the investigators concluded that neonatal outcomes were similar between groups. The epidural group showed a much better overall labour experience, and the investigators concluded that epidural analgesia was superior to other forms of analgesia and provided a better maternal experience (50).

1.5.6 Major and minor side effects

1.5.6..1 Maternal adverse effects

There are numerous adverse maternal effects associated with labour epidurals, however, most are easy to treat and are not associated with significant morbidity or mortality. The more severe complications are usually very rare but may be catastrophic in nature and these include unintentional intrathecal and intravascular injection (3, 4, 23, 51). Minor adverse effects include nausea, vomiting, itching, hypotension, maternal pyrexia, postdural puncture headache (PDPH), motor blockade and back pain (3, 4, 23).

Unintentional intrathecal injection

Unintentional intrathecal injection is observed when guidelines for placement of epidural catheters are not respected. Unintentional placement of the drug mixture into the cerebrospinal fluid results in hypotension, weakness of the diaphragm, and intercostal muscles and may result in the patient being intubated and ventilated (3, 4, 23). The incidence is 1 in 3500 (52).

Unintentional intravascular injection

The unintentional injection of local anaesthetic mixture intravascularly during epidural catheter placement will result in circulatory collapse, necessitating cardiopulmonary resuscitation (3, 4, 23).

Nausea, vomiting and itching

Nausea, vomiting and itching are extremely common complications and may result in significant patient dissatisfaction and discomfort. These complications occur secondary to opioid use and are worsened with increased dosing. The opioids act on the central u receptors to produce these side effects (3, 4).

Hypotension

Hypotension occurs in 1 in 20 (4.9%) women post-epidural insertion (52), and is defined as a 20% deviation of mean arterial blood pressure from baseline (3). Hypotension occurs as a result of a loss of vascular tone below the level of the

labour epidural. A sympathectomy causes a decrease in blood returning to the heart and together with uterine compression of the aorta and inferior vena cava, may result in a decrease in cardiac preload. Treatment entails the preventative measure of maternal positioning with full lateral tilt (53), inserting epidurals in fluid replete patients and the use of crystalloid or colloid pre-loading or co-loading, and the use of phenylephrine in 50 − 100 ug boluses or ephedrine in 5 − 10 mg boluses (3, 4, 23).

The definition of hypotension is important in studies and it is important to adopt standard definitions. Blood pressure may differ significantly antenatally and during labour, and it is important to have a baseline blood pressure prior to the onset of labour (54). Blood pressure monitoring with an intra-arterial device shows that the pressures are similar in patients lying in the lateral, supine and sitting positions. With a non-invasive cuff, the blood pressure in the lateral position of the uppermost arm is lower than in the dependant arm, while the dependant arm's blood pressure is similar to the supine position and in a patient at 45 degrees (54).

Kinsella and Black (54) demonstrated that if a 20% drop in blood pressure from admission baseline was used, a varying number of patients fit the definition of hypotension depending on which arm was used. The rate of hypotension was higher if the uppermost arm was used and no hypotension was found if the dependant arm was used in the lateral position whether the baseline blood pressure was taken antenatally or taken in the labour admissions ward (54).

Maternal pyrexia

Maternal fever has been associated with labour epidural analgesia, and mothers may be over investigated for chorioamnionitis, and sepsis (37, 55). The mechanisms of epidural-associated fever remain incompletely understood; however, it is suggested that epidural analgesia may cause an "imbalance between heat-producing and heat-dissipating mechanisms". It can result in a foetal tachycardia which is sometimes misinterpreted as foetal distress and may result in unnecessary emergency caesarean sections (56).

Postdural puncture headache

Postdural puncture headache is a complication resulting from puncture of the dura during placement with a continuous leak of cerebrospinal fluid through the puncture. Although a PDPH may affect patient satisfaction, it is usually self-limiting and responds to conservative management including bedrest, the administration of intravenous fluid, simple analgesics, and caffeine. However, a sterile epidural blood patch may need to be performed, to which over 90% of patients respond (57, 58). Transnasal sphenopalatine ganglion block should be considered due to safety of the procedure and the immediate and sustained pain relief for the treatment of PDPH (59). PDPH occurs in 1 in 160 (52).

Motor blockade

Motor blockade may occur as a result of the labour epidural. The likelihood of motor blockade and the degree of blockade increases with the increase in concentration of local anaesthetic and maintenance technique employed. Motor blockade may increase the risk for an assisted delivery (60, 61).

The ability to ambulate may increase the rate of spontaneous vaginal deliveries, result in shorter labours, decrease the likelihood of malpresentations, and increase patient satisfaction (47). The Comparative Obstetric Mobile Epidural Trial (COMET) (62) compared low dose combined spinal epidural to low dose continuous, and traditional epidural techniques. The low dose combined spinal epidural group had a higher rate of normal vaginal deliveries than the traditional epidural group with a reduction in instrumental deliveries (62).

Motor blockade is traditionally assessed using the Bromage or modified Bromage score, however, these scoring systems do not assess the pelvis in terms of muscle function, tone and power (63). The Bromage score has four categories:

- Grade 0 no motor block
- Grade 1 able to move knees and feet with a 35% motor block
- Grade 2 inability to raise leg and move knees only able to move feet with a 65% motor block
- Grade 3 complete motor block (64).

Modification of the Bromage score was subsequently developed to differentiate patients between grade 0 – 1, Grades 1 – 3 are unchanged with Grade 0 being no motor block, Grade 0+ able to raise straight leg but slight weakness and Grade 0++ able to raise straight leg but significant weakness. The Breen modified Bromage score also exists. It is a six-point scale to assess motor block and is used to differentiate patients in the last category of the Bromage score (64).

Back pain

Labour epidurals are not associated with chronic postpartum backache (13). There is a study that shows that 50% of patients irrespective of means of delivery or method of analgesia have chronic backache. The epidural may cause temporary pain at the site of injection and local discomfort (65).

Effect on the duration of labour and risk for caesarean section or assisted delivery

A review done by Cambric and Wong (28) on labour epidural analgesia and obstetric outcomes showed that labour epidural analgesia does not increase the risk of caesarean section delivery (28). This has also been demonstrated in other studies (26, 34). However, there are still studies that continue to argue that labour epidurals increase the rate of caesarean sections in parturient (66, 67).

Many factors have been implicated in the risk for instrumental delivery such as forceps or vacuum delivery (18, 28). Factors such as maternal age, parity, level of the head in relation to the pelvis, maternal pain, urge to bear down, degree of motor blockade, and the technique of maintenance of labour epidural have all been implicated (18, 68). The use of labour epidurals has not been shown to clinically affect the duration of labour (51).

1.5.6..2 Foetal adverse effects

The COMET study found that continuous epidural bolus (CEI) was associated with increased neonatal resuscitation, as compared to intermittent boluses (62).

Agrawal et al. (69) studied the effect of epidural anaesthesia on labour and neonatal outcomes in India. They compared labouring women who received an

epidural versus those who did not. The study revealed no significant difference in the mode of delivery, and the authors concluded that there was no poor neonatal outcome associated with labour epidurals. These findings are supported by findings of other studies (50, 70).

1.6 Labour epidural maintenance techniques

Epidural labour analgesia, once established, requires maintenance until labour is completed. The techniques employed to maintain analgesia include the intermittent epidural bolus (IEB) technique also referred to as manual boluses, the CEI technique, patient controlled epidural analgesia (PCEA) as stand-alone method or as a supplement to other techniques and the programmed intermittent epidural bolus (PIEB) technique (11, 36, 61, 71).

1.6.1 Intermittent epidural bolus

The IEB is the traditional regimen for maintaining labour analgesia. The anaesthetist will assess the level of the block on an hourly basis, check for the displacement of the epidural catheter and may provide a bolus of epidural mixture (46). The technique is associated with haemodynamic instability (72), but is safe, reproducible and cost effective as it does not require procurement of infusion pumps. Although considered to be labour intensive, it has been shown to reduce local anaesthetic consumption as opposed to CEI (73). This technique may limit the number of epidurals that may be placed by a single anaesthetist (36) and is associated with breakthrough pain (11, 71).

1.6.2 Continuous epidural infusion

The CEI technique involves the connection of the catheter to a pump that delivers the epidural mixture as a continuous infusion. This technique can be supplemented with PCEA for breakthrough pain (74). This technique has been postulated to allow for smoother analgesia, decreased workload for the attending anaesthetist and increased maternal satisfaction, however, studies have not demonstrated that workload is reduced (11, 73).

This technique has been recently improved using automated pumps that can provide PIEB with or without PCEA (60, 61, 75, 76). Some studies have shown that PIEB provides superior analgesia and higher levels of satisfaction than CEI (61, 77, 78).

A study comparing CEI and IEB showed that the IEB group had decreased consumption of bupivacaine per hour, decreased motor blockade, increased maternal satisfaction, but similar neonatal outcomes. With regards to mode of delivery the groups were also similar (79). Capogna et al. (60) showed that CEI is associated with increased local anaesthetic agent consumption and increased motor block (60).

It has been postulated that the PIEB technique is associated with fewer maternal adverse effects and higher levels of maternal satisfaction when compared to other techniques. Systematic reviews and meta-analyses have demonstrated that local anaesthetic drug consumption per hour was increased with CEI as opposed to PIEB (34, 80), maternal satisfaction was lower using the visual analogue scale, maternal motor blockade was decreased, but the two methods were comparable in terms of foetal, and labour outcomes (60, 61, 75).

A study comparing CEI with PCEA to PIEB with PCEA showed that the former had greater local anaesthetic consumption and required more physician rescue boluses. However, there was no differences in time to first rescue bolus, and the rate of instrumental deliveries remained the same (81).

1.6.3 Patient controlled epidural analgesia

PCEA is not usually used as a sole method but rather as a supplementary method to CEI or PIEB. As a sole method, it may be comparable to manual boluses given by the anaesthetist. It allows for patient autonomy but reduces maternal satisfaction as it requires the pain to return before administering a bolus since no background infusions are provided. The pump has a set lockout time and allowable volume per hour to avoid overdose and undesirable complications (74). It may reduce physician workload, especially in busy labour wards (82).

PCEA has been shown to result in a reduction in local anaesthetic consumption (82-84), better analgesia and maternal satisfaction (85). Srivastava et al. (86) compared the PCEA bolus technique to PCEA with a background CEI. Patients receiving PCEA boluses needed the treating anaesthesiologist to administer a greater number of rescue boluses for distressing breakthrough pain. Consumption of the local anaesthetic agents and opiates in terms of total volume was greater in the PCEA bolus only group, and there was no difference in analgesia using the visual analogue pain score, neonatal Apgar score, mode of delivery, or maternal satisfaction (86).

Boselli et al. (87) showed that CEI with PCEA resulted in increased consumption of local anaesthetics. There were no differences between PCEA alone as compared to CEI with PCEA in terms of pain scores, motor block, maternal drowsiness, nausea and vomiting, one and five-minute Apgar scores, or mode of delivery. It was found that PCEA was superior to PCEA with CEI as it reduced cost and anaesthetic workload (87).

Halpern and Carvalho (88) have demonstrated that PCEA as opposed to PCEA with CEI decreases local anaesthetic agent consumption but increases the incidence of breakthrough pain and was associated with increased maternal dissatisfaction. However, Bremerich et al. (89) showed that PCEA with CEI did not increase consumption of the local anaesthetic mixture and had similar maternal and foetal outcomes.

Chua et al. (90) compared PCEA with ropivacaine 0.125% to bupivacaine 0.125%. The consumption of local anaesthetics was found to be similar but the ropivacaine group had a lower number of PCEA boluses. There were no differences in the duration of labour, one and five-minute Apgar scores, mode of delivery, or maternal satisfaction. The authors concluded that the analgesia provided by PCEA using low dose ropivacaine and bupivacaine was similar (90). Increasing ropivacaine to 0.2% has been shown to have equal analgesic effect to lower concentrations, however, lower concentrations are associated with less motor blockade (91). Bernard et al. (92) explored whether increasing concentration of a local anaesthetic agent and lockout time on the PCEA would improve maternal satisfaction. Patients demonstrated better visual analogue pain scores and

maternal satisfaction with increased concentration and lockout times (92). A study by Boutros et al. (93) comparing IEB, CEI and PCEA found that the CEI group required more rescue boluses than PCEA, motor blockade was more frequent in the CEI than IEB group and local anaesthetic consumption per hour was less in IEB than PCEA. No differences in the incidence of itching and hypotension were demonstrated between the three groups. The authors concluded that PCEA is better than CEI with regards to local anaesthetic consumption (93).

PCEA may also be provided as computerised integrated patient controlled epidural analgesia. With this technique, pumps have integrated algorithms and adjust infusion rates based on patient demands. This technique has been associated with increased maternal satisfaction (94).

1.6.4 Programmed intermittent epidural bolus

PIEB employs an automated pump to give the local anaesthetic and opioid mixture through the epidural catheter into the epidural space at a fixed calculated dose and at scheduled intervals. As with CEI, it can be supplemented with PCEA. Numerous benefits over CEI have been postulated (60, 61, 74, 75, 95).

Hogan (56) studied the technique using cadavers, and found that high injecting pressures caused a more uniform spread of the mixture in the epidural space, intervertebral foramina and nerve sheath. These benefits are further enhanced by using a multi-orifice epidural catheter as opposed to a single orifice catheter (96, 97). Comparing CEI with PIEB anatomically and physiologically sheds some light into possible explanations in differences seen. The local anaesthetic agent needs to move against a concentration gradient from outside the nerve cell to the inside. By giving the epidural mixture as a continuous infusion, a steady state can be reached by allowing the intra-neural concentration to be higher resulting in a reverse polarity with the movement of local anaesthetic agent extraneurally reducing sensory block. With CEI, the drugs are able to penetrate the entire nerve cell as opposed to PIEB where the concentrating ion is higher on the outside giving the benefits of a reduced motor block (61, 98).

A focus on PIEB as a technique is due to the development of new pump technology. New automated pumps with upgraded software can now be used in

clinical practice. To achieve PIEB combined with PCEA, previously two pumps were used, one for PIEB and the other for the PCEA component. With the latest software upgrades, one pump can be now be used to achieve the high flow rate bolus that is fixed at scheduled intervals and PCEA component (99). With the old software, a maximum infusion rate of 175 ml/hour could be achieved. Advancements have resulted in pumps that can now deliver up to 500 ml/hour using specialised high flow tubing. PIEB incorporates the benefits of IEB and CEI (61).

A randomised controlled study by Wong et al. (75) showed that PIEB combined with PCEA resulted in less bupivacaine consumption compared with CEI plus PCEA while providing equivalent labour analgesia. Fewer physician provided additional boluses were required in the PIEB group, and fewer manual rescue boluses were needed (75).

Fettes et al. (100) conducted a study to compare CEI and PIEB. The study demonstrated a reduced local anaesthetic agent usage in the PIEB group (100).

Leo et al. (83) compared CSE and PIEB with PCEA and showed that PIEB with PCEA is associated with a reduction in the use of local anaesthetics (83). A reduction in local anaesthetic consumption has been demonstrated with bupivacaine, ropivacaine, and levobupivacaine (60, 61). Capogna et al. (60) have demonstrated reduced bupivacaine and fentanyl consumption and cost with PIEB combined with PCEA when compared to CEI combined with PCEA. Tien et al. (99), however, conducted a study comparing CEI with PCEA, and PIEB with PCEA. The study showed no difference in the local anaesthetic agent consumption but can be criticised as it was a retrospective study, and patients were not randomised (99).

As previously described, motor blockade and instrumental delivery are complications associated with epidural analgesia (3, 4). Capogna et al. (60) conducted a double blind randomised control study to determine the incidence of motor blockade and instrumental delivery with PIEB. The study compared PIEB with PCEA to CEI with PCEA using a two-pump system and demonstrated a 37% incidence of motor blockade in the former using the Breen modified Bromage

score. The incidence of motor block at full cervical dilatation was higher in the CEI group, the incidence of instrumentation in labour was three times lower in the PIEB group, and there was no difference in caesarean section rates between two groups (60).

Nunes et al. (95) however, have described no difference in instrumental delivery rates in patients receiving PIEB and CEI (95). Other studies have shown no difference in mode of delivery between PIEB and CEI (80, 95, 99, 101, 102).

Much controversy exists regarding pain scores in patients receiving PIEB compared to other techniques. Fettes et al. (100) have shown that PIEB reduced the amount of local anaesthetic agent used with similar pain scores when compared to CEI, and therefore conclude that PIEB offers better analgesia. Nunes et al. (95) conducted a study comparing CEI and PIEB that demonstrated no difference in pain scores and maternal satisfaction between the techniques (95). Further studies have also demonstrated no difference in pain scores between PIEB and CEI techniques (60, 99, 102).

A retrospective review of electronic maternal records demonstrated that PIEB with PCEA required less rescue boluses as compared to CEI with PCEA (101). Other studies have also demonstrated reduced requirements for rescue boluses in PIEB with PCEA (75, 83, 103).

Lin et al. (102) conducted a study comparing maternal and foetal outcomes in PIEB and CEI. The study showed no difference in duration of labour between the two techniques, and no difference in foetal outcomes (102). Nunes et al. (95) conducted a study that demonstrated similar findings.

Haemodynamic instability is seen with epidural analgesia, sometimes requiring anaesthetist intervention with intravenous fluids and pressors. Haemodynamic instability is defined as a drop in mean arterial blood pressure of more than 20% from baseline (3). Leonard et al. (104) reported the incidence of 12.3% for hypotension at Rahima Moosa Mother and Child Hospital in a retrospective audit. This was similar to an audit performed at Tygerberg hospital (105) where the incidence was 13.4%. In their audits both authors did not mention the type of technique used to maintain the labour epidural. Ferrer et al. (106) compared CEI

with PCEA to PIEB with PCEA and showed no difference between the groups. Leo et al. (83) also demonstrated the same.

1.7 Summary

The studies have demonstrated that using automated technology with upgraded software for PIEB with PCEA results in decreased local anaesthetic usage, less motor blockade, fewer subsequent rescue boluses and better maternal satisfaction. Some studies have shown better haemodynamic stability with PIEB as opposed to CEI and IEB. However, no difference in neonatal and maternal outcomes and breakthrough pain have been demonstrated. The use of different pain rating scales, parity, local anaesthetics and opiates used, number of pumps used and dosing intervals differed between the studies. None of these studies were conducted in the South African context.

Appropriately powered studies comparing PIEB with PCEA to CEI in South African women using a single automated pump technique according to set algorithms are required to demonstrate better maternal outcomes and foetal outcomes. These studies will have to consistently show that PIEB with PCEA offers less breakthrough pain, higher levels of maternal satisfaction, better maternal haemodynamic control and less motor blockade, and a lower rate of assisted deliveries (80).

1.8 References

1. Jones L. Pain management for women in labour: An overview of systematic reviews. Int J Evid Based Healthc. 2012;5(2):101-2. doi:10.1002/14651858.CD009234.pub2.

2. Lowe NK. The nature of labor pain. Am J Obstet Gynecol. 2002;186(5):S16-S24. doi:10.1016/S0002-9378(02)70179-8.

3. Miller RD. Miller's Anesthesia. 8th ed. Philadelphia, PHL: Churchill Livingstone; 2015.

4. Morgan GE, Mikhail MS. Clinical Anesthesiology. 5th ed. New York, NY: McGraw Hill 2006.

5. Labor S, Maguire S. The pain of labour. Rev Pain. 2008;2(2):15-9. doi:10.1177/204946370800200205.

6. Jamison RN, Gracely RH, Raymond SA, Levine JG, Marino B, Herrmann TJ, et al. Comparative study of electronic vs. paper VAS ratings: A randomized, crossover trial using healthy volunteers. Pain. 2002;99(1-2):341-7. doi:10.1016/s0304-3959(02)00178-1.

7. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. J Clin Nurs. 2005;14(7):798-804. doi:10.1111/j.1365-2702.2005.01121.x.

8. Aun C, Lam Y, Collett B. Evaluation of the use of visual analogue scale in Chinese patients. Pain. 1986;25(2):215-21. doi:10.1016/0304-3959(86)90095-3.

9. Jensen MP, Turner JA, Romano JM. What is the maximum number of levels needed in pain intensity measurement? Pain. 1994;58(3):387-92. doi:10.1016/0304-3959(94)90133-3.

10. Hawkins JL. Epidural analgesia for labor and delivery. N Engl J Med. 2010;362(16):1503-10. doi:10.1056/NEJMct0909254.

11. Reena KH, Bandyopadhyay MA, Mishra AP. Labor epidural analgesia: Past, present and future. Indian Journal of Pain. 2014;28(2):71. doi:10.4103/0970-5333.132843.

12. Russell R, Reynolds F. Back pain, pregnancy, and childbirth. BMJ. 1997;314(7087):1062-3. doi:10.1136/bmj.314.7087.1062.

13. Loughnan BA, Carli F, Romney M, Doré CJ, Gordon H. Epidural analgesia and backache: A randomized controlled comparison with intramuscular meperidine for analgesia during labour. Br J Anaesth. 2002;89(3):466-72. doi:10.1093/bja/89.3.466.

14. Ding T, Wang D-X, Qu Y, Chen Q, Zhu S-N. Epidural labor analgesia is associated with a decreased risk of postpartum depression: A prospective cohort study. Anesth Analg. 2014;119(2):383-92. doi:10.1213/ane.0000000000000107.

15. Garthus-Niegel S, Knoph C, von Soest T, Nielsen CS, Eberhard-Gran M. The role of labor pain and overall birth experience in the development of posttraumatic stress symptoms: A longitudinal cohort study. Birth. 2014;41(1):108-15. doi:10.1111/birt.12093.

16. American College of Obstetricians and Gynecologists. Practice bulletin no. 177 summary: Obstetric analgesia and anesthesia. Obstet Gynecol. 2017;129(4):766-8. doi:10.1097/aog.0000000000002009.

17. American Society of Anesthesiologists. Practice guidelines for obstetric anesthesia: An updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. Anesthesiology. 2016;124(2):270-300. doi:10.1097/ALN.0000000000000935.

18. Cambic CR, Wong CA. Impact of central neuraxial analgesia on the progress of labor. Adv Anesth. 2009;27(1):167-89. doi:10.1016/j.aan.2009.07.001.

19. Reena, Bandyopadhyay K, Afzal M, Mishra A, Paul A. Labor epidural analgesia: Past, present and future. Indian Journal of Pain. 2014;28(2):71-81. doi:10.4103/0970-5333.132843.

20. Findley I, Chamberlain G. Relief of pain. BMJ. 1999;318(7188):927-30. doi:10.1136/bmj.318.7188.927.

21. Brennan F, Carr DB, Cousins M. Pain management: A fundamental human right. Anesth Analg. 2007;105(1):205-21. doi:10.1213/01.ane.0000268145.52345.55.

22. Pandya ST. Labour analgesia: Recent advances. Indian J Anaesth. 2010;54(5):400-8. doi:10.4103/0019-5049.71033.

23. South African Society of Anaesthesiologists. Guidelines for Regional Anaesthesia in South Africa. Available from: https://sasaapi.sasaweb.com/Document/SASRAguidelines2016_636722590664755485.pdf [date accessed 26 August 2017.

24. South African Society of Anaesthesiologists. South African Acute Pain Guidelines. Available from: https://sasaapi.sasaweb.com/Document/SASA%20Pain%20Guidelines%202015_636052806593689611.pdf [date accessed 08 August 2018.

25. Yeo ST, Holdcroft A, Yentis SM, Stewart A, Bassett P. Analgesia with sevoflurane during labour: II. Sevoflurane compared with entonox for labour analgesia. Br J Anaesth. 2007;98(1):110-5. doi:10.1093/bja/ael327.

26. Loughnan BA, Carli F, Romney M, Doré CJ, Gordon H. Randomized controlled comparison of epidural bupivacaine versus pethidine for analgesia in labour. Br J Anaesth. 2000;84(6):715-9. doi:10.1093/oxfordjournals.bja.a013580.

27. Yeo ST, Holdcroft A, Yentis SM, Stewart A. Analgesia with sevoflurane during labour: I. Determination of the optimum concentration. Br J Anaesth. 2007;98(1):105-9. doi:10.1093/bja/ael326.

28. Cambic CR, Wong CA. Labour analgesia and obstetric outcomes. Br J Anaesth. 2010;105(Suppl 1):i50-60. doi:10.1093/bja/aeq311.

29. Volikas I, Butwick A, Wilkinson C, Pleming A, Nicholson G. Maternal and neonatal side-effects of remifentanil patient-controlled analgesia in labour. Br J Anaesth. 2005;95(4):504-9. doi:10.1093/bja/aei219.

30. Volikas I, Male D. A comparison of pethidine and remifentanil patient-controlled analgesia in labour. Int J Obstet Anesth. 2001;10(2):86-90. doi:10.1054/ijoa.2000.0831.

31. Balki M, Kasodekar S, Bernstein P, Carvalho JC. Remifentanil patient-controlled analgesia for labour: Optimizing drug delivery regimens. Can J Anaesth. 2007;54(8):626-33. doi:10.1007/BF03022956.

32. Schnabel A, Hahn N, Broscheit J, Muellenbach RM, Rieger L, Roewer N, et al. Remifentanil for labour analgesia: A meta-analysis of randomised controlled trials. Eur J Anaesthesiol. 2012;29(4):177-85. doi:10.1097/EJA.0b013e32834fc260.

33. Wilson MJA, MacArthur C, Cooper GM, Shennan A. COMET Study Group UK. Ambulation in labour and delivery mode: A randomised controlled trial of high-dose vs mobile epidural analgesia. Anaesthesia. 2009;64(3):266-72. doi:10.1111/j.1365-2044.2008.05756.x.

34. Sng BL, Leong WL, Zeng Y, Siddiqui FJ, Assam PN, Lim Y, et al. Early versus late initiation of epidural analgesia for labour. Cochrane Database Syst Rev. 2014(10):CD007238. doi:10.1002/14651858.CD007238.pub2.

35. Okojie NQ, Isah EC. Perception of epidural analgesia for labour among pregnant women in a Nigerian tertiary hospital setting J West Afr Coll Surg. 2014;4(4):142-62.

36. Silva M, Halpern SH. Epidural analgesia for labor: Current techniques. Local Reg Anesth. 2010;3:143-53. doi:10.2147/LRA.S10237.

37. Philip J, Alexander J, Sharma S, Leveno K, McIntire D, Wiley J. Epidural analgesia during labor and maternal fever. Anesthesiology. 1999;90(5):1271-5. doi:10.1097/00000542-199905000-00008.

38. Saberski LR, Kondamuri S, Osinubi OY. Identification of the epidural space: Is loss of resistance to air a safe technique?: A review of the complications

related to the use of air. Reg Anesth Pain Med. 1997;22(1):3-15. doi:10.1136/rapm-00115550-199722010-00002.

39. Beilin Y, Arnold I, Telfeyan C, Bernstein HH, Hossain S. Quality of analgesia when air versus saline is used for identification of the epidural space in the parturient. Reg Anesth Pain Med. 2000;25(6):596-9. doi:https://doi.org/10.1053/rapm.2000.9535.

40. Hoffmann VL, Vercauteren MP, Vreugde JP, Hans GH, Coppejans HC, Adriaensen HA. Posterior epidural space depth: Safety of the loss of resistance and hanging drop techniques. Br J Anaesth. 1999;83(5):807-9. doi:10.1093/bja/83.5.807.

41. Carvalho JC. Ultrasound-facilitated epidurals and spinals in obstetrics. Anesthesiol Clin. 2008;26(1):145-58, vii-viii. doi:10.1016/j.anclin.2007.11.007.

42. Riley ET, Carvalho B. The Episure syringe: A novel loss of resistance syringe for locating the epidural space. Anesth Analg. 2007;105(4):1164-6. doi:10.1213/01.ane.0000281935.78144.82.

43. Teng WN, Tsou MY, Chang WK, Ting CK. Eyes on the needle: Identification and confirmation of the epidural space. Asian journal of anesthesiology. 2017;55(2):30-4. doi:10.1016/j.aja.2017.05.009.

44. Atiénzar MC, Palanca JM, Torres F, Borràs R, Gil S, Esteve I. A randomized comparison of levobupivacaine, bupivacaine and ropivacaine with fentanyl, for labor analgesia. Int J Obstet Anesth. 2008;17(2):106-11. doi:https://doi.org/10.1016/j.ijoa.2007.10.003.

45. Gautier P, De Kock M, Van Steenberge A, Miclot D, Fanard L, Hody J. A double-blind comparison of 0.125% ropivacaine with sufentanil and 0.125% bupivacaine with sufentanil for epidural labor analgesia. Anesthesiology. 1999;90(3):772-8. doi:10.1097/00000542-199903000-00020.

46. McGrady E, Litchfield K. Epidural analgesia in labour. Br J Anaesth. 2004;4(4):114-7. doi:10.1093/bjaceaccp/mkh030.

47. Kinsella SM, Pirlet M, Mills MS, Tuckey JP, Thomas TA. Randomized study of intravenous fluid preload before epidural analgesia during labour. Br J Anaesth. 2000;85(2):311-3. doi:10.1093/bja/85.2.311.

48. Hu LQ, Zhang J, Wong CA, Cao Q, Zhang G, Rong H, et al. Impact of the introduction of neuraxial labor analgesia on mode of delivery at an urban maternity hospital in China. Int J Gynaecol Obstet. 2015;129(1):17-21. doi:10.1016/j.ijgo.2014.10.030.

49. Halpern SH, Soliman A, Yee J, Angle P, Ioscovich A. Conversion of epidural labour analgesia to anaesthesia for Caesarean section: a prospective study of the incidence and determinants of failure. Br J Anaesth. 2009;102(2):240-3. doi:https://doi.org/10.1093/bja/aen352.

50. Fyneface-Ogan S, Mato CN, Anya SE. Epidural anesthesia: Views and outcomes of women in labor in a Nigerian hospital. Ann Afr Med. 2009;8(4):250-6. doi:10.4103/1596-3519.59580.

51. Anim-Somuah M, Smyth RMD, Jones L. Epidural versus non-epidural or no analgesia in labour. Cochrane Database Syst Rev. 2011(12):Cd000331. doi:10.1002/14651858.CD000331.pub3.

52. Paech MJ, Godkin R, Webster S. Complications of obstetric epidural analgesia and anaesthesia: a prospective analysis of 10 995 cases. Int J Obstet Anesth. 1998;7(1):5-11. doi:10.1016/S0959-289X(98)80021-6.

53. Wang X, Xu J-M, Zhou F, He L, Cui Y-L, Li Z-J. Maternal position and development of hypotension in patients undergoing cesarean section under combined spinal-epidural anesthesia of intrathecal hyperbaric ropivacaine. Med Sci Monit. 2015;21:52-8. doi:10.12659/MSM.892224.

54. Kinsella SM, Black AMS. Reporting of 'hypotension' after epidural analgesia during labour. Anaesthesia. 1998;53(2):131-5. doi:10.1046/j.1365-2044.1998.00315.x.

55. Lieberman E, Lang JM, Frigoletto F, Richardson DK, Ringer SA, Cohen A. Epidural analgesia, intrapartum fever, and neonatal sepsis evaluation. Pediatrics. 1997;99(3):415-9. doi:10.1542/peds.99.3.415.

56. Segal S. Labor epidural analgesia and maternal fever. Anesth Analg. 2010;111(6):1467-75. doi:10.1213/ANE.0b013e3181f713d4.

57. Turnbull DK, Shepherd DB. Post-dural puncture headache: Pathogenesis, prevention and treatment. Br J Anaesth. 2003;91(5):718-29. doi:10.1093/bja/aeg231.

58. Bezov D, Lipton RB, Ashina S. Post-dural puncture headache: Part I diagnosis, epidemiology, etiology, and pathophysiology. Headache. 2010;50(7):1144-52. doi:10.1111/j.1526-4610.2010.01699.x.

59. Channabasappa S, Manjunath S, Bommalingappa B, Ramachandra S, Banuprakash S. Transnasal sphenopalatine ganglion block for the treatment of postdural puncture headache following spinal anesthesia. Saudi J Anaesth. 2017;11. doi:10.4103/sja.SJA_59_17.

60. Capogna G, Camorcia M, Stirparo S, Farcomeni A. Programmed intermittent epidural bolus versus continuous epidural infusion for labor analgesia: The effects on maternal motor function and labor outcome. A randomized double-blind study in nulliparous women. Anesth Analg. 2011;113(4):826-31. doi:10.1213/ANE.0b013e31822827b8.

61. Capogna G, Stirparo S. Techniques for the maintenance of epidural labor analgesia. Curr Opin Anaesthesiol. 2013;26(3):261-7. doi:10.1097/ACO.0b013e328360b069.

62. Effect of low-dose mobile versus traditional epidural techniques on mode of delivery: A randomised controlled trial. Lancet. 2001;358(9275):19-23. doi:10.1016/s0140-6736(00)05251-x.

63. Bromage PR. Epidural Analgesia. Philadelphia,Pa: WB Saunders; 1978.

64. Graham AC, McClure JH. Quantitative assessment of motor block in labouring women receiving epidural analgesia. Anaesthesia. 2001;56(5):470-6. doi:10.1046/j.1365-2044.2001.01524-6.x.

65. Macarthur AJ, Macarthur C, Weeks SK. Is epidural anesthesia in labor associated with chronic low back pain? A prospective cohort study. Anesth Analg. 1997;85(5):1066-70. doi:10.1097/00000539-199711000-00019.

66. Ramin SM, Gambling DR, Lucas MJ, Sharma SK, Sidawi JE, Leveno KJ. Randomized trial of epidural versus intravenous analgesia during labor. Obstet Gynecol. 1995;86(5):783-9. doi:10.1016/0029-7844(95)00269-w.

67. Thorp JA, Hu DH, Albin RM, McNitt J, Meyer BA, Cohen GR, et al. The effect of intrapartum epidural analgesia on nulliparous labor: A randomized, controlled, prospective trial. Am J Obstet Gynecol. 1993;169(4):851-8. doi:http://dx.doi.org/10.1016/0002-9378(93)90015-B.

68. Yancey MK, Pierce B, Schweitzer D, Daniels D. Observations on labor epidural analgesia and operative delivery rates. Am J Obstet Gynecol. 1999;180(2):353-9. doi:10.1016/s0002-9378(99)70213-9.

69. Agrawal D, Makhija B, Arora M, Haritwal A, Gurha P. The effect of epidural analgesia on labour, mode of delivery and neonatal outcome in nullipara of India, 2011-2014. J Clin Diagn Res. 2014;8(10):OC03-6. doi:10.7860/JCDR/2014/9974.4930.

70. Fratelli N, Prefumo F, Andrico S, Lorandi A, Recupero D, Tomasoni G, et al. Effects of epidural analgesia on uterine artery Doppler in labour. Br J Anaesth. 2011;106(2):221-4. doi:10.1093/bja/aeq317.

71. Gupta S, Partani S. Neuraxial techniques of labour analgesia. Indian J Anaesth. 2018;62(9):658-66. doi:10.4103/ija.IJA_445_18.

72. Holte K, Foss N, Svensén C, Lund C, Madsen J, Kehlet H. Epidural anesthesia, hypotension, and changes in intravascular volume. Anesthesiology. 2004;100(2):281-6.

73. McGrady E, Litchfield K. Epidural analgesia in labour. Continuing Education in Anaesthesia Critical Care & Pain. 2004;4(4):114-7. doi:10.1093/bjaceaccp/mkh030.

74. Onuoha OC. Epidural analgesia for labor: Continuous infusion versus programmed intermittent bolus. Anesthesiol Clin. 2017;35(1):1-14. doi:10.1016/j.anclin.2016.09.003.

75. Wong CA, Ratliff JT, Sullivan JT, Scavone BM, Toledo P, McCarthy RJ. A randomized comparison of programmed intermittent epidural bolus with continuous epidural infusion for labor analgesia. Anesth Analg. 2006;102(3):904-9. doi:10.1213/01.ane.0000197778.57615.1a.

76. Mosadeghrad AM. Factors influencing healthcare service quality. Int J Health Policy Manag. 2014;3(2):77-89. doi:10.15171/ijhpm.2014.65.

77. Spoerel WE, Thomas A, Gerula GR. Continuous epidural analgesia: experience with mechanical injection devices. Can Anaesth Soc J. 1970;17(1):37-51. doi:10.1007/bf03004526.

78. Evans KR, Carrie LE. Continuous epidural infusion of bupivacaine in labour: A simple method. Anaesthesia. 1979;34(4):310-5. doi:10.1111/j.1365-2044.1979.tb04927.x.

79. Russell R, Reynolds F. Epidural infusion of low-dose bupivacaine and opioid in labour: Does reducing motor block increase the spontaneous delivery rate? Anaesthesia. 1996;51(3):266-73. doi:10.1111/j.1365-2044.1996.tb13645.x.

80. George RB, Allen TK, Habib AS. Intermittent epidural bolus compared with continuous epidural infusions for labor analgesia: A systematic review and meta-analysis. Anesth Analg. 2013;116(1):133-44. doi:10.1213/ANE.0b013e3182713b26.

81. Carvalho B, George RB, Cobb B, McKenzie C, Riley ET. Implementation of programmed intermittent epidural bolus for the maintenance of labor analgesia. Anesth Analg. 2016;123(4):965-71. doi:10.1213/ane.0000000000001407.

82. van der Vyver M, Halpern S, Joseph G. Patient-controlled epidural analgesia versus continuous infusion for labour analgesia: A meta-analysis. Br J Anaesth. 2002;89(3):459-65. doi:10.1093/bja/aef217.

83. Leo S, Ocampo CE, Lim Y, Sia AT. A randomized comparison of automated intermittent mandatory boluses with a basal infusion in combination with patient-controlled epidural analgesia for labor and delivery. Int J Obstet Anesth. 2010;19(4):357-64. doi:10.1016/j.ijoa.2010.07.006.

84. Vallejo MC, Ramesh V, Phelps AL, Sah N. Epidural labor analgesia: Continuous infusion versus patient-controlled epidural analgesia with background infusion versus without a background infusion. J Pain. 2007;8(12):970-5. doi:10.1016/j.jpain.2007.07.002.

85. Sezer OA, Gunaydin B. Efficacy of patient-controlled epidural analgesia after initiation with epidural or combined spinal-epidural analgesia. Int J Obstet Anesth. 2007;16(3):226-30. doi:10.1016/j.ijoa.2007.02.007.

86. Srivastava U, Gupta A, Saxena S, Kumar A, Singh S, Saraswat N, et al. Patient controlled epidural analgesia during labour: effect of addition of

background infusion on quality of analgesia & maternal satisfaction. Indian J Anaesth. 2009;53(6):649-53.

87. Boselli E, Debon R, Cimino Y, Rimmelé T, Allaouchiche B, Chassard D. Background infusion is not beneficial during labor patient-controlled analgesia with 0.1% ropivacaine plus 0.5 µg/ml sufentanil. Anesthesiology. 2004;100(4):968-72. doi:10.1097/00000542-200404000-00030.

88. Halpern SH, Carvalho B. Patient-controlled epidural analgesia for labor. Anesth Analg. 2009;108(3):921-8. doi:10.1213/ane.0b013e3181951a7f.

89. Bremerich DH, Waibel HJ, Mierdl S, Meininger D, Byhahn C, Zwissler BC, et al. Comparison of continuous background infusion plus demand dose and demand-only parturient-controlled epidural analgesia (PCEA) using ropivacaine combined with sufentanil for labor and delivery. Int J Obstet Anesth. 2005;14(2):114-20. doi:https://doi.org/10.1016/j.ijoa.2004.12.005.

90. Chua NP, Sia AT, Ocampo CE. Parturient-controlled epidural analgesia during labour: Bupivacaine vs. ropivacaine. Anaesthesia. 2001;56(12):1169-73. doi:10.1046/j.1365-2044.2001.02321.x.

91. Evron S, Glezerman M, Sadan O, Boaz M, Ezri T. Patient-controlled epidural analgesia for labor pain: Effect on labor, delivery and neonatal outcome of 0.125% bupivacaine vs 0.2% ropivacaine. Int J Obstet Anesth. 2004;13(1):5-10. doi:10.1016/S0959-289X(03)00092-X.

92. Bernard JM, Le Roux D, Vizquel L, Barthe A, Gonnet JM, Aldebert A, et al. Patient-controlled epidural analgesia during labor: The effects of the increase in bolus and lockout interval. Anesth Analg. 2000;90(2):328-32. doi:10.1097/00000539-200002000-00017.

93. Boutros A, Blary S, Bronchard R, Bonnet F. Comparison of intermittent epidural bolus, continuous epidural infusion and patient controlled-epidural analgesia during labor. Int J Obstet Anesth. 1999;8(4):236-41. doi:10.1016/S0959-289X(99)80103-4.

94. Lim Y, Sia AT, Ocampo CE. Comparison of computer integrated patient controlled epidural analgesia vs. conventional patient controlled epidural analgesia for pain relief in labour. Anaesthesia. 2006;61(4):339-44. doi:10.1111/j.1365-2044.2006.04535.x.

95. Nunes J, Nunes S, Veiga M, Cortez M, Seifert I. A prospective, randomized, blinded-endpoint, controlled study: Continuous epidural infusion versus programmed intermittent epidural bolus in labor analgesia. Braz J Anesthesiol. 2016;66(5):439-44. doi:10.1016/j.bjane.2014.12.006.

96. Kaynar AM, Shankar KB. Epidural infusion: Continuous or bolus? Anesth Analg. 1999;89(2):534. doi:10.1213/00000539-199908000-00063.

97. Segal S, Eappen S, Datta S. Superiority of multi-orifice over single-orifice epidural catheters for labor analgesia and cesarean delivery. J Clin Anesth. 1997;9(2):109-12. doi:https://doi.org/10.1016/S0952-8180(97)00232-8.

98. Gibiino G, Distefano R, Camorcia M, Capogna G. Maternal epidural pressure changes after programmed intermittent epidural bolus (PIEB) versus continuous epidural infusion (CEI). Eur J Anaesthesiol. 2014;31:183-4.

99. Tien M, Allen TK, Mauritz A, Habib AS. A retrospective comparison of programmed intermittent epidural bolus with continuous epidural infusion for maintenance of labor analgesia. Curr Med Res Opin. 2016;32(8):1435-40. doi:10.1080/03007995.2016.1181619.

100. Fettes PD, Moore CS, Whiteside JB, McLeod GA, Wildsmith JA. Intermittent vs continuous administration of epidural ropivacaine with fentanyl for analgesia during labour. Br J Anaesth. 2006;97(3):359-64. doi:10.1093/bja/ael157.

101. McKenzie CP, Cobb B, Riley ET, Carvalho B. Programmed intermittent epidural boluses for maintenance of labor analgesia: an impact study. Int J Obstet Anesth. 2016;26:32-8. doi:10.1016/j.ijoa.2015.11.005.

102. Lin Y, Li Q, Liu J, Yang R, Liu J. Comparison of continuous epidural infusion and programmed intermittent epidural bolus in labor analgesia. Ther Clin Risk Manag. 2016;12:1107-12. doi:10.2147/TCRM.S106021.

103. Lim Y, Sia AT, Ocampo C. Automated regular boluses for epidural analgesia: A comparison with continuous infusion. Int J Obstet Anesth. 2005;14(4):305-9. doi:10.1016/j.ijoa.2005.05.004.

104. Leonard TGA, Perrie H, Scribante J, Chetty S. An audit of the labour epidural analgesia service at a regional hospital in Gauteng Province, South Africa. SAJOG. 2018;24(2). doi:10.7196/sajog.1314.

105. Jacobs-Martin GG, Burke JL, Levin AI, Coetzee AR. Labour epidural analgesia audit in a tertiary state hospital in South Africa. South Afr J Anaesth Analg 2014;20(4):174-8. doi:http://dx.doi.org/10.1080/22201181.2015.959344.

106. Ferrer LE, Romero DJ, Vasquez OI, Matute EC, Van de Velde M. Effect of programmed intermittent epidural boluses and continuous epidural infusion on labor analgesia and obstetric outcomes: A randomized controlled trial. Arch Gynecol Obstet. 2017;296(5):915-22. doi:10.1007/s00404-017-4510-x.

Section 2: Author's guidelines

Southern African Journal of Anaesthesia and Analgesia (SAJAA)

How to submit your paper online:

1. Registered authors must login to submit a paper
    1. REGISTER HERE if you do not have a username and password
    2. LOGIN HERE if you have already registered with SAJAA
2. Select Author
3. Click on CLICK HERE TO FOLLOW THE FIVE STEPS TO SUBMIT YOUR MANUSCRIPT
4. Follow the five steps to submit your paper
5. To view a video on how to submit a paper online CLICK HERE
6. To download instructions to authors CLICK HERE

Review policy and timelines

1. Immediate notification if submitted successfully
2. Notification within 3 weeks if not accepted for further review
3. Notification within 3 months if accepted for publication, if revisions are required or if rejected by both reviewers.
4. Publication within 6 months after submission.

Aims, scope and review policy

The *SA Journal of Anaesthesia and Analgesia* aims to publish original research and review articles of relevance and interest to the anaesthetist in academia, public sector and private practice. Papers are peer reviewed to ensure that the contents are understandable, valid, important, interesting and enjoyed. All manuscripts must be submitted online.

SAJAA is accredited by the Department of Education for the measurement of research output of public higher institutions of South Africa (SAPSE accredited). All articles in SAJAA will be peer reviewed.

Article sections and length

The following contributions are accepted (word counts exclude abstracts, tables and references):

- **Original Research** (2 800 – 3 200 words / 4-5 pages)
- **Clinical Reviews** (2 400 words / 3-4 pages)
- **Drug Reviews** (2 400 words / 3-4 pages)
- **Case Studies** (1 800 words / 3 pages)
- **Scientific Letters** (2 400 words / 3-4 pages)
- **Letters to the Editor** (400-800 words]

Please see the journal's section policies section policies for further details.

FULL AUTHOR GUIDELINES

Title page

All articles must have a title page with the following information and in this particular order: Title of the article; surname, initials, qualifications and affiliation of each author; The name, postal address, e-mail address and telephonic contact details of the corresponding author and at least 5 keywords.

Abstract

All articles should include an abstract. The structured abstract for an Original Research article should be between 300 words and should consist of four paragraphs labelled Background, Methods, Results, and Conclusions. It should briefly describe the problem or issue being addressed in the study, how the study was performed, the major results, and what the authors conclude from these results. The abstracts for other types of articles should be no longer than 250 words and need not follow the structured abstract format.

Keywords

All articles should include keywords. Up to five words or short phrases should be used. Use terms from the Medical Subject Headings (MeSH) of Index Medicus

when available and appropriate. Key words are used to index the article and may be published with the abstract.

Acknowledgements

In a separate section, acknowledge any financial support received or possible conflict of interest. This section may also be used to acknowledge substantial contributions to the research or preparation of the manuscript made by persons other than the authors.

References

Cite references in numerical order in the text, in superscript format (Format> Font> Click superscript). Please do not use brackets or do not use the foot note function of MS Word.

In the References section, references must be typed double-spaced and numbered consecutively in the order in which they are cited, not alphabetically.

The style for references should follow the format set forth in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org) prepared by the International Committee of Medical Journal Editors. Abbreviations for journal titles should follow Index *Medicus* format. Authors are responsible for the accuracy of all references. Personal communications and unpublished data should not be referenced. If essential, such material should be incorporated in the appropriate place in the text.

List all authors when there are six or fewer; when there are seven or more, list the first three, then “;et al.”; When citing URLs to web documents, place in the reference list, and use the following format: Authors of document (if available). Title of document (if available). URL. (Accessed [date]).

The following are sample references:

1. Jun BC, Song SW, Park CS, Lee DH, Cho KJ, Cho JH. The analysis of maxillary sinus aeration according to aging process: volume assessment by 3-

dimensional reconstruction by high-resolutional CT scanning. Otolaryngol Head Neck Surg. 2005 Mar;132(3):429-34.

2. Polgreen PM, Diekema DJ, Vandeberg J, Wiblin RT, Chen YY, David S, et al. Risk factors for groin wound infection after femoral artery catheterization: a case-control study. Infect Control Hosp Epidemiol [Internet]. 2006 Jan [cited 2007 Jan 5];27(1):34-7. Available from: http://www.journals.uchicago.edu/ICHE/journal/issues/v27n1/2004069/2004069.web. pdf.

More sample references can be found at:

http://www.nlm.nih.gov/bsd/uniform_requirements.html

Tables

Tables should be self-explanatory, clearly organised, and supplemental to the text of the manuscript. Each table should include a clear descriptive title on top and numbered in Roman numerals (I, II, etc) in order of its appearance as called out in text. Tables must me inserted in the correct position in the text. Authors should place explanatory matter in footnotes, not in the heading. Explain in footnotes all non-standard abbreviations.

For footnotes use the following symbols, in sequence:*,†,‡,§,||,**,††,‡‡

Figures

All figures must be inserted in the appropriate position of the electronic document. Symbols, lettering, and numbering (in Arabic numerals e.g. 1, 2, etc. in order of appearance in the text)

should be placed below the figure, clear and large enough to remain legible after the figure has been reduced. Figures must have clear descriptive titles.

Photographs and images

If photographs of patients are used, either the subject should not be identifiable or use of the picture should be authorised by an enclosed written permission from the subject. The position of photographs and images should be clearly indicated in the

text. Electronic images should be saved as either jpeg or gif files. All photographs should be scanned at a high resolution (300dpi, print optimised). Please number the images appropriately.

Permission

Permission should be obtained from the author and publisher for the use of quotes, illustrations, tables, and other materials taken from previously published works, which are not in the public domain. The author is responsible for the payment of any copyright fee(s) if these have not been waived. The letters of permission should accompany the manuscript. The original source(s) should be mentioned in the figure legend or as a footnote to a table.

Review and action

Manuscripts are initially examined by the editorial staff and are usually sent to independent reviewers who are not informed of the identity of the author(s). When publication in its original form is not recommended, the reviewers' comments (without the identity of the reviewer being disclosed) may be passed to the first author and may include suggested revisions. Manuscripts not approved for publication will not be returned.

Ethical considerations

Papers based on original research must adhere to the Declaration of Helsinki on "Ethical Principles for Medical Research Involving Human Subjects"; and must specify from which recognised ethics committee approval for the research was obtained.

Conflict of interest

Authors must declare all financial contributions to their work or other forms of conflict of interest, which may prevent them from executing and publishing unbiased research. [Conflict of interest exists when an author (or the author's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her opinions or actions.] **Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability.

(Editorial) JAMA 2001: 286(10) The following declaration may be used if appropriate: “I declare that I have no financial or personal relationship(s) which may have inappropriately influenced me in writing this paper.”

Submissions and correspondence

All submissions must be made online at www.sajaa.co.za and correspondence regarding manuscripts should be addressed to:

The Editor, SAJAA, E-mail: toc@sajaa.co.za

Note: Ensure that the article ID [reference] number is included in the subject of your email correspondence.

Electronic submissions by post or via email

Authors with no e-mail or internet connection can mail their submissions on a CD to: SAJAA, PO Box 14804, Lyttelton Manor, 0140, Gauteng, South Africa.

All manuscripts will be processed online. Submissions by post or by e-mail must be accompanied by a signed copy of the following indemnity and copyright form. CLICK HERE to download and save it to your computer.

Submissions by email should be send as an attachment to

Tips on Preparing your manuscript

1. Please consult the “Uniform requirements for manuscripts submitted to biomedical journals” at www.icmje.org
2. Please consult the guide on Vancouver referencing methods at: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=citmed.TOC&depth=2
3. The submission must be in UK English, typed in Microsoft Word or RTF with no double spaces after the full stops, double paragraph spacing, font size 10 and font type: Times New Roman.
4. All author details (Full names, Qualifications and affiliation) must be provided.
5. The full contact details of corresponding author (Tel, fax, e-mail, postal address) must be on the manuscript.
6. There must be an abstract and keywords.

7. References must strictly be in Vancouver format. (Reference numbers must be strictly numerical and be typed in superscript, not be in brackets and must be placed AFTER the full stop or comma.)
8. It must be clear where every figure and table should be placed in the text. If possible, tables and figures must be placed in the text where appropriate. If too large or impractical, they may be featured at the end of the manuscript or uploaded as separate supplementary files.
9. All photographs must be at 300dpi and clearly marked according to the figure numbers in the text. (Figure 1, Table II, etc.)
10. All numbers below ten, without percentages or units, must be written in words.
11. Figure numbers: Arabic, table numbers: Roman

Section 3: Draft article

Comparison between two epidural analgesia maintenance techniques at a regional hospital

Mathabe Sehlapelo, MBChB, DA (SA), FCA (SA)

Helen Perrie, MSc

Juan Scribante, PhD

Janine Wagner, MBChB, DA (SA), FCA (SA)

Department of Anaesthesiology, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand

Corresponding Author

Dr. Mathabe Sehlapelo

Department of Anaesthesiology
Chris Hani Baragwanath Academic Hospital
26 Chris Hani Rd
Diepkloof, Soweto
Johannesburg
1860

mmathabe@yahoo.com

011 933 1843

Key words: Labour epidural, Programmed intermittent epidural bolus, continuous epidural infusion, patient satisfaction, motor blockade

Abstract

Background

Maintaining a labour epidural with programmed intermittent epidural bolus (PIEB) with patient controlled epidural analgesia (PCEA) using automated pumps has been shown to be beneficial compared to continuous epidural infusion (CEI) with intermittent epidural bolus (IEB). The aim of the study was to compare these two techniques for labour analgesia with regards to haemodynamics, drug consumption, motor blockade, mode of delivery and to describe patient satisfaction and adverse effects.

Methods

A prospective, contextual and comparative study was used. One hundred and twenty patients in the active phase of labour were recruited. Participants were randomly assigned to either the CEI with IEB (Group A, n = 60) or PIEB with PCEA (Group B, n = 60). The labour epidural was activated and maintained with bupivacaine 0.0625% and fentanyl 2 ug/ml. Achieving a bilateral T10 sensory level and a visual analogue score less than 30 mm was considered as Time Zero (T0), this timing was continued until delivery.

Results

There were no significant differences in participants' characteristics between the groups. A higher percentage of satisfaction was recorded in Group B. Hypotension occurred significantly more often in Group A ($p = 0.002$). Group B had less drug consumption ($p < 0.01$), rescue boluses ($p < 0.01$) and motor blockade ($p = 0.02$). Group A had more assisted deliveries ($p = 0.01$). Adverse effects occurred similarly in both groups.

Conclusion

PIEB with PCEA for maintenance of labour epidural analgesia results in better participant satisfaction, more cardiovascular stability, less drug consumption and less motor blockade with more unassisted deliveries. Labour epidural analgesia techniques using algorithms are proving to be superior to other maintenance techniques. Although more costly, PIEB with PCEA appears to convey benefits.

Introduction

Labour pain is an unpleasant, subjective, emotional and complex experience (1, 2). It is a dynamic process and the perception of its severity can be affected by various factors (3, 4). Severe uncontrolled labour pain is associated with numerous maternal and foetal psychological and physiological adverse effects and as a result of this labour analgesia should be offered (3-5). Neuraxial techniques, particularly epidural analgesia, have been recognised as the gold standard for providing labour analgesia (5-9). The primary goal is to provide adequate, safe (6, 10), reliable and reproducible maternal analgesia with minimal motor blockade (11, 12), less haemodynamic instability and fewer adverse effects (3, 10, 13).

Once labour epidural analgesia has been established, it requires maintenance until completion of labour. The techniques employed for maintenance include intermittent epidural boluses (IEB) also referred to as manual boluses, patient controlled epidural analgesia (PCEA), continuous epidural infusion (CEI) and programmed intermittent epidural boluses (PIEB) with or without PCEA (6, 10, 12, 14). Each maintenance technique has advantages and disadvantages (5, 6, 15-19).

IEB is generally a safe, reproducible and cost-effective technique as it does not require automated pumps, but it is associated with haemodynamic instability and is labour intensive (17). PCEA as the sole technique may be compared to IEB. PCEA offers patients autonomy to deliver medication to themselves with a lockout time, but is associated with breakthrough pain and increased requirements for rescue boluses as compared to IEB (19). CEI offers a consistent level of analgesia and a decreased workload for the treating anaesthetist but is associated with increased local anaesthetic consumption and therefore an increased risk of motor blockade (6, 11, 17, 18).

PIEB with a PCEA employs an automated pump with set algorithms to deliver a premixed local anaesthetic and opioid mixture through the epidural catheter at a fixed calculated dose and at scheduled intervals. It is hypothesised that due to its nature of delivery it offers numerous benefits over the other techniques (6, 11, 12, 20-22). Capogna et al. (11) demonstrated a decreased consumption of local

anaesthetic and therefore less motor blockade with PIEB (11). Wong et al. (12) compared PIEB to CEI and found that PIEB demonstrated less local anaesthetic consumption, fewer rescue boluses for breakthrough pain, a lower incidence of motor blockade, fewer assisted and operative deliveries and better maternal satisfaction when using the visual analogue scale (VAS) (12).

It has been shown that the technique of PIEB with PCEA using automated pumps is beneficial to the parturient and foetus in terms of maternal satisfaction, local anaesthetic consumption, less motor blockade and fewer subsequent rescue boluses as compared with CEI (11, 12, 14, 23). PIEB is costly compared to CEI and although the equipment is available at Rahima Moosa Mother and Child Hospital (RMMCH) it is not often used due to the unavailability and high cost of consumables. At RMMCH, CEI is currently the epidural analgesia maintenance technique of choice and it is not known whether the benefits of PIEB with PCEA outweigh the cost. The aim of the study was to compare CEI with IEB to PIEB with PCEA for labour analgesia at RMMCH. The techniques were compared with regards to haemodynamics, drug consumption, motor blockade and mode of delivery. Patient satisfaction and adverse effects were described.

Methods

Approval was obtained from the Human Research Ethics Committee (Medical) and other relevant authorities. A prospective, contextual, comparative research design was followed in this study.

The study was conducted from 03 August to 16 December 2018. The study population included patients in active labour admitted to the labour ward at RMMCH. A convenience sampling method was used. Once participants were enrolled in the study, they were randomly assigned to one of the two treatment groups using simple random sampling. A consecutively numbered envelope containing the group assignment (a computer generated randomly numbered sequence) was opened by the researcher at the time of randomisation. Participants receiving CEI with IEB were allocated to Group A and those receiving PIEB with PCEA to Group B. The sample size was determined in consultation with a biostatistician. A sample size of 59 participants per group was determined based on a reduction of 60% in the VAS score at two and a half hours starting with a

mean of 12.17 and a SD of 14.00 using a study (24) that compared CEI with IEB to PIEB with PCEA with similar objectives powered to 80% with, a significance level set to 0.05. Inclusion criteria in this study were term ASA I and II patients in the active phase of labour with a cephalic presentation. Exclusion criteria were participants with known neurological disease, psychiatric disease, allergy to local anaesthetic and opioids, weight greater than 110 kg, height less than 140 cm and foetal heart rate abnormalities.

The insertion of the epidural catheter in both groups followed the current practice at RMMCH. The epidural catheter was placed according the South African Society of Anaesthesiologist Regional Anaesthesia Guidelines (25). Insertion of the epidural catheter and collection of data were performed by one author (MS) and a trained research assistant who was an anaesthetist rotating through the pain service. Insertion of the labour epidural catheter was standardised. A pre-procedural (preload) intravenous fluid bolus of 10 ml/kg of a crystalloid was infused over 20 − 30 minutes using an 18 − 20G cannula. A midline approach using an 18 – 20G Perifix® B/Braun multi-orifice epidural catheter was used. Normal saline was used for the loss of resistance technique to identify the epidural space. The catheter was threaded 6 cm into the epidural space.

A mixture consisting of bupivacaine 0.0625% and fentanyl 2 ug/ml was used for loading the epidural. All participants received a 10 ml bolus loading dose of the mixture. Further doses of the epidural mixture were titrated according to block height. Achieving a bilateral T10 sensory level and a VAS score less than 30 mm was considered as Time Zero (T0). T1 was one hour after the sensory level was determined to be at the T10 dermatome, T2 was two hours after this. This timing was continued until time of delivery. The Alaris® CC Syringe Pump (Carefusion) was used for Group A and the CADD®-Solis pump (Smiths Medical) for Group B. In Group A the infusion was started at T0 at 8 ml/hr and titrated to the participants' sensory level. Rescue boluses of 5 ml were given for breakthrough pain, considered as a VAS score greater than 30 mm. The IEB and PCEA were regarded as rescue boluses, and the sensory level was re-assessed prior to administration of any intermittent or top up boluses. In Group B the pump delivered 10 ml of the epidural mixture once every hour from 60 minutes after T0. The pump

allowed patient activated boluses of 5 ml with a lockout time of 10 minutes to a maximum volume of 15 ml per hour.

Patient satisfaction was measured using the VAS. Haemodynamic instability was defined in the study as a 20% drop in the non-invasive mean arterial pressure (MAP). Motor blockade was defined as any degree of motor block in one or both lower limbs at any time during labour as described using the Bromage score. In this study the mode of delivery was divided into unassisted and assisted delivery. Unassisted being a normal vaginal delivery and assisted being a vaginal delivery with either forceps or vacuum, or a caesarean section.

All data were entered onto a Microsoft Excel® spreadsheet and analysed in consultation with a biostatistician. The statistical programme STATA® version 15 was used. Categorical variables were described using frequency and percentages. Continuous variables which were normally distributed were described using means and standard deviations and those not normally distributed using medians and interquartile ranges. Comparisons between groups depending on distribution were made using unpaired t- tests or Mann-Whitney U-tests. Comparison between the groups with regards to haemodynamics and motor blockade were censored using log-rank tests. The censored data were represented using the Kaplan-Meier survival curves. A p value of <0.05 was considered statistically significant.

Results

One hundred and twenty participants were recruited and randomised to Group A and Group B with 60 participants in each group. Participants' characteristics are shown in Table I. There were no significant differences between the groups.

Table I - Participants' characteristics

Participants' characteristics	Group A Mean (SD)	Group B Mean (SD)	p value
Age (years)	26.6 (5.8)	26.8 (6.3)	0.85
Parity	0.7 (0.7)	0.8 (1.0)	0.35
BMI ($kg/m^{2)}$	28.6 (4.8)	28.8 (3.7)	0.76
Cervical dilation (cm)	5 (1.1)	4.7 (0.8)	0.07
VAS (mm)	93.5 (6.0)	93.0 (7.8)	0.66
Duration of labour (hours)	4.0 (1.7)	3.8 (1.9)	0.55
Gestational age (weeks)	38.6 (4.8)	39.2 (1.0)	0.41
Mean arterial pressure (mmHg)	91.8 (6.9)	93.6 (10.0)	0.24
Thoracic sensory level post insertion	8.7 (0.8)	8.5 (0.8)	0.19

Participants' satisfaction at different time intervals is shown in Table II. The number of participants was censored due to delivery. The maximum VAS score is reported per time interval. A higher percentage of participants in Group B were satisfied at all time intervals.

Table II - Participants' satisfaction at different time intervals

	Group A			Group B		
Time	**n**	**VAS <30 mm n (%)**	**Max VAS score (mm)**	**n**	**VAS <30 mm n (%)**	**Max VAS score (mm)**
T1	60	53 (88.3)	42	60	59 (98.3)	73
T2	60	46 (76.7)	50	60	59 (98.3)	10
T3	50	32 (64.0)	55	42	40 (95.2)	30
T4	29	21 (72.4)	85	25	25 (100)	0
T5	19	12 (63.2)	90	15	15 (100)	6
T6	11	7 (63.6)	90	9	9 (100)	0
T7	5	4 (80.0)	4	6	6 (100)	0
T8	4	4 (100)	20	5	5 (100)	0

A drop of 20% in MAP occurred at least once during labour in 27% of participants in Group A and in 5% of participants in Group B ($p = 0.002$). The combined group incidence was 15.8%. Proportions of participants from Group A and Group B who had a 20% drop in MAP are represented in Figure 1. MAP versus time after induction of labour analgesia was censored due to delivery ($p < 0.001$). The Kaplan-Meier curve demonstrates that time to event (drop in MAP) occurred earlier (T2) in Group A. The more time the participants in Group A continued in the study, the more likely that the event (drop in MAP) would occur.

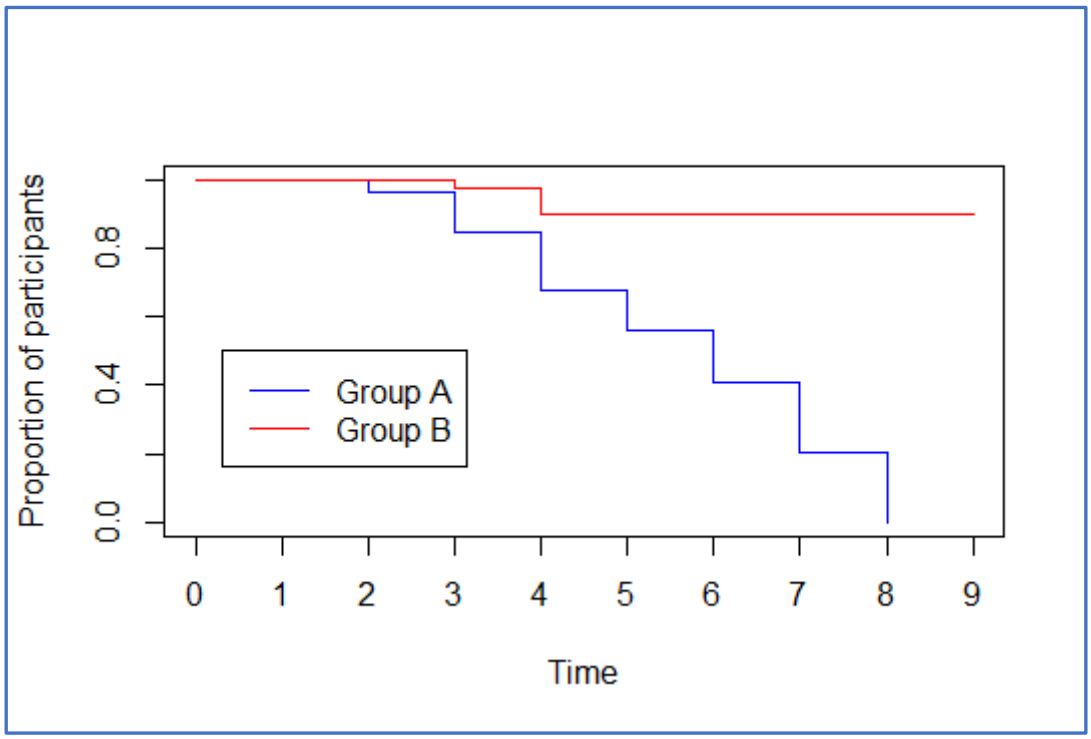


Figure 1- Drop in MAP censored due to delivery

Total bupivacaine and fentanyl consumption and rescue boluses required are reported in Table III. The bupivacaine and fentanyl consumption and rescue boluses required were significantly different between the groups.

Table III - Drug consumption

	Group A	Group B	p value
Bupivacaine (mg) Mean (SD)	31.7 (13.9)	25 (13.1)	<0.01
Fentanyl (mcg) Mean (SD)	101.3 (44.4)	80.2 (42.0)	<0.01
Rescue bolus required (proportions)	0.70	0.35	<0.01

Motor block occurred at least once during labour in 43% of participants in Group A and 21% in Group B (p = 0.02). Proportions of participants from Group A and Group B who had a motor block are shown in Figure 2. Motor block versus time after induction of labour analgesia was censored due to delivery (p = 0.002). The Kaplan-Meier curve demonstrates that time to event (motor block) occurred at the

same time (T1) between the groups. The more time the participants in Group A continued in the study, the more likely that the event (motor blockade) would occur.

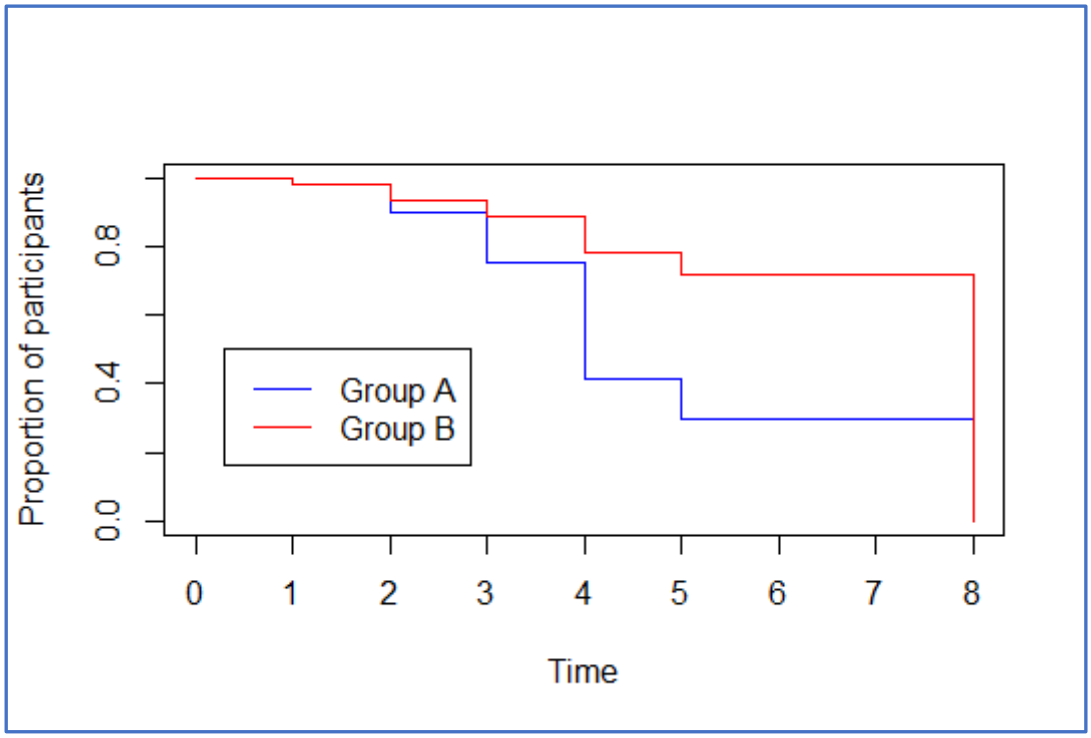


Figure 2 – Motor block censored due to delivery

Comparison between groups regarding mode of delivery is demonstrated in Table IV. In Group A had 7 (12%) participants had having an instrumental delivery, whereas in Group B no participants required an instrumental delivery.

Table IV - Mode of delivery

Mode of delivery	Group A n (%)	Group B n (%)	P value
Unassisted delivery	30 (50)	44 (73)	0.01
Caesarean section	23 (38)	16 (27)	0.24

The incidence of adverse effects was similar between the two groups and is shown in Table V.

Table V - Incidence of adverse effect

Adverse effects	Group A	Group B
	n (%)	
Pruritus	2 (3.3)	1 (1.7)
Shivering	4 (6.7)	5 (8.3)
Nausea and vomiting	7 (11.7)	9 (15.0)
Maternal pyrexia	2 (3.3)	3 (5.0)

Discussion

Participants in Group B (PIEB with PCEA) were more satisfied with their pain management than those in Group A (CEI with IEB). Leo et al. (26) and Sia et al. (27) comparing the same techniques as in our study similarly reported a higher overall patient satisfaction in patients that received PIEB with PCEA. Wong et al. (12) comparing CEI with PCEA to PIEB with PCEA also found a higher overall patient satisfaction in the latter group. A possible explanation is that in our study a multi-orifice epidural catheter was used. This type of catheter has been shown to give better sensory blockade (28, 29) and has differential flow (30). However, it has been shown that CEI has a low injection pressure and flow, with flow only in the proximal port and not the distal port, hence acting as a single orifice catheter. On the other hand PIEB shows the expected differential flow rate with a wider spread and better sensory blockade and better participant satisfaction (30).

The overall incidence of a 20% drop in MAP in our study was 15.8%. This is similar to incidences of 12.3% and 13.4% reported by Leonard et al. (31) and Jacobs-Martin et al. (32), respectively. However, when comparing CEI with IEB to PIEB with PCEA in our study, there was a significant difference. Group A had a 27% incidence of participants who had a 20% drop in MAP as opposed to the 5%

in Group B. This significant difference is not demonstrated in the literature. Ferrer et al. (33) compared CEI with PCEA to PIEB with PCEA and showed no significant difference between the groups. Leo et al. (26) in a study similar to ours showed no difference between the groups. This could be due to the increased drug consumption, rescue boluses and motor block in Group A which may have contributed to a sympathectomy with subsequent vasodilation of the venous capacitance vessels and drop in blood pressure.

Total bupivacaine and fentanyl consumption and rescue boluses were significantly reduced in Group B. The reduction in rescue boluses in Group B implies that PIEB with PCEA reduces the risk of breakthrough pain. Fidkowski et al. (34) compared three groups, CEI with IEB to two different PIEB regimens, that is PIEB with PCEA 5 ml every 30 minutes and 10 ml every 60 minutes. Their study showed that the PIEB regimen with higher volumes and longer intervals reduces rescue boluses and therefore breakthrough pain. In a study similar to ours, Fettes et al. (35) showed that participants using CEI with IEB needed three times more rescue boluses. The wider spread and better sensory blockade with PIEB may be responsible.

Participants in Group B had significantly less motor blockade than those in Group A. Capogna et al. (11) compared CEI with PCEA to PIEB with PCEA, using an epidural mixture containing levobupivacaine 0.0625% and sufentanil 0.5 ug/ml. Their study reported a 37% incidence of motor blockade when CEI with PCEA was used and 2.7% in the latter, this difference was statistically significant. Bullingham et al. (36) compared CEI to PIEB with PCEA using ropivacaine and reported a 21.8% lower limb weakness with CEI and 1% with PIEB with PCEA. This could be due to the fact that PIEB is injected at higher pressures than CEI and therefore produces a more uniform spread in the epidural space (30, 37). PIEB creates a greater diffusion gradient around the nerve cell than CEI. This allows the local anaesthetic to enter the nerve cell rapidly producing an effective sensory block and with time to exit the nerve cell decreasing the motor blockade (6).

It is important to note that Capogna et al. (11) used the Breen modified Bromage score which is more sensitive than the Bromage score used by Bullingham et al. (36) and in our study. Both studies found the incidences for motor blockade for the

PIEB with PCEA were lower than in our study. The different type and concentrations of the local anaesthetic agent used may have resulted in this difference. Atienzar et al. (38) compared levobupicaine, bupivacaine and ropivacaine with fentanyl for labour analgesia and showed that motor blockade was significantly higher with bupivacaine compared to levobupicaine between the groups. When levobupivacaine was compared to ropivacaine no difference in motor blockade between the groups was found (38).

In our study participants in Group B had significantly fewer assisted deliveries and caesarean sections. George et al. (39) performed a systematic review comparing CEI to PIEB for labour analgesia. Their review looked at nine randomised controlled trials and showed no significant difference in instrumental delivery and caesarean sections between the groups. Sng et al. (23) performed a systematic review comparing automated mandatory bolus to basal infusions. The data of 11 randomised controlled trials was pooled and showed no significant differences between the two techniques with regards to instrumental deliveries and caesarean sections (23). This was, however, different to the study by Capogna et al. (11) which was specifically powered to detect the difference between CEI with PCEA and PIEB with PCEA with regards to motor blockade and instrumental deliveries. Motor blockade interferes with the bearing down reflex and failure of the foetal head to internally rotate (40).

Pruritus, shivering, nausea and vomiting and maternal pyrexia was experienced similarly in both groups in our study. Leo et al (26) described similar adverse effects. PIEB with PCEA in their study had a decreased proportion of participants who had pruritis and shivering but more maternal pyrexia. Interesting to note is that in their study there was no participant that had nausea and vomiting between the groups. The reasonable explanation is that during our study period there was a month that RMMCH had oxytocin shortages and syntometrine was used. One of the described side effects of syntometrine is nausea and vomiting.

There are potential limitations to our study. The study was contextual in that the population is limited to the labour ward of RMMCH. The results may therefore not be generalised to other hospitals. The decision for instrumental delivery and

caesarean section were made by the treating obstetrician with varying institutional practices.

Conclusion

PIEB with PCEA for maintenance of labour epidural analgesia results in better participant satisfaction, more cardiovascular stability, less drug consumption and less motor blockade with more unassisted deliveries. The benefits of this technique are not only patient centred but also for the health care team, it decreases the workload. With research being done around PIEB, the algorithms are proving to be superior as opposed to the other maintenance techniques. Even though PIEB with PCEA is costly the benefits do outweigh the cost.

Conflict of interest

The authors declare that we have no financial or personal relationships which may have inappropriately influenced us in writing this paper.

Acknowledgement

This research was done in partial fulfilment of a Master of Medicine degree.

References

1. Jones L. Pain management for women in labour: An overview of systematic reviews. Int J Evid Based Healthc. 2012;5(2):101-2. doi:10.1002/14651858.CD009234.pub2.

2. Lowe NK. The nature of labor pain. Am J Obstet Gynecol. 2002;186(5):S16-S24. doi:10.1016/S0002-9378(02)70179-8.

3. Miller RD. Miller's Anesthesia. 8th ed. Philadelphia, PHL: Churchill Livingstone; 2015.

4. Morgan GE, Mikhail MS. Clinical Anesthesiology. 5th ed. New York, NY: McGraw Hill 2006.

5. Reena KH, Bandyopadhyay MA, Mishra AP. Labor epidural analgesia: Past, present and future. Indian Journal of Pain. 2014;28(2):71. doi:10.4103/0970-5333.132843.

6. Capogna G, Stirparo S. Techniques for the maintenance of epidural labor analgesia. Curr Opin Anaesthesiol. 2013;26(3):261-7. doi:10.1097/ACO.0b013e328360b069.

7. Ogboli-Nwasor E, Adaji S, Bature S, Shittu O. Pain relief in labor: A survey of awareness, attitude, and practice of health care providers in Zaria, Nigeria. J Pain Res. 2011;4:227-32. doi:10.2147/JPR.S21085.

8. Findley I, Chamberlain G. Relief of pain. BMJ. 1999;318(7188):927-30. doi:10.1136/bmj.318.7188.927.

9. Hawkins JL. Epidural analgesia for labor and delivery. N Engl J Med. 2010;362(16):1503-10. doi:10.1056/NEJMct0909254.

10. American Society of Anesthesiologists. Practice guidelines for obstetric anesthesia: An updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. Anesthesiology. 2016;124(2):270-300. doi:10.1097/ALN.0000000000000935.

11. Capogna G, Camorcia M, Stirparo S, Farcomeni A. Programmed intermittent epidural bolus versus continuous epidural infusion for labor analgesia: The effects on maternal motor function and labor outcome. A randomized double-blind study in nulliparous women. Anesth Analg. 2011;113(4):826-31. doi:10.1213/ANE.0b013e31822827b8.

12. Wong CA, Ratliff JT, Sullivan JT, Scavone BM, Toledo P, McCarthy RJ. A randomized comparison of programmed intermittent epidural bolus with continuous epidural infusion for labor analgesia. Anesth Analg. 2006;102(3):904-9. doi:10.1213/01.ane.0000197778.57615.1a.

13. McGrady E, Litchfield K. Epidural analgesia in labour. Br J Anaesth. 2004;4(4):114-7. doi:10.1093/bjaceaccp/mkh030.

14. Gupta S, Partani S. Neuraxial techniques of labour analgesia. Indian J Anaesth. 2018;62(9):658-66. doi:10.4103/ija.IJA_445_18.

15. Boselli E, Debon R, Cimino Y, Rimmelé T, Allaouchiche B, Chassard D. Background infusion is not beneficial during labor patient-controlled analgesia with 0.1% ropivacaine plus 0.5 μg/ml sufentanil. Anesthesiology. 2004;100(4):968-72. doi:10.1097/00000542-200404000-00030.

16. Boutros A, Blary S, Bronchard R, Bonnet F. Comparison of intermittent epidural bolus, continuous epidural infusion and patient controlled-epidural analgesia during labor. Int J Obstet Anesth. 1999;8(4):236-41. doi:10.1016/S0959-289X(99)80103-4.

17. McGrady E, Litchfield K. Epidural analgesia in labour. Continuing Education in Anaesthesia Critical Care & Pain. 2004;4(4):114-7. doi:10.1093/bjaceaccp/mkh030.

18. Silva M, Halpern SH. Epidural analgesia for labor: Current techniques. Local Reg Anesth. 2010;3:143-53. doi:10.2147/LRA.S10237.

19. Srivastava U, Gupta A, Saxena S, Kumar A, Singh S, Saraswat N, et al. Patient controlled epidural analgesia during labour: Effect of addition of background Infusion on quality of analgesia & maternal satisfaction. Indian J Anaesth. 2009;53(6):649-53.

20. Nunes J, Nunes S, Veiga M, Cortez M, Seifert I. A prospective, randomized, blinded-endpoint, controlled study: Continuous epidural infusion versus programmed intermittent epidural bolus in labor analgesia. Braz J Anesthesiol. 2016;66(5):439-44. doi:10.1016/j.bjane.2014.12.006.

21. Onuoha OC. Epidural analgesia for labor: Continuous infusion versus programmed intermittent bolus. Anesthesiol Clin. 2017;35(1):1-14. doi:10.1016/j.anclin.2016.09.003.

22. Wong CA, McCarthy RJ, Hewlett B. The effect of manipulation of the programmed intermittent bolus time interval and injection volume on total drug use for labor epidural analgesia: A randomized controlled trial. Anesth Analg. 2011;112(4):904-11. doi:10.1213/ANE.0b013e31820e7c2f.

23. Sng BL, Zeng Y, de Souza NNA, Leong WL, Oh TT, Siddiqui FJ, et al. Automated mandatory bolus versus basal infusion for maintenance of epidural analgesia in labour. Cochrane Database Syst Rev. 2018;5:Cd011344. doi:10.1002/14651858.CD011344.pub2.

24. Mukherjee S, Das S, Mukhopadhyay S, Basu SR. Comparison between continuous epidural infusion and intermittent epidural bolus of bupivacaine fentanyl combination for labour analgesia. Sch J App Med Sci. 2013;1(6):953-8.

25. South African Society of Anaesthesiologists. Guidelines for Regional Anaesthesia in South Africa. Available from: https://sasaapi.sasaweb.com/Document/SASRAguidelines2016_636722590664755485.pdf [date accessed 26 August 2017.

26. Leo S, Ocampo CE, Lim Y, Sia AT. A randomized comparison of automated intermittent mandatory boluses with a basal infusion in combination with patient-controlled epidural analgesia for labor and delivery. Int J Obstet Anesth. 2010;19(4):357-64. doi:10.1016/j.ijoa.2010.07.006.

27. Sia AT, Leo S, Ocampo CE. A randomised comparison of variable-frequency automated mandatory boluses with a basal infusion for patient-controlled epidural analgesia during labour and delivery. Anaesthesia. 2013;68(3):267-75. doi:10.1111/anae.12093.

28. Segal S, Eappen S, Datta S. Superiority of multi-orifice over single-orifice epidural catheters for labor analgesia and cesarean delivery. J Clin Anesth. 1997;9(2):109-12. doi:https://doi.org/10.1016/S0952-8180(97)00232-8.

29. D'Angelo R, Foss ML, Livesay CH. A comparison of multiport and uniport epidural catheters in laboring patients. Anesth Analg. 1997;84(6):1276-9. doi:10.1097/00000539-199706000-00019.

30. Kaynar AM, Shankar KB. Epidural infusion: Continuous or bolus? Anesth Analg. 1999;89(2):534. doi:10.1213/00000539-199908000-00063.

31. Leonard TGA, Perrie H, Scribante J, Chetty S. An audit of the labour epidural analgesia service at a regional hospital in Gauteng Province, South Africa. SAJOG. 2018;24(2). doi:10.7196/sajog.1314.

32. Jacobs-Martin GG, Burke JL, Levin AI, Coetzee AR. Labour epidural analgesia audit in a tertiary state hospital in South Africa. South Afr J Anaesth Analg 2014;20(4):174-8. doi:http://dx.doi.org/10.1080/22201181.2015.959344.

33. Ferrer LE, Romero DJ, Vasquez OI, Matute EC, Van de Velde M. Effect of programmed intermittent epidural boluses and continuous epidural infusion on labor analgesia and obstetric outcomes: A randomized controlled trial. Arch Gynecol Obstet. 2017;296(5):915-22. doi:10.1007/s00404-017-4510-x.

34. Fidkowski CW, Shah S, Alsaden M-R. Programmed intermittent epidural bolus as compared to continuous epidural infusion for the maintenance of labor analgesia: a prospective randomized single-blinded controlled trial. Korean J Anesthesiol. 2019;72(5):472-8. doi:10.4097/kja.19156.

35. Fettes PD, Moore CS, Whiteside JB, McLeod GA, Wildsmith JA. Intermittent vs continuous administration of epidural ropivacaine with fentanyl for analgesia during labour. Br J Anaesth. 2006;97(3):359-64. doi:10.1093/bja/ael157.

36. Bullingham A, Liang S, Edmonds E, Mathur S, Sharma S. Continuous epidural infusion vs programmed intermittent epidural bolus for labour

analgesia: a prospective, controlled, before-and-after cohort study of labour outcomes. Br J Anaesth. 2018;121(2):432-7. doi:https://doi.org/10.1016/j.bja.2018.03.038.

37. Hogan Q. Distribution of solution in the epidural space: Examination by cryomicrotome section. Reg Anesth Pain Med. 2002;27:150-6. doi:10.1053/rapm.2002.29748.

38. Atiénzar MC, Palanca JM, Torres F, Borràs R, Gil S, Esteve I. A randomized comparison of levobupivacaine, bupivacaine and ropivacaine with fentanyl, for labor analgesia. Int J Obstet Anesth. 2008;17(2):106-11. doi:https://doi.org/10.1016/j.ijoa.2007.10.003.

39. George RB, Allen TK, Habib AS. Intermittent epidural bolus compared with continuous epidural infusions for labor analgesia: A systematic review and meta-analysis. Anesth Analg. 2013;116(1):133-44. doi:10.1213/ANE.0b013e3182713b26.

40. Grant EN, Tao W, Craig M, McIntire D, Leveno K. Neuraxial analgesia effects on labour progression: facts, fallacies, uncertainties and the future. Br J Obstet Gynaecol. 2015;122(3):288-93. doi:10.1111/1471-0528.12966.

Section 4: Proposal

Comparison between two epidural analgesia maintenance techniques at a regional hospital

Mathabe Sehlapelo

772642

Supervisor	Helen Perrie Department of Anaesthesiology
Co-supervisor	Juan Scribante Department of Anaesthesiology
Co-supervisor	Janine Wagner Department of Anaesthesiology

4.1 Introduction and problem statement

Labour pain is an unpleasant, subjective, emotional and complex experience (1, 2). It is a dynamic process and the perception and its severity can be affected by various factors (3, 4). Severe uncontrolled labour pain is associated with numerous maternal and foetal psychological and physiological adverse effects and as a result of this labour analgesia should be offered (3-5). Neuraxial techniques particularly epidural analgesia have been recognised as the gold standard for providing labour analgesia (5-9). The primary goal is to provide adequate, safe (6, 10), reliable, and reproducible maternal analgesia with minimal motor blockade (11, 12), haemodynamic instability and other adverse effects (3, 4, 6, 10).

Once labour epidural analgesia has been established, it requires maintenance until completion of labour. The techniques employed for maintenance includes intermittent epidural bolus (IEB) also referred to as manual bolus, patient controlled epidural analgesia (PCEA), continuous epidural infusion (CEI) and programmed intermittent epidural bolus (PIEB) with or without PCEA (3, 4, 6, 10, 12).

IEB is a generally safe, reproducible and cost-effective technique as it does not require automated pumps, but it is associated with haemodynamic instability and is labour intensive (6). PCEA as the sole technique may be compared to IEB. PCEA offers patients autonomy to deliver medication to themselves with a lockout time, but has an association with breakthrough pain and increased requirement of rescue boluses as compared to IEB (13). CEI offers a consistent level of analgesia and a decreased workload for the treating anaesthetist but is associated with increased local anaesthetic consumption and therefore an increased risk of motor blockade (6, 11, 14, 15).

PIEB with a PCEA employs an automated pump with set algorithms to deliver a premixed local anaesthetic and opioid mixture through the epidural catheter at a fixed calculated dose and at scheduled intervals. It is hypothesised that due to its nature of delivery it offers numerous benefits over the other techniques (6, 11, 12, 16-18). Capogna et al (11) demonstrated a decreased incidence of consumption of local anaesthetic and therefore less motor blockade with PIEB (11). Wong et al

(12) compared PIEB to CEI and found that PIEB demonstrated less local anaesthetic consumption, fewer rescue boluses for breakthrough pain, lowered incidence of motor blockade, assisted and operative deliveries and better maternal satisfaction with PIEB when using the visual analogue scale (VAS) (12).

Problem Statement

Labour epidural analgesia maintenance can be achieved using IEB, PCEA, CEI and PIEB or combinations of these techniques (3, 6, 10). Each maintenance technique has advantages and disadvantages (6, 13, 14, 19-22).

It has been shown that the technique of PIEB with PCEA using automated pumps are beneficial to the parturient and foetus in terms of maternal satisfaction, local anaesthetic consumption, less motor blockade and fewer subsequent rescue boluses as compared with CEI (11, 12). PIEB is costly compared to CEI and although the equipment is available at Rahima Moosa Mother and Child Hospital (RMMCH) it is not often used. Data for South Africa on labour epidural analgesia maintenance techniques is limited. At RMMCH CEI is currently the epidural analgesia maintenance technique of choice and it is not known whether the benefits of PIEB with PCEA outweigh the cost.

4.2 Aim and objectives

4.2.1 Aim

The aim of the study is to compare CEI with IEB to PIEB with PCEA for labour analgesia at RMMCH.

4.2.2 Objectives

The primary objectives of this study are to**:**

- compare participants satisfaction using VAS
- compare participants haemodynamics
- compare the bupivacaine and fentanyl consumption

- compare level of motor blockade using the Bromage score
- compare mode of delivery
- describe adverse effects.

4.3 Research assumptions

The following definitions will be used in this study.

Patient: a person 18 years and older who is in active labour.

Active phase of labour: cervical dilatation between 2 − 5 cm.

Term pregnancy: pregnancy at or above 37 weeks.

Patient satisfaction: measured using the VAS, a linear measure between 0 – 100 mm. Satisfaction will be regarded as a score of 30 mm or less.

Haemodynamic instability: a 20% drop in the mean arterial non invasive blood pressure.

Motor blockade: any degree of motor block in one or both lower limbs at any time during labour as described using the Bromage score.

Mode of delivery:

- unassisted: normal vaginal delivery
- assisted: vaginal delivery with either forceps, vacuum or caesarean section.

Epidural mixture: Bupivacaine 0.0625% with fentanyl 2 ug/ml in 0.9% normal saline.

Epidural record: a pre-printed RMMCH specific record that is completed by the anaesthetist performing the epidural with regards to placement and management (Appendix A).

Time: T0 is the time the sensory level is determined to be at the T10 dermatome.

T1 is one hour after sensory level is determined to be at T10 dermatome

T2 is two hours after sensory level is determined to be at T10 dermatome

This will be continued until time of delivery.

4.4 Demarcation of study field

The study will be conducted in the labour ward of RMMCH, which is affiliated to the Department of Anaesthesiology at the University of the Witwatersrand. The hospital is a 338-bed regional hospital with approximately 12 000 deliveries a year.

4.5 Ethical considerations

Approval to conduct the study will be obtained from the Human Research Ethics Committee (Medical) and the Graduate Studies Committee of the University of the Witwatersrand. Approval will be obtained from the CEO of RMMCH (Appendix B).

Participants that meet the inclusion criteria will be approached. The purpose of the study will be explained, they will be invited to participate and if they agree an information letter (Appendix C) will be given and written consent (Appendix D) will be obtained. Participants who decline to participate in the study and qualify for an epidural will still have access to the routine labour epidural analgesia service offered at RMMCH.

The names of participants from whom data are collected will not be recorded on the data collection sheet. Each patient will be allocated a study number. A list with patient names and corresponding study numbers will be generated and filed separately. Confidentiality will be maintained as only the researcher and supervisors will have access to the raw data.

All data collected will be stored securely in a locked cupboard for six years after completion of the study. This study will be conducted according to the principles of the Declaration of Helsinki (23) and the South African Guidelines for Good Clinical Practice (24).

4.6 Research methodology

4.6.1 Research design

A prospective, contextual, comparative research design will be followed in this study.

In a prospective study, outcomes are measured after following a certain population for a period of time (25). This study will be prospective as the data will be collected at the time the study takes place.

A contextual study refers to a particular group or population or specific place referred to as a “small scale world such as hospital wards, gangs, school classrooms and restaurants” (26). This study is a contextual study as it will be taking place in the labour ward at RMMCH.

A comparative study is “a study in which intact groups are compared on some dependent variable. The researcher is not able to manipulate the independent variable, which is frequently some inherent characteristics of the subjects, such as age or educational level” (25). This study is comparative, as it compares CEI with IEB to PIEB with PCEA.

4.6.2 Study population

The study population will include participants in active labour admitted to the labour ward at RMMCH during the study period.

4.6.3 Study sample

Sample size

The sample size was determined in consultation with a biostatistician. A sample size of 59 participants per group was determined based on a reduction of 60% in VAS at two and a half hours starting with a mean of 12.17 and a SD of 14.00 using a study that compared CEI with IEB to PIEB with PCEA with similar objectives (27).

Sampling method

In this study a convenience sampling method will be used. Convenience sampling collects participants readily available to the researcher (25). Once participants are enrolled in the study, they will be randomly assigned to one of the two treating

groups using simple random sampling. Simple random sampling according to Endacott and Botti (28) is where “All elements in a sampling frame have an equal chance of selection. Selection is through the use of random numbers or similar method.” A consecutively numbered envelope containing the group assignment (computer generated randomly numbered sequence) will be opened by the researcher at the time of randomisation. Participants receiving CEI with IEB will be allocated to Group A and those receiving PIEB with PCEA to Group B.

Inclusion and exclusion criteria

Inclusion criteria in this study are:

- ASA I and II patients
- participants who consent to take part in the study
- term participants in the active phase of labour with a cephalic presentation.

Exclusion criteria in this study are participants with known:

- neurological disease
- psychiatric disease
- allergy to local anaesthetic and opioid
- foetal heart rate abnormalities
- weight >110 kg
- height <140 cm.

4.6.4 Data collection

Data collection

Once with relevant approvals have been received, data will be collected from the labour ward at RMMCH.

The insertion of the epidural catheter in both groups will follow the current practice at RMMCH. The current practice does not assess the VAS and Bromage score.

Once admitted to the labour ward of RMMCH, participants fulfilling the inclusion criteria will be approached to participate in the study. The study will be explained and those participants agreeing to participate will be given an information letter

(Appendix C) and asked to provide written consent (Appendix D). A consecutively numbered envelope containing the group assignment (computer generated randomly numbered sequence) will be opened by the researcher at the time of randomisation. Participants receiving CEI with IEB will be allocated to Group A and those receiving PIEB with PCEA to Group B. The epidural analgesia insertion, side effects, complications and removal will be explained to participants.

Participant will be placed in the lateral position. A pre-anaesthetic check-up will be performed and will include but not be limited to baseline blood pressure, heart rate, VAS and Bromage score assessment. A pre-procedural intravenous fluid bolus of 10 ml/kg of a crystalloid will be infused over 20 − 30 minutes using an 18 − 20G cannula. The epidural catheter and management will be placed according the South African Society of Anaesthesiologist Regional Anaesthesia Guidelines (29). Placement of epidural analgesia catheter between the two groups will be standardised. Patient will be placed in the sitting position, the area cleaned with antiseptic solution and draped. The Iliac crests will be palpated for anatomical landmarks to identify L4 − L5 vertebrae. The Touhy needle will be inserted in the midline between spinous processes. Normal saline will be used for loss of resistance technique to identify epidural space. The catheter will be threaded 6 cm into the epidural space. A test dose of 5 ml lignocaine 2% will be used to ascertain placement. A 10 ml dose bupivacaine 0.0625% with fentanyl 2 ug/ml will be given to all participants as a first dose. Further bupivacaine doses will be titrated according to block height. Achieving a bilateral T10 sensory level will be considered as Time Zero. The epidural mixture will be prepared in 50 ml syringes, bupivacaine 6.25 ml of a 0.5% solution and 100 ug fentanyl will be diluted in normal saline up to 50 ml. This will result in an epidural mixture consisting of bupivacaine 0.0625% and fentanyl 2 ug/ml.

Blood pressure, heart rate, VAS and Bromage score, adverse effects and epidural mixture consumption will be recorded hourly after T0 until delivery. The sensory level, a routine measurement, will be assessed using an ice pack.

The Alaris® CC Syringe Pump (Carefusion) will be used for Group A and the CADD®-Solis pump (Smiths Medical) for Group B. Both the syringe and cassette and hold 50 ml of solution. They will be connected to the epidural catheter. In

Group A the infusion will be started at Time Zero at 8 − 16 ml/hr, titrated to sensory level. Rescue boluses of 5 ml will be given for breakthrough pain, considered as VAS greater than 30 mm. In Group B the pump will deliver 10 ml of the epidural mixture once off every hour from 60 minutes after Time Zero. The pump will allow patient activated boluses of 5 ml with a lockout time of 10 minutes to a maximum volume of 15 ml per hour.

Insertion of the epidural and collection of data will be performed by the primary researcher and a trained research assistant who is an anaesthetist rotating through the pain service. All collected data will be entered on the data collection sheet (Appendix E).

Progress of labour will be managed by attending obstetricians. Sips of water and juices will be allowed. Patient will be managed in the lateral position during labour with posture changing. Ambulation will not be encouraged but will be allowed only in the presence of labour ward staff.

4.6.5 Data analysis

All data will be entered onto a Microsoft Excel® spreadsheet and analysed in consultation with a biostatistician. The statistical programme STATA version 15 (STATACorp, USA) will be used. Descriptive and inferential analysis will be done. Categorical variables will be described using frequency and percentages. Continuous variables which are normally distributed will be described using means and standard deviations and those not normally distributed using medians and interquartile ranges. Comparisons between groups will be made using unpaired t-tests or Mann-Whitney U-tests depending on the distribution of the data. A p value of <0.05 will be considered statistically significant.

4.7 Significance of the study

Labour pain can have multiple adverse effects on the mother and foetus (3, 4, 6). Epidural analgesia is considered the gold standard for relief of pain during labour (6). It has been shown that the technique of PIEB with PCEA using automated pumps is beneficial for both the parturient and foetus in terms of maternal satisfaction, local anaesthetic consumption, less motor blockade and fewer

subsequent rescue boluses as compared with CEI with IEB (11, 12). Should the use of PIEB with PCEA result in maternal satisfaction, less local anaesthetic consumption, less motor blockade and fewer subsequent rescue boluses it could be a safe alternative to CEI with IEB.

4.8 Validity and reliability of the study

The validity of the study refers to the extent to which a true value is being represented by a measurement. Reliability is the consistency of the measure achieved (30).

In this study validity and reliability will be maintained by the following measures:

- applying an appropriate study design
- using a standardised data collection sheet
- sample size being determined in consultation with a biostatistician
- data will be collected by one researcher and a trained assistant
- CADD®- Solis pumps used are standardised to administer a set concentration and volume bolus of epidural mixture
- the Alaris® CC Syringe Pumps (Carefusion) used are standardised to administer a set volume.
- data analysis will be done in consultation with a biostatistician.

4.9 Potential limitations

The study is contextual in that the population is limited to the labour ward of RMMCH. The results may therefore not be generalised to other teaching hospitals affiliated with the University of the Witwatersrand or to other hospitals in South Africa.

The VAS although regarded as a valid and reliable scale is a subjective measurement of pain. Even though the procedure might have been explained to participants, they may not understand how to use the pumps, and this may affect the total local anaesthetic consumption documented.

4.10 Project outline

4.10.1 Time frame

ACTIVITY	Mar 2018	Apr 2018	May 2018	June 2018	Jul 2018	Aug 2018	Sep 2018	Oct 2018	Nov 2018	Dec 2018	Jan 2019
Proposal preparation and submission											
Ethics approval											
Postgrad approval											
Data collection											
Analysis of results											
Writing results											
Article/ chapters											
Literature review											
Submit											

4.10.2 Budget

The Department of Anaesthesiology will bear the cost of printing and paper for the proposal, ethics and post graduate approvals. Additional funding will be received from Gabler Medical in the form of cassettes for automated pumps as sponsorship for study (Appendix F). Each cassette costs R554.10 and each extension set costs R91.27. These prices include VAT.

	Price per page	Number of pages	Copies	Total
Paper and printing	R1	1076	1	R1076
Binding	R200		3	R600
Subtotal				**R1676**
	Price per box (10/box)	Number of participants		
Cassettes	R554.10	60		**R 6649,2**
Extension set	R91.27	60		**R 1095,24**
Total				**R 9420.44**

4.11 References

1. Jones L. Pain management for women in labour: An overview of systematic reviews. Int J Evid Based Healthc. 2012;5(2):101-2. doi:10.1002/14651858.CD009234.pub2.

2. Lowe NK. The nature of labor pain. Am J Obstet Gynecol. 2002;186(5):S16-S24. doi:10.1016/S0002-9378(02)70179-8.

3. Miller RD. Miller's Anesthesia. 8th ed. Philadelphia, PHL: Churchill Livingstone; 2015.

4. Morgan GE, Mikhail MS. Clinical Anesthesiology. 5th ed. New York, NY: McGraw Hill 2006.

5. Reena KH, Bandyopadhyay MA, Mishra AP. Labor epidural analgesia: Past, present and future. Indian Journal of Pain. 2014;28(2):71. doi:10.4103/0970-5333.132843.

6. Capogna G, Stirparo S. Techniques for the maintenance of epidural labor analgesia. Curr Opin Anaesthesiol. 2013;26(3):261-7. doi:10.1097/ACO.0b013e328360b069.

7. Ogboli-Nwasor E, Adaji S, Bature S, Shittu O. Pain relief in labor: A survey of awareness, attitude, and practice of health care providers in Zaria, Nigeria. J Pain Res. 2011;4:227-32. doi:10.2147/JPR.S21085.

8. Findley I, Chamberlain G. Relief of pain. BMJ. 1999;318(7188):927-30. doi:10.1136/bmj.318.7188.927.

9. Hawkins JL. Epidural analgesia for labor and delivery. N Engl J Med. 2010;362(16):1503-10. doi:10.1056/NEJMct0909254.

10. American Society of Anesthesiologists. Practice guidelines for obstetric anesthesia: An updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. Anesthesiology. 2016;124(2):270-300. doi:10.1097/ALN.0000000000000935.

11. Capogna G, Camorcia M, Stirparo S, Farcomeni A. Programmed intermittent epidural bolus versus continuous epidural infusion for labor analgesia: The effects on maternal motor function and labor outcome. A randomized double-blind study in nulliparous women. Anesth Analg. 2011;113(4):826-31. doi:10.1213/ANE.0b013e31822827b8.

12. Wong CA, Ratliff JT, Sullivan JT, Scavone BM, Toledo P, McCarthy RJ. A randomized comparison of programmed intermittent epidural bolus with continuous epidural infusion for labor analgesia. Anesth Analg. 2006;102(3):904-9. doi:10.1213/01.ane.0000197778.57615.1a.

13. Srivastava U, Gupta A, Saxena S, Kumar A, Singh S, Saraswat N, et al. Patient controlled epidural analgesia during labour: Effect of addition of background Infusion on quality of analgesia & maternal satisfaction. Indian J Anaesth. 2009;53(6):649-53.

14. Silva M, Halpern SH. Epidural analgesia for labor: Current techniques. Local Reg Anesth. 2010;3:143-53. doi:10.2147/LRA.S10237.

15. McGrady E, Litchfield K. Epidural analgesia in labour. Br J Anaesth. 2004;4(4):114-7. doi:10.1093/bjaceaccp/mkh030.

16. Nunes J, Nunes S, Veiga M, Cortez M, Seifert I. A prospective, randomized, blinded-endpoint, controlled study: Continuous epidural infusion versus programmed intermittent epidural bolus in labor analgesia. Braz J Anesthesiol. 2016;66(5):439-44. doi:10.1016/j.bjane.2014.12.006.

17. Onuoha OC. Epidural analgesia for labor: Continuous infusion versus programmed intermittent bolus. Anesthesiol Clin. 2017;35(1):1-14. doi:10.1016/j.anclin.2016.09.003.

18. Wong CA, McCarthy RJ, Hewlett B. The effect of manipulation of the programmed intermittent bolus time interval and injection volume on total drug use for labor epidural analgesia: A randomized controlled trial. Anesth Analg. 2011;112(4):904-11. doi:10.1213/ANE.0b013e31820e7c2f.

19. Bandyopadhyay KH, Afzal M, Mishra AK, Paul A. Labor epidural analgesia: Past, present and future. Indian Journal of Pain. 2014;28(2):71.

20. Boselli E, Debon R, Cimino Y, Rimmelé T, Allaouchiche B, Chassard D. Background infusion is not beneficial during labor patient-controlled analgesia with 0.1% ropivacaine plus 0.5 µg/ml sufentanil. Anesthesiology. 2004;100(4):968-72. doi:10.1097/00000542-200404000-00030.

21. Boutros A, Blary S, Bronchard R, Bonnet F. Comparison of intermittent epidural bolus, continuous epidural infusion and patient controlled-epidural analgesia during labor. Int J Obstet Anesth. 1999;8(4):236-41. doi:10.1016/S0959-289X(99)80103-4.

22. McGrady E, Litchfield K. Epidural analgesia in labour. Continuing Education in Anaesthesia Critical Care & Pain. 2004;4(4):114-7. doi:10.1093/bjaceaccp/mkh030.

23. The Helsinki Declaration of the World Medical Association. Ethical principles of medical research involving human subjects. JAMA. 2013;310(20):2191-4. doi:10.1001/jama.2013.281053.

24. Guidelines for good practice in the conduct of clinical trials with human participants in South africa; . Available from: http://www.kznhealth.gov.za/research/guideline1.pdf [date accessed.

25. Brink H, Van der Walt C, Van Rensburg G. Fundementals in research methodology for healthcare professionals. 3rd ed ed. Cape Town Juta; 2012.

26. De Vos A SH, Fouche C, Poggenpoel M, Schurink E, Schurink W. Research at grass roots. Pretoria: Van Schaik; 1998.

27. Mukherjee S, Das S, Mukhopadhyay S, Basu SR. Comparison between continuous epidural infusion and intermittent epidural bolus of bupivacaine fentanyl combination for labour analgesia. Sch J App Med Sci. 2013;1(6):953-8.

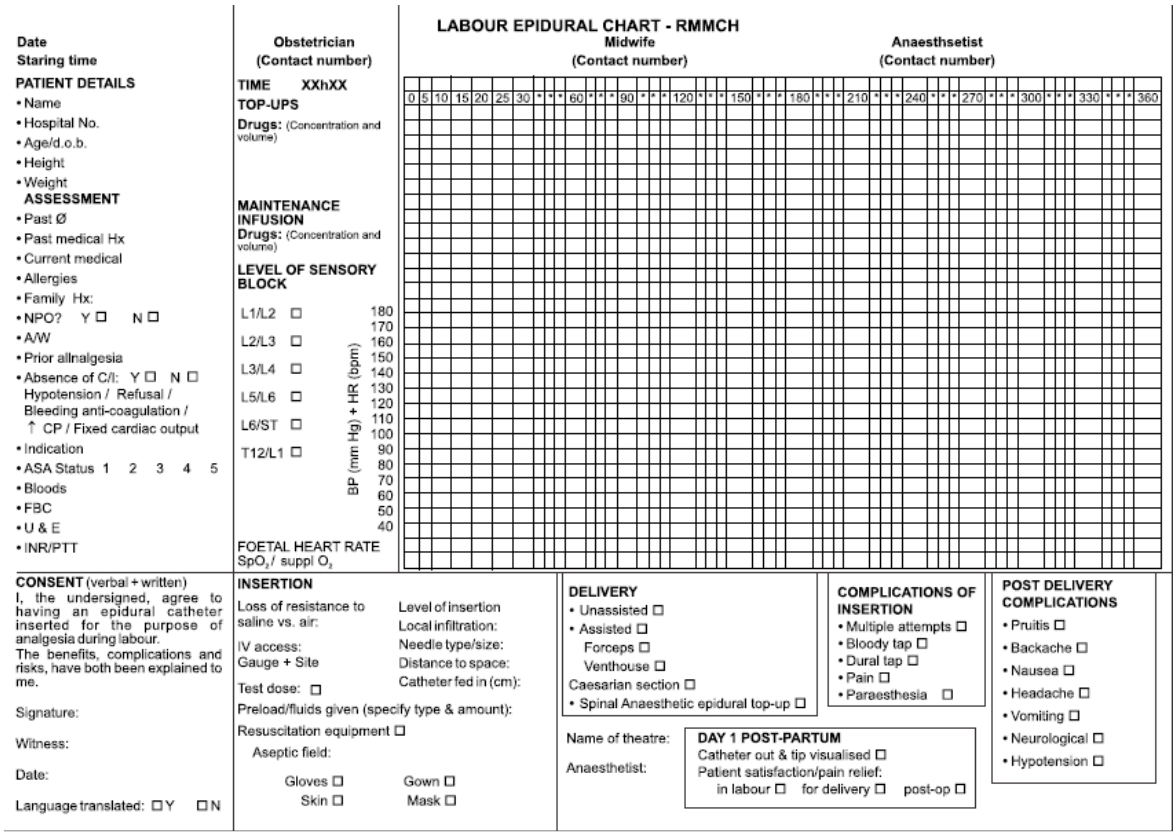
28. Endacott R, Botti M. Clinical research 3: Sample selection. Accid Emerg Nurs.15(4):234-8. doi:10.1016/j.aaen.2006.12.006.

29. South African Society of Anaesthesiologists. Guidelines for Regional Anaesthesia in South Africa. Available from: https://sasaapi.sasaweb.com/Document/SASRAguidelines2016_636722590664755485.pdf [date accessed 26 August 2017.

30. Botma Y, Greff M, Mulaudzi M, Wright S. Research in health sciences. South Africa: Pearson Education; 2010.

4.12 Appendices

Appendix 1: RMMCH epidural record



LABOUR EPIDURAL CHART - RMMCH

Date
Staring time

PATIENT DETAILS
- Name
- Hospital No.
- Age/d.o.b.
- Height
- Weight

ASSESSMENT
- Past Ø
- Past medical Hx
- Current medical
- Allergies
- Family Hx:
- NPO? Y ☐ N ☐
- A/W
- Prior allnalgesia
- Absence of C/I: Y ☐ N ☐ Hypotension / Refusal / Bleeding anti-coagulation / ↑ CP / Fixed cardiac output
- Indication
- ASA Status 1 2 3 4 5
- Bloods
- FBC
- U & E
- INR/PTT

Obstetrician (Contact number)

Midwife (Contact number)

Anaesthsetist (Contact number)

TIME XXhXX

TOP-UPS

Drugs: (Concentration and volume)

MAINTENANCE INFUSION

Drugs: (Concentration and volume)

LEVEL OF SENSORY BLOCK

L1/L2 ☐
L2/L3 ☐
L3/L4 ☐
L5/L6 ☐
L6/ST ☐
T12/L1 ☐

BP (mm Hg) + HR (bpm)

FOETAL HEART RATE
SpO_2 / suppl O_2

0 5 10 15 20 25 30 * * * 60 * * * 90 * * * 120 * * * 150 * * * 180 * * * 210 * * * 240 * * * 270 * * * 300 * * * 330 * * * 360

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40

CONSENT (verbal + written)
I, the undersigned, agree to having an epidural catheter inserted for the purpose of analgesia during labour.
The benefits, complications and risks, have both been explained to me.

Signature:

Witness:

Date:

Language translated: ☐Y ☐N

INSERTION

Loss of resistance to saline vs. air:
Level of insertion
Local infiltration:
IV access:
Gauge + Site
Needle type/size:
Distance to space:
Test dose: ☐
Catheter fed in (cm):
Preload/fluids given (specify type & amount):
Resuscitation equipment ☐
Aseptic field:
Gloves ☐ Gown ☐
Skin ☐ Mask ☐

DELIVERY
- Unassisted ☐
- Assisted ☐
  - Forceps ☐
  - Venthouse ☐
- Caesarian section ☐
- Spinal Anaesthetic epidural top-up ☐

COMPLICATIONS OF INSERTION
- Multiple attempts ☐
- Bloody tap ☐
- Dural tap ☐
- Pain ☐
- Paraesthesia ☐

POST DELIVERY COMPLICATIONS
- Pruitis ☐
- Backache ☐
- Nausea ☐
- Headache ☐
- Vomiting ☐
- Neurological ☐
- Hypotension ☐

Name of theatre:

Anaesthetist:

DAY 1 POST-PARTUM
Catheter out & tip visualised ☐
Patient satisfaction/pain relief:
in labour ☐ for delivery ☐ post-op ☐

Appendix B: Letter to CEO of RMMCH

16 March 2018

Rahima Moosa Mother and Child Hospital

Fuel & Oudtshoorn Streets, Coronationville, Johannesburg 2112

Attention: Chief Executive Officer Rahima Moosa Mother and Child Hospital

RE: Permission to conduct research at RMMCH

I am a registrar in the Department of Anaesthesiology of the University of the Witwatersrand registered for the Master of Medicine degree. The title of my proposed research: Comparison between two epidural analgesia maintenance techniques at a regional hospital approved by the Graduate Studies Committee and the Human Research Ethics Committee of the University of the Witwatersrand (Certificate number…).

I hereby apply for permission to collect prospective data comparing two epidural analgesia maintenance techniques with maternal satisfaction, haemodynamics, drug consumption, motor blockade and mode of delivery. Data will be collected on data collection sheet and analysed with a statistician.

There will be no financial implications for the hospital in order to conduct this study.

Attached please find a copy of my M Med proposal and HREC clearance.

Thank you in advance for your assistance.

Kind Regards

Dr. Mathabe Sehlapelo

Appendix C: Patient information letter

Dear Patient,

Hello, my name is Dr Mathabe Sehlapelo and I am currently a registrar in the Department of Anaesthesiology. I would like to invite you to participate in my research study entitled: Comparison between two epidural analgesia maintenance techniques at a regional hospital. This will be submitted to the University of the Witwatersrand as part of my Master of Medicine degree.

Giving birth may be a painful experience. We can place an injection into your back to decrease the pain. The injection is standard practice for decreasing pain during giving birth. This is done by placing a small tube into a space in your back to allow me to give you the medication without many injections. In order to do this, you will sit on the bed, your back will be cleaned and an injection to numb the skin will be injected. Once the area is numb, I will place the tube for the medication into your back through a second injection. The second injection should not be painful as the skin should now be numb. I will give medication through the tube to make sure it is in the correct space. I will then give you the medication to decrease the pain. There are two methods by which I can give you the medication and I will choose an envelope to decide which method you will receive. Choosing an envelope to decide is a random process like flipping a coin and you can end up receiving any one of the methods. In the one method the medication can run through the tube all the time while you are waiting for your baby to be delivered. In the other method the medication can run in every hour while you are able to give yourself more medication in between to decrease your pain. I will measure your pain, your blood pressure and your ability to bend your knees.

If you don’t want to be part of my study, you don’t have to and if you want help with your pain, I will still give you the injection in your back. If you decide that you would like to be in my study and then change your mind you can stop being in my study at any time. Only my supervisors and I will look at your results and I will not use any information that can be used to identify you.

For more information you can phone me at (011) 470 9106 or the Chairman of the Ethics Committee on (011) 717-1234.

My study has been approved by the Human Research Ethics Committee Medical (Mxxxxxx) and the Graduate Studies Committee at the Witwatersrand University.

Signing the consent form attached means that you agree to take part in my study. You will be given a copy of this form to keep.

Thank you for your time.

Dr Mathabe Sehlapelo

Appendix D: Patient consent form

Consent Form

I, _____agree to participate in the study: Comparison between two epidural analgesia maintenance techniques at a regional hospital.

I have read and understood the information letter provided to me by Dr Sehlapelo. I understand that I may withdraw from the study at any point if I do not wish to participate.

I have had the opportunity to ask questions about the study and my participation in it.

Participant name

Participant signature Date

Doctor’s name

Doctor’s signature Date

Appendix E: Data collection sheet

Comparison between two epidural analgesia maintenance techniques at a regional hospital

Study number:

1. Group allocation

Group A (CEI)	
Group B (PIEB)	

2. Demographic information

Age (years)	
Body weight (kg)	
Height (cm)	
Gestational age (weeks)	
Parity	
Cervical dilatation (cm)	

3. Pre-procedure assessment

Heart rate (beats/min)	
Systolic blood pressure (mm/Hg)	
Diastolic blood pressure (mm/Hg)	
Mean Arterial blood pressure(mm/Hg)	
Bromage score	
VAS (mm)	

4. Drug consumption

Pump mls	
PCEA mls	
Rescue boluses mls	
Total	

5. Assessments during study period

Variable	T0	T1	T3	T4	T5	T6	T7	T8	T9
VAS									
Heart rate									
Systolic BP									
Diastolic BP									
Mean Arterial BP									
Epidural mixture (ml)									
Rescue bolus (ml)									
PCEA (ml)									
Bromage									
Pruritus									
Nausea/vomiting									
Residual paraesthesia									
Other									

6. Mode of delivery

Unassisted	Normal vaginal delivery	
Assisted	Forceps	
	Vacuum	
	Caesarean section	

Appendix E: Funding from Gabler Medical

- Dear George

Thank you for your support! The epidural spike sets will be perfect.

I will forward your reply to Dr M Sehlapelo who will be conducting the study. She is currently busy with her study proposal and will contact you in the coming months to finalize further arrangements.

We are very excited to be able to conduct this study at RMMCH as it will help us to improve our acute pain service.

Thank you and kind regards

Dr Thomas Kleyenstuber

Department of Anaesthesia

Rahima Moosa Mother & Child Hospital

kleyenstuber@hotmail.com

From: George Nieuwoudt <gnieuwoudt@gablermedical.com>
Sent: 25 May 2017 08:25 AM

To: Thomas Kleyenstuber
Cc: Suzanne Swart; Ronel de Haan
Subject: RE: MMED study

Good day Dr. Kleyenstuber

Thank you for your email.

- We will be happy to help with this MMED study.
- I recommend that we do this study Epidural spike sets (*below)
  - Help with the stock control.
  - All the lines are colour yellow and we are not limited to only 100ml.

*21-7324 CADD® Yellow Striped Administration Set
With bag spike, flow stop, clamp, and one-way checkvalve
with male Luer, Non-DEHP Plasticized (TOTM)
Length: 312 cm Priming Volume: 3.2 mL

Should you have any queries or require any further information, please do not hesitate to contact me.

Best regards
George (Sebastiaan)

G NIEUWOUDT Product / Service Manager
email: gnieuwoudt@gablermedical.com, web: www.gablermedical.com
cell no: + 27-76-427 5661,
cape town office: + 27-21-531 0820, fax: + 27-21-531 0829, P.O. Box 563, Eppindust, 7475, South Africa
JHB office: + 27-12-665-1811, Suite 7 -Groundfloor, Manhatten Office park, 16 Pieter street, Centurion

This email is intended solely for the addressee and all attached information is confidential. All reasonable steps are taken to ensure the accuracy and integrity of the information. Gabler Medical does not accept liability or responsibility whatsoever if the information or data is, for whatever reason, corrupted, inaccurate or does not reach its intended destination. Please consider the environment before printing this email.

From: Suzanne Swart
Sent: Friday, 19 May 2017 2:12 PM
To: Thomas Kleyenstuber <kleyenstuber@hotmail.com>; George Nieuwoudt <gnieuwoudt@gablermedical.com>
Subject: Re: MMED study

Afternoon Dr Kleyenstuber,

Trust you are well.

Doctor we will get back to you with a answer on Monday 22 May 2017 regarding this matter as we need to finalise some arrangements from our side.

Sorry for any inconvenience.

Best regards
Suzanne

S SWART Medical Sales Representative
email: sswart@gablermedical.com, web: www.gablermedical.com
cell no: + 27-82-495 0928,
cape town office: + 27-21-531 0820, fax: + 27-21-531 0829, P.O. Box 563, Eppindust, 7475, South Africa

This email is intended solely for the addressee and all attached information is confidential. All reasonable steps are taken to ensure the accuracy and integrity of the information. Gabler Medical does not accept liability or responsibility whatsoever if the information or data is, for whatever reason, corrupted, inaccurate or does not reach its intended destination. Please consider the environment before printing this email.

From: Thomas Kleyenstuber <kleyenstuber@hotmail.com>
Sent: Friday, May 19, 2017 11:29:43 AM
To: George Nieuwoudt; Suzanne Swart
Subject: MMED study

Dear George and Suzanne

One of our registrars is interested in doing her MMED study using our CADD pumps. She wants to compare the haemodynamic effects of PIEB vs continuous infusion in our labour epidural patients. The statisticians have come up with a provisional study sample of 64-70 patients. We would therefore need about 32-35

CADD cassettes and extension lines. Because this is an MMED research project the registrar will have to get permission from the CEO of RMMCH to do the study and she will only give permission if there is no additional cost to RMMCH.

I am therefore asking if Gabler Medical would be prepared to sponsor the required consumables?

Furthermore, please send me a quote for 10 Boxes of 50ml cassettes for our regular acute pain service. We still have enough stock of the extension lines.

Lastly, please send me the articles on PIEB that you mentioned during our last meeting.

Kind regards

Dr Thomas Kleyenstuber
Department of Anaesthesia
Rahima Moosa Mother & Child Hospital
kleyenstuber@hotmail.com

Section 5: Annexures

5.1 Ethics approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Mathabe Sehlapelo

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M180418

NAME: (Principal Investigator)	Dr Mathabe Sehlapelo
DEPARTMENT:	Anaesthesiology Rahima Moosa Mother and Child Hospital
PROJECT TITLE:	Comparison between two epidural analgesia maintenance techniques at a regional hospital
DATE CONSIDERED:	04/05/2018
DECISION:	Approved Uncodintionally
CONDITIONS:	
SUPERVISOR:	Helen Perrie
APPROVED BY:	CB Penny Professor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	03/08/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **April** and will therefore be due in the month of **April** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 03/08/2018

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

5.2 Graduate studies approval

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

02 July 2018
Person No: 772642
PAG

Dr M Sehlapelo
497 Block L
Soshanguve
0152
South Africa

Dear Dr Sehlapelo

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Comparison between two epidural analgesia maintenance techniques at a regional hospital* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

5.3 Hospital CEO approval

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

RAHIMA MOOSA MOTHER AND CHILD HOSPITAL

Enquiries : Karen Marshall
Tel : (011) 470 9284
Fax : 086 553 4623
Email : Karen.Marshall@wits.ac.za

TITLE OF RESEARCH PROJECT:
"Comparison between two epidural analgesia maintenance techniques at a regional hospital"

PRINCIPAL INVESTIGATOR OF THE PROJECT:
Dr Mathabe Sehlapelo

DEPARTMENT:
Anaesthesiology

SUPERVISOR:
Dr Janine Wagner

NHRD REF NO: GP_201807_003

Dear Dr Sehlapelo,

Permission is granted for you to conduct the research as indicated in the title above.

The terms under which this permission is granted is contained in the Researcher Declaration form that you have signed. Failure to comply with these conditions will result in the withdrawal of such permission.

It is crucial for you to inform the Research Coordinator, Karen Marshall of the actual start and end dates of your study. This could be done by e-mail.

Should the study commence more than 12 months after receipt of this approval letter you will have to go through the process of applying again.

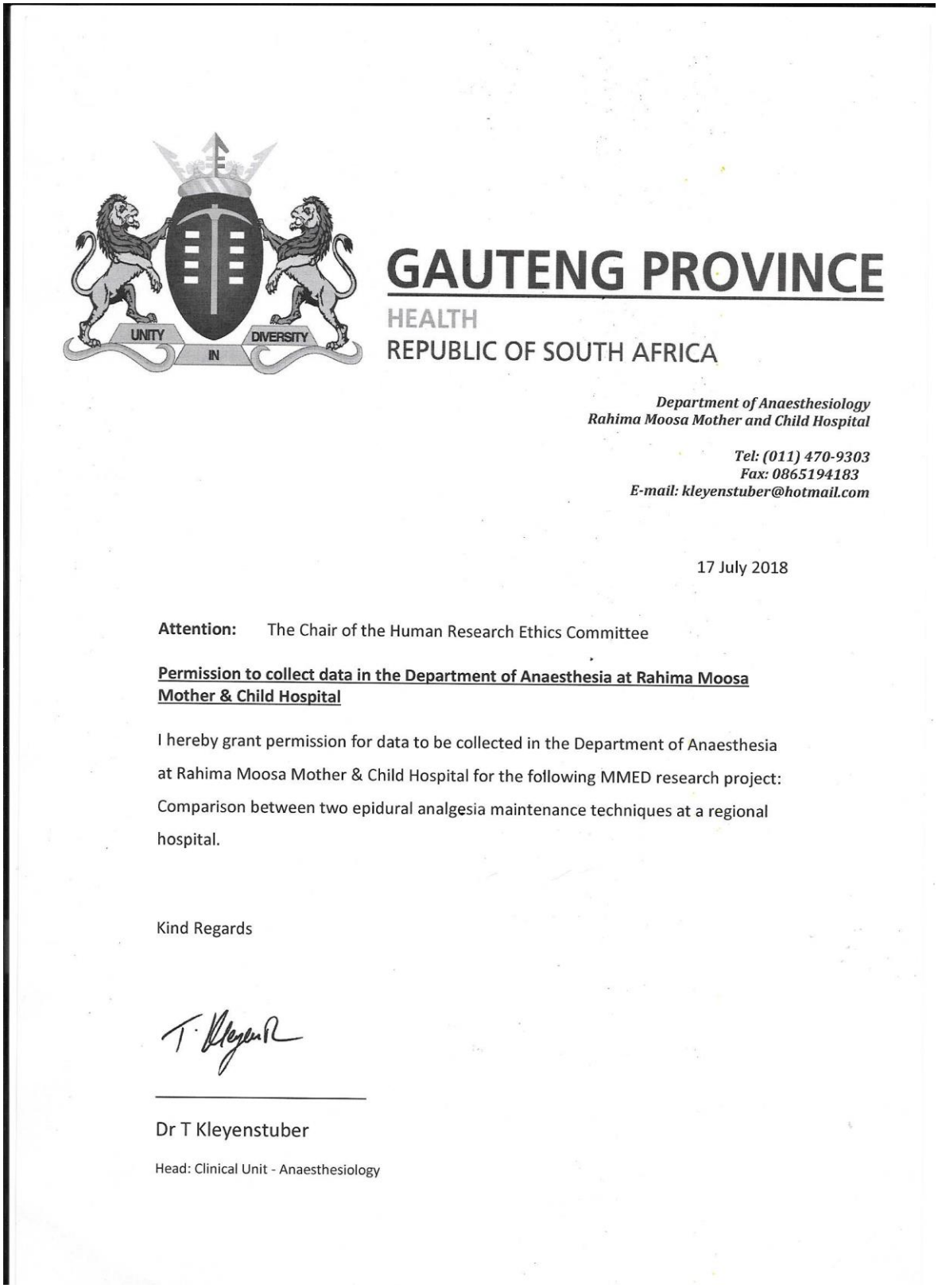
You are strongly advised to keep a signed copy of the declaration form so as to ensure that the terms of this agreement are complied with at all times.

Yours sincerely,

DR FREW BENSON
CLINICAL EXECUTIVE
2018:07:11

ADDRESS: Cnr FUEL & OUDSTHOORN STREET CORONATIONVILLE 2093 / PRIVATE BAG X20 NEWCLARE 2112 JHB

5.4 Head of department approval



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Department of Anaesthesiology
Rahima Moosa Mother and Child Hospital

Tel: (011) 470-9303
Fax: 0865194183
E-mail: kleyenstuber@hotmail.com

17 July 2018

Attention: The Chair of the Human Research Ethics Committee

Permission to collect data in the Department of Anaesthesia at Rahima Moosa Mother & Child Hospital

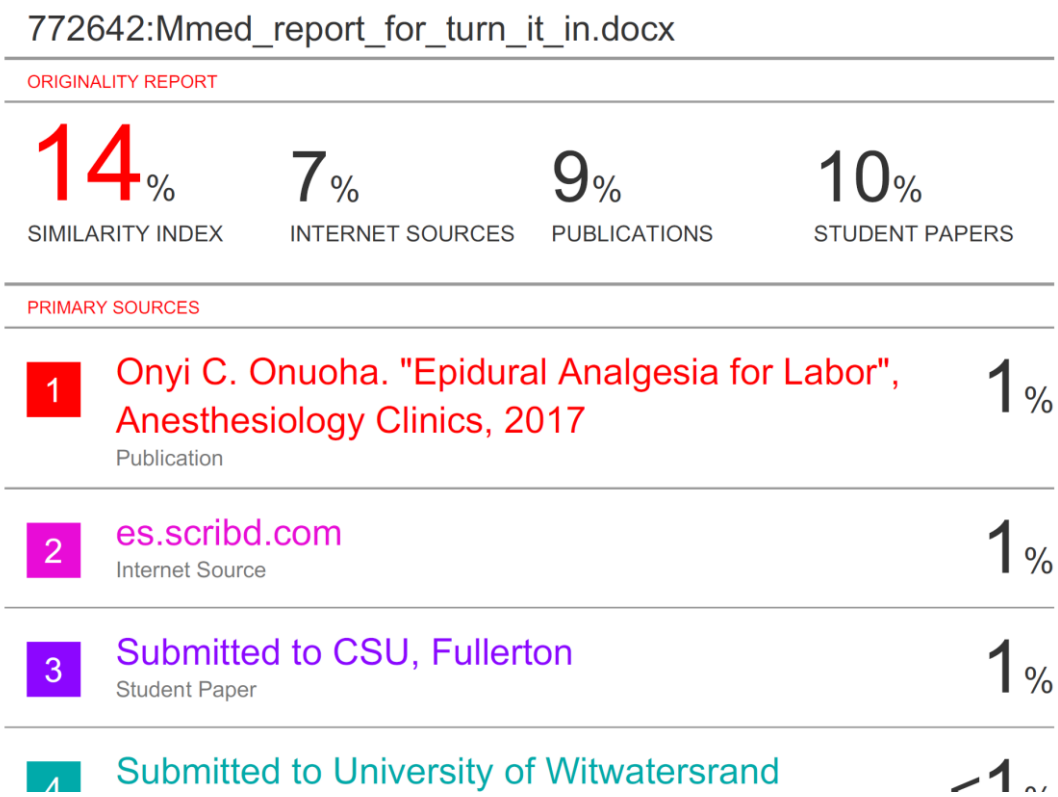
I hereby grant permission for data to be collected in the Department of Anaesthesia at Rahima Moosa Mother & Child Hospital for the following MMED research project: Comparison between two epidural analgesia maintenance techniques at a regional hospital.

Kind Regards

Dr T Kleyenstuber

Head: Clinical Unit - Anaesthesiology

5.5 Turnitin report



772642:Mmed_report_for_turn_it_in.docx

ORIGINALITY REPORT

14%	7%	9%	10%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Onyi C. Onuoha. "Epidural Analgesia for Labor", Anesthesiology Clinics, 2017 Publication	1%
2	es.scribd.com Internet Source	1%
3	Submitted to CSU, Fullerton Student Paper	1%
4	Submitted to University of Witwatersrand	1%

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

25th October, 2019

The Chairperson
Graduate Studies Committee
Faculty of Health Sciences
University of the Witwatersrand

Dear Madam,

Re: M Med: **Comparison between two epidural analgesia maintenance techniques at a regional hospital**

Dr Mathabe Sehlapelo, student number: 772642, has submitted her research report to Turnitin which revealed a similarity index of 14%. These similarities appear not to be plagiarism but mainly the use of common terminology and phrases specific to the topic of the research.

Yours sincerely,

H C Perrie

Helen Perrie
Supervisor

1