A Randomized Double Blinded Study Comparing The Haemodynamic Effects Of Intravenous Bolus Of 3 IU Vs. 5 IU Oxytocin During Caesarean Section Delivery Under Spinal Anaesthesia At Dr. George Mukhari Academic Hospital

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210011898

A research report submitted to the faculty of Medicine at University of Limpopo (Medunsa Campus) in partial fulfilment for the degree of Master of Medicine in Anaesthesiology.

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DECLARATION

In submitting this report, in partial fulfilment of the requirements for the degree of Master of Medicine in Anaesthesiology at the University of Limpopo (Medunsa Campus), I do declare that this dissertation is my original work in design and execution and has not been previously submitted by me for a degree at this or any other university; and that all the material herein has been duly acknowledged.

____________________  210011898  __________________
DR V.Y. PHASWANA       Student Number            DATE:
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DEDICATION

This research report is dedicated to my family at large; specifically my father, Mr T.E. Phaswana and, my mother, Mrs T.F. Phaswana for their unconditional love, support, guidance and encouragement from childhood and throughout my studies. You were always there when one needed you most, during both happy and sad times. Thank you for giving me a chance to prove and improve myself through all my walks of life. I love you and May God bless you dearly forever!

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My brother, Phathutshedzo, the foundation we have laid proves that there is no mountain higher as long as God is with us. Yours is to study and the rest shall follow. With dedication and commitment anything is possible, chance favours the prepared mind. Take the spear forward!!!
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<td>Intramuscular injection</td>
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ABSTRACT

Caesarean section is a surgical procedure used to deliver a baby. Caesarean delivery may be performed because of maternal or fetal problems that arise during labour and may be planned before mother goes to labour. It requires regional or general anaesthesia to prevent pain. After the delivery of the baby, mother is given oxytocin to aid the uterus contraction but the problem is its haemodynamic effects mostly cardiovascular.

Different dose regimens of oxytocin during caesarean section have been described but appear to be experimental. Several empirical regimens have been proposed for oxytocin administration during caesarean delivery and these has led to many different practices in its administration worldwide including specifically at Dr. George Mukhari Academic Hospital.

A prospective randomized double blinded study was conducted at Dr. George Mukhari Academic Hospital. The study involved pregnant women who had completed thirty seven weeks of pregnancy in line with American Society of Anaesthesiologist (ASA) I and II with singleton pregnancy to be delivered under spinal anaesthesia. The age range was from 18 - 45 years. The sample population was divided into Group A (103 patients) and Group B (100 patients). Group A patients were administered a dose of 3 IU oxytocin while Group B patients were administered a dose of 5 IU oxytocin during caesarean section delivery. The haemodynamic effects between the two groups were then monitored. A statistical analysis performed on SAS Release 9.2 running on Microsoft Windows was conducted.

In this study, the 5 IU oxytocin intravenous bolus demonstrated a higher impact on the haemodynamic changes compared to the 3 IU oxytocin intravenous bolus. Administration of 5 IU oxytocin resulted in a greater increase in heart rate than the administration of 3 IU, which was only significantly different at 1 minute (p value = 0.047). In addition, 5 IU oxytocin intravenous bolus resulted in greater decreases in both systolic and diastolic blood pressures than in 3 IU oxytocin intravenous bolus. These decreases were particularly significantly different for systolic blood pressures.
at 1, 2 and 5 minutes follow-up points (p values: 0.005, 0.001 and 0.014, respectively) while for diastolic blood pressures the decreases were significantly different at 1 and 2 minutes follow-up points (p values: 0.043 and 0.016, respectively).

Despite the haemodynamic changes, the other most significant difference was in the percentage in nausea which was significantly greater in Group B (5 IU) at 32.0% than Group A (3 IU) at 10.7% (p value = 0.0003). In addition, the percentage patients with chest pain side effects in Group B (17%) was significantly greater than the percentage in Group A (4.9%) (p value = 0.0063).

The 3 IU oxytocin intravenous bolus produced less haemodynamic effects than 5 IU oxytocin intravenous bolus. This study confirms that adequate uterine tone can be achieved with small doses of oxytocin in patients undergoing caesarean section. The use of 3 IU or even less as a preferred dose of use during caesarean delivery at Dr. George Mukhari Academic Hospital should be considered further. In fact, DR George Mukhari Academic Hospital should rather maybe consider the adoption of a 2.5 IU oxytocin intravenous dose in line with the National ESMOE guidelines for district and regional hospitals’ protocol for caesarean section under spinal anaesthesia.
CHAPTER 1: INTRODUCTION

1.1. Study Problem Statement

Caesarean section is a surgical procedure used to deliver a baby. A vertical or horizontal incision in the mother’s lower abdomen is made to expose uterus. Another incision is made in the uterus to allow removal of baby and placenta. The caesarean section rate is steadily increasing and regional anaesthesia has become the preferred method.1

Caesarean delivery may be performed because of maternal or fetal problems that arise during labour. It may be planned before mother goes to labour. It requires regional or general anaesthesia to prevent pain. After the delivery of the baby, patient is given oxytocin to contract the uterus but the problem is its haemodynamic effects mostly cardiovascular.2 Oxytocin is used to aid uterine contraction after delivery at caesarean section, the optimum dose is unclear. Intravenous oxytocin causes cardiovascular effects including tachycardia, hypotension, myocardial infarction, cardiovascular collapse, death, nausea and vomiting.3 Dose regimens of oxytocin drugs during caesarean section have been described but appear to be empirical.2

The magnitude of these side effects is dose related and an inadequate dose can result in increased uterine bleeding.4 Attempts to reduce haemodynamic side effects of oxytocin have focused on reduction in speed of injection and dose.5

Several empirical regimens have been proposed for oxytocin administration during caesarean delivery and these has led to many different practices in its administration worldwide.6

1.2. Aim of the study

The aim of the study was to compare the haemodynamic effects caused by intravenous bolus 3 IU and 5IU doses of oxytocin during caesarean section delivery.
1.3. Objectives of the study

- To determine which of the two intravenous bolus dose 3 IU vs. 5 IU of oxytocin will have the least haemodynamic effects during caesarean section delivery.
CHAPTER 2: LITERATURE REVIEW

Oxytocin is a natural occurring peptide hormone produced by the periventricular nuclei of the hypothalamus. It is transported in secretory granules to the posterior pituitary for subsequent release. It has two main effects; uterine contraction and milk ejection from the lactating mammary gland. Oxytocin has very weak antidiuretic hormone activity which necessitates infusion in an isotonic solution. This peptide, Oxytocin, was discovered by Sir Henry Dale and synthesized by Du Vigneaudin in 1953. It is currently used in the majority of deliveries in developed and developing countries worldwide. Oxytocin is commonly employed to induce or augment the process of labour to effect vaginal delivery. Oxytocin is also used as the first line drug to restore uterine tone and minimize post-partum blood loss following caesarean section delivery.

Oxytocin is given routinely to women after delivery of baby during caesarean section or normal vaginal delivery to aid contraction of the uterus and therefore reduce blood loss. When given as a rapid intravenous bolus it causes cardiovascular side effects, which are widely known, but there is little agreement as to the mechanism by which they occur. Some studies suggest that the preservative, chlorobutanol is the cause of these haemodynamic effects.

The mechanism by which oxytocin act is by binding to the G-protein on the surface of the uterine myocyte, resulting in the generation of 1,2 diacylglycerol and inositol 1,4,5-triphosphate (IP3) via the action of phospholipase C. IP3 triggers Ca\(^{2+}\) release from sarcoplasmic reticulum. Oxytocin also increases Ca\(^{2+}\)intracellular entry via L-type Ca\(^{2+}\) channels and decrease Ca\(^{2+}\) efflux. Calcium ions binds to calmodulin and activate myosin light chain kinase, which is a central mechanism of contraction of uterine smooth muscle. The concentration of myometrial oxytocin receptors increases with advancing gestation.

The haemodynamic changes in pregnant women after caesarean section delivery may be caused by the elimination of the aorta-caval compression, auto transfusion from uterine contraction, haemorrhage and vasoconstriction. However, some studies have reported that uterotonic drug is the dominant factor. Uterotonic drug which is
frequently used for caesarean section is oxytocin. It induces uterine contraction and peripheral vasodilation along with a decrease in arterial pressure after delivery\textsuperscript{3,4}.

Intravenous injection of oxytocin during caesarean section has been reported to cause cardiovascular side effects such as tachycardia or hypotension, chest pain and arrhythmias. In most severe cases, it is further reported to cause even cardiovascular collapse and death. Other reported side effects include nausea and vomiting, headache, fluid pooling or pulmonary edema\textsuperscript{2,13,14}.

Rarely as a result of structural similarities with vasopressin, large doses of oxytocin may cause water retention, hyponatraemia, seizures and coma. Although oxytocin causes less emetic effects compared with other uterotonics, the incidence of nausea and vomiting is 29 and 9\% respectively after a low dose 5 IU oxytocin, as reported by Dyer et. al. (2011). The most common side effects after oxytocin administration at caesarean section are dose-related hypotension and tachycardia. Hypotension is caused by transient relaxation of vascular smooth muscle cells, probably via calcium-dependent stimulation of the nitric oxide pathway\textsuperscript{11}.

Rapid bolus injection of any dose of oxytocin results in marked vasodilation of arteries and capacitance vessels. Arterial vasodilation decrease cardiac output up to two fold. Vasodilation of capacitance vessel decrease venous return leading to a fall in blood pressure, increase in heart rate and myocardial ischemia\textsuperscript{5}. When oxytocin is administered in bolus dose it may be associated with adverse effects including hypotension, nausea, vomiting, headache and myocardial ischemia\textsuperscript{15}. Its potential to produce adverse haemodynamic effects has now featured in the reports of Confidential Enquires into Maternal Death (CEMD) in the United Kingdom\textsuperscript{16}.

Maternal morbidity and mortality are the most relevant concern after oxytocin administration. The 1997 -1999 triennial audit of (CEMD) in the United Kingdom reported death of two women from cardiovascular instability following an intravenous bolus of 10 international units (IU) oxytocin dose\textsuperscript{17}.

Awareness of these deaths resulted in dose reduction in United Kingdom to an intravenous bolus of 5 IU. Even this dose and method of administration may cause hypotension, tachycardia, peripheral flushing, nausea and vomiting \textsuperscript{16,17}.  
Intravenous oxytocin has an onset of action of one to two minutes. It's rapidly degraded in the liver and kidney with plasma half-life of four to ten minutes. Given intramuscularly the onset of action is two to four minutes and duration of action is thirty to sixty minutes. Therefore the potential advantage of an oxytocin infusion at caesarean section is that it maintains uterine contractility throughout the surgical procedure and immediate postpartum period when most primary hemorrhage occurs.

Historically a 10 IU intravenous bolus of oxytocin was given after caesarean delivery of baby. More recent guidelines largely resulting from Confidential Enquires into Maternal Deaths in United Kingdom recommended a 5 IU bolus to be administered as a slow injection because of the potential for haemodynamic instability after a rapid 10 IU bolus.

Few studies have compared different doses of oxytocin during caesarean section. Pinder et. al. (2002) shows that there was only small decrease in mean arterial blood pressure (MAP) in both groups after oxytocin bolus. As Pinder et. al. (2002) reported, a statistical significant decrease occurred only at 30s after 10 IU of oxytocin. Both regimens 5 IU and 10 IU produced clinically and statistically significant increase in heart rate over baseline from 30 to 60 s after 5 IU and from 30 to 120 s after 10 IU. Stroke volume increased following 10 IU of oxytocin but not after 5 IU. There was significant difference between the groups for cardiac output at 1 minute. Haemodynamics returned to baseline by 2 minutes in both groups.

Khan et. al. (2014), in similar study comparing 3 IU and 5 IU of oxytocin, observed that “oxytocin infusion 3 IU results in less haemodynamic response than oxytocin 5IU although the difference was not statistically significant”. They further conclude that “adequate uterine tone can be achieved with small doses of oxytocin in patients undergoing caesarean section”. Recent literature either avoid describing a specific oxytocin dose during caesarean delivery or provide a range of 5-40 IU while current guidelines for the administration of oxytocin during caesarean delivery are diverse, empiric and vague. Despite this notion, it appears more anaesthetists are mostly using 5 IU as mentioned in various literatures, described herein below. Interestingly, other studies have demonstrated the use of lower doses of oxytocin to achieve adequate uterine tone.
Sartain et al (2008) has found that 2 IU of oxytocin results in less haemodynamic changes when compared to 5 IU\(^3\). There was an increase in heart rate which was significantly greater in 5 IU than 2 IU. The mean decrease in MAP was also significantly greater in 5 IU sustaining a decrease of more than 30 mmHg compared to none in 2 IU group. There was a marked reduction in frequency of nausea and vomiting in 2 IU compared to 5 IU and reduced antiemetic therapy. There was no difference between the groups in blood loss and uterine tone\(^3\).

Sartain et al (2008) showed significant decrease in haemodynamic effects when using lower dose of oxytocin 2 IU compared with Pinder et. al. (2002) 10 and 5 IU. The higher doses of oxytocin resulted in significantly greater increase in heart rate and decrease in MAP\(^3,16\). Thomas et al (1997) administered oxytocin 5 IU as a bolus and the other group 5 IU as an infusion. Baseline MAP and heart rate were similar in both groups, mean arterial pressure bolus group 89 mmHg, infusion group 87 mmHg, mean heart rate bolus group 102 beats per minute, infusion group 93 beats per minute\(^4\). There was an increase in heart rate seen at 35 s in bolus group with apparent rebound bradycardia at 120 s. There was an increase by 10 beats per minute over the duration of infusion. A decrease in MAP up to 27 mmHg in bolus group and a decrease of 8 mmHg in infusion group was noticed during the study. The study demonstrated an average decrease in MAP and significant changes in heart rate in the two groups\(^4\).

Sarna et. al. (1997) compared four groups each receiving 5, 10, 15, and 20 IU oxytocin administered as infusion at rate 1.0 IU/min via infusion pump after clamping umbilical cord\(^3\). There was no significant difference in haemodynamic effects of patients in four groups at each recorded intervals (5, 10, 15 & 20 minutes) uterine tone and estimated blood loss were the same. Since a constant infusion rate of infusion of oxytocin was maintained the duration of administration was varied, it appears more a duration than dosage study\(^2\).

Pinder et al (2002) showed a decrease in MAP and a significant increase in heart rate in 10 IU compared to 5 IU\(^16\). Sartain et. al. (2008) showed decrease in MAP and increase heart rate in 5 IU than 2 IU which showed less haemodynamic effects, less nausea and vomiting\(^3\). Thomas et al (2007) studies showed a decrease in MAP and increase in heart rate in both groups\(^4\). Sarna et. al. (1997) showed no difference in
haemodynamic effects, uterine tone and estimated blood loss since constant infusion was maintained\(^2\). Pinder et. al. (2002), Thomas et. al. (2007) and Sartain et al (2008) showed a decrease in MAP, nausea and vomiting and significant increase in heart rate\(^3,4,16\). Khan et. al. (2014) concluded that there is a need to reevaluate the use of 5 IU oxytocin as a standard dose to achieve adequate uterine tone during caesarean section following their successful achievement of adequate uterine tone with 3 IU oxytocin\(^23\).

Tsimas, et. al. (2013) reported that oxytocin use during caesarean section in Botswana does not follow recommended practice and current literature, resulting in potential harmful consequences, such as increased morbidity and mortality\(^24\). In a recent review study, Yamaguchi, et. al. (2016) re-emphasizes that “oxytocin is the uterotonic of choice for the prevention and treatment of uterine atony and further that there is no consensus on the optimal dose and rate of its administration in caesarean sections”\(^25\). In addition, Yamaguchi, et. al. (2016) also concluded as follows:

- That “drip infusion of 5-20 IU oxytocin seems to be the usual mode of use in caesarean sections in Brazil,
- That high doses of or prolonged exposure to oxytocin can lead to desensitization of its receptors and be translated clinically as therapeutic inefficacy.
- That the use of oxytocin bolus (e.g. 10 IU) should be avoided, particularly in hypovolemic patients or those with low cardiovascular reserve”\(^25\).

Kiran, et. al. (2013) reported that small bolus dosage of oxytocin (0.5 – 2 IU) results in adequate uterine tone in women undergoing elective caesarean section delivery with minimal side effects on haemodynamic parameters and fewer incidences of nausea and vomiting\(^26\). Interestingly, in South Africa, the National ESMOE guidelines for district and regional hospitals’ protocol for caesarean section under spinal anaesthesia recommends a dose of 2.5 IU oxytocin administered slowly intravenously\(^27\).
CHAPTER 3: METHOD OF THE STUDY

3.1. Study setting.

The study was conducted at Dr. George Mukhari Academic Hospital, a tertiary level hospital in the province of Gauteng, north of Pretoria.

3.2. Study design

The study was conducted as a prospective double blinded randomized methodology.

3.3. Study Population

The study was done on pregnant women who had completed thirty seven weeks of pregnancy in line with American Society of Anaesthesiologists (ASA) I and II with singleton pregnancy to be delivered under spinal anaesthesia. The age range was from 18-45 years. The inclusion and exclusion criteria for the study population was as described below.

3.3.1. Inclusion criteria

Indication for caesarean section including:

- Healthy ASA I and II pregnant patient at term
- Previous caesarean section delivery
- Pre-eclampsia
- Gestational diabetes
- Breech presentation
- Fetal distress
- Poor fetal reserve

3.3.2. Exclusion criteria

Exclusion criteria including risk factors for post-partum haemorrhage:
- Placenta previa and abruption
- Multiple pregnancy
- Uterine fibroids
- History of uterine atony
- Bleeding disorder
- Use of anticoagulants
- Significant renal, liver, heart and endocrine disease
- Patient refusal
- Allergy to oxytocin
- Patient requiring more than 5IU intravenous bolus dose

3.4. Sample size

The sample population included 103 patients in Group A, administered with a bolus dose of 3 IU oxytocin, and 100 patients in Group B, administered with a bolus dose of 5 IU oxytocin.

With a sample size of two hundred and three (203) patients (103 on 3 IU and 100 on 5 IU) a difference of 20% in the occurrence of any of the critical side effects as described in the two groups were detected with 80% power using the chi-squared test at the 5% level of significance. Sample size estimation was done on query Advisor Release 7.

3.5. Sample selection

The sample population was selected on the basis of a Singleton pregnancy with indication for cesarean section delivery fitting the inclusion criteria.

3.6. Data collection

Anaesthesiology registrars were trained through a workshop on how to help with data collection in preparation for the study. The researcher recruited all patients who were booked with indication for caesarean section delivery. The study sample included patients who agreed to participate when approached and gave informed consent. Patient demographics and haemodynamic parameters were recorded on a
pre-designed sheet (Appendix I, II, and III). The researcher prepared the bolus dose to be administered by the pre-trained registrars but did not participate in the data collection. Anaesthesiology registrars were administering intravenous bolus dose 3 IU and 5 IU of oxytocin followed by infusion of 20 IU of oxytocin in one litre of ringers lactate at 125 ml/hr. Patients who subsequently required more than the prescribed dose were excluded from the study. Prepared drugs were labeled A and B. Only the researcher knew what was in A or B. Anaesthesiology registrars and the patient did not know the doses of oxytocin to be given. Collection of data was done over a period of six months after approval from Research Committee.

3.7. Method of data collection

Two hundred and three envelopes were prepared for packaging over the period of the study. Hundred and three envelopes had prepared syringe of oxytocin labelled A for Group A. The other hundred envelopes were allocated with prepared syringe labelled B for Group B. Each group was allocated number from one to hundred e.g. A 1. After the Registrar picked up the envelope with the labelled group and number, they wrote into the designed sheet with patient demographics and haemodynamic parameters. Doses of oxytocin were known by the chief researcher as the one who had prepared the bolus doses (a limited number of doses per day) and did not administer to any patient.

Anaesthesia was standardized with 500 ml Ringers lactate preloading infusion before the start of anaesthesia with an 18 gauge intravenous cannula. Haemodynamic monitoring included non-invasive blood pressure (NIBP) electrocardiogram (ECG) and pulse oximeter. Premedication consisted of oral 0.3 M Sodium Citrate 30 ml, Ranitidine 50 mg intravenous and 1 g Ampicillin, given before anaesthesia in the ward just after informed consent. Blood pressure and heart rate were each measured three times and then averaged to determine the baseline. Aseptic method was followed before the start of spinal anaesthesia. A 22, 25 and 26 gauge spinal needle (depending on availability) was inserted at L3/L4 interspace. Once cerebrospinal fluid was detected, hyperbaric bupivacaine 7.5-10 mg with 25 microgram fentanyl were injected intrathecally with patient in the sitting position. After spinal injection the patient was placed supine with 15 degrees left lateral tilt and slight head lift. Patients were then requested to lift their lower limbs and if they could
not then the spinal block was confirmed. In addition, the Obstetrician would test for pain with toothed forceps in the umbilical region.

After delivery of the baby and clamping of umbilical cord, oxytocin bolus dose was given intravenously over five to ten seconds followed by 20 IU in one litre of ringers lactate to run as an infusion at 125 ml/hr to maintain uterine contraction. Blood pressure and heart rate of the two groups were recorded using the automated noninvasive blood pressure monitor and electrocardiogram, respectively. Blood pressure and heart rate were recorded in the designed sheet with other patient demographics.

If any patient developed hypotension (Systolic blood pressure less than 100mmHg), bolus of Ephedrine 5-10 mg or Phenylephrine 50 µg were given to restore the mean arterial pressure to within 20% of preoperative values. Colloid or crystalloid fluids were also used to correct hypotension. Hypotension is the reduction of mean arterial value of 20% of the preoperative values. If any of the patients experienced nausea, vomiting or chest pain, then that side effect was recorded on a pre-designed chart. Chest pain resulting from increased myocardial demand due to tachycardia which shortens diastolic filling time were corrected by supplemental oxygen given by face mask. Blood loss was estimated by visual assessment of suction bottles and swabs. A fully soaked large swab holds 100-150 ml. Blood loss of up to 750 milliliters was expected during caesarean section. Blood loss more than a litre at operation was replaced with colloid or blood as deemed necessary by the anaesthetist.

Post-operative pain relief was standardized to multimodal analgesia with a combination of opioids, non-steroidal anti-inflammatory drugs, paracetamol and wound infiltration with local anaesthetic.

Data generated from the two groups of study was recorded in a data sheet designed for each patient and the strength of drug dosage.

**3.8. Data analysis**

The statistical analysis was descriptive and inferential.
Demographic data was summarized by descriptive measures e.g. mean, standard deviation, quartile range, minimum and maximum values, frequency counts and percentiles, as appropriate.

Within each group (3 IU and 5 IU) mean value of the changes over time in blood pressure and heart rate were tested for significance by the paired t-test. Mean values for the two groups were compared by the two sample t tests.

The occurrences of side effects in the two groups were compared by the chi-squared test. Results were reflected graphically as appropriate.

All statistical procedures were performed on SAS, Release 9.2 running under Microsoft Windows for a personal computer. All Statistical tests were two sided and p values ≤ 0.05 was considered significant.

3.9. Reliability and validity of study

Reliability is the extent to which test scores are accurate and consistent. To prevent errors the researcher trained registrars who helped with data collection. Standard monitoring equipment for blood pressure and heart rate used were calibrated. Proper selection of blood pressure cuff and placement on the arm covered 80% of the arm circumference. Smaller inflatable bladder can lead to false elevated blood pressure as bigger cuff will give low readings.

Validity refers to extent to which a research design is scientifically sound or appropriately conducted. It is used to determine whether research measures what it intended to measure and appropriate truthfulness of results. An average of three different readings of blood pressure and heart rate were used as the base line for validity purposes. This study was randomized double blinded study meaning it was blind to patient and anaesthesiology registrars giving the prepared doses by the researcher. The sample size for the study has been calculated by a statistician and the p values ≤ 0.05 were considered significant.

3.10. Bias

Random error due to sampling variability or measurement precision occurs in all quantitative studies. They can be minimized but not avoided. Bias was minimized by
getting a large number of sample size. Registrars participating in the study were trained and informed about recording the facts (correct readings) without editing any values. Random error were easily determined and addressed using statistical analysis. Bias can arise from innumerable resources and human factors. In this study we encountered selection bias (non-probability sampling). In this type of population, sampling members of population do not have an equal chance to be selected i.e. there is no way to ensure that all members of population would be selected.

Due to this, it was not safe to assume that the sample fully represent the target population. The researcher was also deliberately choosing each individual that participated in the study. The sample size was sufficient to warrant statistical analysis. Data was collected over six month’s period to get a bigger sample size. The researcher cannot guarantee representativeness due to time constrains.

3.11. Ethical consideration

Before the study was conducted, written informed consent was required from the patient and the documents with patients particulars were kept confidential. Patients were provided with study information leaflet including side effects so they can make an informed decision before they participate in the study. Approval from the Clinical Manager of Dr. George Mukhari Academic Hospital and Medunsa Research and Ethics committee was granted.
CHAPTER 4: RESULTS

4.1. Demographic Characteristics

The study involved two groups of patients where in one group (Group A) was administered with 3 IU oxytocin and the other group (Group B) with 5 IU oxytocin. Group A consisted of 103 patients while Group B had 100 patients. The average age of patients in both groups was more or less similar at 26.5 vs. 26.6, as described in table 1 and depicted in figure 1 below.

Table 1. Age, years

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<th>Group B: 5 IU</th>
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<td>N</td>
<td>103</td>
<td>100</td>
<td></td>
</tr>
<tr>
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<td>26.5</td>
<td>26.6</td>
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<tr>
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<tr>
<td>Minimum/Maximum</td>
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More importantly, the mean ages of patients in the two groups did not differ significantly (two-sample t test, p=0.8437). The mean ages of the two groups are displayed in the following figure.

Figure 1. Mean Age
4.2. Duration of Pregnancy

**Table 2. Duration of pregnancy**

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<thead>
<tr>
<th>Duration, weeks</th>
<th>Number (%) patients</th>
<th>Group A: 3 IU</th>
<th>Group B: 5 IU</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>19 (18.4)</td>
<td>12 (12.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>29 (28.2)</td>
<td>39 (39.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>24 (23.3)</td>
<td>24 (24.0)</td>
<td></td>
<td>0.0936</td>
</tr>
<tr>
<td>39</td>
<td>15 (14.5)</td>
<td>15 (15.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>14 (13.6)</td>
<td>4 (4.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>1 (1.0)</td>
<td>3 (3.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>1 (1.0)</td>
<td>3 (3.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>103 (100)</strong></td>
<td><strong>100 (100)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The distribution of the duration of pregnancy was more or less similar between the two groups.

**Figure 2. Duration of Pregnancy**
As summarized and depicted in table 2 and figure 2 above, the distribution of the duration of pregnancy does not differ significantly between Group A and Group B (Fisher Exact test, p=0.0936).

4.3. Heart Rates

The mean values of the heart rates of patients in the two groups are summarized in table 3 and depicted in figure 3 below.

**Table 3. Heart rates, bpm**

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A: 3 IU</th>
<th>Group B: 5 IU</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
<td>Min/Max</td>
</tr>
<tr>
<td>Baseline</td>
<td>103</td>
<td>96.8 ± 16.9</td>
<td>59/143</td>
</tr>
<tr>
<td>1 min</td>
<td>103</td>
<td>97.6 ± 15.3</td>
<td>60/132</td>
</tr>
<tr>
<td>2 min</td>
<td>103</td>
<td>97.0 ± 17.3</td>
<td>62/168</td>
</tr>
<tr>
<td>5 min</td>
<td>103</td>
<td>97.4 ± 16.9</td>
<td>52/160</td>
</tr>
<tr>
<td>10 min</td>
<td>103</td>
<td>93.8 ± 16.1</td>
<td>52/156</td>
</tr>
<tr>
<td>15 min</td>
<td>103</td>
<td>92.1 ± 15.4</td>
<td>54/140</td>
</tr>
<tr>
<td>20 min</td>
<td>97</td>
<td>90.7 ± 14.7</td>
<td>60/128</td>
</tr>
</tbody>
</table>

*Statistically significant

In both groups the mean heart rate initially increased, compared to baseline, and then dropped below the baseline level. The increase in heart rate at 1, 2 and 5 minutes was much higher in patients who received 5 IU oxytocin than those who received 3 IU oxytocin. The changes in heart rates were however statistically significantly different at 1 minute follow-up point (p values= 0.047).
**HEART RATE**

**Figure 3. Heart Rate**

The mean values of the changes, relative to baseline, in the heart rates at the follow-up points of 1, 2, 5, 10, 15 and 20 minutes are displayed in the following table.

**Table 4. Changes in heart rate, bpm**

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A: 3 IU</th>
<th>Group B: 5 IU</th>
<th>P value A vs B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
<td>Min/Max</td>
</tr>
<tr>
<td>Baseline</td>
<td>103</td>
<td>96.8 ±16.9</td>
<td>59/143</td>
</tr>
<tr>
<td><strong>Change at</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 min (p value)</td>
<td>103</td>
<td>0.79 ± 14.7 (0.5855)</td>
<td>-36/45</td>
</tr>
<tr>
<td>2 min (p value)</td>
<td>103</td>
<td>0.13 ± 15.8 (0.9324)</td>
<td>-31/48</td>
</tr>
<tr>
<td>5 min (p value)</td>
<td>103</td>
<td>0.53 ± 16.2 (0.7398)</td>
<td>-45/46</td>
</tr>
<tr>
<td>10 min (p value)</td>
<td>103</td>
<td>-3.0 ± 15.6 (0.0529)</td>
<td>-36/36</td>
</tr>
<tr>
<td>15 min (p value)</td>
<td>103</td>
<td>-4.8 ± 15.7 (0.0027*)</td>
<td>-37/43</td>
</tr>
<tr>
<td>20 min (p value)</td>
<td>97</td>
<td>-6.3 ± 15.4 (0.0001*)</td>
<td>-41/30</td>
</tr>
</tbody>
</table>

* Statistically significant
The mean changes in heart rate did not, at any point, differ significantly between the two groups (Two-sample t-test, all p values in last column of the table are > 0.05).

4.4. Systolic Blood Pressure

The mean systolic blood pressures of patients in the two groups are summarized in table 5 and depicted in figure 4 below.

**Table 5. Systolic blood pressures, mmHg**

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A: 3 IU</th>
<th></th>
<th>Group B: 5 IU</th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
<td>Min/Max</td>
<td>n</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Baseline</td>
<td>103</td>
<td>128.7 ± 16.3</td>
<td>81/171</td>
<td>100</td>
<td>121.6 ± 13.9</td>
</tr>
<tr>
<td>1 min</td>
<td>103</td>
<td>118.4 ± 17.4</td>
<td>69/182</td>
<td>100</td>
<td>111.8 ± 16.1</td>
</tr>
<tr>
<td>2 min</td>
<td>103</td>
<td>117.2 ± 16.9</td>
<td>72/172</td>
<td>100</td>
<td>109.7 ± 15.2</td>
</tr>
<tr>
<td>5 min</td>
<td>103</td>
<td>115.2 ± 16.9</td>
<td>68/167</td>
<td>100</td>
<td>109.8 ± 14.4</td>
</tr>
<tr>
<td>10 min</td>
<td>103</td>
<td>112.7 ± 15.8</td>
<td>79/160</td>
<td>100</td>
<td>111.5 ± 13.2</td>
</tr>
<tr>
<td>15 min</td>
<td>103</td>
<td>111.5 ± 15.8</td>
<td>72/177</td>
<td>89</td>
<td>112.8 ± 13.8</td>
</tr>
<tr>
<td>20 min</td>
<td>97</td>
<td>113.5 ± 12.4</td>
<td>82/147</td>
<td>81</td>
<td>116.4 ± 12.7</td>
</tr>
</tbody>
</table>

* Statistically significant

In both Group A and Group B, the drop in systolic blood pressures were all statistically significant at 1, 2 and 5 minutes follow-up points (Paired t test, all p values in brackets are < 0.05).

![SYSTOLIC BLOOD PRESSURE](image_url)

**Figure 4. Systolic Blood Pressure**
The mean values of the decreases, relative to baseline, in the systolic blood pressures at the follow-up points of 1, 2, 5, 10, 15 and 20 minutes are displayed in the following table.

**Table 6. Decreases in systolic blood pressures, mmHg**

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A: 3 IU</th>
<th>Group B: 5 IU</th>
<th>P value A vs B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
<td>Min/Max</td>
</tr>
<tr>
<td>Baseline</td>
<td>103</td>
<td>128.7 ± 16.3</td>
<td>81/171</td>
</tr>
<tr>
<td>Change at</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 min (p value)</td>
<td>103</td>
<td>-10.3 ± 16.5 (&lt;0.0001*)</td>
<td>-61.0/21.7</td>
</tr>
<tr>
<td>2 min (p value)</td>
<td>103</td>
<td>-11.5 ± 17.4 (&lt;0.0001*)</td>
<td>-62.3/23.3</td>
</tr>
<tr>
<td>5 min (p value)</td>
<td>103</td>
<td>-13.5 ± 16.5 (&lt;0.0001*)</td>
<td>-80.3/24.7</td>
</tr>
<tr>
<td>10 min (p value)</td>
<td>103</td>
<td>-16.0 ± 16.6 (&lt;0.0001*)</td>
<td>-69.3/32.3</td>
</tr>
<tr>
<td>15 min (p value)</td>
<td>103</td>
<td>-17.2 ± 19.1 (&lt;0.0001*)</td>
<td>-71.7/27.0</td>
</tr>
<tr>
<td>20 min (p value)</td>
<td>97</td>
<td>-15.3 ± 18.1 (&lt;0.0001*)</td>
<td>-69.7/30.0</td>
</tr>
</tbody>
</table>

* Statistically significant

The changes in systolic blood pressures did not differ significantly between Group A and Group B at 1, 2 and 5 minutes follow-up points. The changes differed significantly at 10, 15 and 20 minutes follow-up points. (Two-sample t test, p values in last column of the table).

**4.5. Diastolic Blood Pressure**

The mean diastolic blood pressures of patients in the two groups are as displayed in table 7 and depicted in the following graph 5 below.
Table 7. Diastolic blood pressures, mmHg

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A: 3 IU</th>
<th></th>
<th>Group B: 5 IU</th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
<td>Min/Max</td>
<td>n</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Baseline</td>
<td>103</td>
<td>78.1 ± 12.7</td>
<td>47/108</td>
<td>100</td>
<td>73.5 ± 10.3</td>
</tr>
<tr>
<td>1 min</td>
<td>103</td>
<td>69.2 ± 13.9</td>
<td>34/93</td>
<td>100</td>
<td>65.4 ± 12.6</td>
</tr>
<tr>
<td>2 min</td>
<td>103</td>
<td>67.4 ± 13.4</td>
<td>35/97</td>
<td>100</td>
<td>63.1 ± 11.5</td>
</tr>
<tr>
<td>5 min</td>
<td>103</td>
<td>65.8 ± 12.2</td>
<td>33/94</td>
<td>100</td>
<td>63.6 ± 11.1</td>
</tr>
<tr>
<td>10 min</td>
<td>103</td>
<td>62.4 ± 12.4</td>
<td>33/94</td>
<td>100</td>
<td>63.4 ± 11.5</td>
</tr>
<tr>
<td>15 min</td>
<td>103</td>
<td>62.7 ± 11.4</td>
<td>38/94</td>
<td>89</td>
<td>64.2 ± 11.5</td>
</tr>
<tr>
<td>20 min</td>
<td>97</td>
<td>63.2 ± 10.2</td>
<td>40/98</td>
<td>81</td>
<td>65.8 ± 11.1</td>
</tr>
</tbody>
</table>

* Statistically significant

In both Group A and Group B, the drop in diastolic blood pressures were all statistically significant at 1 and 2 minutes follow-up points (Paired t test, all p values in brackets are < 0.05).

Figure 5. Diastolic Blood Pressure

The mean values of the decreases, relative to baseline, in the diastolic blood pressures at the follow-up points of 1, 2, 5, 10, 15 and 20 minutes are displayed in the following table.
### Table 8. Decreases in diastolic blood pressures, mmHg

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A: 3 IU</th>
<th>Group B: 5 IU</th>
<th>P value A vs B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean±SD</td>
<td>Min/Max</td>
</tr>
<tr>
<td>Baseline</td>
<td>103</td>
<td>78.1±12.7</td>
<td>47/108</td>
</tr>
<tr>
<td>Change at</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 min</td>
<td>103</td>
<td>-9.0±12.6</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>(p value)</td>
<td></td>
<td>-55.7/21.3</td>
<td></td>
</tr>
<tr>
<td>2 min</td>
<td>103</td>
<td>-10.7±14.7</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>(p value)</td>
<td></td>
<td>-51.3/27.7</td>
<td></td>
</tr>
<tr>
<td>5 min</td>
<td>103</td>
<td>-12.3±13.8</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>(p value)</td>
<td></td>
<td>-60.7/24.3</td>
<td></td>
</tr>
<tr>
<td>10 min</td>
<td>103</td>
<td>-15.7±12.4</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>(p value)</td>
<td></td>
<td>-58.7/25.7</td>
<td></td>
</tr>
<tr>
<td>15 min</td>
<td>103</td>
<td>-15.5±13.5</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>(p value)</td>
<td></td>
<td>-66.7/15.0</td>
<td></td>
</tr>
<tr>
<td>20 min</td>
<td>97</td>
<td>-14.8±13.7</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>(p value)</td>
<td></td>
<td>-54.7/21.0</td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant

The changes in diastolic blood pressures did not differ significantly between Group A and Group B at 1, 2 and 5 minutes follow-up points. However, the changes differed significantly at 10, 15 and 20 minutes follow-up points. (Two-sample t test, p values in last column of the table).

### 4.6. Blood Loss

Blood loss was recorded in both groups of patients as summarized in table 9 and depicted in figure 6 below.
Table 9. Blood loss

<table>
<thead>
<tr>
<th>Blood loss, ml</th>
<th>Number (%) patients</th>
<th>Group A: 3 IU (n=103)</th>
<th>Group B: 5 IU (n=100)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 500</td>
<td>44 (43.1%)</td>
<td>54 (54.6%)</td>
<td>0.2178</td>
<td></td>
</tr>
<tr>
<td>500 – 750</td>
<td>50 (49.0%)</td>
<td>41 (41.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>750 – 1000</td>
<td>8 (7.9%)</td>
<td>4 (4.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>102* (100)</td>
<td>99* (100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* One missing value

There was no huge difference in blood loss between the two groups as per different categories of blood loss.

![BLOOD LOSS](image)

Figure 6. Blood Loss

The distribution of patient’s blood loss in the two groups does not differ significantly (Fisher Exact test, p=0.2178).

4.7. Side Effects

The study outcome with respect to side effects are as summarized in table 10 below.
### Table 10. Side effects

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Number (% patients with side effect)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A: 3 IU (n=103)</td>
<td>Group B: 5 IU (n=100)</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>5 (4.9%)</td>
<td>17 (17.0%)</td>
</tr>
<tr>
<td>Headache</td>
<td>10 (9.7%)</td>
<td>6 (6.0%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (10.7%)</td>
<td>32 (32.0%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>8 (7.8%)</td>
<td>7 (7.0%)</td>
</tr>
</tbody>
</table>

* Fisher Exact test

Patients administered with 5 IU oxytocin recorded high levels of chest pain (17%) compared to patients administered with 3 IU (4%). In addition, those administered with 5 IU also recorded high levels of nausea (32%) compared to the 3 IU patients. Headache and vomiting recorded comparable results between the two groups of patients.

The distribution of side effects between the two groups is depicted graphically in figure 7 below:

![Figure 7. Side Effects](image-url)
The percentage of patients with chest pain side effects in Group B (17.0%) is significantly greater than the percentage in Group A (4.9%). The percentage of patients with headache in Group B (6.0%) does not differ significantly from the percentage in Group A (9.7%). The percentage of patients with nausea in Group B (32.0%) is significantly greater than the percentage in Group A (10.7%). The percentage of patients who vomited in Group B (7.0%) does not differ significantly from the percentage in Group A (7.8%).
CHAPTER 5: DISCUSSION

5.1. Haemodynamic Changes

Maternal haemodynamic changes after caesarean delivery may have many potential causes, including removal of aorto-caval compression, auto transfusion from uterine contraction, blood loss, vasopressors and emotional excitement. Other studies have shown that uterotonic drugs were a dominant factor. The most cardiovascular changes observed after oxytocin are dose related decrease in systolic and diastolic blood pressure with a compensatory increase in heart rate.

5.1.1. Heart Rates

This study found that intravenous bolus of 3 IU oxytocin (Group A) resulted in less haemodynamic changes than 5 IU bolus (Group B). As summarized in Table 3, in patients administered with 3 IU, there was a significant increase in heart rates from baseline of 96.8 (±16.90) beats/min. The greatest change occurred at 1 minute with a heart rate of 97.6 (±15.3) beats per minute and decreased after 5 minutes to baseline. Patients administered with 5 IU however showed an even greater heart rate increase peaking at 102 (±18.3) beats per minute at 1 minute and decreased to baseline after 5 minutes. As depicted in figure 3, in both groups the mean heart rate initially increased, compared to the baseline, and then dropped below baseline level. The increase in heart rates at 1, 2 and 5 minutes follow-up points was much higher in patients who received 5 IU oxytocin than those who received 3 IU oxytocin. The changes were however statistically significant, in particular at 1 minute (Paired t test, p value = 0.047). Interestingly, the mean changes in heart rates did not, at any point, differ significantly between the two groups.

The haemodynamic findings as described above are consistent with those by Khan et. al. (2014), where in a similar study comparing 3 IU and 5 IU of oxytocin, observed that “oxytocin infusion (in 15 ml ringers lactate over 5 minutes) 3 IU results in less haemodynamic response (blood pressure) than oxytocin 5 IU although the difference
was not statistically significant. Sartain et. al. (2008) also reported similar results, where there was greater increase in mean (SD) heart rate in patients who received 5 IU of oxytocin [32(17) beats/minute] than those who received 2 IU of oxytocin [24(13) beats/minute], p=0.015. Kim et. al. (2011) also found that the haemodynamic changes (heart rate) were lower in 2 IU bolus-continuous group than those in the 5 IU group. Pinder et. al. (2002) also reported significant increases in heart rate in both groups following administration of a 5IU oxytocin compared to 10 IU, although much higher in the 10 IU group.

Interestingly, Bhattacharya et. al. (2013) study showed a higher increase in heart rate (approximately 25-30 beat/minute) in 3 IU bolus given over 15 seconds group at 30 seconds which did not return to baseline even after 10 minutes as compared to the infusion group where the heart rate raised by 10 beats/minute and gradually touched the baseline value. In addition, Murshid, et. al. (2011) reported in a study comparing 5 IU bolus and 5 IU infusion that the mean difference of all haemodynamic parameters at 2 to 5 minutes of administration of oxytocin were statistically significant (P<0.05).

In another interesting similar study, Kiran, et. al. (2013) reported that small bolus dosage of oxytocin (0.5 – 2 IU) results in adequate uterine tone in women undergoing elective caesarean section delivery with minimal side effects on haemodynamic parameters and less incidence of nausea and vomiting.

### 5.1.2. Systolic and Diastolic Blood Pressures

There was a significant decrease in systolic blood pressure relative to baseline of 128 (±16.3) mmHg at 1 and 2 minutes, i.e. 118 (±17.4) mmHg and 117 (±16.9) mmHg for Group A (3 IU). Group B (5 IU) also showed a significant decrease in systolic blood pressure relative to baseline of 121 (±13.9) mmHg at 1 and 2 minutes, i.e. 111.8 (±16.1) mmHg and 109 (±15.2) mmHg, respectively. As summarized in Table 5, in Group A as well as Group B the drop in systolic blood pressure were all statistically significant at 1, 2 and 5 minutes follow-up points (paired t-test, p<0.05). The changes in systolic blood pressure did not differ significantly between Group A
and Group B at 1, 2 and 5 minutes follow-up points. The changes differed significantly at 10, 15 and 20 minutes follow-up time points (paired t-test, p<0.05), as illustrated in figure 4.

In Group A (3 IU), there was a drop in diastolic blood pressure at 1, 2 and 5 minutes follow-up points, i.e. 69.2 (±13.9) mmHg, 67.4 (±13.4) mmHg, 65.8 (±12.2) mmHg relative to the baseline 78.1 (±12.7) mmHg. Also in Group B (5 IU), there was an even greater drop in diastolic blood pressure at 1, 2 and 5 minutes follow-up points, i.e. 65.4 (±12.6) mmHg, 63.1 (±11.5) mmHg and 63.6 (±11.1) mmHg relative to baseline of 73.5 (±10.3) mmHg. In both Group A and B, the drop in diastolic blood pressure (Table 7) were all statistically significant at 1 and 2 minutes follow-up points (paired t-test, all p values <0.05). The changes in diastolic blood pressure did not differ significantly between Group A and B at 1, 2 and 5 minutes follow-up points, as illustrated in figure 5. However, the changes differed significantly at 10, 15 and 20 minutes follow-up points (paired t-test, p value < 0.05).

In line with this study results’, Sartain et. al. (2008) reported a significant decrease in mean arterial pressure (MAP) from baseline at 1 minute in both groups p≤0.005 in patients who received 5 IU [13 (15) mmHg] than those who received 2 IU [6 (10) mmHg], p=0.030³. Thomas et. al. (2007), in comparing 5 IU bolus IV against 5 IU infusion, MAP decreased up to 27 mmHg and heart rate increased by 7 beats/minute at 35 seconds in the bolus group which recovered to baseline at 110 seconds. The infusion group in contrast had a decrease in MAP of only 8 mmHg and heart rate increased by 10 beats/minute⁴. However, in a comparative study by Pinder et. al. (2002), there was a small but statistically significant (P < 0.05) reduction in mean arterial pressure (MAP) from baseline 30 seconds after administration of a 10 IU oxytocin bolus¹⁶.

5.1.3. Blood Loss

In Group A, the percentage of blood loss <500ml was 43% as compared to 54% in Group B. Between 500 – 750 ml, Group A percentage blood loss was 49% as compared to 41.4% in Group B. Between 750 -1000ml, Group A was 7.9% and
Group B was 4.0%. As indicated in Table 9 and depicted in figure 6, the distribution of patient blood loss in the two groups did not differ significantly (Fischer exact test p=0.2178).

Consistent with this study results, both Taj and Ommid (2014) and Khan et. al. (2014) reported no difference in blood loss between the two groups. In contrast, Carvalho et. al. (2004) reported estimated blood loss at 693±487 ml while concluding that the bolus dose of oxytocin used at elective caesarian deliveries in non-laboring women can be significantly reduced while maintaining effective uterine contraction.

5.2. Other Side Effects

The number of pregnant women who experienced nausea and vomiting was greater in Group B (5 IU) than Group A (3 IU). Percentage in nausea in Group B (32.0%) was significantly greater than Group A (10.7%), as indicated in Table 10 and depicted in figure 7 (p value = 0.0003). The percentage of those who vomited in Group B (7.09%) does not differ significantly from the percentage in Group A (7.8%). The percentage patients with chest pain side effects in Group B (17%) is significantly greater than the percentage in Group A (4.9%) (p value = 0.0063). The percentage of patients with headache in Group B (6 %) does not differ significantly from the percentage in Group A (9.7%).

In line with this study findings, Sartain et. al. (2008) reported that the frequency of nausea was higher in the 5 IU (32.5%) group than in the 2 IU (5%) group, p=0.003. Taj and Ommid (2014) found that there were no differences in uterine tone, nausea, vomiting or the need to give further uterotonics in their study comparing two groups administered with 10 IU either as bolus injection over 15 seconds or infusion over 5 minutes. Bhattacharya et. al. (2013) reported chest pain (12.5%) in the bolus group while no such adverse effects were noticed in the infusion group.

Overall, the results as observed in this study are consistent with literature knowledge as the drop in blood pressure in the 5 IU group is consistent with the high incidence of nausea and vomiting in the same group.
CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1. CONCLUSION

As reported in previous studies, Oxytocin has demonstrated again to be an effective uterotonic drug for caesarean sections. The most effective dose, as the study intended to establish, remains a widely contested phenomenon. Different doses have been used widely with different results with the most common being haemodynamic changes including increased heart rate, cardiac output and decreased mean arterial pressure.

In this study, the 5 IU oxytocin intravenous bolus demonstrated a higher impact on the haemodynamic changes compared to the 3 IU oxytocin intravenous bolus. Administration of 5 IU oxytocin resulted in a greater increase in heart rate than the administration of 3 IU, which was only significantly different, in particular, at 1 minute (p value = 0.047). In addition, 5 IU oxytocin intravenous bolus resulted in greater decreases in both systolic and diastolic blood pressures than in 3 IU oxytocin intravenous bolus. These decreases were particularly significantly different for systolic blood pressures at 1, 2 and 5 minutes follow-up points (p values: 0.005, 0.001 and 0.014, respectively) while for diastolic blood pressures the decreases were significantly different at 1 and 2 minutes follow-up points (p values: 0.043 and 0.016, respectively).

Despite the haemodynamic changes, the other most significant difference was in the percentage in nausea which was significantly greater in Group B (5 IU) at 32.0% than Group A (3 IU) at 10.7%, as indicated in Table 10 and depicted in figure 7 (p value = 0.0003). In addition, the percentage patients with chest pain side effects in Group B (17%) is significantly greater than the percentage in Group A (4.9%, p value = 0.0063).

Dyer et al (2011) showed that slow administration of 1-3 IU intravenous bolus dose is sufficient for uterine contraction for both non-laboring and laboring women and decreases side effects during caesarean section\(^\text{11}\). This dose should be administered in the form of infusion rather than bolus and maintenance of infusion to
be administered over 8 hours. Butwick et al. (2010) concluded that the routine use of 5 units oxytocin for caesarean deliveries should no longer be recommended, as effective uterine tone occurs with lower doses of oxytocin (0.5 – 3 units). In another similar study, Kiran, et. al. (2013) reported that small bolus dosage of oxytocin (0.5 – 2 IU) results in adequate uterine tone in women undergoing elective caesarean section delivery with minimal side effects on haemodynamic parameters and less incidence of nausea and vomiting.

In this study, the administration of 3 IU oxytocin intravenous bolus resulted in less haemodynamic response than 5 IU oxytocin intravenous bolus. However, in contrary to Khan et. al., the results were statistically significantly different for certain haemodynamic effects at certain follow-up time points. This study confirms that adequate uterine tone can be achieved with small doses of oxytocin in patients undergoing caesarean section. The findings of this study are therefore consistent with the recommendation of a 2.5 IU oxytocin intravenous dose by the National ESMOE guidelines for district and regional hospitals’ protocol for caesarean section under spinal anaesthesia. The use of 3 IU or less as a preferred dose of use during caesarean delivery at Dr. George Mukhari Academic Hospital should be considered.

In conclusion, the most haemodynamic changes observed in this study after oxytocin administration are the increase in heart rate, and dose related decrease in systolic and diastolic blood pressure. The impact was higher in the 5 IU group than in the 3 IU group of patients. In addition, high doses of oxytocin induced higher levels of nausea and chest pain.
6.2. LIMITATIONS OF THE STUDY

1. The study was undertaken in healthy pregnant patients with singleton undergoing caesarean section delivery under regional anaesthesia.
2. These results may not be applicable to pregnant patients with a high risk for post-partum haemorrhage.
3. Patients in labour may exhibit unpredictable response to oxytocin because of either prolonged labour or use of intravenous oxytocin to augment labour which may desensitize and may render unresponsive and may require other uterotonics.
4. Use of non-invasive monitors missing the detection of transient haemodynamic change.

6.3. RECOMMENDATIONS

At Dr. George Mukhari Academic Hospital there is no formal protocol as to what dose of oxytocin to give after caesarean section or vaginal delivery to contract the uterus. Most doctors administer oxytocin dose ranging from 5 IU to 10 IU bolus or as per request from the obstetrician after assessing the tone of uterus for contractility.

The development of an appropriate oxytocin protocol for caesarean section is a subject of further investigation and local studies at Dr. George Mukhari Academic Hospital would be even more useful and probably relevant for the South African population. Similarly, Tsimane, et. al. (2013) reported similar challenges in Botswana and recommended “education and guidance through local national guidelines and local protocols to alleviate potential harmful consequences, such as increased morbidity and mortality.” This recommendation is also true for South Africa and should contribute positively to the reduction of local morbidity and mortality rates following caesarean section delivery.

In consistent with Khan et. al. (2014), the following points should be integrated when designing a protocol:

1. Oxytocin should be given slowly in small boluses of 1-3 IU and not 5IU.
2. It should not be administered as a rapid intravenous bolus.
3. A smaller initial rapid infusion of oxytocin should be followed by a maintenance infusion.

4. If effective uterine contraction is not maintained by oxytocin other uterotonic drugs acting via different pathways should be considered.

According to Tsen L.C. (2013) there is an Oxytocin Rule of Three for caesarean section to be followed:

I. 3 IU iv loading dose to be administered no faster than 15 seconds
II. 3 minutes assessment interval, if inadequate contraction give 3 IU oxytocin iv rescue dose
III. 3 total doses of oxytocin (initial + 2 rescue doses)
IV. 3 IU/h oxytocin iv maintenance dose (30 IU/L @100ml/h)
V. 2 Pharmacologic options (carboprost and misoprostol).

In determining the appropriate oxytocin protocol, the National ESMOE guidelines for district and regional hospitals’ protocol for caesarean section under spinal anaesthesia\(^\text{27}\) is of more critical importance. Therefore, this researcher recommends that based on this study’s outcomes and other literature, as cited above amongst others, DR George Mukhari Academic Hospital should consider the adoption of a 2.5 IU oxytocin intravenous dose in line with the National ESMOE guidelines for district and regional hospitals’ protocol for caesarean section under spinal anaesthesia\(^\text{27}\).
REFERENCES


10. Taj A, Ommid M. Haemodynamic effects of Oxytocin as intravenous bolus or infusion on women undergoing caesarian section. JK Science 2014; 16(2): 52-56


27. ESMOE Aneasthesia Working Group, National ESMOE guidelines for district and regional hospitals’ protocol for caesarean section under spinal aneasthesia, July 2009 revision May 2011
APPENDIX

APPENDIX I

A RANDOMISED DOUBLE BLINDED STUDY COMPARING THE HAEMODYNAMIC EFFECTS OF INTRAVENOUS BOLUS OF 3 IU VS 5 IU OXYTOCIN DURING CEASAREAN SECTION DELIVERY UNDER SPINAL ANAESTHESIA AT Dr GEORGE MUKHARI ACADEMIC HOSPITAL.

PATIENT GROUP .......... A OR B NUMBER ..........

DATE OF COLLECTION ........................................................................................................

NAME OF DATA COLLECTOR ..........................................................................................

PATIENT AGE ...................................................................................................................

DURATION OF PREGNANCY ..........................................................................................

PREMEDICATION ............................................................................................................... 

ADDITIONAL BOLUS DOSE ............................................................................................

TIME OF SIDE EFFECTS POST BOLUS ........................................................................

SEVERITY OF SIDE EFFECTS ........................................................................................
APPENDIX II

Table 1: Haemodynamic effects variables and rescue measures
Phenylephrine (PEP) or Ephedrine

<table>
<thead>
<tr>
<th></th>
<th>Blood Pressure in mmHG</th>
<th>Heart rate in beats per minute</th>
<th>Systolic BP &lt;100mm Hg PEP/Ephedrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before injection of oxytocin bolus to be followed by infusion. Baseline 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 minute</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX III

Table 2: Side effects profile

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Blood loss estimation by swabs and in the suction bottle

<table>
<thead>
<tr>
<th></th>
<th>&lt;500ml</th>
<th>500ml-750ml</th>
<th>750ml-1000ml</th>
<th>&gt;1000ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Emfundo yesiguli

Phrojekthi: Impiphumele ehlukahlukene laphonalaphayayo
imnika imbumba emva ubelekwe ngokusikwa ungalalisiwa
nga ujovwe emgodleni lapha esibhedlela sase Dr. George
Mukhari Academic Hospital

Emva kokubelethwa kwengane ngoku sikwa isibeletho
kufanele sifingcweno masishwabane ukuza angalahlekelwa
yigazi. I oxytocin inikizelwa ukusiza ukushwabanisa isibeletho
kepha futhi nalokho kune miphumela e fanele nenga
fanelekanga. Leyo miphumela ingaba isihlabi sesifuba,
inhliziyo I shaya masinyane, igazi liya phansi, uma kuthi
uphalaze. Uma isigulani sibenokugula lokhu esikhulume lapha
kulephepha uzothola ukulatshwa.

E kufundeni kwethu sizohlukanisa ukuthi iyiphi kwezimbili
izilinganiso zokujoviwa ngokudlulele phakathi kuka 3IU no
5IU ukuthi yiphi ezobane miphumela engasiyingozikodwa
ikwazi u kushwabanisa isibeletho emva koku fakwa kwe
oxytocin.

Ngifunde ngazwisisa lemfundo
Igama lesiguli ............................................................................................................
Umsayino ....................................................................................................................
Patient leaflet of the study

Title: A randomized double blinded study comparing the haemodynamic effects of intravenous bolus 3IU vs. 5IU oxytocin during caesarean section delivery under spinal anaesthesiology at Dr. George Mukhari Academic Hospital.

After delivery of the baby through caesarean section uterus must contract to prevent blood loss. Oxytocin is given to aid contraction but also comes with side effects. Those side effects include chest pain, tachycardia, hypotension, nausea and vomiting. Patients who will develop any side effects will be given treatment according to presentation of symptoms.

In our study we are going to compare which of two doses intravenous bolus 3 U and 5 IU will have least side effects but still contracting the uterus followed by an infusion of oxytocin.

I read and understand the study details.

Name of a patient ..........................................................

Signature ..........................................................
Thuto ka molwetse

Leina la porojeke: Dipatlisiso di le pedi di farologaneng di dirilwe ka gotlhopha batho fale le fale le go bapisa ditlamorago tsa meento ya 3 IU le 5 IU mo mading mo nakong ya pelegiso (Ceasarean) mo sepetleng sa Dr George Mukhari Academic Hospital.

Morago ga go belega ka karo popelo e tswanetse go ngotlafala go thibela go felelwa ke madi. Popelo e ngotlega fa o file moletswi oxytocin ee nang le ditlamorago. Ditlamorago e leng ditlhabi mafatlheng, pelo e itaya ka bonako, kgatelelo ya madi e godimo, go sellega le go tlhatsa. Ge eba molwetsi a humana tshwatso morago ga go humana kalahi otla humana hlokomelo ya kalahi.

Go se re i thutang ka sona re ya go bapisa gore meento ya 3IU le 5IU di ka baana le ditlhmorago tse nnye empa popelo e ngotlega morago o neela molwetse oxytocin.

Ke buisitse le go tlhaloganya thuto ee fa godimo

Leina la molwetse ........................................................................................................................................

Tshaeno ya molwetse ....................................................................................................................................