POTENTIAL OF KETOFOL TO PROVIDE ADEQUATE SEDATION AND ANALGESIA IN WOMEN UNDERGOING MANUAL VACUUM ASPIRATION IN EMERGENCY DEPARTMENT AT THE UNIVERSITY TEACHING HOSPITALS, LUSAKA ZAMBIA

BY

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A Dissertation Submitted to the University of Zambia in Fulfilment of the Requirement for the Master of Medicine in Anaesthesia and Critical Care

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DEDICATION

To my gorgeous wife Lerato, and my two wonderful children; Michael and Laura, without their endurance and backing, this could not have been possible.

DECLARATION

I, Dr. Kaunda Lwimba, hereby declare that this dissertation represents my own work, and it has not previously been submitted either in all or in part for a degree, diploma or other qualification at this or another University.

SIGNED

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APPROVAL

This Masters dissertation of Dr. Kaunda Lwimba is approved as fulfilling part of the requirements for the award of degree in Master of Medicine in Anaesthesia and Critical Care by the University of Zambia.

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ABSTRACT

Diagnosis of abortion in Zambia relies on clinical findings coupled with ultrasound examination. The treatment of choice in the first trimester is manual vacuum aspiration (MVA). Reducing the physical pain and anxiety during MVA is the ultimate goal of management for which, several drugs have been used solely or in combination to try to alleviate the pain associated with the procedure with variable results. However, the aspect of anxiety, which is a crucial aspect of care, is not adequately taken care of and perhaps raises ethical issues around performing MVA under local anaesthesia in emotionally vulnerable miscarrying women.

A previous study done at University Teaching Hospital (UTH), Lusaka, Zambia showed that more than 90% of women undergoing MVA experience severe pain, despite receiving preoperative analgesics such as Paracetamol, Ibuprofen and Morphine. Ketofol sedation has not been tried in MVA in our setting in spite of successfully producing adequate sedation action for many short painful procedures.
A pre-post interventional study with historical controls was conducted as a quality improvement study at UTH in the Department of Gynaecology to explore the potential of Ketofol sedation to provide adequate sedation and analgesia in women undergoing MVA. Pain scores were recorded using a Faces Pain Scale during the procedure (reported immediately after the procedure), at 10 minutes and at 60 minutes. During the procedure, sedation scores were determined using Ramsay Sedation Scale as well measuring heart rates and oxygen saturation. Time to discharge was also measured.

A total of 94 women were studied; 54 patients who received UTH standard care in the previous study (oral Paracetamol 1g, Ibuprofen 400mg and Morphine 30mg) and 40 patients who received Ketofol sedation in addition to the UTH standard care which the patients in the historical group also received. Data from 2015 included 54 (57.4%) women who received UTH standard care (oral Paracetamol, Ibuprofen and Morphine). In the current study Ketofol sedation was administered in addition to standard care to 40 women during MVA. There was no statistical difference in all baseline characteristics of participants in both groups; p value >0.05. Pain scores were measured during the procedure (reported immediately afterwards), at 10 minutes and 60 minutes after the procedure. Women in the standard care group reported significantly higher pain scores, median 10 (IQR,8-10) compared to women in the Ketofol group median 2 (IQR 0–2); $p<0.001$ during the procedure, and also reported more pain at 10 minutes after the procedure however, there was no statistically significant difference in pain recorded at 60 minutes after the procedure. It was further noted that patients in the Ketofol group had significantly lower heart rates during the procedure. addition to this, it was noted, contrary to expectations, that the time to discharge was reduced in the Ketofol group compared to the standard care group, potentially due to reduced pain experienced.

In conclusion, the results suggest that addition of Ketofol sedation to the current UTH standard of care reduced procedural pain experienced during MVA compared to standard care alone as well as producing effective sedation and rapid recovery.

Keywords: Miscarriage, Manual Vacuum Aspiration, Sedation, Ketofol

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ABBREVIATIONS AND ACRONYMS

ED	Emergency Department
FPS	Faces Pain Scale
FPR	R Faces Pain Scale – Revised
IASP	International Association for the Study of Pain
LMIC	Low and Middle Income Countries
MVA	Manual Vacuum Aspiration
NRS	Numerical Rating Scale
PSA	Procedural sedation and analgesia
REC	Research Ethics Committee
RPOC	Retained products of conception
RSS	Ramsay Sedation Scale
UTH	University Teaching Hospital
WNBH	Women and New Born Hospital
VAS	Visual Analogue Scale
VRS	Verbal Rating Scale
WHO	World Health Organization

DEFINITIONS OF TERMS

Pain	'an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage' (International Association for the Study of Pain, 1994).
RPOC	persistence of placental or fetal tissue in the uterus after delivery, termination of pregnancy or a miscarriage (Radiopaedia, 2018).
MVA	procedure performed to remove retained products of conception.
Septic Abortion	any abortion with signs of infection (Udoh *et al.*, 2016).
Induced Abortion-	an abortion accomplished by the pregnant woman herself or with the help of other, non-medical help (Carolyn, 2016).
Spontaneous Abortion	the loss of pregnancy without external intervention before 20 weeks' gestation (Zegers-Hochschild *et al.*, 2009).
Sedation	a semi-conscious state that allows patients to be comfortable during certain surgical or medical procedures (American Society of Anesthesiologists).
Analgesia	loss of sensation of pain that results from an interruption in the nervous system pathway between sense organ and brain (Encyclopedia Britannica).
Recovery Time	duration of time, in minutes, from the end of the MVA to the time the patient is deemed fit for discharge.
Ketofol	mixture of ketamine and propofol (1:4) ratio used in this study
Standard Care	protocol of care which involves giving oral paracetamol, ibuprofen and morphine.

CHAPTER ONE: INTRODUCTION

1.1 Background

Early pregnancy failure is a significant public health problem throughout the world. Up to 20% of recognised pregnancies miscarry, and up to 25% of women will experience a miscarriage up to some point (Shwekerela *et al.,* 2007). Although approximately 15% of all pregnancies end in spontaneous miscarriage, there are also an estimated 22% induced abortions annually (Alan Guttmacher Institute 1999). Many of these are performed in unsafe situations resulting in approximately 47,000 deaths annually worldwide representing 13% of all maternal deaths (WHO, 2011). The majorities of these maternal deaths occur as a result of septicaemia and haemorrhage (Hill *et al., 2001*). Also, many more women suffer long-term morbidity such as pelvic infections, uterine perforation and anaemia (Finer *et al.,* 2005). Because spontaneous and induced abortions are usually impossible to distinguish both groups of women in this situation are managed the same (Mupeta *et al.,* 2009).

Diagnosis of abortion in Zambia relies on clinical findings coupled with ultrasound examination (Mupeta *et al.,* 2009). The treatment of choice in the first trimester is manual vacuum aspiration (MVA) (Weeks*et al.,* 2013; Allison *et al.,* 2011). In our setting, MVA is a short gynaecological procedure performed in the emergency department, and is characterised by anxiety and pain. Reducing the physical pain and anxiety that most women undergo during MVA of retained products of conception (RPOC) is the ultimate goal of management while lowering medication-induced side effects (Antonella *et al*., 2015; Baird *et al.,* 2002).

Management of procedural pain during miscarriage or abortion is a crucial aspect of patient care (Meckstroth *et al.,* 2009). Several drugs have found their use solely or in combination to try to alleviate the pain associated with the procedure, with variable results. Generally, the following categories exist for pain management: Firstly, we have analgesics, which alleviate the sensation of pain at the level of receptors of the spinal cord and brain (Stern *et al*., 2009; Margolis *et al*., 1993). Peripherally acting analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) act by inhibiting cyclo-oxygenase-1 (COX-1) and COX-2 enzymes, involved in prostaglandin synthesis, resulting in analgesic, anti-inflammatory, and antipyretic effects (Day *et al*., 2013). Secondly, we have anaesthetics, some of which eliminate only the recollection of pain by means of hypnosis, like propofol (Ilyas *et al.,* 2017) while other anaesthetics provide both hypnosis and analgesia. Local anaesthesia, injected into the cervix and areas around the cervix, interrupts the

transmission of painful impulses to the brain (Tangsiriwatthana *et al*., 2013, Maltzer *et al.*, 1999). Para-cervical block using lignocaine 1% is effective as a safe alternative to procedural sedation in the management of incomplete miscarriages (Arora *et al.*, 2016; Renner *et al*., 2012). However, the aspect of anxiety, which is a crucial aspect of care, is not adequately taken care of and perhaps raises ethical issues around performing MVA under local anaesthesia in emotionally vulnerable miscarrying women (Sharma *et al.*, 2015). Thirdly, we have anxiolytics which decrease anxiety and facilitate relaxation (Farach *et al.*, 2012; Rawling and Wiebe, 1998). Other modalities such verbal support has been found to be useful in the management of MVA. Verbal support to provide reassurance and diversion during the MVA procedure and para-cervical block use, generally, proved inadequate for pain relief (Renner *et al.*, 2010).

A combination of propofol and ketamine (Ketofol) has successfully produced adequate sedation for many short painful procedures such as in oncology (Andolfatto *et al*., 2012; Aouad *et al.*, 2008). Its effectiveness has also been shown in interventional radiology (Aydin Erden *et al.*, 2009), cardiac catheterization, (Akin *et al.*, 2005) and haematological diseases (da Silva *et al.*, 2011) in children. In practice, clinical effects of propofol and ketamine complement each other well. While propofol provides hypnosis, ketamine offers analgesia and stable hemodynamic activity (Sakai *et al.*, 1995).

A study done as part of a previous dissertation at University Teaching Hospital (UTH), Lusaka, Zambia showed that more than 90% of women undergoing MVA of RPOC experience severe pain (Mumphansha *et al.*, 2015), despite receiving pre-operative analgesiain the form of oral Paracetamol, Ibuprofen and Morphine, which is the standard care protocol in this institution. Studies of other painful procedures such as circumcision and colonoscopy have shown that Ketofol significantly reduces pain compared to other analgesic and sedative drugs. However, Ketofol has not been used in MVA in our setting. Thus, this study was set out looking at a new intervention which could potentially be considered optimal in many contexts and comparing it with our local standard care in reducing pain among women undergoing MVA at UTH.

1.2 Statement of the problem

Management of procedural pain during miscarriage or abortion is a critical aspect of patient care (Meckstroth, 2009). Despite advances in pain management and research, millions of people continue to suffer unnecessarily (Mackey, 2016; Board, 2011). In many low and middle-income countries (LMIC), pain management takes a low priority (Sasaki *et al.*, 2017; Travis, 2004). There is a general lack of personnel, drugs and basic equipment in this field of healthcare (Hodges *et al.*, 2007). Despite their recognised effectiveness in treating pain, adequate analgesics are still not readily accessible in many hospitals in LMIC (Size *et al.*, 2007; Soyannwo, 2010). Currently, at the University Teaching Hospital, Lusaka, Zambia, a combination of oral paracetamol, morphine and ibuprofen is used to alleviate pain during MVA. However, this regimen is inadequate because a recent study showed more than 90% women undergoing MVA experience severe pain (Mumphansha *et al*., 2015). Uncontrolled acute pain not only leads to discomfort and suffering but also has unwanted consequences such as delayed healing, increased morbidity, prolonged stay in hospital and risk of developing chronic persistent pain (Harsoor, 2011; Board, 2011).

1.3 Study justification

The University Teaching Hospital lacks equipment to perform general anaesthesia on women undergoing MVA of RPOC, a short procedure characterised by anxiety and pain. In spite of administration of a combination of oral paracetamol, ibuprofen and morphine, women still experience severe pain (Mumphansha *et al.*, 2015). The use of propofol and ketamine for procedural sedation and analgesia has grown in popularity, but the unwanted effects of each drug alone have limited their adoption in painful procedures such as during circumcision (Yousef and Elsa yed, 2013). Thus, the use of Ketofol has been reported to reduce pain, provide sedation and amnesia with little impact on human resource (Yousef and Elsayed, 2013). This study therefore was set out to determine the potential of sedation with a combination of two well-known medications in women undergoing MVA. It was hypothesized that Ketofol sedation, in addition to the local standard care protocol (oral analgesia), would reduce acute pain and anxiety associated with the procedure.

1.4 Research question

Would the use of Ketofol (in addition to standard care) provide adequate sedation and analgesia in women undergoing MVA compared to women on standard care (oral analgesia) alone in the ED at the University Teaching Hospitals, Lusaka, Zambia?

1.5 Objectives

1.5.1 General objective

To explore the potential of Ketofol to provide adequate sedation and analgesia compared to standard care (oral analgesia) in women undergoing manual vacuum aspiration of retained products of conception at University Teaching Hospital (UTH).

1.5.2 Specific objectives

1. To determine sedation scores of women undergoing MVA who receive Ketofol sedation
2. To determine the pain experienced by women undergoing MVA under Ketofol sedation compared to those receiving the UTH standard care (oral analgesia) only
3. To determine the time to discharge of women undergoing MVA with Ketofol Sedation compared to those receiving the UTH standard care (oral analgesia) only

CHAPTER TWO: LITERATURE REVIEW

2.1 Management of abortions

Both spontaneous and induced abortions can lead women to seek care at health facilities. In most cases, it is difficult to distinguish between spontaneous and induced abortions of which first trimester miscarriages have considerable human and financial burden (WHO, 1997). Not surprisingly, these women make up a significant part of the gynaecological patient load presenting to emergency gynaecological clinics.

Treatment of first-trimester miscarriage can either be medical and expectant or via MVA. MVA is a more attractive method in comparison to expectant management and medical management because it is inexpensive, has fewer complications (Rausch *et al.,* 2012; Kinariwala *et al.,* 2013) and can be performed by a non-physician health worker at primary health care facilities (De Jonge *et al.,* 1994). Pain and distress during a surgical evacuation are elicited via different routes throughout the entirety of the procedure.

The evacuation procedure includes placement of the tenaculum, traction of the cervix and dilatation of the os. Pain sensation is transmitted via the sensory and sympathetic pathways from the postero-lateral aspect of the cervix to the lateral spinal thalamic tract of the spinal cord (Al-Chalabi and Gupta, 2018). Also, a deep intrinsic pain caused by the evacuation of the uterus is elicited, occurring as a diffuse pain with cramping. Pain is experienced with the movement of the uterus and scraping of the uterine wall as well as muscle contraction related to emptying (Zhang *et al.,* 2010). Uterine pain is transmitted from the fundus along major uterine nerves which follow the uterosacral and utero ovarian ligaments. Women who have experienced miscarriage or early pregnancy loss have bereavement actions such as grief, resentment, guilt and anxiety (Kersting and Wagner, 2012). High levels of anxiety also tend to lead to an increase in pain reporting (Olav *et al.,* 2018; Cardno, 2002). Another very important consequence of inadequately controlled acute pain is eventual development of chronic pain, with its morbidity and sequelae, which is difficult to treat. Chronic pain may result from disease or injury, however, its persistence and extent maybe inadequately explained based on the low level of underlying pathology as the pain may persists for a long period.

The current available treatment options are rarely capable of eliminating chronic pain totally. Due to the persistence of pain, it is possible that environmental, emotional, and cognitive factors do play a role or certainly contribute to persistence of pain as well as its related illness behaviours (Hadjistavropoulos *et al.*, 2011).

The first and necessary step to ensure optimal pain management is an accurate assessment and one of the utmost critical barriers to adequate pain treatment is that it is not evaluated in the first place (Ardery *et al.,* 2003). The International Association of Pain defines pain as "an unpleasant sensory or emotional experience associated with actual or possible tissue harm or described regarding such damage" (Allison *et al.*, 2009). In 1968, McCaffery coined the statement that "pain is whatever the experiencing person says it is, occurring whenever he says it does". As pain is an individual experience, self-report is the most appropriate way of describing pain (Market al., 2012). Therefore, acceptance of the patient's report is the cornerstone of pain management. However, pain assessment is problematic and complicated (Sternbach *et al.,* 1978) because of its subjective nature and difficulties in communicating pain (Melzack *et al*., 1973). Parameters that are vital, such as heart rate and blood pressure, are unreliable in the assessment of pain as they rely on several other factors (Buttner *et al.,* 2000). Cardiovascular and respiratory parameters are non-specific and prone to error. Their use in clinical practice is unproven and therefore not recommended as a sole modality (van Dijk *et al*., 2001).

2.2 Faces Pain Scale

Faces Pain Scale(FPS), (Wong-Baker faces pain scale) (Wong and, Baker, 1988), which was initially adapted for use in children and is validated for use in adults (Herr, 1998; Mumphansha *et al.,* 2015) has a series of faces ranging from a broadly smiling face to crying faces. The faces pain scale-revised (FPS-R) is a validated tool for use in adults particularly with low education and/language difficulties and can be scored along the 0-10 metric as the numerical rating scale (Hick, 2001)**.**

The FPS-R shown in Figure 2.1 below was used during the study to assess the pain during and after the MVA.

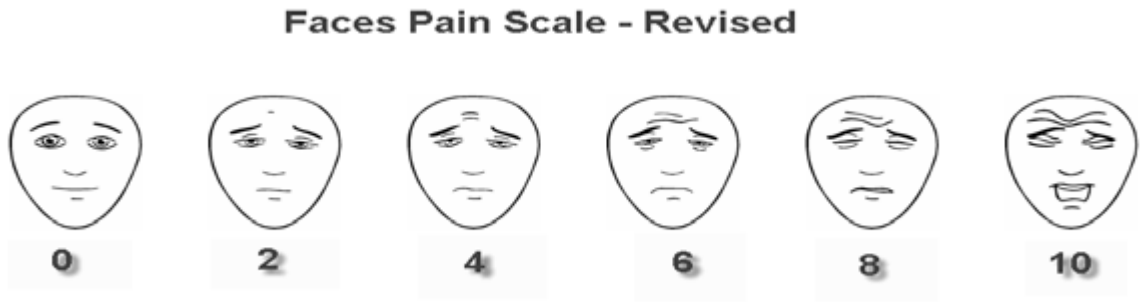

Figure 2.1 Shows faces pain scale.

In clinical practice and research, simple pain scales that are multidimensional have been employed. However, in our population, FPS was found as the most preferred, requiring the least explanation and was easier to understand and complete. It produced results that were reliable and reproducible therefore, it has been validated to be used in women undergoing MVA of RPOC at UTH, Lusaka, Zambia (Mumphansha *et al.,* 2015).

2.3 Ketamine

Ketamine is a derivative of phencyclidine and is classified as a non-competitive N-methyl-D-Aspartate glutamate (NMDA) receptor antagonist. The commercial preparations contain two enantiomers, which differ in potency and clinical effects (Neuhauser *et al.,* 2008). Ketamine affects multiple receptors: NMDA is the main one, but mu and sigma opioid receptors and monoaminergic receptors are also involved (Roelofse *et al.,* 2010). In high doses, ketamine also affects sigma opioid receptors, blocks muscarinic cholinergic receptors, and potentiates GABAergic neurotransmission. Systemically administered ketamine has also a local anaesthetic action (Weinbroum *et al.,* 2017).

The principal pharmacology of ketamine is vitally altered from that of other procedural sedation and analgesic agents. It exerts its effects by “disconnecting” the thalamocortical and limbic systems, which is, dissociating the central nervous system from stimuli, permitting for thorough analgesia as well. It prompts a state referred to as dissociative anaesthesia (Daabiss *et al*., 2009). The two primary metabolites, norketamine and hydroxynorketamine, are both active and

analgesia will persist after awakening. The central respiratory drive depression is minimal; upper airway muscle, pharyngeal, and laryngeal reflexes are preserved, and there is a bronchodilator effect. Protective reflexes, such as the pharyngeal, laryngeal, eyelid, and the corneal, are active under the effects of ketamine (Daabiss *et al.*, 2009).

Patients given anaesthetic doses of ketamine have a typical catatonic appearance. They are unconscious and amnesic, but their eyes usually remain open and exhibit nystagmus (Oranje, 2000).

2.4 Ketamine for procedural sedation

Ketamine has raised a lot of interest outside the operating room recently, especially in the aspect of ambulatory surgery largely because of its acceptably short duration of action, safety profile, its administration through almost any route, but above all, its sedative/analgesic effects (McCarty *et al*., 2000). This, therefore, has brought about rapid advancement in paediatric sedation techniques especially using ketamine. It has become a very well-known drug for use in a lot of fields of medicine such as the emergency department, dentistry, and interventional radiology, producing its classic state of dissociative sedation (Green *et al.*, 1990). Green and Krauss (2004) report that ketamine, fundamentally, is different to other sedative/analgesic drugs because it does not operate on the sedation continuum. Its clinical effects should therefore be defined from a different sedation category (Green *et al.*, 1990). Ketamine is attractive because it produces complete analgesia due to its dissociative state and hence it allows for more painful operations to be performed outside the operating room (Krauss *et al*., 2003).

Pharmacologically and pharmacodynamically, the understanding of ketamine has improved, thus it has become progressively popular partly because of its ability, without harm, to be combined with other drugs, e.g. propofol, for various procedures (Topsun *et al*., 2007). Herd and Anderson (2007) demonstrated that ketamine was effective in providing adequate sedation and fast recovery times in children.

2.5 Propofol

Propofol, (2, 6-di-isopropylphenol), a non-barbiturate sedative hypnotic, has an excellent pharmacokinetic profile in short procedures (Absalom, 2009) as depicted by Figure 2.2 below showing the various propofol receptor binding sites. Propofol causes global central nervous system (CNS) depression, ɣ-amino butyric acid A (GABAA) receptor agonism, *N*-- methyl-*D*-aspartate (NMDA) receptor antagonism and leads to amnestic effects (Hudson *et al.,* 2014; Patel *et al.,* 2011).

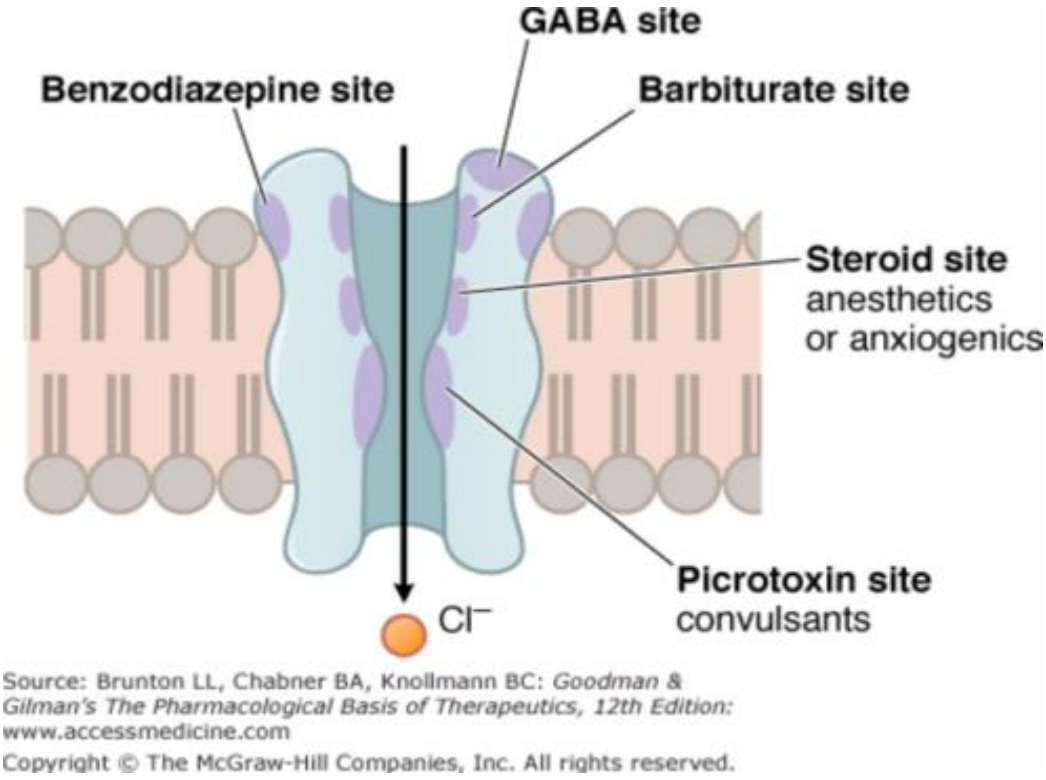

Figure 2. 2 Shows Propofol-GABA receptor activities

Propofol's high lipid solubility facilitates quick onset with a short recovery time. Additionally, it has a pleasant recovery with few contraindications and little hangover effect. It also has the advantages of operating as an antiemetic, an anticonvulsant, and amnestic substance; besides, it can be administered to patients with a predisposition to or suspected malignant hyperthermia, epilepsy, and muscular diseases (Kim, 2007). Although extremely effective and potent, propofol use is limited by a relatively high incidence of dose dependent hypotension and respiratory depression (Arora *et al.,* 2007). Therefore, propofol should only be used when strict precautionary measures are observed. One of its significant shortcomings is the fact that it has no

analgesic effect. For painful procedures it needs to be combined with a drug which can complement its weaknesses (Roelofse *et al.,* 2010).

2.6 Ketofol

Ketamine and propofol are physically compatible; one study found that they could be combined for 1 hour at 23°C with no increase in particle content at Y site injection (De Moraes *et al.,* 2015; Elsherbiy *et al.,* 2007). In another study, (Donnelly *et al.,* 2008) found that Ketofol solutions have been found to be stable up to 3 hours when stored at room temperature with exposure to light in 50:50 and 30:70 proportions.

Propofol and Ketamine have different effects on the hemodynamic and respiratory systems and therefore combining the two allows for the administration of smaller dosages of each, which may lead to less dose-related side effects (Nejati *et al.,* 2010). The side-effects of propofol include a painful infusion, transient cognitive dysfunction, cardiovascular and respiratory depression and the absence of any analgesic effect. This is in clear contrast with ketamine, which is a dissociative sedative, a systemic analgesic, and has amnestic properties, whilst preserving muscle tone, airway reflexes and spontaneous respiration (Arora *et al*., 2007).

Ketamine's side effects include emergence phenomena, post-operative dysphoria, vomiting and laryngospasm. The antiemetic and anxiolytic effects of propofol, together with the use of lower dosages, should decrease these side effects, thus theoretically balancing each other out when used together (Arora *et al*., 2007; Nejati *et al*.,2010). Several studies have been performed comparing the efficacy of Ketofol to propofol and propofol-fentanyl combination and have found Ketofol to be very effective. Studies comparing Ketofol to propofol (Akin *et al.,* 2005) found that compared to propofol group, onset of sedation was faster in the Ketofol group. Thus, they concluded that the addition of ketamine to propofol decreased the respiratory depression and produced the faster onset of sedation.

2.7 Ketofol versus Propofol

In a randomized double-blind study involving patients undergoing cardiac catheterization, some patients received propofol monotherapy for sedation (1.5 mg/kg) while some received propofol (1.5 mg/kg) plus ketamine (0.5 mg/kg) (Akin *et al.,* 2005). They found a significant (defined a priori as >20%) decrease in mean arterial pressure (MAP) in the propofol only group compared

to the Ketofol group. However, no significant differences where noted in terms of other vital parameters between the two groups. Based on these finding, it can therefore be concluded that the addition of low-dose ketamine to propofol (Ketofol) preserved MAP without delaying recovery as well as reducing the incidence of adverse outcomes.

In a non-randomized trial in which propofol (1.5 mg/kg) was compared to Ketofol (propofol (1.5 mg/kg) plus ketamine (0.5 mg/kg) in patients undergoing auditory brainstem response testing (Akin *et al.,* 2005), sedation was maintained with repeat aliquots of propofol determined by the treating physician. The investigators noted that a repeat dose of medication was needed in more than 2/3 of patients in the propofol group compared to less than 1/3 required in the Ketofol group. Therefore, it was concluded that the addition of low dose ketamine to propofol reduced the risk of respiratory depression and the need for repeat medication administration.

In adults there is only one study that compared propofol alone to Ketofol (Frey *et al*., 1999).In a randomized double-blind study involving patients receiving retrobulbar nerve blocks for cataract extraction patients were assigned to receive either propofol or Ketofol (Frey *et al*., 1999). Patients in the Ketofol group had a significantly shorter time until sedation. This led these researchers to conclude that Ketofol resulted in faster onset of sedation while decreasing respiratory compromise.

2.8 Ketofol in the Emergency Department

There is only one published prospective study using Ketofol for procedural sedation and analgesia (PSA) conducted in the Emergency Department (ED) setting. In a descriptive study involving 114 patients requiring PSA for mainly orthopaedic procedures, Ketofol was given in aliquots titrated at the discretion of the treating physician (William *et al*., 2007). It was found that no patient became hypotensive or had evidence of poor perfusion. Transient hypoxia occurred in 2.6% of patients and of these (0.02 to 4.8%) required bag valve mask ventilation.

2.9 Ketofol versus Propofol-Fentanyl

Propofol and fentanyl is another drug combination popular in PSA. In patients undergoing endometrial biopsy, the combination of propofol (1 mg/kg) plus fentanyl (1 µg/kg) was compared to Ketofol, ketamine (0.5 mg/kg) plus propofol (1 mg/kg) (Akin *et al*., 2005). Heart rate, systolic and diastolic blood pressure, respiratory rate, peripheral oxygen saturation, adverse events, time to recovery, and time to discharge were recorded. Time to recovery was similar; though the Ketofol group had increased nausea, vertigo, and visual disturbances which contributed to longer time to discharge. However, despite documenting five-times more respiratory depression in the Ketofol group, longer time to discharge due to increased presence of such adverse events such as nausea, vertigo and visual disturbances, there were no statistically significant differences found not even in vital signs between the two groups. This is attributed to the ketamine to propofol ratio of 1:2 similar to the finding in our pilot study.

CHAPTER THREE: METHODS

3.1 Study Design

This is a pre-post intervention study for quality improvement using historical control

3.1.1 Participants and Setting

The study was conducted at the Women and Newborn Hospital (WNH), gynaecology department of the UTH, Lusaka, Zambia.

3.1.2 Study Population

The study involved all women presenting to the gynaecology emergency ward requiring MVA of retained products of conception from 18 years and above who meet the inclusion criteria.

Inclusion Criteria

Women with retained products of conception requiring MVA and able to consent

Exclusion Criteria

I. Septic abortion

II. Missed abortion

III. Women in shock, which was defined by the sedation anaesthetist as:

BP < 90/60, CRT > 4 seconds, Urine output <0.5mls/kg/ hour, altered Glasgow Coma Score

3.1.3 Sampling Technique

Consecutive sampling technique was used until the sample size was reached.

3.1.4 Recruitment Method

A direct recruitment method of all potential study participants by the clinicians was conducted by talking to women who were identified with RPOC and were eligible to undergo MVA. The study and the procedures were explained to the women. It was explained to the women in the sense that there was no pressure to participate in the study.

3.1.5 Sample Size

Sample size was based on the expected change in pain in women undergoing MVA with Ketofol (Mupeta, 2009**).** From the literature, a clinically significant difference in pain score is considered to be at least 10-20%, that is, a change in pain score of 1 to 2 (Powell *et al*., 2001). Table 3.1 below shows various assumptions made during the sample size calculation.

Table 3.1 Sample size calculation

Calculations of sample size considering alpha (α) and beta (β) errors	
Study characteristics	**Assumptions**
Type of study	Quality Improvement Study
Data sets	Observation in pain scores between Ketofol sedation group and historical data
Variables	Measurement of pain
Losses to follow up	10%
Standard deviation(SD)	15 (Tosun *et al* ., 2009)
Variance $(s)^2$	
Data for alpha(Zα)	P=0.05; 95%confidence desired (two-tailed test); Zα=1.96
Data for beta(Zβ)	20% beta error;80% power desired (one tailed test); (Zβ =0.84
Difference to be detected (d)	10% mean difference

Formula $= (Z\alpha + Z\beta)^2 * 2 * (SD)^2 / d^2$

$=35+ (10\%)$

$=40$

3.2 Assignment Method

For the purpose of comparison, there were two groups: The "No Sedation" group consisted of patients from a previous local study (Mumphansha *et al.,* 2015).These patients received the standard oral analgesia prescribed in our institution, and there was no statistically significant difference in characteristics from the intervention group.

The "Ketofol" intervention group not only received the intervention but also received the standard care at our institution – namely the oral analgesia which is explained in more detail in the following section. The reason that this group of patients also received the oral analgesia was because Ketofol sedation provides analgesia and sedation for a short time such that provision of oral analgesics was envisioned to have post procedure analgesic effect.

3.3 Experimental Intervention

Prior to undertaking the experimental intervention, we undertook a pilot study to determine the ratio of ketamine to propofol that would give the best results; reasonable sedation, analgesia and quick recovery. It is from that pilot study that the ratio of 1:4 ketamine to propofol was determined.

Patients in the Ketofol group received the same pre-procedure analgesia protocol as in the "no sedation" group, (Paracetamol 1g, Ibuprofen 400mg and Morphine 30mgorally).This was administered thirty minutes before the procedure. All patients that met the inclusion criteria were enrolled for the study, however, a detailed explanation of the benefits and possible complications was given by nurses with prior training before consent for the procedure was obtained. Using a structured questionnaire, baseline characteristics were obtained including weight which was measured by means of a standard scale. The patient weight obtained was used to calculate the ketamine to propofol requirement in the ratio 1:4 respectively. An analgesic dose of ketamine at 0.5mg/kg was calculated in milligrams after which propofol dose was found as four times the ketamine dose in milligrams too. Standard monitoring for a sedation procedure was attached; pulse oximetry, electrocardiography and blood pressure. After placement of an intravenous cannula, sedation was commenced with an initial bolus of ketamine 0.5mg/kg followed by 0.6mg/kg of propofol. Propofol aliquots of 10mg were then given until the patient was sedated to a targeted Ramsay score of 2 or 3 (see table 3.2).Medication dosages, administration times, total procedure time, vital signs (non-invasive blood pressure, oxygen saturation, heart rate, and respiratory rate), side effects, and sedation scores were recorded by the same trainee anaesthesiologist and nursing assistants at the beginning of the procedure and during the procedure at every 5 minutes until the end of the procedure. The sedation levels of the patients were assessed using Ramsay sedation scale (RSS); applied to target score of 2 or 3. Throughout the MVA procedure, when the drug doses were not sufficient to achieve the targeted sedation scores or when the patient moved, additional boluses of 10mg Propofol was administered and supplemental drug requirements were documented**.**

3.4 Sedation and pain scores

The RSS used to determine the response to sedation and analgesia is shown below (Table 3.2). After the procedure was completed, the patients were transferred to the recovery room where pain scores were recorded at three points – pain during the procedure was measured by asking the patient to recall as soon as they reached the recovery room (time 0), and then pain scores were recorded at ten minutes and sixty minutes, using the FPS. Patients were discharged from the ward based on the ward doctors' assessment of patients as being fit for discharge.

Table 3.2 Ramsay Sedation Scale used during the sedation

IF AWAKE	**IF ASLEEP**
Ramsay 1 Anxious, agitated, restless	Ramsay 4 Brisk response to light glabellar tap or loud auditory stimulus
Ramsay 2 Cooperative, oriented, tranquil	Ramsay 5 Sluggish response to light glabellar tap or loud auditory stimulus
Ramsay 3 Responsive to commands only	Ramsay 6 No response to light glabellar tap or loud auditory stimulus

3.5 Data Collection

Pain during the procedure was measured by asking patients to report their recall of pain during the procedure, as soon as it finished (time 0). Pain scores at 10 minutes and 60 minutes were measured using standard tool (Faces Pain Scale), heart rates were also recorded using a cardiac monitor while sedation scores were measured using a standard tool (Ramsay Sedation Scale). Sedation scores were measured during the procedure based on the patient responses. For patients that remained awake, the target was cooperation and ability to respond to commands. On the other hand, for patients that were deeply sedated, the anesthesiologist target was their brisk response to light glabellar tap or loud auditory stimulation.

Recovery time was estimated as the time from the end of the procedure to the time the patient was deemed fit for discharge from the ward. Discharge was not protocolized and the decision was solely made by the ward doctors. This study decided to maintain that practice without any deviation to avoid creating a unique environment. It should be stated that there were no monetary or any form of incentives offered to the participants. The data collection started on April 6th2108 and ended on May 5th 2018.

3.6 Measures

Table 3.1 shows the variables which were measured during the study and their corresponding scale of measurement. Pain score measurements were further categorized into four groups, no pain (0), mild pain (1-3), moderate pain (4-6) and severe pain (7-10). No instruments were developed for the study but the pain scale method that was used is a reliable and validated tool in our population (Mumphansha *et al*., 2015).Translation of English into the local language was done with the help of expert in translating the language so that the meaning and context remained the same and for reliability and validity of results.

Table 3.3 Scale of Measurements

Independent variables	**Scale of measurement**
Age	Continuous
Weight	Continuous
Marital status	Categorical
Educational level	Ordinal
Co morbidities e.g. HIV, HTN,DM, migraine, epilepsy, cardiac disease	Categorical
Allergy	Categorical
History of anaesthetic exposure	Categorical
History of miscarriage	Categorical
Gravidity	Categorical
Parity	Categorical
Recovery time	Continuous
Level of pain	Ordinal
Level of sedation	Ordinal
Surgical history	Categorical
Drug history	Categorical

3.7 Ethical Considerations

Permission was obtained from University Teaching Hospitals management to carry out the study in the institution. Approval was sought from ERES CONVERGE IRB while clearance was obtained from the departments of anaesthesia and critical care, and obstetrics and gynaecology. Patient autonomy and privacy was maintained. Their participation was entirely on voluntary basis, no form of coercion or payment to the participants was involved.

3.8 Data Analysis

Firstly, all descriptive analysis of data of the baseline characteristics of the study participants was conducted. For quantitative variables, Shapiro-Wilk test was used to perform normality test of the numerical variables and data was not normally distributed. For categorical variables, the chi-square test or Fisher's test exact test if a predicted cell count was less than five and absolute and relative frequencies for categorical variables were calculated. The bivariate analysis comparison of the main variables between the study groups was conducted using Mann-Whitney test.

For all data analysis significance level was considered when $p<0.05$. All statistical analyses were conducted using GraphPad Prism, version 6.01 (GraphPad Software Inc., La Jolla, California, USA) and STATA, version 13 (STATA Corp, College Station, Texas, USA).

3.9 Study Limitations

The MVA procedure was performed by different gynaecology doctors at different stages of their training. If only one specific doctor performed the MVA, consistency would have been guaranteed. However, this was a pragmatic study looking at service provision in the real world, and this was a fair representation of how MVAs are performed in routine clinical setting at the study site area and also all doctors who performed the procedures were expected to be competent and well qualified for it. Inability to distinguish between spontaneous and induced abortions but relying on information given by the women, could have affected the perception of pain as women presenting with spontaneous abortions tend to be more anxious and distressed because of the pregnancy loss. However, there is no any other way to distinguish the two apart from asking women themselves. Again, because this is pragmatic; treating both groups homogenously as one

is realistic to the setting. Another limitation was that memory of procedural pain may have been inadequate as this study relied on the patient recall of pain, measured immediately afterwards. However, this is the only way to assess pain perceived during the procedure as patients were sedated.

Pain scores during the procedure, could have been affected by the residual sedation. However, this can be argued that it is the recollection of pain that is important for the patients anyway, and so recording their memory of the procedural pain immediately afterwards is more meaningful than asking a sedated patient about pain while the procedure is ongoing. This study could not be a randomised controlled trial to possibly remove systemic bias because from the previous study, patients were suffering very high level of pain. It would, therefore, be completely unethical to have a control group which was going to experience similar pain levels.

CHAPTER FOUR: RESULTS

4.1 Baseline characteristics of study participants

Table 4.1 shows the baseline characteristics of the study participants. A total of 94 women underwent MVA. 54 (57.4%) were in the "no sedation" group (previous study) and 40 (42.6%) were in the Ketofol group. The dosages in milligrams for ketamine and propofol expressed as median and interquartile ranges were 30 (26-31.75) and 125 (110-160) respectively. The median age in the "no sedation" group was 31 (28- 35) and 33 (29-36) in the Ketofol group. There was no difference in gravidity and parity between the "standard care" group and the "Ketofol" group; p values 0.68 and 0.77 respectively. History of allergies, history of miscarriages and HIV status were also not significantly different between the two groups.

Table: 4.1 Baseline characteristics of study participants

Characteristics	**No sedation**	**Ketofol**
Age	31 (28- 35)	33 (29- 36)
Marital status	27 (52%)	18 (47.5%)
Education, secondary or more (n, %)	23 (44.2%)	27 (67.5%)
Gravidity	2 (1- 4)	2 (1- 3)
Parity	1 (0- 3)	1 (0- 2)
History of miscarriage	9 (19.2%)	8 (20%)
History of allergies	12 (23.1%)	6 (15%)
HIV status	9 (17.3%)	4 (10%)

HIV = human immunodeficiency virus; percentages are in parentheses. For continuous variables median (interquartile range) are shown.

4.2 Adverse events occurring in different groups

Adverse events that occurred in both groups were also assessed during the MVA procedure. The following were recorded: dizziness (p=0.83), headache (p=0.45), apnea (p=0.95), hallucination (p=0.98), vomiting (p=0.98) and agitation (p=0.99). There was no significant difference between the two groups (Table 4.2).

Table 4.2 Adverse events occurring in different groups

Parameter	**No sedation (n=54)**	**Ketofol (n=40)**	**P value**
Dizziness	7	5	0.83
Headache	6	3	0.45
Apnea	0	1	0.95
Hallucination	0	0	0.98
Vomiting	0	1	0.95
Agitation	0	0	0.99

4.3 Comparison of pain scores

The study hypothesized that pre-operative oral analgesia ("standard care") in addition to Ketofol is likely to produce better analgesia in women undergoing MVA compared to those having oral analgesia alone. In testing the hypothesis, recollection of pain during the procedure was measured immediately afterwards in both groups. Women in the "no sedation" group had significantly higher pain scores, median 10 (IQR, 8 - 10) compared to women in the Ketofol group 2(IQR, 0 – 2); $p<0.001$ as shown in Figure 4.1. Mann-Whitney test was used to compare between the groups and the results are shown with significance where applicable ($p< 0.05$).

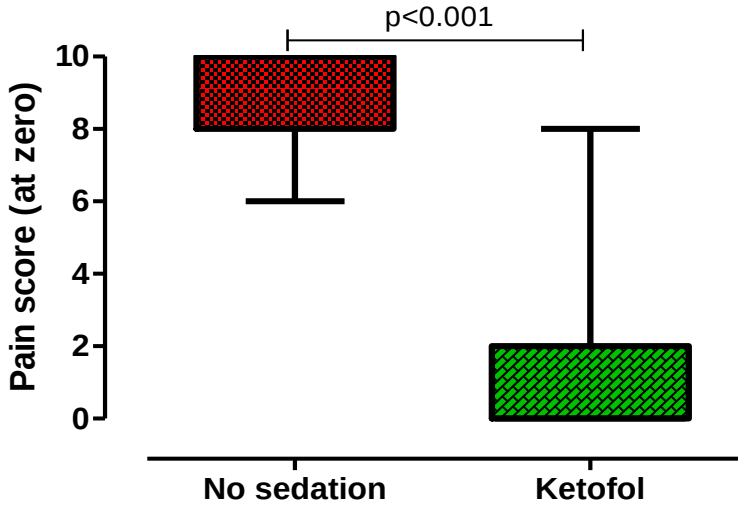

Figure: 4. 1 Comparison of pain score at 0 between women who received standard care ("no sedation") compared to those who received standard care plus Ketofol (Ketofol). Box and whiskers plot are shown.

After measuring pain scores at 0 (the recollection of pain during the procedure, measured immediately afterwards) and noting significant difference between the two groups, next the study sought to measure the pain score at 10 minutes. There were higher pain scores in the "no sedation" group; 2 (2-4) compared to the Ketofol group; 0 (0-2); $p<0.001$ as shown in Figure 4.2. Mann-Whitney test was used to compare between the groups and the results are shown with significance where applicable ($p< 0.05$).

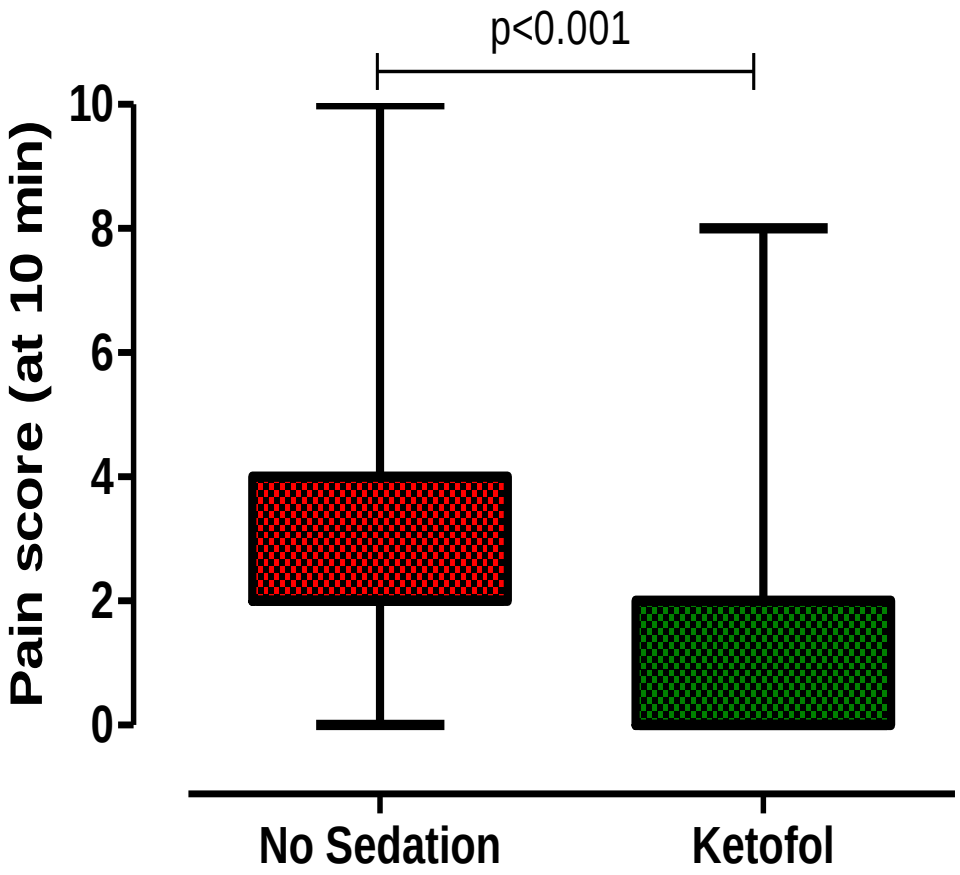

Figure: 4. 2 : Comparison of pain scores at 10 minutes between women who were on standard care ("no sedation") and those on standard care plus Ketofol (Ketofol). Box and Whiskers plot are shown.

After the measuring of pain scores during the procedure and 10 minutes after the procedure ended, and noting the differences, next the study sought to measure the pain score at 60 minutes. There was no statistical difference in pain score at 60 between the "no sedation" group; 2 (0-2) and the Ketofol group; 0 (0-2); p=0.82 as shown in Figure 4.3. Mann-Whitney test was used to compare the groups.

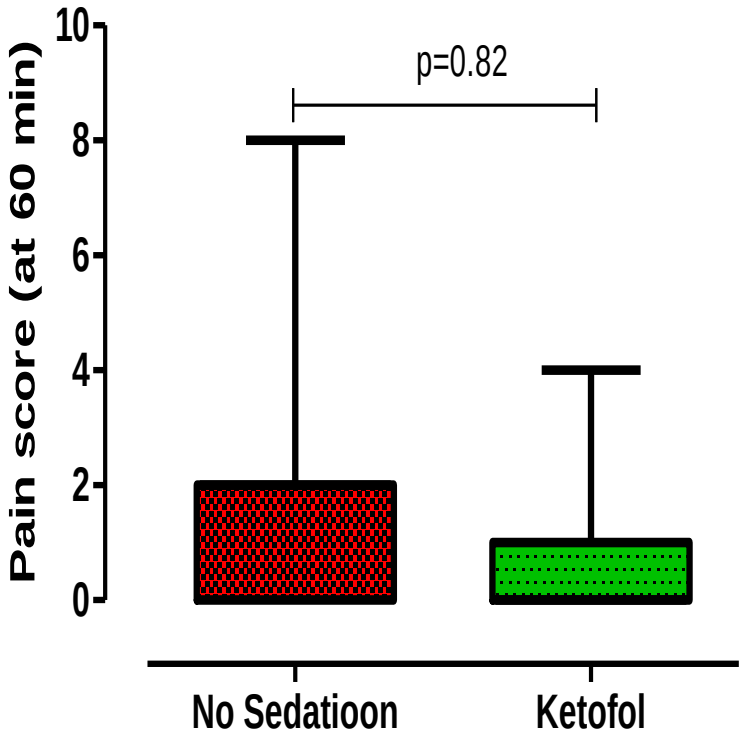

Figure: 4. 3 Comparison of pain score faces at 60 minutes post-procedure between women who were on standard care ("no sedation") and those on standard care plus Ketofol (Ketofol). Box and Whiskers plot are shown.

4.4 Sedation scores

Using the RSS a median score of 4 (IQR, 3-4) was obtained as shown in the Figure 4.4.

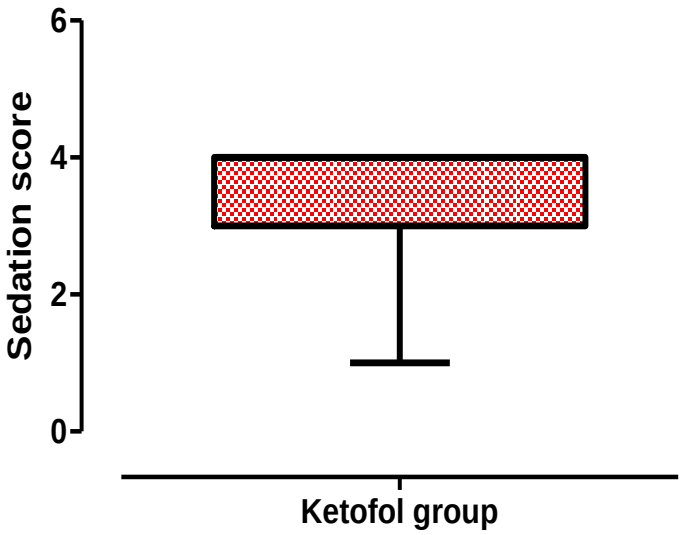

Figure 4.4 Sedation scores of women in the Ketofol group. Box and Whiskers plot are shown.

4.5 Comparison of heart rates

It was interesting to note in this study that over three-quarters of the women examined reported that the loss of their pregnancies was of spontaneous origin, contrary to the physical examination findings. It was found that about two-thirds were induced illegally despite abortion being legal in Zambia. This finding was extremely surprising, and alone requires further research to establish barriers to accessing abortion services in Zambia in spite of the service being free.

During the MVA procedure, the heart rates of women in the two groups were compared. Heart rates in the "no sedation" group were significantly higher, median 111 (99 – 125) compared to the Ketofol group, 95.5 (85.5 – 103); p<0.001 as shown in Figure 4.5.

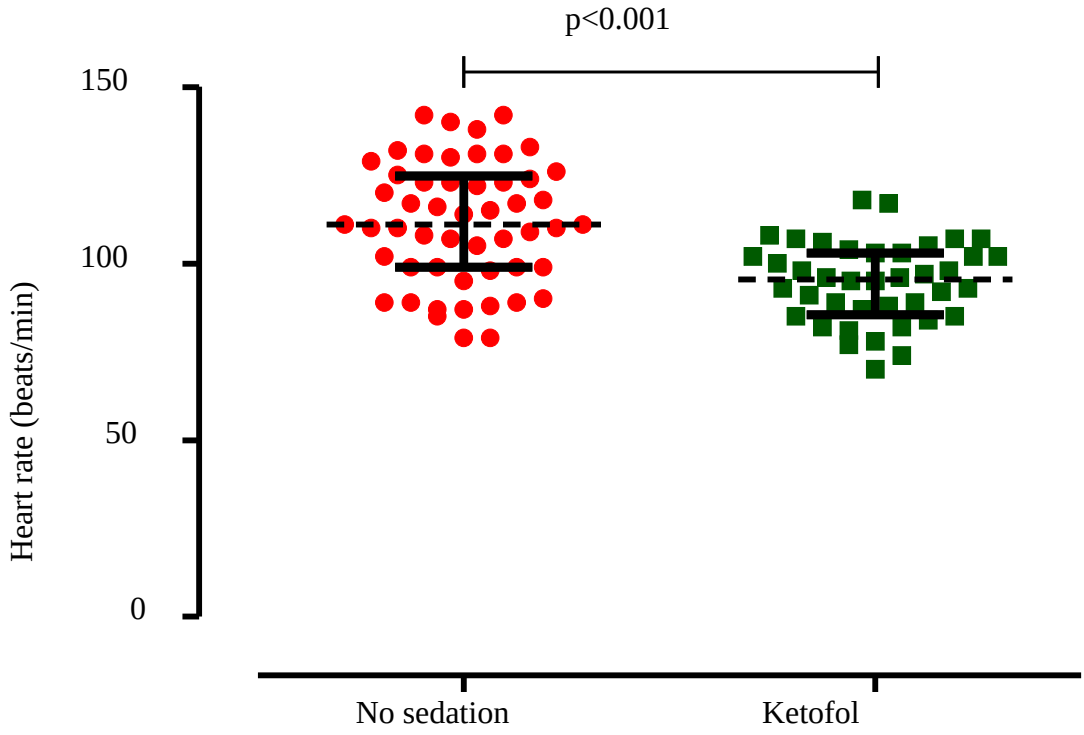

Figure 4.5 Comparison of heart rate between the two groups. The broken line in the dot plots are medians and the lower and upper lines represent the 25th and 75th percentiles respectively.

4.6 Comparison of time to discharge

Determining the recovery time was difficult because the discharge of patients was done by the ward doctors and the criteria for discharge from the wards was not protocolized. Therefore, time to discharge, as determined by the unit doctors, was used as a surrogate to recovery time and compared between the historical no sedation group and the Ketofol group. Surprisingly, women who were in the "no sedation" group had significantly longer time to discharge, median 345 (IQR, 169 – 742) than the Ketofol group 191 (133 – 394); p=0.009 as shown in Figure 4.6. Mann- Whitney test was used and results are shown with significance where applicable (p< 0.05).

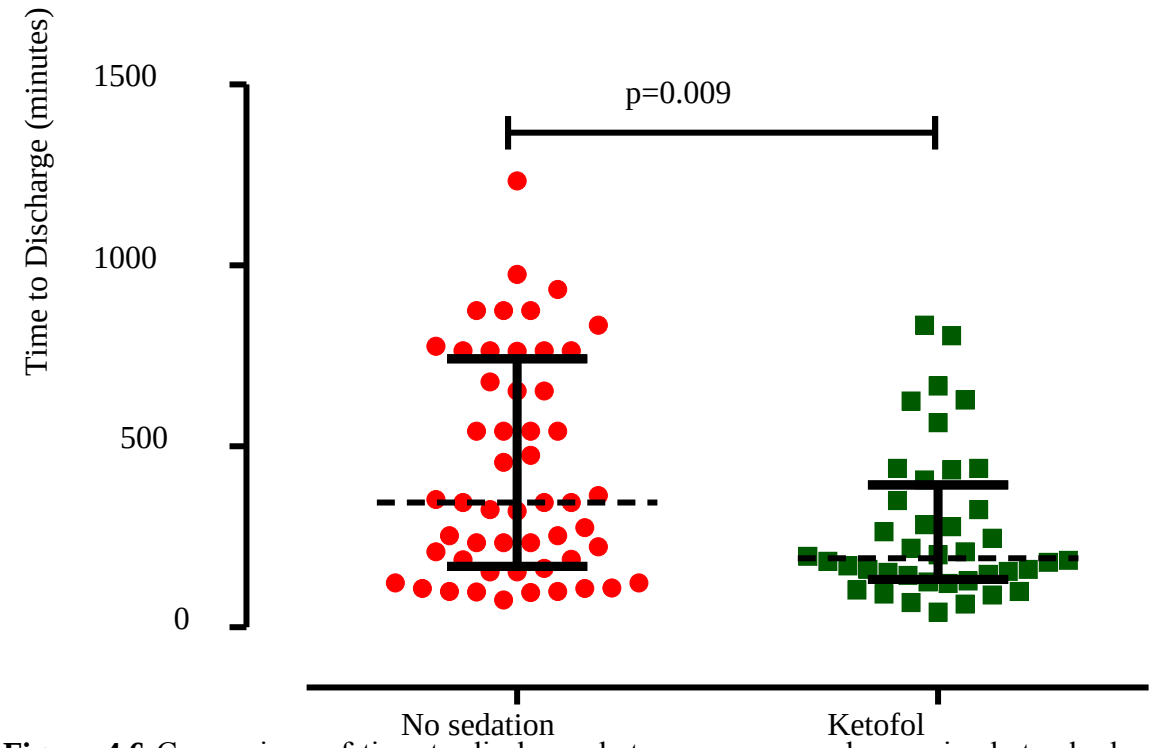

Figure 4.6 Comparison of time to discharge between women who received standard care ("no sedation") and those in the Ketofol group. The broken lines within the dot plots are medians.

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

This study found that women undergoing manual evacuation of retained products of conception with Ketofol sedation experienced significantly less pain during and immediately after the procedure, and that the technique was safe and produced satisfactory levels of sedation. Given the number of cases seen per month, it is clear that many women each year are likely to suffer high level of pain unnecessarily and result in lasting psychological sequelae.

This technique could potentially prevent suffering in many of women. This study found that sedation technique was a viable one in our setting and that with the presence of an anaesthetist, staff training and the availability of a minimum set of monitoring and equipment, it was possible to provide the service on an ongoing basis. The technique was found to be safe with minimum adverse effects and a quick time to discharge, which can be used as a surrogate for recovery time. In this quality improvement study, this study did not experience adverse effects requiring intervention.

It is clear that patient comfort is an important aspect of care. The MVA procedure is associated with some adverse events such anxiety, agitation and headache (Baird *et al.,* 2002). As patients present for MVAs, one of their chief complaints is anxiety surrounding the procedure they are about to undergo and the act of losing a pregnancy therefore treating the pain and anxiety are critical to patient satisfaction and quality of care. From the results of this study, using the RSS the patients were comfortable during and after the sedation which can imply adequate sedation and patient satisfaction. All patients were adequately sedated according to RSS, median score of 4 (IQR, 3-4).In this study, the Ketofol and standard care groups reported less anxiety, agitation and headache, suggesting that patients in both groups were comfortable, probably due to the fact that both standard care and Ketofol sedation provided analgesic effects. This finding is in keeping with other studies reviewed (Wang *et al.,* 2012).

Pain scores measured between the two groups immediately after the MVA and 10 minutes later showed a significant difference with the Ketofol group registering lower pain scores. However, there was no difference after 60 minutes suggesting that the effect of Ketofol had completely worn off. Statistically, there was no difference between women who received Ketofol sedation compared to those on standard care in terms of baseline characteristics. Essentially the two

groups were comparable and as far as literature was searched, no study was found which had reported similar findings.

The difference in pain scores recorded immediately after the MVA between the two groups was highly clinically significant, as well as meeting criteria for statistical significance. It clearly showed women in the Ketofol group had significantly lower pain score suggesting that they experienced less pain compared to the women who were given standard care during the procedure. It provided adequate sedation and analgesia to allow for the safe performance of the MVA. The women were calm and relaxed during the procedure as sympathetic stimulation could have been dampened by analgesia and sedation. Further evidenced could be provided by low HR recorded during the procedure in the Ketofol sedation group compared to the historical cohort.

At 10 minutes however, it was noticed that the difference in the pain scores was significant but less marked than when recorded immediately after the procedure between the two groups. At this time the analgesic effect of Ketofol was slowly wearing off but still provided better analgesia than the oral analgesics in the historical group. From clinical assessment at 10 minutes' women in the Ketofol sedation group appeared more comfortable and potentially dischargeable from the ward.

At 60 minutes there was no difference in the pain scores recorded, which could be primarily attribute to the low levels of pain in both groups at this time point, as well as the short half-lives of both Ketamine and Propofol. The lack of difference at this stage again may also be partly attributed to oral analgesics which could have reached clinical efficacy by that time. This suggests that morphine, ibuprofen and paracetamol are probably appropriate and effective analgesics only for this stage of the post-procedure and not for the actual procedure.

In this study, lower heart rates among the Ketofol sedation group were observed compared to the historical UTH standard care group; this could essentially be because of the reduced sympathetic discharge associated with reduction in pain as well as the reduced anxiety as a result of Ketofol sedation. Pain and anxiety increase sympathetic discharge which explains the observed higher heart rates in the group that had not sedation. That being the case, Ketofol provided both analgesia and sedation and explains why the Ketofol group had lower heart rates. The findings of

this study, as well as others (Frey *et al.*, 1999), suggest that Ketofol has effective analgesic properties.

Compared to the historical cohort, those that underwent sedation recovered faster. This may imply that providing Ketofol sedation could not prolong the patient stay on the ward, causing strain on the hospital resources. It is a well-known fact that ketamine may produce unwanted psychomimetic reactions, also referred to as "emergence reactions", usually occurring during awakening from sedation. Factors such as age, dose, gender, psychological susceptibility, and concurrent drugs are known to be related to this 'emergence reaction' phenomenon (Edwin et al., 2018). Additionally, psycho-mimetic reactions may occur when a large dose of ketamine is injected (Badrinath *et al.* 2000). In this study, however, only an analgesic dose of 0.5mg/kg was given to the patient and this maybe one reason explaining why no such emergence reactions were observed in patients in the current study. Combining ketamine with propofol is undoubtedly the main factor similar to what others studies have reported (Akin *et al.*, 2005).

Akin and colleagues (2005) reported that Ketofol was associated with quick onset of sedation and recorded no patients requiring ventilatory support. Furthermore, in another study conducted by Akin and colleagues (2005), patients receiving Ketofol for endometrial biopsy had a short time to discharge due to fewer adverse events such as visual disturbance, nausea and vertigo. These findings are in keeping with results that have been reported elsewhere (Messenger *et al.*, 2007; Goh *et al.*, 2005).In our study, the use of propofol combined with ketamine reported fewer adverse events such as respiratory depression which has been reported in procedures where propofol alone has been used (Amornyotin, 2013). However, regarding potential complications associated with Ketofol sedation, this study did not record any statistically significant adverse effects. Despite the fact that no significant adverse effects were recorded, it should be noted that being a remote site, where it is difficult to get immediate help when required, safety precautions have to be adhered to at all times. Presence of a trained or senior anaesthesia trainee with appropriate skills should always be at hand. Sedation and general anaesthesia are not binary events but exist on a continuum. Ketofol sedation may potentially progress to a general anaesthesia in certain instances and therefore, should be performed only when basic monitoring and resuscitation drugs and equipment are available. This places responsibility on the anaesthesia

provider as well as the gynaecologists/ obstetricians to work as a team to make sure the practice is effective and safe for the patient.

The use of Ketofol for sedation and analgesia in the emergency department has become popular (Loh and Dalen, 2007). There have been numerous studies regarding how effective Ketofol is in many medicinal and surgery procedures, especially in the emergency rooms where it has been used as an agent for procedural sedation and analgesia (Donnelly *et al.*, 2008). Despite previous studies not supporting the use of a bolus dose of propofol-ketamine (Ketofol) for sedation and analgesia (Slavik *et al*., 2007); the results of this study revealed that use of Ketofol sedation produced acceptable sedation as well as analgesia for the patients.

With regards to the dose ratio of ketamine to propofol used in this study, Ketofol (ketamine: propofol) in the ratio 1:4 produced adequate sedation and analgesia with no recorded hemodynamic, psychotomimetic and respiratory side effects during the procedure. Similar results have been reported in other studies where Ketofol (1:4) has been used in women undergoing termination of pregnancy (Wang *et al*., 2012). Surprisingly, a higher number of women who experienced postoperative dizziness in the Ketofol group were reported by Wang and colleagues (2012) but not in this study. Furthermore, this study did not record any intraoperative respiratory depression in the Ketofol group or the standard care group. Also, faster recovery time and absence of clinically significant adverse events were recorded, similar to what others have reported (Frey *et al.*, 1999).

5.1 Conclusion

Ketofol sedation significantly reduced intraoperative pain experienced during manual vacuum aspiration of retained products of conception compared with the local standard care (oral analgesia) protocol and produced effective sedation and absence of clinically significant adverse events. Furthermore, the technique was safe and effective, by using two-dose ratios described above.

5.2 Recommendation

Ketofol sedation should be adopted as a service for management of pain in women undergoing MVA of RPOCs at the WNH, department of gynaecology. The pain management protocol for women undergoing MVAs should be revised by the WNH Pain Team.

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APPENDICES

Appendix 1: INFORMATION SHEET

A quality improvement study on the women undergoing Manual Vacuum Aspiration of Retained Products of Conception with Ketofol

INTRODUCTION

My name is Dr. Kaunda Lwimba, a student in the School of Medicine at the University of Zambia pursuing a degree of Master of Medicine in Anaesthesiology and Intensive Care. I kindly request your participation in the above mentioned study. Completing a research study is a requirement for the award of this masters' degree. Before you decide on participation, I would like to explain to you the purpose of this study and what is expected of you. If you agree to take part in this study, you will be asked to sign a consent form in the presence of a witness.

NATURE AND PURPOSE OF THE STUDY

This study is being conducted to explore the potential of Ketofol to provide sedation and analgesia among women undergoing manual vacuum aspiration of retained products of conception at university teaching hospitals (UTH).

PROCEDURE OF THE STUDY

If you agree to participate in this research, we will obtain information about you using a data entry sheet. Your contact details will be required and then u will be given Ketofol as you undergo the procedure.

POSSIBLE RISKS AND DISCOMFORTS

You may experience discomfort during the administration of the drug, you will be made to sleep during which time you will entirely be in the hands of the attending doctor. You may also experience vivid dreams.

POSSIBLE BENEFITS

You will be able to undergo Manual Vacuum Aspiration sedated and unlikely to experience pain during and after the procedure.

CONFIDENTIALITY

All the collected information is strictly confidential. All the data that will be collected, analysed, and reported on will not include your name and therefore cannot be traced to you.

CONSENT

Your participation is strictly voluntary. You will not suffer any consequences if you decide not to participate in this study. You may also withdraw from the study at any time for any reason without consequences to you.

Thank you for considering participation in this study. If you have any questions, concerns, and clarifications, please contact myself or ERES Converge committee on the following addresses:

Dr. Kaunda Lwimba
University Teaching Hospital
P. O Box 51292,
Lusaka
Telephone:0955-155-633
0955-155-634/0966-765-503

ERES Converge,
33 Joseph Mwilwa Road
Rhodespark,
Lusaka

ICHAKUTAMPILAPO

Ishinalyandi nine Dr Kaunda Lwimba Ndimwana we sukulu pa University of Zambia eponde sambilila ifyabu Shingánga, Inonshita ndecita ama sambililo ayakulalika abalwele abama opaleshoni nokutungilila abalwalisha sana. Ndemilomba ukuti mwasukeko amepesho muli study ndecita.Tetimpwishe isukulu nokupoka setifiketi kano nacita iyi study elyonkapoka Master's degree. Ilyo tamulati musumine ukwasuka amepusho, ndefwaya uku milondolwelako ico ndecitila iyi study elyo nefyakucetekela. Nga mwasumina ukwasuka amapusho, mulingile ukusaina icipepala cakutila mwasumina ukwasuka amepusho pamenso yakwa Kambone.

IFYO IYI STUDY YABA ELYO NECO NDECITILA IYI STUDY

Iyi study yakulolekesha pafyo umuti wa Ketofol wingafwilishako ukulalika nokulesha ubukali kuli banamayo ilyo balebasuka mumala panuma yakuponya amafumo pafipatala nkalamba fya University Teaching Hospitals (UTH).

IFYO IYI STUDY IKACITIWA

Ngacakutila mwasumina ukuba muli iyi study ninshi tuli nokusunga amashina yenu pamo natelefoni namba yenu.panuma yaicho mukapelwa umutiwa Ketofol ilyobalemisuka mumala.

IFINGA MISAKAMIKA NANGULA UBWAFYABUMBI

Lintu umuti ulepelwa limbi kuti mwaunfwa ububi kukuboko, Lelo umulandu wakuti mukaba abalalikwa, bashing'anga bakamilolekeshapo ukufika nakukupwisha kwa procedure.

IFISUMA IFINGA TUMBUKA MU KUCITA IYI STUDY

Banamayo bakalabasuka mumala ninshi nababalalika ukwabula ukunfwa ubukali ilyo balebawamya nelyo bapwisha ukubawamya.

INKAMA

Fyonse ifyo tulelemba nangula ukulanda fyamunkama. Ifishinka fyonse nga twapoka, tukaloleshapo elyo napakulemba report, tatwakabikepo ishina lyenu pakutila takwingaba umuntu nangula umo uwingamwishiba iyoo.

UKUSUMINA

Ukwasuka amepusho nimukufwaya kwenu ukwabula ukupatikishiwa. Takwabe nangula cimo icingamicitikila ngamwakana ukwasuka amepusho. Elyo ngamwatampa ukwasuka amepusho elyo mwamona ukutila tamulefwaya kukonkanyapo kuti mwaleka ukwasuka inshita iliyonse ukwabula nangu cimo icinga micitikila.

Namitotela nganshi pakusumina ukuba muli iyi study. Ngamuli namepusho yonse ayo mulefwaya ukwipusha pali iyi study kuti mwaipusha ine nagula akabungweka ERES Coverage committee paliiyi address

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Appendix 2: **INFORMED CONSENT**

I have understood the explanation given to me by Dr. Kaunda Lwimba about the study concerning Ketofol use in women undergoing manual vacuum aspiration and hereby give my informed consent to participate in this study.

1. I agree to participate in this study
2. I agree to be interviewed and receive Ketofol during the procedure.
3. I understand that the information I give will be treated with confidentiality
4. I understand that my participation in this study is entirely voluntary and I am free to withdraw from the study at any point. Withdrawal from the study will not, in any way, affect the treatment I will receive at the UTH.

Participant's	Signature	Thumb print
……	……	…….

Investigator:	Signature
……	……

UKUSUMINA

Natesha ifyo ba Dr. Kaunda Lwimba banondolwela pali iyi study yamuti wa Ketofol ukupelwa kuli banamayo abaponeshe amafumo pakubawamya mumala. Elyo nasumina ukuba muli iyi study

1. Nasumina ukuba muli iyi study
2. Nasumina ukwasuka amapesho nokupoka umuti wa Ketofol ilyo balengwamya mumala.
3. Naishiba nokuti ifyo tukalanshanya fyonse fikaba munkama
4. Nasumina nokutila ukuba muli iyi study nimukutemwa kwandi nemwine ukwabula ukupatikishiwa. Elyo kuti nafumamo muli iyi study inshita iliyonse ukulingana no kutemwa kwandi. Ukufuma muli iyi study teti kulenge ukufulunganya ukundapwa kwandi iyo nangu panono.

Ishina lya abalaasuka: Sigineca: Ichifwatiko

…… …… ……

Ishina lya Kambone: Sigineca:

…… ……

Appendix 3: QUESTIONAIRE

1. Demographics.

Patient Identification number:_____

Age ……

Weight ……

Marital status (single/married/separated/divorced/widowed)

Gravidity …….. Parity…….

History of miscarriage (Yes/No)

History of anaesthetic exposure – general (yes/no)

- Spinal (yes/no)
- Other (yes/no)

Co morbidities (HIV, HTN, DM, migraine, epilepsy, cardiac disease)……..

Allergy (Yes/No)

Level of Education (None/Primary/Secondary/Tertiary)

Analgesia received before procedure……...

- Starting time of MVA…….
- Finishing time of MVA……..

2. Level of sedation (RAMSEY SEDATION SCALE)…….

IF AWAKE	IF ASLEEP
Ramsey 1 Anxious, agitated, restless	Ramsey 4 Brisk response to light glabellar tap or loud auditory stimulus
Ramsey 2 Cooperative, oriented, tranquil	Ramsey 5 Sluggish response to light glabellar tap or loud auditory stimulus
Ramsey 3 Responsive to commands only	Ramsey 6 No response to light glabellar tap or loud auditory stimulus

3. Any Side Effects?

Hypotension……

Desaturation……

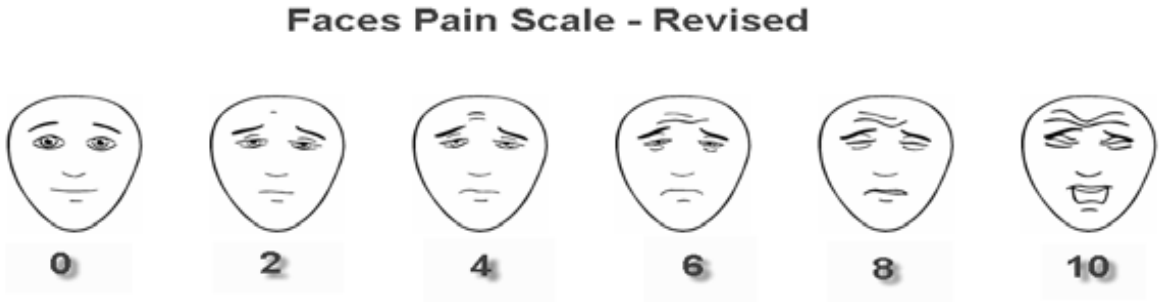
Nausea/vomiting……..

Hallucinations…….

Catatonia…….

Other ……

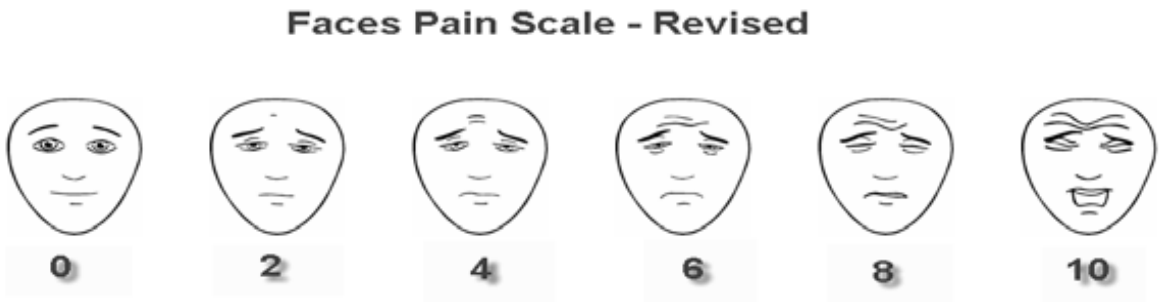
4. Recall of Pain (During the MVA)……..



- These faces show how much something can hurt.
- The faces show more and more pain *[from left to right]*
- Point to the face that shows how much you hurt [right now]."

"0" = "no pain" and "10" = "very much pain

5. Recall of Pain (10min)……



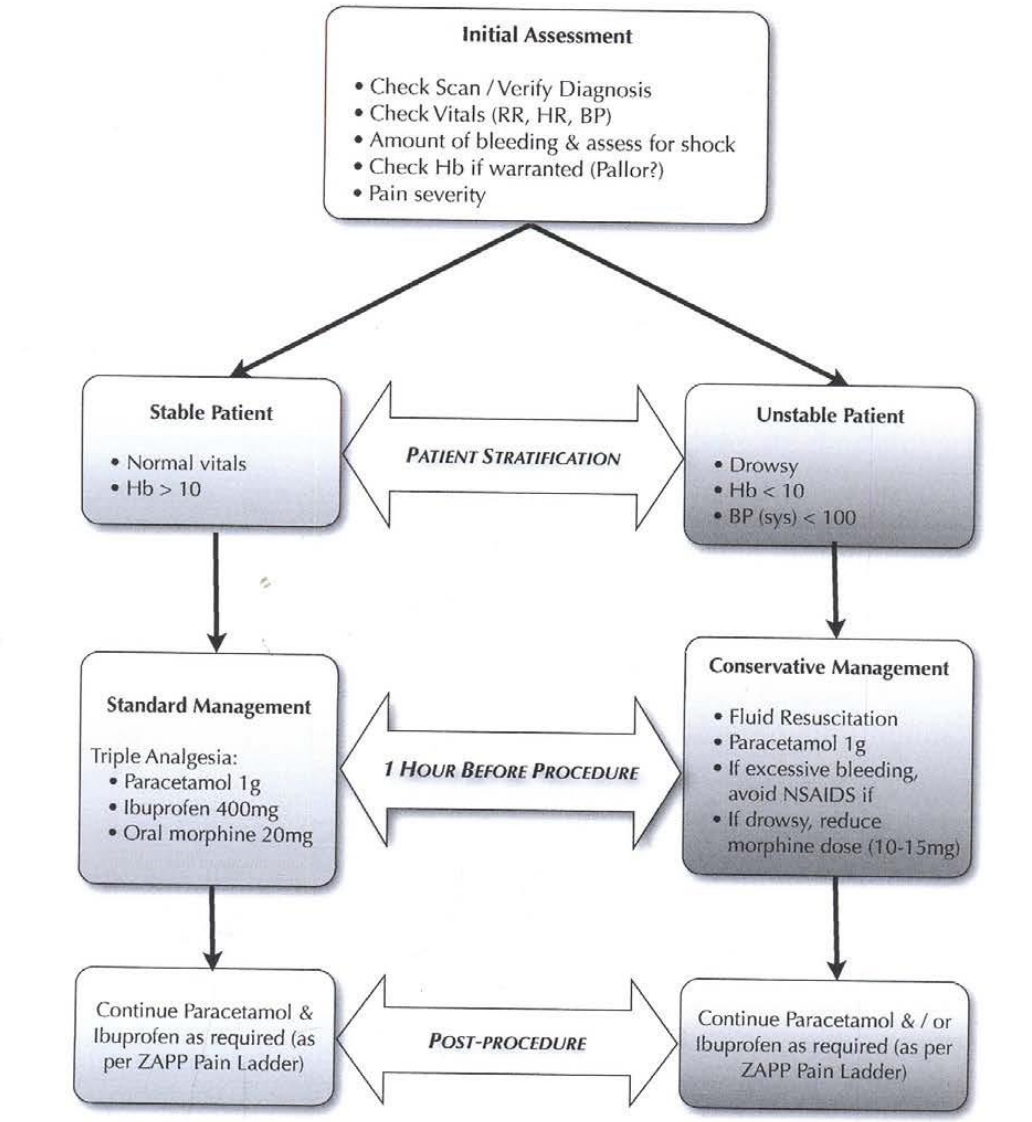
6. Recall of Pain (1:00hour)…….

Faces Pain Scale - Revised

7. Discharge Time ……

ZAMBIA ACUTE PAIN PROGRAMME (OTA PROJECT)

MVA Preemptive Analgesia Protocol



'Lusaka Link' Project
Out to Africa

Version 1.2; 6/7//12; Niven Akotia & Julie Windass