The effect of a single low dose propofol at the end of the operation in reducing post operative nausea and vomiting (PONV) in women undergoing laparoscopic gynaecological surgery at Parirenyatwa hospital.

by

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ABSTRACT

Objectives

To determine the effectiveness of single low dose propofol in reducing PONV in women undergoing laparoscopic gynaecological surgery.

To describe factors associated with nausea and vomiting in women undergoing laparoscopic gynaecological surgery.

Study design: Randomized single blinded controlled study

Setting: Parirenyatwa Hospital

Subjects: Eighty women aged between 19-55 years booked for laparoscopic surgery.

Statistical methods: Summary descriptive statistics, student's t-test, and Chi-square test.

Results: Incidence of nausea within one hour was 7.5% in the propofol group and 2.5% in the nonpropofol group (P = 0.6) and 10% and 15% nausea incidence after one hour in the respective groups. There were no reported incidences of vomiting after one hour from both study groups. Two participants from the propofol group (B) vomited within the first hour postoperatively and none from the nonpropofol group. Four participants (10.5%) complained of either nausea or vomiting from the propofol group compared to 9 (21.4%) from the non-propofol group (P = 0.23) which was not statistically significant.

Conclusion: Administration of single low dose propofol 0.5mg/kg at the end of laparoscopic gynaecological surgery does not reduce the incidence of PONV after propofol (2mg/kg) induction.

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LIST OF ABBREVIATIONS

ASA - American Society of Anaesthesiologists

BMI- Body mass index

CTZ - Chemoreceptor trigger zone

ENT - Ear, nose and throat

GIT- Gastrointestinal tract

5-HT - 5-hydroxytryptamine

LMP- Last menstrual period

NK- Neurokinin

NSAID- Nonsteroidal anti inflammatory drugs

PACU- Post anaesthetic care unit

PONV- Postoperative nausea and vomiting

NMDA- N-methyl D-aspartate

GABA- gamma-Aminobutyric acid

CI- Confidence Interval

PKa- Acid dissociation constant

Mg/ml- milligrams per milliliter

IV- Intravenous

EEG- Electroencephalography

P6- Point 6

FiO_2- Fraction of inspired oxygen

TIVA- Total intravenous anaesthesia

ETT- Endotracheal Tube

Introduction

It is now well recognized that post operative nausea and vomiting (PONV) is no longer just a trivial inconvenience but a significant cause of postoperative morbidity. It has physiological, psychological and economic disadvantages for both the patient and health care provider. Every effort should therefore be made to reduce it. Like pain, PONV is no longer acceptable in modern anaesthetic practice [(1)].

Post operative vomiting results in complications which affect both the success of the procedure and patient safety. It is associated with esophageal rupture, pulmonary aspiration, dehydration, electrolyte imbalances, raised intracranial and intraocular pressure. Wound complications such as bleeding and hematoma formation, increased pressure on suture lines, venous hypertension in skin flaps and wound dehiscence can also occur. Recovery is delayed in patients with persistent PONV. Amelioration of PONV has become even more important in day care surgery, an essential part of modern health care[(2;3)]. PONV has a bearing on length of hospital stay and unplanned overnight admission after day care surgery. Return to normal daily activities is delayed by PONV and so is employment. It has a negative influence on patient attitude to day surgery[(2)].

More resources are spent on PONV as this disrupts patient throughput. More nursing time is required, extra drugs and intravenous fluids are needed, hospital bed stay is increased and care to other patients is adversely affected through a knock on effect. PONV is feared by most patients and is the yard stick by which they judge their anaesthetist [(4)].

There are many factors associated with PONV and these can be related to the patient, the surgery, perioperative drugs and other perioperative events .There is also considerable variation among patients: women are three times more likely to suffer PONV than men under the same surgical condition. Patients with a history of PONV have a threefold increased risk of PONV [5].

PONV has equally been noted to be increased in some disease conditions and certain surgical procedures. It is increased with laparoscopic surgery where incidences of up to 80% have been reported and this area has been used more in antiemetic studies [6]. Gynaecological laparoscopic surgery has an incidence of 40% to 77% while general incidence of PONV for all surgical patients is estimated to be 25-30% [1;2;7]. A local study done in Zimbabwe in 1995, revealed an incidence of PONV of 21.5% and post operative vomiting of 13% [8].

Propofol, an alkyl phenol derivative is primarily a hypnotic agent thought to act via gamma-aminobutyric acid (GABA) and N-methyl D-aspartate(NMDA) receptors. Two effects of propofol exist: its antiemetic effect and sense of wellbeing to the patient after its administration. Its use has been shown to be associated with less PONV and a reduction in antiemetic use [9]. Evidence has shown that it possesses inherent antiemetic activity and has shown good results in treating refractory PONV after day case surgery [10].

Although routine prophylaxis for nausea and vomiting would seem appropriate, the choice of antiemetic agents is wide, and some are too expensive in our setting to be cost effective for routine use [11]. This study therefore sought to evaluate the effectiveness of single low dose propofol, a relatively cheaper antiemetic in reducing PONV in our local population.

Literature Review

Nausea is an unpleasant and uncomfortable sensation of an impending episode of vomiting [7]. It is often associated with prodromal symptoms such as salivation, swallowing, pallor and tachycardia. Vomiting is a complicated process, mediated by a central coordinating vomiting centre thought to reside in the brainstem (close to the tractus solitarius).Certain risk factors are unavoidable, such as those caused by the procedure or those associated with patient characteristics. Since these cannot be modified when present, diligent prophylaxis should be pursued. The choice of anaesthetic is one factor that the anesthetist has control over.

Fig1 is a diagrammatic illustration of the physiology of vomiting:

The medullary vomiting centre is located in the lateral reticular formation of the medulla, close to the fourth ventricle. It receives afferents from the chemoreceptor trigger zone (CTZ), vestibular apparatus, cerebellum, higher cortical and brainstem centers and solitary tract nucleus. These structures are rich in dopaminergic, muscarinic, serotoninergic, histaminergic and opioid receptors. Blockade of these receptors may be the mechanism of the antiemetic action of drugs. Efferents for the vomiting centre are transmitted via cranial nerves V, VII, IX, X, and XII to the gastrointestinal tract and through the spinal nerves to the diaphragm and abdominal muscles to cause the mechanical act of vomiting. The CTZ is in or near the area postrema, on the lateral walls of the fourth ventricle near the obex. It includes serotonin, dopamine, histamine, muscarinic and opioid receptors. The CTZ can be activated by chemical stimuli received through the systemic circulation as well as the cerebral spinal fluid. The cerebral cortex is stimulated by smell and physiological stresses. Motion can stimulate the vestibular apparatus, which may also stimulate the CTZ.

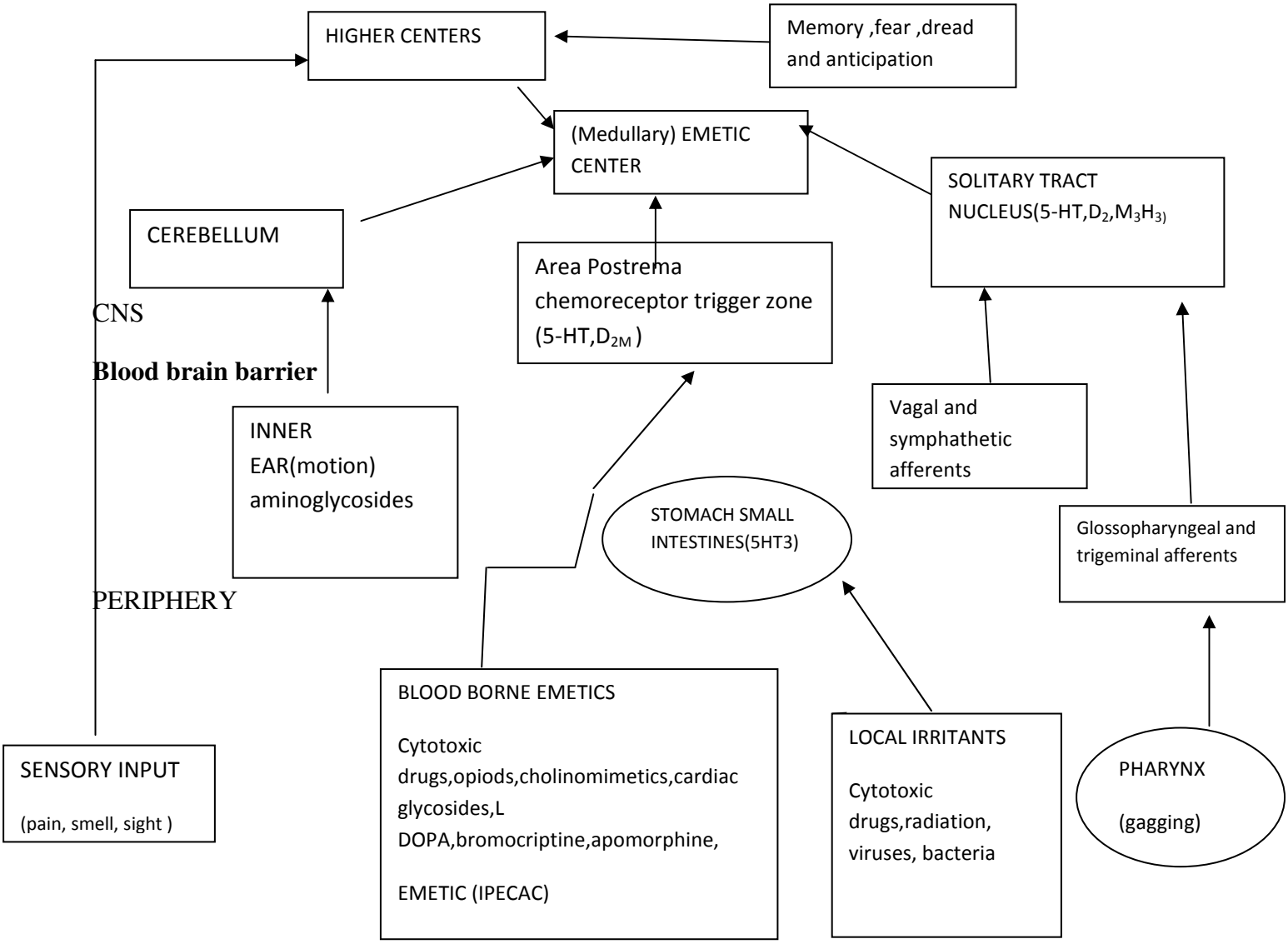


Fig 1: Pharmacologist view of emetic stimuli

Factors affecting PONV

The origin of PONV is multifactorial.Factors that are not under anaesthetic control include patient age, sex, history of previous PONV or motion sickness, smoking, surgical procedure, duration of surgery and anaesthesia, and patient and parental anxiety.A study by Moyo P revealed that PONV was a problem in black Zimbabweans. Incidence of nausea in both male and female patients was found to be 21.5% while vomiting was 13% [(8)] (P<0.03).

Age decreases the chances of vomiting. A study by Sinclair et al reported that the incidence of PONV decreased by 13% for each 10 year increment. The same study also showed that PONV incidence decreased after the age of 50 years [(12)].

Women are three times more likely to experience PONV than men. This has been attributed to variations in serum gonadotropin or other hormone levels. Moyo P showed that women suffered significantly more often from nausea and vomiting than men. Incidence of nausea and vomiting was 25% and 16.5% in women compared to 14% and 6% in men (P<0.05 nausea,P<0.03 vomiting) [(8)].A study by Sinclair showed that the risk for PONV for men was 1/3 that of women[(12)].The model predicted PONV accurately and yielded an area under the receiver operating characteristics curve of 0.785+/_0.011 using an independent validation set.

History of previous PONV or motion sickness has been reported to be a strong predictor of PONV. It increases the risk of PONV by two to three folds.

Smoking is associated with decreased risk of PONV. Sinclair et al reported that smoking decreased likelihood of vomiting by 34% [(12)]. Rodrigo also reported that smoking significantly

decreased PONV [13].However Saidi A showed that exposure to cigarette smoke at home was not protective against PONV in children undergoing tonsillectomy [14].

Certain types of surgery are associated with a higher incidence of PONV than others. Examples include plastic (breast augmentation), ophthalmic (strabismus repair), ear nose and throat,dental, gynaecologic, laparoscopic (sterilization), genitourinary, orthopaedic surgery (shoulder procedures), mastectomy or lumpectomy [15]. It is unclear if the association is caused by the different anaesthetic agents, the different lengths of the surgical operation, or the surgery itself. Generally patients for plastic and orthopaedic shoulder surgery have a six fold increase in the risk of PONV. [12]

The risk of PONV increases with increasing duration of surgery and anaesthesia probably because of greater accumulation of emetogenic anaesthetic agents. PONV increases from 2.8%

incidence in patients with a surgical duration of less than 30 minutes to 27.7% incidence in those with surgical duration of 151 to 180 minutes. The duration of anaesthesia increases the risk of PONV by 59% for each 30 minute increase [12].A study by Lesliie K also showed that longer duration of anaesthesia was a predictor of PONV [area under receiver operating characteristic curve=0.70 (95%CI:0.667-0.73)][16].

The anaesthetic technique employed contributes to PONV.The type of premedication administered also affects the incidence of PONV.The α2 agonist clonidine reduces PONV in children after strabismus repair probably by reducing anxiety while use of opioid analgesics for premedication on the other hand, increases the risk of PONV [12].

Patients receiving general anaesthesia were eleven times more likely to experience PONV than those receiving regional anaesthesia or a chronic pain block because of the emetogenic effects of opioids [1].Nitrous oxide has been reported to produce a greater incidence of vomiting .Its omission reduces vomiting incidence but only if the baseline risk of vomiting is higher in the patient population [17;18]. Nitrous oxide has been suggested to contribute to PONV through three mechanisms: activation of the medullary dopaminergic system, increasing cerebrospinal opioid peptides, and gastrointestinal distension through transfer to the gastrointestinal tract. In addition, nitrous oxide is routinely administered during general anaesthesia as 60-70% of the total gas mixture, which restricts the fraction of inspired oxygen to levels below those associated with reduced risk of PONV and surgical site infection.Clinical experience suggests that the routine use of nitrous oxide as an adjunct to the maintenance of general anaesthesia is on the decline, particularly among more recently appointed anaesthetists. This observation is supported by Yoshimura and Ushijima (2005) who found that in their institution nitrous oxide was used in the maintenance of 97% of general anaesthetics in 1995 but by 2004 this figure had decreased to 49% [19].

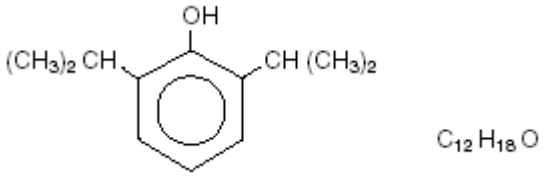
Volatile anaesthesia may be the main cause of early (0-6 hours) but not delayed (6-24 hours) PONV[20].In a randomized controlled trial of factorial design, in the early post operative period (0-2hours), the leading risk factor for vomiting was the use of volatile anaesthetics with similar odds ratio (95% CI) being found for isoflurane,(19.8(7.7-51.2),enflurane,(16.1(6.2-41.8).A dose response relationship was present for the use of volatile anaesthetics [20].

Regional anaesthesia, used as the sole anaesthetic or as a supplement to general anaesthesia can reduce PONV. It reduces the requirement of general anaesthesia and opioids and serves as

residual analgesia in the early postoperative period with subsequent decreased use of postoperative opioids.The general assumption that regional anaesthesia is associated with less PONV than general anaesthesia is generally correct, although newer general anaesthetic agents like propofol have narrowed the gap [21].

Propofol (2,6-diisopropylphenol) has become the intravenous anaesthetic of choice for ambulatory surgery. Propofol injectable emulsion is a sterile, nonpyrogenic emulsion containing 10 mg/mL of propofol suitable for intravenous administration. Propofol is chemically described as 2,6-diisopropylphenol and has a molecular weight of 178.27.

The structural and molecular formulas are:



Propofol is slightly soluble in water and, thus, is formulated in a white, oil-in-water emulsion. The pKa is 11. The octanol/water partition coefficient for propofol is 6761:1 at a pH of 6-8.5. In addition to the active component, propofol, the formulation also contains soybean oil (100 mg/mL), glycerol (22.5 mg/mL), egg lecithin (12 mg/mL); and disodium edetate (0.005%); with sodium hydroxide to adjust pH. The propofol injectable emulsion is isotonic and has a pH of 7-8.5.[22]

Propofol injectable emulsion is a single-use parenteral product which contains 0.005% disodium edetate to inhibit the rate of growth of microorganisms, for up to 12 hours, in the event of accidental extrinsic contamination. However, Propofol injectable emulsion can still support the growth of microorganisms, as it is not an antimicrobially preserved product. Accordingly, strict aseptic technique must still be adhered to.It should not be used if contamination is suspected. Unused portions should be discarded as directed within the required time limits[23].

Propofol is highly protein-bound *in vivo* and is metabolised by conjugation in the liver.[24] Its rate of clearance exceeds hepatic blood flow, suggesting an extrahepatic site of elimination as well. The half life of elimination of propofol has been estimated at between 2 and 24 hours. However, its duration of clinical effect is much shorter, because propofol is rapidly distributed into peripheral tissues. When used for intravenous (IV) sedation, a single dose of propofol typically wears off within minutes. Propofol is versatile; the drug can be given for short or prolonged sedation as well as for general anesthesia. Its use is not associated with nausea as is often seen with opioid medications. These characteristics of rapid onset and recovery along with its amnestic effects [25] have led to its widespread use for sedation and anesthesia.

Electroencephalography (EEG) research upon those undergoing general anesthesia with propofol suggests that it causes a prominent reduction in the brain's information integration capacity at gamma wave band frequencies.[26]

Propofol is extensively metabolized, with most of the administered dose appearing in the urine as glucuronide conjugates.Favourable operating conditions and rapid recovery are claimed as the main advantages in using propofol whereas disadvantages include relatively high incidences of

apnea and hypotension. Another disadvantage of propofol administration is pain on injection, which is sometimes very distressing to patients.[27] Although various pharmacological and non-pharmacological methods to decrease pain due to propofol injection have been tried, the most effective technique has not been identified.[28] Picard and Tramer carried out a meta-analysis of 56 studies (n = 6264 patients) in the prevention of pain on injection of propofol, and concluded that lidocaine was the most effective drug for minimising pain during propofol administration[27].The action of propofol involves a positive modulation of the inhibitory function of the neurotransmitter gama-aminobutyric acid (GABA) through GABA receptors[29].

Propofol, an intravenous hypnotic agent, is considered to possess antiemetic action[23].It is associated with a lower incidence of PONV when used for induction of anaesthesia compared with thiopentone [30]. Sub hypnotic doses of propofol were shown to be effective in reducing PONV associated with general anaesthesia [10].A study by Ramanathan et al looking at the efficacy of single low dose propofol at the end of surgery in preventing PONV found out that the incidence of nausea was reduced in the propofol group and was statistically significant ($P<0.05$) in the 4^{th}-24^{th} hour period. The incidence of vomiting was also significantly reduced ($P<0.05$) in the propofol group [31].

A randomized controlled trial evaluating whether propofol could effectively reduce PONV showed that in early period (0-5 hours), PONV in thiopentone/nitrous, propofol/nitrous, propofol/propofol groups was 72%, 44% and 31% respectively ($p=0.00014$)[23].The study therefore concluded that total intravenous anaesthesia (TIVA) using propofol and propofol/nitrous anaesthesia can significantly reduce the incidence of PONV in the early

postoperative period[23]. Total intravenous anaesthesia with propofol has been used with low emetogenic potential that is clinically relevant.

Reversal of non-depolarizing neuromuscular blocking drugs with anticholinesterases such as neostigmine can increase the incidence of PONV due to the muscarinic effects on the gastrointestinal tract [32]. Neostigmine is often used to antagonize residual neuromuscular block. Because anticholinesterases such as neostigmine have cholinergic effects on the gastrointestinal tract (increased motility and gastric acid secretion) and on the heart (bradycardia, cardiac arrest), they are co-administered with anticholinergics, such as atropine or glycopyrrolate [33]. Atropine is a tertiary amine and can cross the blood-brain barrier to cause central effects. In contrast, glycopyrrolate is a quaternary amine that does not easily cross the blood-brain barrier and thus has no important central effects[34]. Interestingly, some authors have reported no significant difference in PONV between those who received a reversal and those who did not. Ching-Rong Cheng reported that neostigmine does not produce a clinically important increase in PONV [32]. The combination of neostigmine with either atropine or glycopyrrolate did not significantly increase the incidence of overall (0-24 h) vomiting (relative risk (RR) 0.91 [0.70-1.18], P=0.48) or nausea (RR 1.24 [95% CI: 0.98-1.59], P=0.08) [32].

Pain can increase the risk of PONV by prolonging gastric emptying time resulting in nausea and vomiting. Use of opioids to treat postoperative pain can also add to increased PONV.

Various scores are available for nausea and vomiting. A review found three predictive scores for postoperative nausea and vomiting and attempted to validate them in 1,444 patients[35]. A different review identified three additional predictive scores and attempted to validate all six scores in 1,566 patients[36]. Participants in both validation studies underwent general anesthesia

without prophylactic antiemetics. A subsequent study used a neural network (i.e. artificial intelligence software) to predict postoperative nausea and vomiting; however, this is not practical for physicians without specialized software[37].

The scores vary considerably in complexity. Some are multivariate equations that are not practical for bedside use without a calculator; however, simpler scores consisting of four or five items have been shown to be as accurate or nearly as accurate as more complex equations[38-39].

Apfel is renowned to have done a lot of research in PONV.The Apfel score (table 1 below) includes four variables and assigns one point for each. The score was prospectively validated in 520 patients from a different hospital than that used in the original study and was found to have good predictive accuracy [36-39].

TABLE 1

Apfel Score to Predict Postoperative Nausea and Vomiting

Characteristics	**Points**
Female sex	1
History of motion sickness or postoperative nausea and vomiting	1
Nonsmoker	1
Postoperative opioid treatment is planned	1
Total:	____

Score	***Probability of postoperative nausea and vomiting (%)***
0	10
1	21
2	39
3	61
4	78

The PONV risk score by Apfel consists of four predictors: female gender,history of motion sickness or PONV,non smoking and use of postoperative opioids.If none,one,two,three or four of these risk factors were present,the incidence of PONV were 10%,21%,39%,61% and 78% respectively[40;41].

Hypovolemia postoperatively can result in orthostatic hypotension, dehydration and dizziness, all of which can increase PONV. Appropriate intraoperative fluid administration reduces PONV following ambulatory surgery [21,42]. Kathrine Holte et al showed that liberal versus restrictive fluid administration improved recovery after laparoscopic cholecystectomy [43]. Magner J.J et al reported that intravenous administration of crystalloid 30ml/kg to healthy women undergoing day case gynaecological laparoscopy reduced the incidence of vomiting, nausea and antiemetic use compared to crystalloid 10ml/kg [44].

Early motion postoperatively including nursing procedures, ambulation and transfer on stretchers, wheelchair or vehicle can all increase PONV especially in those patients who have received opioids.Postoperative oral feeds can affect PONV. Van den Berg et al have shown that many patients who vomit postoperatively do so after taking their first drink [45].Another study by Van der Bilt found out that in 23% of the 62 patients of group A (fed within 4 hours) and in 6% of the 102 patients of group B (fed after 4 hours) (p = 0.003), vomiting was so severe that it necessitated modification of the feeding schedule. According to this study, it appears that it would be better to withhold feeding for the first 4 hours after surgery[46].

Antiemetic drugs

Several classes of drugs constitute the mainstay of antiemetic therapy. These include the older drugs like droperidol, metoclopramide and more recently 5-hydroxytryptamine (5-HT3) antagonists of which many studies and clinical trials were done in the nineteen nineties. Despite extensive research and introduction of newer antiemetic drugs with better efficacy and safety profiles, little progress has been done in reducing incidence of PONV.

Butyrophenones

Droperidol is the commonest antiemetic in the butyrophenone class of drugs. It is a heterocyclic neuroleptic inhibiting dopaminergic receptors in the CTZ of the medulla. Side effects include sedation, drowsiness (dose dependent), dysphoria, restlessness and rarely extra pyramidal reactions which are common in children. It also causes prolonged QT interval which has led to its loss of favour. Droperidol, in doses as low as 0.625 to1.25mg has been shown to be as effective as ondansetron 4mg without increasing sedation, agitation, anxiety or delaying discharge [(11;47)].

Benzamides

Metoclopramide has been used for almost 45 years and is the most effective of this class. It is a dopamine antagonist in the CTZ. At high doses, it also antagonizes 5-HT3 receptors. It also increases the lower esophageal sphincter tone and facilitates gastric emptying into the small intestine through its dopaminergic and cholinergic actions on the gastrointestinal tract [(48)]. Thus it reverses the gastric immobility and cephalad peristalsis that accompany the vomiting reflex. Best documented doses in adults are 10mg (IV) and 0,25mg/kg (IV) in children. Side effects include

abdominal cramping, sedation, dizziness and rarely dystonic extra pyramidal reactions (oculogyric crises, opisthotonus, trismus, torticolis) and cardiac dysarrhythmias [2;9;49].A study by Yoshitaka F et al evaluated the effect of small doses of propofol,droperidol and metoclopramide at the end of thyroid surgery in reducing PONV.The study showed that the incidence of PONV during the first 24 hours after anaesthesia was recorded in 13 %,47 % and 50% of patients who had received propofol 0.5mg/kg,droperidol 20ug/kg and metoclopramide 0.2mg/kg respectively ($P<0.05$)[50].

Histamine receptor antagonists (HRA)

Among the histamine receptor antagonists, the most commonly used is dimenhydrinate. HRA prevent histamine binding and activity by occupying histamine 1 receptors on effector cell membranes. They have sedative effects. A dose of 20mg dimenhydrinate decreases vomiting after outpatient surgery in adults.A study by Ingeborg D showed that 0.5mg/kg in children significantly decreases incidence of vomiting after strabismus surgery and is not associated with prolonged sedation [51].In the placebo group (no dimenhydrinate),the overall incidence of PONV was 60.1% compared with 30.1% in the treatment group ($p<0.0001$) [52].

Muscarinic receptor antagonists

The vestibular apparatus of the inner ear and the nucleus of the tractus solitarius are rich in muscarinic and histamine receptors. Scopolamine is postulated to block transmission to the medulla of impulses arising from overstimulation of the vestibular apparatus. Scopolamine patches applied before induction of anaesthesia protects against PONV after middle ear surgery. Hyun Kyu Lee showed that PONV was reduced after application of scopolamine patches in

patients receiving epidural morphine [28].The proportion of patients who required rescue antiemetics was significantly lower in group DS (dexamethasone and scopolamime) than in group D (dexamethasone) at 12-24 hours (p=0.026)[54].

5-hydroxytryptamine (5-HT3) Receptor antagonists

Drugs in this class produce pure antagonism of the 5-HT3 receptor. Their introduction has resulted in a major improvement in pharmacotherapy of chemotherapy and radiation therapy-induced nausea and vomiting. They are highly effective in both prevention and treatment of PONV. Ondansetron is the most commonly used. Other drugs in this class include granisetron, tropisetron and dolasetron [55].

Ondansetron is a carbazolone derivative which is structurally related to serotonin and has specific 5-HT3 subtype receptor antagonist properties. Serious side effects are rare hypersensitivity reactions. It can also cause headaches, light headaches, dizziness, flushing at intravenous site, transient increases in plasma concentration of liver transaminases, a warm epigastric sensation and constipation. Cardiac dysarrhythmias have been reported. There was no difference in overall incidence of adverse effects with the usual clinical doses of ondansetron (4 to 8 mg) droperidol (0.625 – 1.25 mg) and metoclopramide (10mg) [56].

The antiemetic efficacy of ondansetron was shown to be better than its antinausea efficacy. When administered near the end of surgery rather than before surgery, ondansetron may result in higher efficacy and better patient satisfaction and this was found to be the same with metoclopramide [56].

Tramer et al showed that there were no differences in the effectiveness of 4 or 8mg ondansetron in the treatment of established PONV [57]. They also concluded that ondansetron did not differ significantly in its antiemetic effects from droperidol or metoclopramide when given for established emesis. Other studies have however shown that ondansetron has greater efficacy in controlling established PONV compared to metoclopramide [56;58].

Granisetron is a more selective 5-HT3 receptor antagonist than ondansetron. A dose of 0.04 mg IV is effective in preventing PONV. Its elimination half life of nine hours is 2.5 times longer than that of ondansetron and therefore require less frequent dosing. It is expensive and this may limit its use [59].

Dolasetron is a highly potent and selective 5-HT3 receptor antagonist. Given at induction of anaesthesia, the optimal dose for prophylaxis is 50mg. For rescue antiemetic, dolasetron 12.5mg IV is effective. It is rapidly metabolized to hydrodolasetron which is responsible for the antiemetic effect. Hydrodolasetron has an elimination half-life of approximately eight hours and is 100 times more potent as a serotonin antagonist than the parent compound [60].

Tropisetron is an indoleacetic acid ester of tropine with 5HT3 receptor antagonist activity. A dose of 2mg in adults and 0.1 mg/kg in children may be effective against PONV [61].

Glucocorticoids

Other drugs like glucorcorticoids (dexamethasone and methylprednisolone) have been used as antiemetics. Besides dexamethasone's traditional use in chemotherapy-related emesis, it has also been used more recently as prophylaxis for PONV. Although the mechanism of its antiemetic action is unclear,meta-analysis have shown that in high risk, single intravenous dexamethasone

8mg or 10mg is effective with no known increase in side effects compared to placebo[62;63]. Its antiemetic effects compares with conventional antiemetic agents.A study by Apfel demonstrated that 4mg dexamethasone given at the beginning of surgery is as effective as 4mg ondansetron or 1.25 mg droperidol[64]. Dexamethasone's antiemetic efficacy is better when used in combination with another antiemetic drug than when used as the sole agent [8;66-68].

Neurokinin-1 antagonists

Neurokinin-1 (NK-1) receptor antagonists represent a new class of antiemetics. NK-1 receptors are abundant in the medullary areas where antiemetic inputs converge. Studies have shown that NK-1 receptor antagonists are more effective than ondansetron for prophylaxis against PONV after gynaecological surgery and better than placebo in the treatment of established PONV [49;56].

No drug can claim to be the miracle cure for this deceptively simple problem. Different pharmacological classes of drugs with different mechanisms of action, in combination should be more effective than single drugs alone in inhibiting the emetic reflex. Combination therapy could result in reduction of dosing of the respective drugs, hence improving the side effect profile [2]. A study by Mangwiro R comparing metoclopramide versus metoclopramide and dexamethasone in preventing PONV in gynaecological patients undergoing laparoscopy showed that combination drugs decrease PONV both in the first few hours postoperatively and 24 hours postoperatively versus monotherapy in high risk PONV groups (P=0.038) [68]. Nanaka et tal evaluated the efficacy of a combination of dexamethasone and metoclopramide for the prophylaxis of PONV after gynaecological abdominal surgery. They showed that a combination of metoclopramide and dexamethasone was more effective in preventing PONV compared with metoclopramide alone [66].

A study by Saidi A comparing the effectiveness of a combination of midazolum with dexamethazone and dolasetron showed that combination therapy was equally effective in preventing PONV in children and can be used as an alternative in high risk patients. [14]

Non pharmacological antiemetic methods

Non pharmacological methods of reducing PONV are available and include acupuncture. This can be done through electroacupunture, transcutaneous electrical nerve stimulation, acupoint stimulation or acupressure. Acupuncture is a technique intended to promote health and well-being, that entails the insertion, into the body of its subject, of very thin needles. The needles are applied into areas described as acupuncture points. The point 6 (P6) acupuncture point lies about four centimeters up the arm from the wrist creases. Stimulation of this point is claimed to reduce PONV effectively. A systemic review by Lee and Done concluded that the P6 acupuncture point stimulation is effective in preventing PONV in adults but not children [69].For adults, the P6 point stimulation halved the incidence of early PONV.Vanita Jindal et al showed that in adults, acupuncture was able to inhibit chemotherapy-related acute vomiting [51].

Supplemental oxygen has also been shown to have a protective effect against PONV [56].But despite this early notion, the ability of supplemental oxygen to decrease the incidence of PONV is inconsistent, with initial studies suggesting benefit while subsequent trials demonstrate no decrease in PONV[70;71;72;73].In a meta analysis of randomized controlled trials assessing role of supplemental oxygen in reducing PONV,Mukadder Orhan et al demonstrated that patients who received perioperative 80% fraction of inspired oxygen (80% FIO_2) compared to 30-40% FIO_2 had similar incidence for early, late and overall PONV[70].They recommended that 80% FIO_2 should therefore no longer be considered an effective or reliable method to reduce PONV[70-73].

Propofol as an antiemetic

Intravenous induction with propofol has long been associated with a modest reduction of PONV. Apfel et al in their study confirmed that replacing an inhaled anaesthetic agent with propofol does reduce PONV by about the same amount as ondansetron and addition of one or more antiemetics to a propofol induction anaesthetic reduces PONV even further [(40)].

When sub hypnotic doses of propofol (10-20mg iv) were given (at the end of laparoscopic surgery) to adult patients to treat PONV, 81% reported overall reduction in PONV compared to 35% in the control group. However 28% of the patients had relapse of nausea and vomiting within 30 minutes [(69)].Compared with newer volatile anaesthetics, propofol anaesthesia offered advantage of lower incidence of PONV[(69)].

McCollum et al's study compared propofol as an induction agent to methohexitone after morphine or pethidine premedication. It showed that the incidence of PONV was significantly reduced for the six hour postoperative period in the propofol group with a tendency of PONV to increase six hours post operatively in both groups [(74)]. This suggested that the anti-emetic effect of propofol is related to its serum concentration which when reduced below the effective level, allows the emetic effects of opioids to become more predominant [(74)].

Gan et al looked at the serum concentration of propofol needed to treat PONV. Ninety-three percent of patients were successfully treated (without increasing sedation) in the recovery room with a mean serum level of 343 ng/ml which could be achieved by a bolus of 10 mg followed by an infusion of 0.6 mg/kg/hr [(5)].

Fuji and Hakura M, compared the percentage of patients experiencing nausea, retching or vomiting after different concentrations of propofol were given at the end of surgery. They reported incidences of 67% in the placebo group, 60% in the propofol 0.25mg/kg group and 33% in the propofol 0.5 mg/kg group. No adverse events attributed to the study drug were observed[11].

Unal et tal compared propofol and metoclopramide in preventing PONV after middle ear surgery. The results showed that administration of a sub hypnotic dose of propofol (0.5mg/kg) at the end of surgery was found to be at least as effective as metoclopramide in preventing PONV in the early postoperative period in adult patients undergoing middle ear surgery [9].

Fuji and Itakwa M compared propofol, droperidol and metoclopramide for prophylaxis of PONV after breast cancer surgery. Prevalence of PONV was not significantly different between propofol 0.5mg/kg and droperidol 20μg/kg 0-24 hours after anaesthesia. Prevalence of PONV was significantly lower with propofol and droperidol compared with metoclopramide 0.2mg/kg and placebo [11].

Rama-Maceiras P et tal's study looked at effects of different opioids on PONV. It showed that propofol and fentanyl anaesthesia resulted in higher incidence of PONV and requirements of antiemetic drugs in the period between 2 - 12 postoperative hours compared with propofol and remifentanil in patients undergoing plastic surgery [75].

Hammas B et al investigated the superiority of prolonged antiemetic prophylaxis with a 4 drug multimodal regimen .They compared the effects of low dose propofol infusion with a 4 drug multimodal regimen .Their results showed antiemetic prophylaxis with a combination of

droperidol ,ondansetron,metoclopramide and dexamethasone was more effective in preventing PONV. Low dose infusion of propofol had short lasting effects and therefore increased incidence of PONV than combination therapy [76].

Numazaki M & Fujiyi evaluated the efficacy of propofol given at the end of surgery for prevention of nausea and vomiting in parturients undergoing caesarian section under spinal anaesthesia. Severity of nausea and vomiting was less, 22% in patients who received propofol than in those who received placebo, 60% ($P<0.05$). They concluded that sub hypnotic dose (0.5mg/ kg/) was effective in preventing nausea and vomiting [10].

In another randomized double –blinded comparison of metoclopramide, ondansetron and cyclizine in day-case laparoscopy patients receiving a standardized propofol/isoflurane anaesthetic but no preoperative antiemetic , 50% of patients in the no antiemetic group had no nausea and vomiting up to 24 hours post-op. Incidence of PONV in the metoclopramide group was 24 %,in ondansetron 20% and in cyclizine 51% [77].There was no detectable difference between ondansetron 4 mg and metoclopramide 10mg.Both metoclopramide and ondansetron may potentially reduce incidence of PONV following gynaecological laparoscopy by up to 50 % when administered intravenously prior to propofol/isoflurane anaesthestic [3;58].Moore J.K compared propofol and halothane versus sevoflurane in paediatric day-case surgery: induction and recovery characteristics. The incidence of both PONV was noted to be significantly higher in the sevoflurane group compared to the propofol and halothane group ($P=0.034$). The increased incidence of adverse events during induction, postoperative nausea and vomiting and postoperative delirium in the sevoflurane group suggests that sevoflurane is not ideal as a sole agent for paediatric day case anaesthesia. There were more adverse events during volatile

induction with sevoflurane, and this was most significant for excitatory movement. This difference is probably attributable to the prolonged time spent in the excitation phase of induction with sevoflurane, compared with the very short excitation phase of induction with an i.v. technique[15].

Diclofenac given perioperatively and postoperatively results in less PONV than opioids.[78].Wennstrom B studied the analgesic and antiemetic properties of rectally administered diclofenac compared with opioid (morphine) given i.v during strabismus surgery in children. Incidence of PONV in the first 24 hours was 12% while it was much higher, 72% (P=0.0000) in the morphine group[78].

Various combinations of antiemetic are available for use in developed countries. Use in resource constrained communities is limited by high cost to both the patients and the institutions. In this study, one vial of propofol would suffice for both induction and the single small dose 0.5mg/kg at the end of surgery.

PONV is one of the most distressing morbidities associated with surgery. The incidence elsewhere can be as high as 30 %[56]. In an unpublished study by Moyo P,the incidence of nausea and vomiting in Zimbabwe, investigated in a variety of different surgical procedures, was found to be 21.5% and 13% respectively. Laparoscopic gynaecological surgery contributes a significant proportion of patients both in private and public sector. The emotional and psychological factors associated with PONV would mean most of these patients may not be stable enough for early discharge. More resources would therefore be needed to manage the complications of PONV with the resultant increased cost both to the patient and the institution. Identification of an effective but cheaper alternative antiemetic therefore needs to be explored.

It is with this background that this study was conducted to investigate if a single low dose propofol 0.5 mg/kg at the end of surgery reduces PONV in women undergoing laparoscopic gynaecological surgery in Harare, Zimbabwe.

Study justification

1. PONV is a problem which can be avoided or at least reduced in incidence. Once reduced, success rates of the procedure and patient satisfaction are both significantly improved.

If more emphasis is put on preventing PONV, this will in the long run be cheaper for both the hospital and the patient.

2. Laparoscopic gynaecological surgery contributes a significant number of surgical operations in both public and private health sectors in Zimbabwe. The study seeks to find out the effectiveness of a single low dose propofol 0.5mg/kg given at the end of laparoscopic gynaecological surgery in reducing PONV.

3. Drug choice

Propofol has been used effectively to reduce PONV. It is available in most theatres both in private and public hospitals in Zimbabwe. The incidence of side effects is low in doses which will be used in this study. It also has an added advantage of a sense of wellbeing to the patient postoperatively.

Objectives

1. To compare the antiemetic effect of propofol induction versus propofol induction plus single low dose propofol at the end of the operation in women undergoing laparoscopic gynaecological surgery.

2. To describe demographic characteristics of the two groups.

3. To investigate factors that may be associated with vomiting in women undergoing laparoscopic gynaecological procedures.

Inclusion Criteria

1. ASA grade 1 and 2.
2. Women on elective laparoscopic gynaecology list.
3. Patients who consent to the study.
4. Women aged 18 to 55 years.

Exclusion Criteria

1. Patients who refuse to consent to the study.
2. ASA 3 – 5 patients
3. Patients with potential difficult airway.
4. Patients with a contraindication to any of the drugs to be used.
5. Patients with a history of PONV in previous surgical operations.

6. Patients with a history of motion sickness.
7. Patients on drugs that reduce PONV.
8. Patients who smoke.

Methodology and patient recruitment

The study was carried out at Parirenyatwa Hospital gynaecological theatre. A day prior to the operation, informed written consent was obtained from each participant by the researcher during the preoperative anaesthetic visit in the ward. The study aims were carefully explained to the participants on the same visit.

Randomisation

Eighty participants were randomly assigned to two groups by the researcher: A or B, comprising of forty participants each. Each participant was randomly assigned a marked questionnaire out of the total of 80.To allocate a participant to a group, a randomization table (see appendix 4) was used. The table was entered at an arbitrary row and position in the tabulated 5 digit numbers. Successive two-digit groups of numbers were picked. The first forty distinct two-digit numbers that were between 01 and 80 were used to select the participants for group A. After the first 40 participants were picked, the remainder belonged to group B.

Group A: anaesthesia was induced using propofol 2mg/kg.

Group B: anaesthesia was induced using propofol 2mg/kg. Patients were then given propofol single dose 0.5mg/kg at the end of surgery. Only one vial of propofol was opened for both induction and single dose 0.5mg/kg at the end of surgery.In the event a participant weighed more than 80kg, then a second vial of propofol would be opened.

Both groups of participants received metoclopramide 10 mg intravenously. All participants were given one litre of Ringers lactate started perioperatively and completed in recovery room. The airway was secured by a Laryngeal Mask Airway or Endotracheal Tube. Maintenance of anaesthesia was through use of isoflurane, oxygen 100% and fentanyl and all were ventilated using the circle system. Muscle relaxation was employed using atracurium. At the end of the operation, when closing the skin, group B participants were given a single dose of propofol 0.5

mg/kg while group A participants/ control group were not given propofol.All the anaesthetic drugs were given by the researcher. Post operatively patients were given diclofenac 75mg intramuscular if they complained of pain in the recovery room. They were allowed to feed when fully awake. Analgesia was continued with diclofenac and codeine plus paracetamol orally at home.

Both groups of participants were followed up post operatively for the first 24 hours by telephone interview assessing the severity of PONV. A check list was completed by looking at primary end points and secondary end points. Primary end points were complete freedom from both nausea and vomiting. Secondary end points were:

- Severity of symptoms – need for rescue antiemetics,number of episodes
- Time to discharge

PONV was assessed using the Apfel et al's scoring system where nausea was assessed on a binary scale at 1 hour and on an 11- point numeric scale (0-10) at 24hr after surgery. The number of vomiting episodes were also recorded for both intervals. See appendix 1.

The following were operational definitions used in the study:

Nausea-an unpleasant sensation associated with awareness of the urge to vomit.

Retching-the laboured rhythmic contractions of the chest wall and abdominal muscles without the expulsion of gastric contents. This was assessed as nausea.

Vomiting-the forceful expulsion of gastric contents from the mouth brought about by sustained contraction of the abdominal muscles.

A detailed questionnaire was used (see appendix 1) which looked into patient history pre-operatively, intra-operative technique and primary and secondary end points of PONV.

Study Design

It was a randomized single blinded study.

Setting

The study was carried out at Parirenyatwa hospital gynaecology theatre.

Sample Size

This was determined with the help of a statistician. Using Pocock's formula, the calculated sample size for this study was 40 participants in each group, giving a total of 80 participants.

Data Analysis

Data was collected using a questionnaire. It was cleaned and coded before it was transferred to SPSS version 16 for statistical analysis. In analyzing the data, summary of statistics i.e. frequency, mean and median were used. Student t-test was used to compare continuous variables between group A and B participants. The Kruskal-Wallis P values and non parametric equivalent of the t-test were used to compare abnormally distributed data. Chi-square test and Fisher's exact test were used to compare discrete variables between group A and B patients.

Ethical Considerations

The study protocol was submitted to the Department of Anaesthesia and Critical Care Medicine, Parirenyatwa Hospital Ethics Committee and the Medical Research Council of Zimbabwe for scrutiny and approval. Both bodies approved the research with some alterations which were duly effected. Informed consent was obtained from each participant. Treatment of breakthrough pain and emesis was made readily available for the participants.

RESULTS

A total of 80 patients were recruited into the study. Group A, comprising of 40 participants was induced with propofol 2mg/kg **(Non propofol group)**. Group B, comprising of 40 participants was induced with propofol 2 mg/kg but received single low dose propofol 0.5mg/kg at the end of the operation **(Propofol group)**. A second vial of propofol was opened for participants who weighed more than 80kg from the propofol group (B). All participants received metoclopramide 10 mg intravenously at induction. Follow up rate within 24 hours was 100%.

Table 2. Baseline characteristics of participants by group

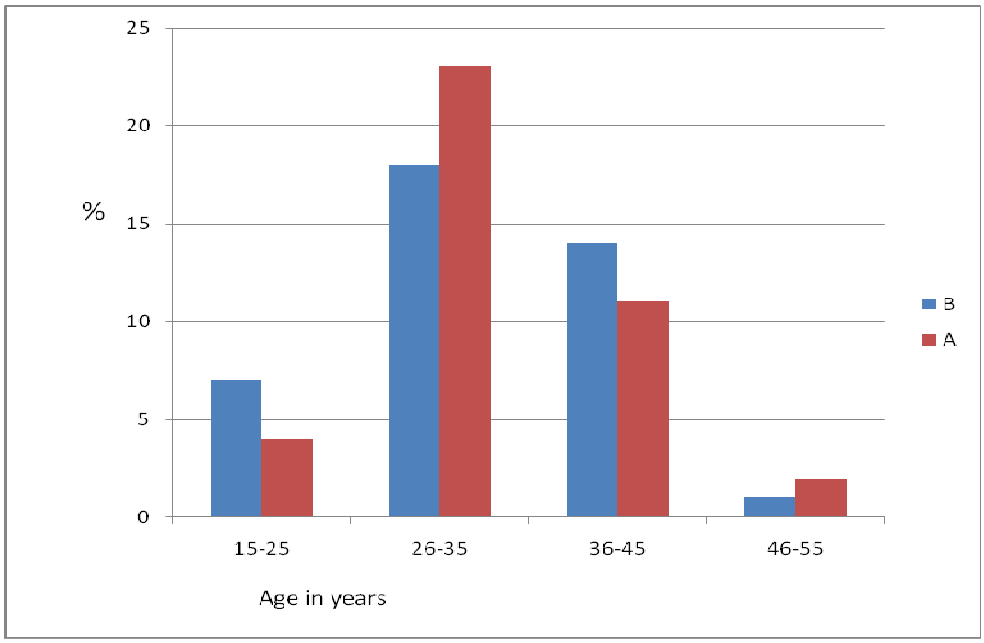
	Non Propofol Group(A) N=40	Propofol group(B) N=40	P value
Mean Age years(SD)	32.1 (7.3)	32.6 (7.1)	0.8
Weight in kg(SD)	74.6(12.0)	72.6(14.9)	0.13
Height in metres(SD)	1.7(0.06)	1.6(0.07)	0.6
BMI(SD)	26.4 (4.2)	25.6(4.0)	0.7
Average duration of anaesthesia in minutes(SD)	35.5(11.4)	36.8(10.3)	0.6
Mean days post LMP(SD)	30.0(63.6)	35.6(81.4)	0.5

Table 3.Procedure type

	Non Propofol Group(A) N=40	Propofol group(B) N=40	P value
Gynaecological procedure type	%	%	
Diagnostic laparoscopy	80.0%	75.0%	0.6
Operative laparoscopy	20.0%	25.0%	0.6

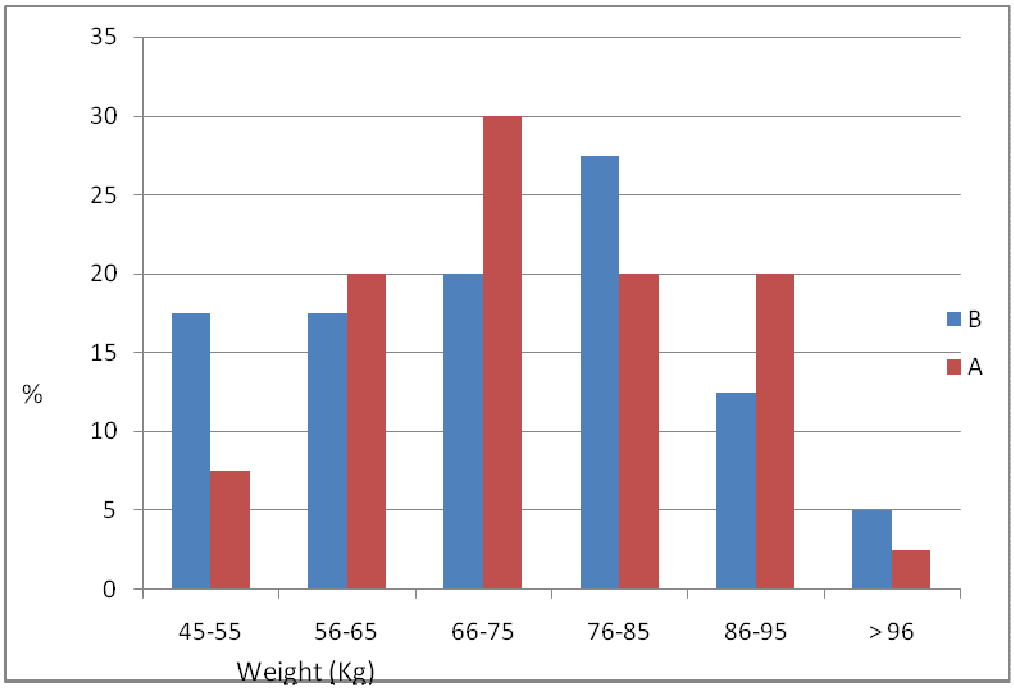
There were no statistically significant differences between the 2 study groups in terms of age, anthropometric measurements, duration of anaesthesia, mean days post LMP and type of procedure.

Figure 2. Bar graph showing age distribution of participants by group.



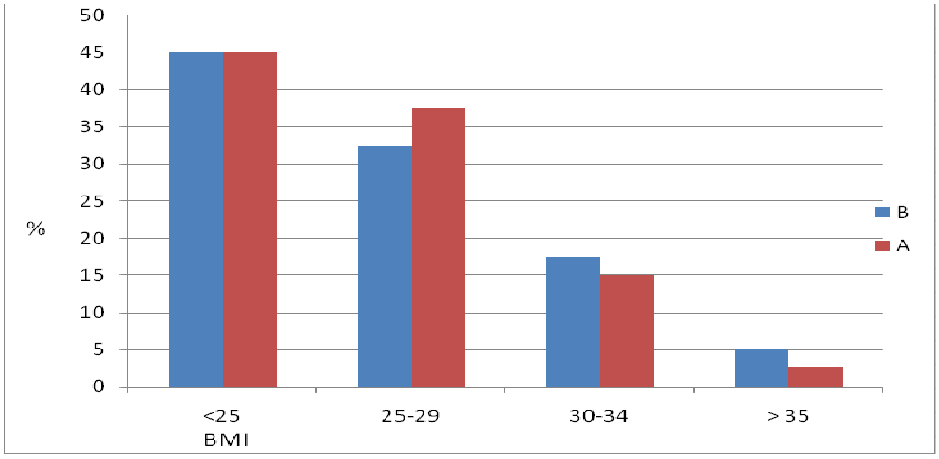
Age of participants ranged from 19 to 55 years. The mean age for the non propofol group (A) was 32.1 with a standard deviation of 7.3 while the mean age for the propofol group (B) was 32.6 with a standard deviation of 7.1(P= 0.8).There was a normal distribution curve representative of a normal population. Mode of age group was 26-35 years for both groups.

Figure 3. Bar graph showing weight distribution of participants by group



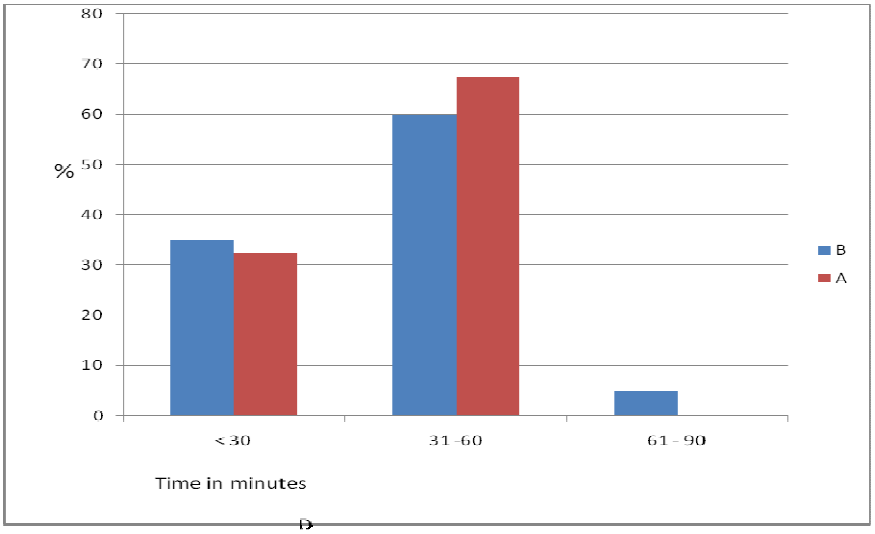
The mean weight in kilograms was 74.6 for the non-propofol group (A) while it was 72.6 for the propofol group (B).The modal weight was 66-75kg for the non-propofol group (A) and 76-85 kg for the propofol group(B) .

Figure 4. Bar graph showing distribution of body mass index(BMI) by group



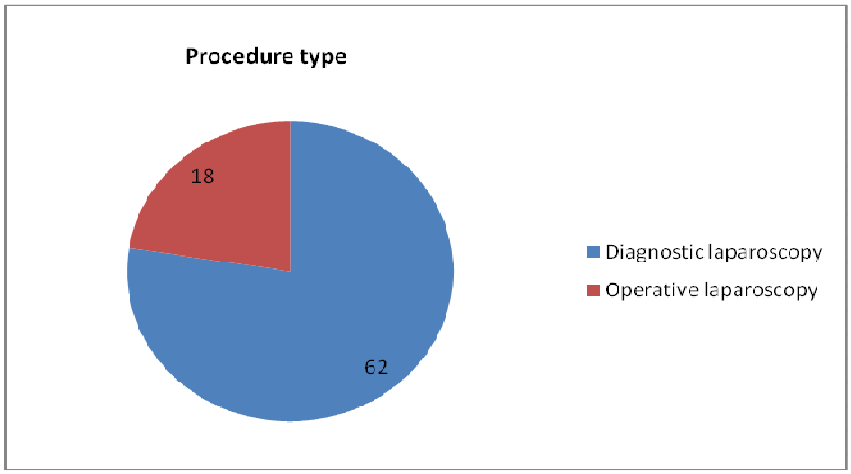
45% of the participants from the non-propofol group (A) had a normal BMI (<25%) while 45% of the participants from the propofol group (B) had a normal BMI.

Figure 5. Comparison of duration of anaesthesia by group



Most of the procedures, 67.5% in the non propofol group (A) and 60% in the propofol group (B) were done within 31-60 minutes.

Figure 6. Pie chart showing proportion of gynaecological procedures for the 80 participants



Procedures done were divided into two basic categories: either diagnostic laparoscopy and dye studies or operative laparoscopy which included tubal ligation, ovarian drilling, drainage of ovarian cysts, release of adhesions or cauterization for endometriosis. The majority of procedures, 77.5% were diagnostic laparoscopy, compared to 22.5% operative laparoscopy.

Table 4. Patterns of nausea, vomiting, pain and use of rescue antiemetics by group.

	Non Propofol (A) N=40(%)	Propofol (B) N=40 (%)	P value
Nausea within one hour Yes	1(2.5)	3(7.5)	0.6
Nausea after one hour Yes	6(15)	4(10)	0.7
Vomiting within one hour Yes	0(0)	2(5)	0.5
Vomiting after one hour Yes	0	0	
Pain within one hour Yes	23(57.5)	20(50.0)	0.5
Pain after one hour Yes	18(45)	13(32.5)	0.25
Rescue antiemetic given Yes	1(2.5)	2(5)	1

Before participants were discharged from the recovery room,1 participant (2.5%) from the non-propofol group (A) admitted to feeling nausea. In the propofol group (B),3 participants (7.5%) felt nausea. This difference was not statistically significant(P =0.6).

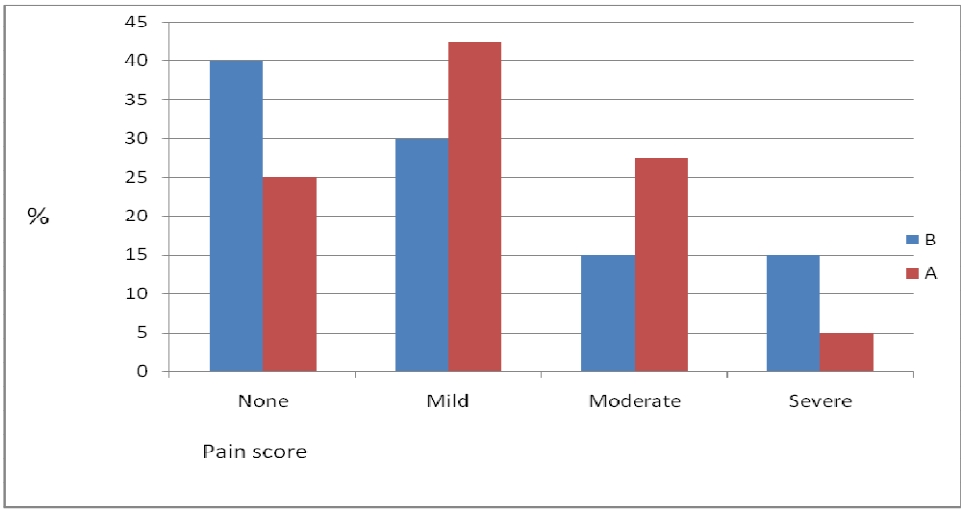
No participant from the non-propofol group (A) vomited in the recovery room. In the propofol group (B), 2 participants (5%) vomited in the recovery room. Twenty three (57.5%) participants in the non-propofol group (A) felt pain in recovery room while twenty (50%) in the propofol group (B) felt the same.

When participants were followed up 24 hours later, 6 (15%) in the non-propofol group (A) felt nausea compared with 4 (10%) in the propofol group (B) (P =0.7). There was no vomiting reported in both study groups.

Eighteen participants (45%) from the non-propofol group (A) felt pain 24 hours later compared to 13(32.5%) in the propofol group (B) (P=0.25).

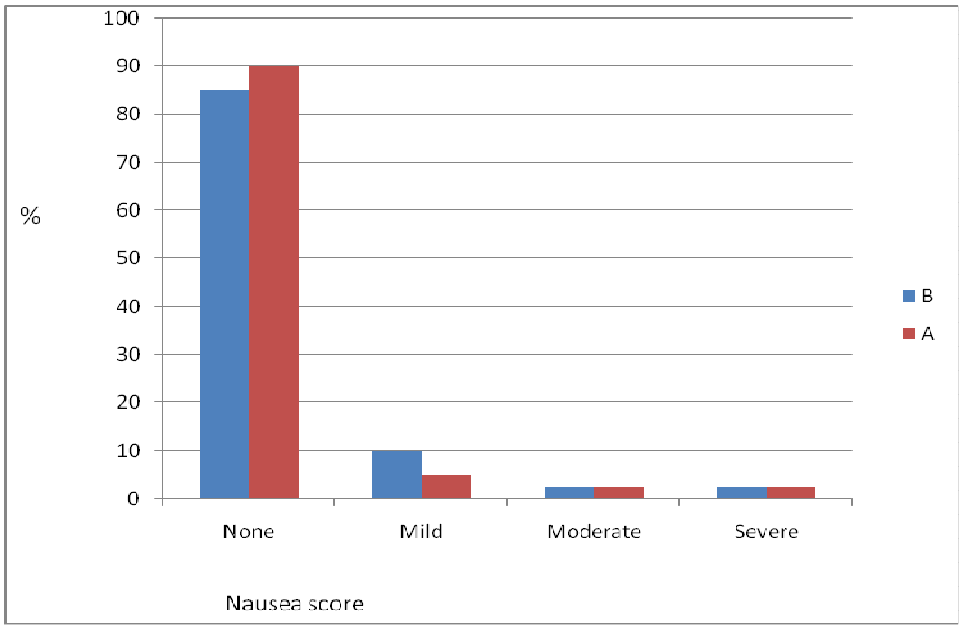
Two participants from the propofol group (B) who vomited in the recovery room were given intravenous prochloperazine 12.5mg. No further vomiting was reported until discharge 24 hours later.

Figure 7. Bar graph showing incidence of pain score between the 2 groups



40% of the participants in the propofol group (B) and 25% in the non-propofol group (A) did not complain of pain. However 30% of participants in the respective groups complained of moderate to severe pain and were given a non steroidal anti-inflammatory drug,diclofenac 50mg three times per day in the first 24 hours postoperatively.

Figure 8. Bar graph showing nausea score by group



The majority of participants had no nausea,85% in the propofol group (B) and 90% in the non-propofol group (A).

Table 5. The effect of propofol on either nausea or vomiting

	Non propofol(A) N=40(%)	Propofol(B) N=40(%)	P value
Either nausea or vomiting Yes	9 (21.4)	4 (10.5)	0.23

Four participants (10.5%) complained of either nausea or vomiting from the propofol group (B) while 9 (21.4%) complained of nausea or vomiting in the non-propofol group (A) (P = 0.23) which was not statistically significant.

Table 6. Effect of propofol on either vomiting or nausea stratified by reported pain

	Non propofol(A) N=16(%)	Propofol(B) N=17(%)		Non Propofol(A) N=24(%)	Propofol(B) N=23(%)	
	No pain reported	No pain reported	P value	Pain reported	Pain reported	P value
Vomiting /Nausea Yes	1 (10.0)	1 (6.7)	1	7 (23.3)	4(16.0)	0.73

Pain was a confounding factor. When pain was reported, 4 participants (16%) had either nausea or vomiting in the propofol group compared to 7(23.3%) in the non-propofol group (P= 0.73).When pain was not reported, 1participant (6.7%) experienced nausea in the propofol group while 1 participant (10.0%) had either nausea or vomiting in the non-propofol group.

Table 7. Comparison of effect of LMP on nausea only within 24 hours

	Non propofol(A) N= 8(%)	Propofol(B) N= 14(%)		Non Propofol(A) N= 19(%)	Propofol(B) N= 14(%)	
	LMP < 14 days	LMP < 14 days	P value	LMP >15 days	LMP >15 days	P value
Nausea Yes	2(18.5)	2(10.5)	0.6	5(22.7)	3(16.7)	0.7

Two participants (10.5%) with an LMP<14 days complained of nausea in the propofol group (B) compared to two(18.5%) in the non-propofol group (A), (P = 0.6).Of the participants with LMP>15 days,three (16.7%) from the propofol group experienced nausea while five (22.7%) had nausea in the non-propofol group ,(P =0.7). The difference between the groups was not statistically significant.It did not matter at which part of the mensrual cycle participants were at.Hormone levels did not have any significant difference in the incidence of PONV.

DISCUSSION

Laparoscopy has frequently been associated with marked PONV possibly due to pain and reduced gastric emptying associated with gas insufflation [(74)]. The increased incidence of PONV with laparoscopy has often resulted in prolonged patient hospital stay, up to 48 hours.

Propofol has been widely used in ambulatory anaesthesia. It has a high metabolic clearance. Its use has been associated with a decreased use of antiemetic medications. Evidence available indicates that propofol possesses inherent antiemetic properties that have been used to treat refractory nausea and vomiting after ambulatory anaesthesia [(7)].

In a study by Alain Borgeat et al,a subhypnotic dose of propofol was shown to possess direct antiemetic properties. Patients treated with propofol experienced a large reduction in nausea and vomiting compared with patients treated with placebo (81% versus 35% success rate; $P < 0.03$) [(80)].

In this study, the incidence of nausea in the first hour post operatively was 2.5% from the non propofol group (A) and 7.5% from the propofol group (B). (P= 0.6).No vomiting was reported from the non propofol group (A) while there was 5% incidence of vomiting from the propofol group (B) (P= 0.5).

A similar pattern was demonstrated 24 hours post operatively. No nausea was reported from the non propofol group (A) while 5% incidence of nausea was reported from the propofol group (B).Both study groups did not report any vomiting after one hour.

Rescue antiemetic was given to 2.5% of the non propofol group (A) compared with 5% from the propofol group (B) (P= 1).

Results from my study do not show statistically significant differences between the use of small dose propofol 0.5mg/kg at the end of laparoscopic gynaecological surgery and the use of propofol single induction dose in reducing PONV. Findings of my study are different from studies done elsewhere which clearly showed that sub hypnotic doses of propofol possess direct antiemetic properties. In their study Borgeat A et al demonstrated that patients treated with subhypnotic doses of propofol in the recovery room experienced a larger reduction in nausea and vomiting than patients treated with placebo. (81% versus 35% success rate) (P= 0.03) [80]. Induction of anaesthesia in their study was achieved through use of various induction agents, not propofol as was the case with my study. Numazaki M et al reported that prophylactic antiemetic efficacy of propofol at subhypnotic dose (1.0mg/kg/hr) is comparable to droperidol 1.25mg, and metoclopramide 10mg in patients undergoing caesarian delivery. Moreover propofol at a sub hypnotic dose is effective in the prevention of severe nausea [10].

Intravenous induction with propofol has long been associated with a modest reduction in PONV. It has become the anaesthetic technique of choice in ambulatory surgery as it affords early patient discharge. A study by Apfel et al confirmed that replacing an inhaled anaesthetic agent with propofol does reduce PONV by about the same amount as a single antiemetic [40].

A study by McCollum et al comparing propofol to methohexitone after morphine or pethidine premedication showed that incidence of PONV was significantly reduced for the first six hours post operatively in the propofol group. There was a tendency for PONV to increase six hours post operatively in both groups. McCollum et al therefore suggest that the antiemetic effect of propofol is related to its serum concentration which when it reduces below the effective level ,leaves the longer acting effects of opioids [74].

In this study, there was no provision for measurement of propofol serum concentration. It would therefore be difficult to comment on the relationship between propofol serum concentration and PONV.

Another study by Gan et al looked at the effective serum concentration of propofol needed to treat PONV.93% of patients were treated successfully (without increasing sedation) with a mean serum level of 343ng/ml. This effective serum concentration could be achieved by a bolus of 10mg followed by an infusion at approximately 10μg/kg/min [(5)].

Fuji et al investigated the dose range effects of propofol for reducing emetic symptoms during caesarian delivery. Their study showed that propofol 1mg/kg/hour is the minimum effective sub hypnotic dose for reducing emetic symptoms during caesarian delivery. Increasing the dose to 2mg/kg/hour provided no further benefit [(81)].

A study survey by Soppitt A.J et al investigated the use of propofol by anaesthesiologists for its antiemetic effect. Evidence available suggests that the antiemetic effect of propofol is associated with a defined plasma concentration range; mean 343ng/ml (10-90% CI 200-600ng/ml). Simulation data demonstrated that after propofol 2mg/kg (like in this study), its concentration will drop below 350ng/ml in 32minutes. After 2mg/kg and 20mg within 10minutes of end of surgery, its concentration will drop below 350ng/ml by 7minutes after the 20mg bolus dose [(82)].

Sopitt A.J et al therefore concluded that the efficacy of propofol as an antiemetic is present only if anaesthesia is maintained by a propofol infusion and also present when used in the post anaesthetic care unit (PACU) at a subhypnotic bolus dose of 0.5mg/kg. There is however little evidence to support propofol use purely at induction of anaesthesia or as part of a 'sandwich'

technique in an attempt to reduce PONV [82]. This is particularly true in surgery lasting longer than a few minutes.

Most studies carried out to find the effect of single low dose propofol in reducing PONV did not use propofol as an induction agent as was done in my study. Patients in other studies were induced with either thiopentone,etomidate or by inhalational induction agents[30;31;50;82].Significant differences in PONV were therefore noted in patients given small dose propofol at the end of surgery compared to those who did not receive propofol.This study has shown that there is no significant difference in reducing PONV when propofol is given either as an induction agent only or when single low dose propofol is added at the end of surgery to a patient induced with propofol.

A study by Helen Ki Shinn compared propofol and sevoflurane in reducing PONV after gynaecologic laparoscopic surgery. The propofol group patients were anaesthetized with propofol during the entire anaesthetic period and the non propofol group received 2mg/kg of propofol intravenously, followed by sevoflurane inhalation. The results showed a statistically significant lower incidence of PONV within one hour of surgery in patients induced and maintained on propofol ($p<0.05$).The study therefore concluded that propofol at induction and during maintenance of anaesthesia can be used to prevent PONV within one hour post-operatively in patients undergoing gynaecologic laparoscopic surgery[83].

LIMITATIONS

1. More information would have been obtained if serum propofol concentrations at the end of the surgical procedure were measured.

2. To pick out smaller details, a larger sample size would have been ideal

3. A better success rate of such a study in our setting in future would require that participants are assisted in paying for their hospital fees. It was noted that most participants were cancelled from the lists as they could not afford the hospital fees. This made the data collection process long and tedious.

4. Lack of funding inhibited the use of recent, better and recommended rescue antiemetic drugs.

CONCLUSION

Administration of low dose propofol 0.5mg/kg at the end of gynaecological laparoscopic surgery does not reduce the incidence of PONV after propofol (2mg/kg) induction.

There is no added advantage of adding a single low dose propofol 0.5mg/kg at the end of the surgery.

RECOMMENDATIONS

1. Further studies need to be carried out co-opting measurement of propofol serum concentration at the end of the surgical procedure.

2. A study with a bigger sample size needs to be carried out to detect small differences in incidence of PONV between the study groups.

Reference List

(1) Watcha F. **The cost effective management of postoperative nausea and vomiting .** Anaesthesiology 2000;92:931-3.

(2) Habib AS, Gan TJ. **Combination therapy for postoperative nausea and vomiting-a more effective prophylaxis?** Ambulatory surgery 2001;9:59-71.

(3) Paxton LD, Mckay AC, Mirakhur RK. **Prevention of nausea and vomiting after day case gynaecological laparosopy .A comparison of ondasentron,droperidol,metoclopramide and placebo.** Anaesthesia 1995;5(50):-403.

(4) Lee Y, Lin YS, Itchen Y. **The effect of dexamethasone on patient contolled analgesia related nausea and vomiting.** Anaesthesia 2002;57:61-5.

(5) Gan TJ. **Post operative nausea and vomiting -can it be eliminated?** JAMA 2002;287(10):1233-6.

(6) Kenny GN. **Risk factors for post operative nausea and vomiting.** Anaesthesia 2010;49:6-10.

(7) Watcha MF, White PF. **Post operative nausea and vomiting ,its etiology,treatment and prevention.** Anaesthesiology 1992;77:162-84.

(8) Moyo P. **Incidence of post operative nausea and vomiting in major central hospitals in Zimbabwe**. MMED thesis,University of Zimbabwe,1995.

(9) Unal y, Ozsolar O. **Comparison of the efficacy of propofol and metoclopramide in preventing postoperative nausea and vomiting after middle ear sugery**. J Clin Anesth 2009;7:521-7.

(10) Numazaki M, Fuji Y. **Subhypnotic dose of propofol for the prevention of nausea and vomiting during spinal anaesthesia for caesarian section.** Anaesth Intensive Care 2002;3(28):262-5.

(11) Fujii Y, Itakura M. **Comparison of propofol ,droperidol and metoclopramide for prophylaxis of post operative nausea and vomiting after breast cancer surgery:a prospective randomised,double blind placebo-controlled study in Japanese patients.** Clin Ther 2008;11(30):224-9.

(12) Sinclair DR, Chung F, Mezei G. **Can postoperative nausea and vomiting be predicted ?** Anaesthesiology 1999;91:108-18.

(13) Rodrigo C. **The effects of cigarette smoking on anaesthesia.** Anest Prog 2000;47:143-50.

(14) Saidi A. **A comparison of the effectiveness of combination of midazolam and dexamethazone versus dolasetron in preventing post -operative vomiting in children undergoing adenotonsillectomy** .MMED thesis University of Zimbabwe college of health sciences; 2006.

(15) Matchock RL. **Susceptability to nausea and motion sickness as a function of the menstrual cycle. Women health issues.Pub Med Central** 2009;18:328-35.

(16) **International multicentre protocol to quantify the relative impact of single and combined antiemetics in a randomised controlled trial of factorial design**.New England Journal of Medicine 2004;350;2441-2451

(17) Singh P, Gupta M , Srivastava A. **Nitrous oxide during anaesthesia for laparoscopic donor nephrectomy:does it matter.** Indian J Urol 2008;24:126-7.

(18) Akca O, Lenhardt R, Fleischmann E, Treschan T, Greif R, et al. **Nitrous oxide increases the incidence of bowel distension in patients under going elective colon resection**. Acta Anaesthesiol Scand 2006;48:894-8.

(19) Yoshimura and Ushijima .**The consumption of nitrous oxide used for general anaesthesia has been markedly reduced in our institute**.Masui ;2005:54(8):904-5

(20) Apfel CC. **Volatile Anaesthesia may be the main cause of early but not delayed PONV; a randomised controlled trial of factorial design**.Br J of Anaeshesia 2002 May:88(5):659-68

(21) Alain Borgeat,MD.**Regional anaesthesia effects on PONV**.Glasgow meeting-May 2003

(22) Trapani G.**Propofol in Anaesthesia.Mechanism of action,structure activity relationship,and drug delivery**.Curr Med Chem.2000 Feb:7(2) 249-71

(23) Chanvei L**.PONV in out patient gynaecologic laparoscopy:a comparison of thiopental-nitrous oxide,propofol-nitrous oxide and TIVA using propofol.**J Med Assoc Thai,2001:84(5)697-704

(24) Favetta P.**Propofol metabolites in man following propofol induction and maintenance**.British Journal of Anaesthesia 2002.(88):653-8

(25) Vaselis RA.**The comparative amnesic effect of midazolum,propofol,thiopental and fentanyl at equisedative concentrations**.Anaesthesiology 1997 Oct;87(4):749-64.

(26) Lee U.**Propofol induction reduces the capacity for neural information intergration:implications for mechanism of consciousness and general anaesthesia.**Consciousness and cognition 2009:(18)56-64

(27) Smith I.**Propofol: An update on its clinical use**.Anaesthesiology 1992:77:162-84.

(28) Picard P.**Prevention of pain on injection with propofol:a quantitative systemic review.**Anasth Analg 2000:90;963-9.

(29) Trapani G.**Propofol in Anaesthesia.Mechanism of action,structure activity relationship,and drug delivery**.Curr Med Chem.2000 Feb:7(2) 249-71

(30) Fujii Y, Itakura M. **Low dose propofol to prevent nausea and vomiting after laparoscopic surgery.** Int J gynae Obstet 2009;268-73.

(31) Ramanathan MD,Augustus MD,DA.**Efficacy of propofol in preventing PONV;single blind randomised control study.**Journal of Anaesthesiology 2003 vol7 number 1

(32) Cheng C, Sessler DI. **Does neostigmine administration produce a clinically important increase in postoperative nausea and vomiting?** Anesthe analg 2006;101:1349 -1355.

(33) Turner DA.**Evaluation of the combined effects of atropine and neostigmine on the lower oesophageal sphincter**.British journal of Anaesth 1985:57:956-9.

(34) Proakis AG:**Comparative penetration of glycopyrrolate and atropine across blood brain and placental barriers in anaesthetised dogs**.Anaesthesiology 1978;48:339-44.

(35) Eberhart LH.**Evaluation of three risk scores to predict PONV**.Acta Anaesthesiol Scand 2000:44 ;480-88.

(36) Apfel. **Comparison for predictive models for PONV**:Br J Anaesth 2002:88:234-40.

(37) Tragger M.**Prediction of PONV using an artificial neural network (in German).** Anaesthetist 2003:52:1132-8.

(38) Apfel CC.**A simplified risk score for prediction of PONV:conclusions from crossvalidation between two centres**. Anaesthesiology 1999:693-700.

(39) Koivuranta M.**A survey of PONV**.Anaesthesia 1997:52:443-9.

(40) Apfel CC. **A simplified risk score for predicting post operative nausea and vomiting.** Anaesthesiology 1999;91:693-700.

(41) Weilbach;PONV; **Usefulness of Apfel score for identification of high risk patients for PONV.** Acta Anaesth.Belg:2006:57:361-363

(42) Lambert.**Preoperative fluid bolus and reduction of PONV in patients undergoing laparoscopic gynaecological surgery**.AANA journal, 2009;77(2);110-4

(43) Holte K. **Liberal versus restrictive fluid administration to improve recovery after laparoscopic cholecystectomy:a randomised double -blind study**. Ann surg 2004;240:892-9.

(44) Magner JJ. **Effect of intraoperative intravenous crystalloid infusion on postoperative nausea and vomiting after gynaecological laparoscopy;comparison of 30 and 10ml/kg**. BMJ 2004;93(3):381-5.

(45) van den Berg AA. **Effects of intra -operative antiemetics and post operative oral fluids restriction.** Anaesthesia 1987;42:270-6.

(46) Van der Bilt J.D.W.**Early feeding after laparoscopic pyloromyotomy:the pros and cons.**2004:18(5):746-748 .

(47) Allen G. **Low dose droperidol**. CAMJ 2002;167:167-8.

(48) Henzi I.**Metoclopramide in the prevention of PONV:A quantitative systemic review of randomised placebo controlled studies**.Br J Anaesth 1999(83) :761-71

(49) Ruhlman C, Herrstedt J. **Casopitant:a novel NK1-receptor antagonist in the prevention of chemotherapy induced nausea and vomiting** . Ther clin risk manag 2009;5:375-84.

(50) Yoshitaka F.**Small dose of propofol,droperidol,metoclopramide for prevention of PONV after thyroidectomy**.Otolaryngo Head Neck surgery 2001(24) 3266-269

(51) Jindal V, Ge A, Mansky PJ. **Safety and efficacy of acupuncture in children,a review of the evidence .** J Pediatr Haematol oncol 2010;30:431-42.

(52) Ingeborg D.**Reduction of PONV by dimenhydrinate suppositories after strabismus surgery in children**.Anaesth Analg 2000:90:311-4.

(53) Kotelko MD. **Transdermal scopolamine decreases nausea and vomiting following caesarian section in patients receiving epidural morphine.** Anaesthesiology 1989;71:675-8.

(54) Hyun Kyu Lee.**The effect of transdermal scopolamine plus intravenous dexamethasone for the prevention of PONV in patients with epidural PCA after major orthopaedic surgery**.Korean J Anaesthesiol 2010:58:50-55.

(55) Kazemi-Kjellberg F, Henzi I, Tramer M. **Treatment of established postoperative nausea and vomiting : a quantitative systemic review** . BMC anasthesiol 2001;1:1471-3.

(56) Ku CM, Ong BC. **Postoperative nausea and vomiting:review of current literature**. Singapore Med J 2003;44:366-74.

(57) Tramer MR. **A quantitative systemic review of ondansetron in treatment of established post operative nausea and vomiting**. BMJ 1997;314:1088-92.

(58) Watts SA. **A randomised double -blinded comparison of metoclopramide ,ondansetron and cyclizine in day case laparoscopy**. Anaesth Intensive Care 1996;5:546-51.

(59) Cieslak GD. **The dose response relation and cost effectiveness of granisetron for the prophylaxis of paediatric postoperative emesis**. Anaesthesiology 1996;85:1076-85.

(60) Kovac AL. **Treatment of postoperative nausea and vomiting with single intravenous doses of dolasentron mesylate:a multicentre trial.** Anaesth Analg 1997;85:546-52.

(61) Alon E. **Tropisetron for treating established postoperative nausea and vomiting:a randomised duble blinded placebo controlled study**. Anaesth Analg 1998;86:617-23.

(62) Henzi et al.**Prevention and treatment of PONV**. Anaesth Analg 2000;91:136-9

(63) Eberhart et al.**Anaesthetic risk score for predicting PONV in adults**.Anaesth Analg 2000:91:117-22

(64) Apfel et al. **A factorial trial of six interventions for prevention of PONV**.New Engand Journal Med ;June 10 2004:350:2441-2451

(65) Apfel et al. **A factorial trial of six interventions for prevention of PONV**.New Engand Journal Med ;June 10 2004:350:2441-2451

(66) Nonaka A, Suzuki S. **Prevention of postoperative nausea and vomiting by metoclopramide combined with dexamethasone in gynaecological surgery**. Masui 2008;8:978-82.

(67) Scuderi PE, James RL, Harris L, Mims GR. **Multimodal antiemetic management prevents early post -operative vomiting after outpatient laparoscopy**. Anaesthesia and analgesia 2002;91:1408-14.

(68) Mangwiro R. **Comparison of metoclopramide versus metoclopramide plus dexamethasone in the prevention of post operative nausea and vomiting in gynaecology patients undergoing laparoscopic surgery**.MMED theisis University of Zimbabwe; 2003.

(69) Lee A Done ML.**The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting:** A meta analysis.Anaesth Analg 1999;88:1362-52

(70) Mukadder Orhan-Sungus,MD.**Does supplemental oxygen reduce PONV ? A meta analysis of randomised controlled trials.**Anaesth and Analg:106:June 2008;1733-38

(71) Purhonen S.**Supplemental 80% oxygen does not attenuate PONV after breast surgery.**Acta Anaesthesiol Scand 2006;50:26-31

(72) Piper SN.**Inspired oxygen fraction of 0.8 does not attenuate PONV after strabismus surgery**.Anaesthesiology 2005:103:6-10

(73) Piper SN.**Inspired oxygen fraction of 0.8 compared with 0.4 does not further reduce PONV in dolasentron treated patients undergoing laparoscopic cholecystectomy**.Br J Anaesth 2006:97:647-53

(74) Miller D. **Miller`s Anaesthesia.** 6th ed. San Francisco: Elsevier; 2010.

(75) Rama-Maceiras P. **Less post operative nausea and vomitting after propofol + remi fentanyl versus propofol + fentanyl during plastic surgery**. Acta Anaesthesiol Scand 2005;3(49):305-11.

(76) Hammas B, Thorn SE, Wattwill M. **Superior prolonged antiemetic prophylaxis with a 4 drug multimodal regimen- comparison with propofol or placebo**. ActaAnaesthesiolo Scand 2002;3(46):232-7.

(77) Mittsunari H, Ashikari E, Tanaka K. **The use of droperidol decreases postoperative nausea and vomiting after gynaecological laparoscopy**. J Anaesth 2007;4(21):507-9.

(78) Wennstrom B.**Rectally administered diclofenac (voltaren) reduces vomiting compared with opioid (morphine) after strabismus surgery in children.**Anaesthesia and pain management J;2002(46):430-434

(79) Borgeat A. **Subhypnotic doses of propofol possess direct antiemetic properties.**

Anaesth Analg 1992;74(4):539-41.

(80) Fuji Y. **Dose-range effects of propofol for reducing emetic symptoms during caesarean delivery.** Obstet Gynaecol 2002;1:75-9.

(81) Soppit AJ. **The use of propofol for its antiemetic effect: a survey of clinical practice in the United States**. Clin Anaesth 2000;12:265-9.

(82) Moore J.K.**Propofol and Halothane versus sevoflurane in paediatric day-case surgery:induction and recovery characteristics.**BJA :90 (4) 461-466

(83) Helen Ki shinn.**PONV after gynaecologic laparoscopic surgery:comparison between propofol and sevoflurane**.Korean J Anaesth 2011;60(1);36-40

(84) Tramer M. **Meta analytic comparison of prophylactic antiemetic efficacy for post operative nausea and vomiting; propofol anaesthesia vs omiting nitrous oxide vs iv anaesthesia with propofol.** BRJ anaesth 1997;78:256-9.

(85) Fujii Y, Itakura M. **Low dose propofol to prevent nausea and vomiting after laparoscopic surgery.** Int J gynae Obstet 2009;268-73.

(86) Eberhart LH.**The menstruation cycle in the postoperative phase.Its effect on the incidence of PONV**;The Anaesthetist 2000;49(6)532-535

(87) Van der Bilt J.D.W.**Early feeding after laparoscopic pyloromyotomy:the pros and cons.**2004:18(5):746-748

Appendix 1
PROPOFOL STUDY QUESTIONNAIRE

Date enrolled …….. ID Number……. Participant signature……..

STUDY GROUP

propofol +metoclopramide (A)	**propofol + metoclopramide +propofol(single low dose) (B)**

Please complete this data collecting form and give this patient drug as indicated above.

PATIENT DETAILS

Age/Zera……

LMP date / Zuva rekuteera……..cycle……..days/mazuva……..

Weight/uremu…….

History of PONV/ kumborutsa kana kusvotwa.

Yes/hongu…… No/kwete……

Height/urefu…….

Previous Nausea and Vomiting/kusvotwa kurutsa pakuvhiiwa.Yes/hongu…No/kwete…….

Current drugs list/mishonga yamurikunwa……..

PROCEDURE……

Drug doses and anaesthetic technique.

Induction		Gases		Relaxant		Analgesia		Airway		Ventilation
Propofol		Isoflurane		Atracurium		Fentanyl		LMA/ETT		IPPV

Dose of propofol induction given…….. Duration of Anaesthesia……

Dose of propofol single low dose given …….mg

OUTCOME

	One Hour		**24 Hours post 1 hour**	
	Yes	**No**	**Yes**	**No**
Nausea/kusvotwa				
Vomiting/kurutsa				
Pain/kurwadza				
Rescue antiemetic/mushonga wekurutsa				

SCORE THE NAUSEA .0….1….2….3….4….5….6….7….8….9….10

| ..mild…. | ……moderate…… | ….severe...

| zvishoma|… zviripakati… |zvakanyanya

SCORE THE PAIN. .0….1….2….3….4….5….6….7….8….9….10|

|..mild….. | ……moderate……. | …severe…… |

| zvishoma|… zviripakati… |zvakanyanya

NB.Please give stimetil (12.5mg i.v) as rescue antiemetic

Rescue antiemetic given : ……..yes / no

Appendix 2

SUBJECT INFORMED CONSENT

PROTOCOL TITLE: The effect of single low dose propofol (a drug used to induce sleep) at the end of the operation in reducing postoperative nausea and vomiting (PONV) in women undergoing laparoscopic gynaecological surgery at Parirenyatwa hospital.

NAME OF RESEARCHER : Dr Tafadzwa Kandawasvika

PHONE : 0772210702 email: tafadzwakandawasvika@yahoo.com

PROJECT DESCRIPTION

Nausea and vomiting in the post operative period is associated with economic disadvantages to both the patient and health care provider. Propofol is a drug used to induce sleep when you are to be operated. It has been associated with less PONV and a reduction in the use of antiemetics. The study seeks to show the effectiveness of a single low dose propofol at the end of the operation in reducing PONV in women undergoing laparoscopic gynecological surgery.

YOUR RIGHTS

Before you decide whether or not to volunteer for this study, you must understand its purpose, how it may help you, the risk to you and what is expected of you. This process is called informed consent.

PURPOSE OF RESEARCH STUDY.

PONV is a common problem and once reduced, success rates of procedures and patient safety are both significantly improved. Reducing PONV may reduce the economic burden on both the patient and the hospital.

PROCEDURES INVOLVED IN THE STUDY

The study will be carried out at Parirenyatwa Hospital gynaecological theatre. A day before the operation, on satisfying the inclusion criteria, you will be randomly assigned to either a non-propofol (A) or propofol (B) group where you will be one of the forty participants in either group .The randomization will follow guidelines stipulated in statistics books in order to reduce bias by giving you an equal opportunity to belong to either group. The anaesthetic treatment assignment which you will finally belong to, will be obtained through the use of a randomization list. On enrolment to the study I will ask you questions about yourself and your health.

At the end of the operation the propofol group patients will be given a single dose of propofol 0.5 mg /kg while the non propofol group will not be given propofol.The anaesthetic drugs for this study are part of anaesthetic standard care for your operation, and you will not incur extra costs by being randomized to either group. You will be observed post operatively for the 24 hours .During that time the severity of PONV will be assessed.

DISCOMFORT AND RISKS

Propofol may cause some pain on injection .This side effect will be alleviated by use of lignocaine on injection and also by injecting into a big vein. If severe PONV occurs you will be given a rescue medication.

STUDY WITHDRAWAL

You may choose not to enter the study or withdraw from the study at any time without loss of benefits entitled to you.

POTENTIAL BENEFITS

There is no material or monetary gains for participating in this study .You are not going to stay in hospital any longer than you will be required by your ward doctors. You will not be charged extra for participating in this study. The anaesthetic drugs for this study are part of anaesthetic standard care for your operation, and you will not incur extra costs by being randomized to either group. If you do complain of severe vomiting postoperatively, you will be given stimetil 12.5 mg intravenously.

CONFIDENTIALITY OF RECORDS

Due to the sensitive nature of some of the questions asked, strict confidentiality will be maintained throughout the study. You will be identified by a unique study identification number. All data will be collected and analyzed according to these numbers. The coded numbers identifying study participants and all records will be locked in a cabinet file. Any links linking participants' identification numbers to other identifying information will be stored separately in a locked cabinet with limited access.

PROBLEMS AND QUESTIONS

Please ask questions about this research or consent now. If you have any questions in future please ask or call Dr Tafadzwa Kandawasvika on cell phone number 0772210702.

If you have any questions concerning this study beyond those answered by the investigator, questions about the research, your rights as a research participant or research related injury or you feel you have been treated unfairly and you would like to talk to someone other than the research team you are free to contact the medical Research council of Zimbabwe on telephone 00263 4 791 792 or 00 263 4 791 193.

AUTHORISATION

I have read this paper about the study or it was read to me. I understand the possible risk and benefits of this study. I know being in this study is voluntary. I choose to be in this study. I know I can stop being in the study and will not lose any benefits entitled to me. I will get a copy of this consent form.

……

Client signature Date

……..

Client Name (Printed)

……..

Researcher signature Date

……..

Witness Signature Date

Appendix 2

FOMU REKUBVUMA KUPINDA MUONGORORO

MUSORO: Ongororo yemadzimai echidiki vanenge vachitarirwa muchibereko nemuchina

Ongororo pakati pemapoka maviri emadzimai vari kuitwa inonzi laparascopy yechibereko tichitsvaka kuona vanonzwa kuda kurutsa (nausea) kana vanorutsa (vomiting) mushure mekunge rimwe boka rakotsiriswa tichishandisa mishonga inoti propofol nemetoclopramide rimwe toshandisa propofol nemetoclopramide tozopa tumwe tumushonga tushoma twe propofol kwekupedzisira kwe oparesheni.

MUONGORORI: Dr Tafadzwa Kandawasvika

NHAMBA DZENHARE :0772210702 email: tafadzwakandawasvika@yahoo.com

TSANANGUDZO YEONGORORO: Kunzwa kuda kurutsa uye kuzorutsa zvinhu zvisingadikanwi zvinoitika mushure mokuvhiyiwa.Izvi zvinoguma zvokonzera kurasikirwa kwenguva nemari kumurapwa nemurapi.Kurutsa mushure mokuvhiyiwa kunovhiringidza kubudirira kwakanaka kwokuvhiyiwa uye kunoita kuti upenyu hwomurapwa husagadzikana.

Propofol yakawonekwa kuti hainyanyi kuunza dambudziko iri uye inoderedza mikana yokushandisa mishonga inidzivirira kurutsa.Propofol inowanikwa muzvipatara zvizhinj zvehurumende nezvisiri uye haina zvizhinji zvakaipa zvainokonzera kana ikashandiswa nechipimo chiduku.Chinangwa chetsvakurudzo kuongorora ,muvanhukadzi,kushanda kwepropofol shoma (0.5mg/kg) mushure mokuvhiyiwa zvichienzaniswa nekusaishandisa.

KODZERO YENYU

Musati masarudza kupinda mu ongorororo iyi tinokupai gwaro rino kuti muzive chinangwa ,zvichaitika ,nekusagadzikana uye zvatichawana kubva muongorororo iyi.Kubatsirwa kunoitwa vanhu kunobva muruzivo rwezvekurapa kunobva mukuongororrwa kwevamwe vanhu.chinangwa chikuru che ongorororo ndechekuwana ruzivo runobatsira varwere vemangwana.Zvamunenge masarudza kuita hazvikanganisi kurapwa kwenyu .Nyatsonzwisisai gwaro iri .Bvunzai mibvunzo munzwisise musati maisa runyoro rwenyu.Kupinda kwenyu muongorororo kunobva mukuzvisarudzira kwenyu

CHINANGWA CHECHIRONGWA

.Tsvakurudzo dzakaitwa munyika dzakabudirira dzaka ratidza kuti Propofol hainyanyi kuunza dambudziko rekunzwa kuda kurutsa kana kuritsa kwacho uye inoderedza mikana yokushandisa mishonga inodzivirira kurutsa.Propofol inowanikwa muzvipatara zvizhinj zvehurumende nezvisiri uye haina zvizhinji zvakaipa zvainokonzera kana ikashandiswa nechipimo chiduku. Chinangwa chetsvakurudzo kuongorora ,muvanhukadzi,kushanda kwepropofol shoma (0.5mg/kg) mushure mokuvhiyiwa zvichienzaniswa nekusaishandisa.

ZVICHAITWA

Ongoro iyi ichaitirwa pachipatara chikuru che ParirenyatwaHospital .Musati maendeswa ku nzwimbo ye operasheni,muchabvunzwa mibvunzo maerereno neupenyu hwenyu uye utano hwenyu. Muchasarudzwa kupinda mubato richapuhwa propofol kana kuti bato risingapuhwi propofol.Tichashandisa maitiro akarondedzerwa mumagwaro e statistics anoita kuti muve nemukana wakafanana wekupinda mune rimwe renabato maviri ,repropofofol kana kuti risiri re

propofol. Divi ramuchapinda richawanikwa mushure mekushandisa randomization list. Panopera kuvhiyiwa pa oparesheni , rimwe boka richapiwa propofol 0.5mg/kg vamwe havapiwe. Muchazoongororwa kwemaawa makumi maviri nemana (24hours) mushure mokuvhiyiwa, vachitariswa udzamu hwedambudziko rekunzwa kuda kurutsa kana kurutsa kwacho.

KURWADZIWA NEKUSAGADZIKANA

Pamuchapihwa propofol nemutsinga zingangorwadza zvishoma.Muchapihwa mushonga unonzi lignocaine kuedza kuderedza marwadzo erudzi urwu.

ZVAMUNOWANA MUONGORORO

Hativimbisi kuti ongororo iyo ichakubatsirai imi mukuwanawo zvinhu kana mari.Kubatsirwa kunoitwa vanhu kunobva muruzivo rwezvekurapa kunobva mukuongororrwa kwevamwe vanhu.Chinangwa chikuru che ongororo ndechekuwana ruzivo runobatsira varwere vemangwana.Hamuzogare muchipatara kupfuura mazuva amunodiwa namachiremba enyu muchiitira ongororo iyi.Hamuzonzi mubhadhare mari pamusoro nepamusana peongororo iyi.Mukarutsa zvakanyanya mushure meoparesheni muchapiwa mushonga uchabhadharwa nevanechekuita neongororo iyi.

KUBUDA MUONGORORO

Makasununguka kurega kana kuzorega pava paya kuva muchirongwa chino pasina kuzoshaiwa rubatsiro pachipatara.

ZVAKAVANZIKA

Zvose zvatichataurirana kana kuita zvinoramba zviripakati pedu neavo vane chokuita neongororo iyi chete.Nokudaro makasununguka kupindura mibvunzo zvizere. Tinoshandisa nhamba kwete zita pamapepa atiri kunyorere nezveutano hwenyu uye achachengetedzwa nemuongorori.Hapana anokwanisa kushandisa mapepa aya kuti aone kuti nderani.

MIBVUNZO NEZVEKODZERO YENYU

Bvunzai mibvunzo nezveongororo iyi .Kana muine mimwe mibvunzo pane ramangwana ridzirai runhare kuna Dr Tafadzwa Kandawasvika pa nhamba idzi 0772210702.

Kana paine zvimwe zvamungade kuziva nezveongoror iyi zvisana kukwanisa kupindurwa zvizere nemuongorori,kodzero yenyu semunhu ari kupinda muongoror kana kumwe kusagutsikana musingakwanise kutaura nemuongorororori makasununguka kubata ve Medical research Council of Zimbabwe panhare 002634791792 kana 002634791193.

KUBVUMA KUPINDA MUONGORORO

Ndaverengerwa zviri muongororo ino ndikanzwisisisa chinangwachacho.Mukunyora zita rangu /kuisa mudhindwa wechigunwe chikuru cherudyi papepa rino ndinotaridza kubvuma kuva muongororo iyi pachangu.

……

Zita remurapwa Zuva

……

Runyoro rwemuongorori Zuva

……………………………………………………………………………………………….

Runyoro rwemufakazi Zuva

Appendix

PROPOFOL STUDY QUESTIONNAIRE

Date enrolled …….. ID Number……. Participant signature……..

STUDY GROUP

propofol+metoclopramide (A)	**propofol+metoclopramide+propofol(single low dose) (B)**

Please complete this data collecting form and give this patient drugs as indicated above.

PATIENT DETAILS

Age/zera…… LMP date/zuva rekuteera……..cycle……..days/mazuva……..

Weight/uremu……. History of PONV/kumborutsa kana kusvotwa. Yes/hongu……No/kwete……

Height/urefu……. Preoperative N&V/kusvotwa kututsa pakuvhiiwa.Yes/hongu…No/kwete……. Current drugs list/mishonga yamurikunwa……..

PROCEDURE……

Drug doses and anaesthetic technique.

Induction		Gases		Muscle relaxation		Analgesia		Airway		Ventilation
Propofol		Isoflurane		Atracurium		Fentanyl		LMA/ETT		IPPV

Dose of propofol induction given…….. Duration of Anaesthesia……

Dose of propofol single low dose given …….mg

OUTCOME

	One Hour		**24 Hours**	
	Yes	**No**	**Yes**	**No**
Nausea/kusvotwa				

Vomiting/kurutsa				
Pain/kurwadza				
Rescue antiemetic/mushonga wekurutsa				

SCORE THE NAUSEA .0….1….2….3….4….5….6….7….8….9….10

| ..mild…. | ……moderate…… | ….severe...

| zvishomal… zviripakati… |zvakanyanya

SCORE THE PAIN. .0….1….2….3….4….5….6….7….8….9….10|

|..mild….. | ……moderate……. | …severe…… |

| zvishomal… zviripakati… |zvakanyany

NB.Please give ondansetron (4mg i.m.) /stimetil (12.5mg i.v) as rescue antiemetic

Rescue antiemetic given : ……..yes / no