A COMPARATIVE STUDY OF GLYCOPYRROLATE AND DEXAMETHASONE IN THE CONTROL OF PONV AFTER INTRATHECAL FENTANYL AND BUPIVACAINE FOR CAESAREAN SECTION.

THIS DISSERTATION IS SUBMITTED TO THE NATIONAL POSTGRADUATE MEDICAL COLLEGE OF NIGERIA IN PART FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE FELLOWSHIP OF THE COLLEGE IN ANAESTHESIA.

BY

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DATE: MAY, 2018.

DECLARATION

It is hereby declared that this work is original and unless otherwise acknowledged. This work has not been presented to any other College for a Fellowship Examination, nor has it been published or submitted elsewhere for publication.

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Dr. Okonkwo Ikemefuna Patrick

February, 2018

CERTIFICATION

The proposal contained in this document was prepared by the author under our supervision. We shall also supervise the study and the writing of the dissertation.

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ATTESTATION BY THE HEAD OF DEPARTMENT

This is to certify that the study titled "**A Comparative Study Of Glycopyrrolate And Dexamethasone In The Control Of Ponv After Intrathecal Fentanyl And Bupivacaine For Caesarean Section"** was conducted by the candidate Dr. Okonkwo Ikemefuna Patrick Under my superintendence as the Head of Department of Anaesthesia.

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LIST OF ABBREVIATIONS

ANOVA---- Analysis of Variance.

APGAR- Appearance, Pulse, Grimace, Activity and Respiration.

ASA---- American Society of Anaesthesiologists.

BBB-----Blood- Brain Barrier.

BP---- Blood Pressure

CNS----Central Nervous System

C/S------Caesarean Section.

CSF----- Cerebrospinal Fluid.

CTZ----- Chemoreceptor Trigger Zone

DA----- Dopaminergic receptor

ECG----- Electrocardiogram.

FIG--- Figure

G--- Guage

Group C---- Normal Saline Group.

Group D----Dexamethasone Group.

Group G ---- Glycopyrrolate Group

HR------- Heart Rate.

ICU------ Intensive Care Unit.

I.M------- Intramuscular.

IONV---- Intraoperative Nausea and Vomiting

IV-------- Intravenous.

Kg------ Kilogram.

L---- Lumbar

MAP---- Mean Arterial Blood Pressure.

MCG----- Microgram.

MG---- Milligram

ML---- Millilitres

N-------- The Estimate of the Population Size.

NaCI---- Sodium Chloride.

NIBP--- Non- Invasive Blood Pressure.

N/S----- Normal Saline.

NSAID- Non-Steriodal Anti-Inflammatory Agent.

%---- Percentage

PACU-- Post Anaesthesia Care Unit.

PCM---- Paracetamol.

PONV---- Postoperative Nausea and Vomiting.

SAB---- Subarachnoid Block.

SBP---- Systolic Blood Pressure

SP02--- Arterial Oxygen Saturation.

SPSS---- Statistical Package for Social Sciences

Tmax---maximum plasma concentration.

UNN--- University of Nigeria Nsukka.

UNTH- University Of Nigeria Teaching Hospital.

DEDICATION

This work is dedicated to my wife, the mother of our children, my rock and pillar.

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My heartfelt gratitude goes to ALL my teachers who over the years have moulded and guided me.

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SUMMARY

BACKGROUND

Postoperative nausea and vomiting (PONV) is an undesirable outcome that parturients who undergo caesarean section experience. Complications of PONV range from discomfort, dehydration, electrolyte imbalance to pulmonary aspiration of gastric contents. Different drugs have been employed as prophylaxis against PONV with varying degrees of success and outcome.

AIM

The aim of this study was to compare the efficacies of IV glycopyrrolate and IV dexamethasone as effective prophyaxis against PONV in women undergoing caesarean section after intrathecal fentanyl and bupivacaine.

PATIENTS AND METHODS

This is a prospective, randomized, double blind placebo controlled study of seventy six (76) ASA II patients aged 18-40 years who underwent elective caesarean section under spinal anaesthesia. Patients were randomly allocated to three groups, group G (glycopyrrolate): n=26, group D (dexamethasone): n=25 and group C (control; normal saline): n=25. Data collection was with the aid of a proforma which included the biophysical profile, ASA physical status, Mallampati scores, patient's haemodynamics, Belville scoring scale for PONV, Likert scale was used for patient satisfaction and side effects were also documented.

The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 17 and presented in tables and figures.

RESULTS

The demographic characteristics and mallampati scores of patients in all 3 groups were similar. Patients in group G had higher mean heart rates compared to groups D and C and this was statistically significant (P=0.046). However, patients in group D recorded the highest mean arterial blood pressure (P=0.028). The results showed that the incidence of PONV in group D was 13.3%, in group G 33.3% and in group C 53.4%. The results showed that the use of 8mg dexamethasone was significantly associated with a lower incidence of PONV (P= 0.048, OR= 0.185, 95% C.I for OR= 0.035 – 0.983). Patients who received IV 8mg dexamethasone were less likely associated with an incidence of PONV. However, the use of IV 0.2mg glycopyrrolate showed a relatively higher incidence of PONV.

All patients expressed satisfaction in the care they received as assessed using the likert scale and only patients who received IV glycopyrrolate experienced side effects in the form of dryness of the mouth. There were no side effects reported in patients who received IV dexamethasone.

CONCLUSION

The study demonstrated the efficacy of 8mg intravenous dexamethasone over 0.2mg intravenous glycopyrrolate in controlling PONV after intrathecal fentanyl and bupivacaine for caesarean section.

CHAPTER ONE

INTRODUCTION

Postoperative nausea and vomiting (PONV) is a common and unpleasant side effect of anaesthesia and surgery, with risk factors including the female gender, smoking, prior history of motion sickness, the use of volatile agents in general anaesthesia, prolonged surgery, opioid use and a previous history of PONV. The worldwide incidence of PONV is 30% and even patients with no known risk factor, have an incidence as high as 10%.[1,2] In pregnant women undergoing caesarean section, the incidence can be as high as 60%.[1,2] Postoperative nausea and vomiting, when severe can lead to dehydration, electrolyte imbalance, bleeding, wound dehiscence and rarely, pulmonary aspiration of gastric contents.[3]

Studies have shown that general anaesthesia increases the risk of PONV and where possible, regional anaesthesia should be used as it significantly lowers the risk of PONV.[2,4] Regional anaesthesia has continued to gain popularity in obstetrics and so has the addition of intrathecal opioids as additives.[5] Opioids like fentanyl can be used as adjuncts for regional anaesthesia and when used, produces intense analgesia. While studies have shown lower incidence of vomiting in the immediate perioperative periods following intrathecal fentanyl administration, the effect on pregnant women undergoing caesarean section is still unclear.[5,6] Dexamethasone and glycopyrrolate have been proven as effective prophylaxis in the prevention of PONV in obstetric surgery.[1,7] A study done by Biswas et al[7] compared the efficacy of glycopyrrolate, dexamethasone and metoclopramide in the control of PONV amongst 80 women who were randomly allocated to one of 3 groups, the results showed that

the glycopyrrolate group had the lowest incidence of nausea and vomiting with a P value of less than 0.05 which was statistically significant. In another study, comparing dexamethasone with a combination of dexamethasone and ondansetron in the prophylactic management of PONV among pregnant women, it was shown that the dexamethasone-ondansetron combination had a lower incidence of PONV.[1] Although serotonin antagonists have been shown to be effective in the prevention of PONV, like in the study above, it is, however, expensive and not readily available, limiting its use in resource poor settings.

The complications of PONV can be life threatening and range from dehydration to pulmonary aspiration of gastric contents and this could be potentially catastrophic to the parturient undergoing surgery. It is therefore important that prophylactic drugs should be studied.

There is no general consensus about the most appropriate antiemetic prophylaxis for the prevention of PONV. Thus, the need to carry out this prospective study to compare IV glycopyrrolate and IV dexamethasone as prophylactic agents against PONV in women undergoing elective caesarean section.

Null Hypothesis (H_0): The average control of PONV with intravenous glycopyrrolate (μ_I) is similar to that of intravenous dexamethasone (μ_R). Any difference detected is due to chance and not to any other measurable factor.

$H_0 : \mu_I = \mu_R, \mu_I - \mu_R = 0, \mu_I - \mu_R = 0.$

Alternate Hypothesis (H_1): The average control of PONV with intravenous glycopyrrolate (μ_I) is not similar to that of intravenous dexamethasone (μ_R). Any difference detected is not due to chance but measurable factor.

$H_0 : \mu_I \neq \mu_R, \mu_I - \mu_R \neq 0, \mu_I - \mu_R \neq 0.$

CHAPTER TWO

GENERAL OBJECTIVE

To compare the efficacies of 0.2mg intravenous glycopyrrolate and 8mg intravenous dexamethasone for the control of PONV after spinal anaesthesia for caesarean section using intrathecal fentanyl/bupivacaine mixture, and intravenous normal saline serves as control.

SPECIFIC OBJECTIVES

1. To determine the incidence of PONV after spinal anaesthesia with bupivacaine and fentanyl, in patients given 0.2mg intravenous glycopyrrolate.
2. To determine the incidence of PONV after spinal anaesthesia with bupivacaine and fentanyl, in patients given 8mg intravenous dexamethasone.
3. To determine the side effects of glycopyrrolate, dexamethasone and fentanyl used in the study.
4. To determine patients' satisfaction using Likert's scale.

CHAPTER THREE

LITERATURE REVIEW

Anaesthesia has gradually become safer over the years with anaesthetic deaths and complications with permanent damage becoming less common, largely due to advancement in monitoring techniques and training.[6] This has caused other complications of anaesthesia to gain more importance.[6] Postoperative nausea and vomiting is defined as any nausea, retching, or vomiting occurring during the first 24-48 hours after surgery in patients. it remains the most common complication following surgery and has become increasing worrisome despite measures targeted against it.[6,8,9]

Most gynaecologic surgeries are associated with a high incidence of PONV.[9,10,11] A prospective study done by Soyanwo et al[11] at Ibadan southwest Nigeria, puts the incidence to be 41.6% and 19.6% for females and males respectively. Although another study done by Okafor et al[9] in South East Nigeria reported an incidence of PONV among women at just 4.0%, but in this study, antiemetic premedicants with metoclopramide and atropine were used. This is much lower than other studies done in Nigeria.[11,12] An explanation could be an intrinsic variation between races and ethnic groups and the methodology.

The effect of PONV on patients range from discomfort, dehydration, electrolyte derangement, bleeding, wound dehiscence and aspiration of gastric contents to delay in discharge and unanticipated hospital re-admission with its antecedent effect on hospital cost.[1,3,6]

General anaesthesia has been implicated as having a greater frequency and severity of PONV

and several studies have supported this fact.[1,9] However, a large proportion of surgical procedures, especially obstetric surgeries are amenable to regional anaesthesia.[1,9] Most reviews on PONV discuss almost exclusively general anaesthesia and largely ignore the effect of regional anaesthesia.[6] This contrasts with the increasing choice of regional anaesthesia for cesarean section.

The introduction of intrathecal morphine in 1979 opened the door for many advances in intrathecal adjuncts for regional anaesthesia.[1] Fentanyl which is lipophilic produces intense, but short acting analgesia, and when used intrathecally, has been shown not to provoke nausea.[5,6]

No single mechanism can explain PONV following regional anaesthesia and several mechanisms of action have been proposed.[6] Studies have shown that hypotension following spinal anaesthesia (systolic blood pressure < 80 mmHg) is associated with nausea, most likely associated with vagal stimulation.[13] Administration of supplemental oxygen has improved PONV, suggesting that hypoxaemia at the vomiting centre could be a culprit.[13] Gut ischaemia leading to the release of emetogenic substances such as serotonin has also been implicated.[6] The incidence of nausea and vomiting decreased by the intravenous administration of atropine, suggesting that vagal stimulation may also play a role via action on higher centres.[13]

Women undergoing laparoscopic procedures had lower incidences of postoperative emesis with epidural anaesthesia, compared to general anaesthesia.[13] This may be due to improved

gastric emptying associated with regional anaesthesia.[13] A 20% incidence of emesis has been reported following 5mg epidural morphine in elective cesarean section.[13] Morphine is hydrophilic and this effect may be caused by the rostral spread of the opioid from the epidural site of injection to the chemoreceptor trigger zone and vomiting centre.[6,13] More lipid soluble opioids like fentanyl, when administered intrathecally or via the epidural space have less rostral spread and are therefore less likely to cause PONV.[6,13]

Baricity of agents also affects cerebrospinal fluid drug kinetics, limiting the rostral spread of agents and subsequently decreasing the incidence of PONV.[13] In the studies by Apfel et al[15] and Pierre et al[16], the female gender has consistently been the strongest risk factor with an odds ratio of ~3, which indicates that females are on the average three times more likely to develop PONV than men. A relationship of nausea and vomiting to the menstrual cycle has been pointed out, with peak incidence occuring during day 25 to the end of the cycle.[6] This influence needs further study.

Non-smoking status with an odds ratio of ~2, doubles the risk of PONV.[16] The specific mechanism is unknown, but one commonly believed theory is that polycyclic aromatic hydrocarbons in cigarette smoke induce cytochrome P450 enzymes, thereby increasing the metabolism of emetogenic volatile anaesthetics.[16] Little evidence exists to support this theory. Patients with a history of motion sickness or previous PONV may have a low threshold for vomiting and are at increased risk for developing emetic symptoms. It is thought that these

individuals may have a well developed arc for vomiting.[13]

Apfel et al, found that younger patients were at increased risk of PONV. For adult patients, age is statistically, though not clinically a relevant risk factor, with the incidence of PONV decreasing as patients age.[16]

Also, the use of volatile anaesthetic agents is associated with a two-fold increase in the risk of PONV.[16] This risk increases in a dose dependent manner, with no difference in incidence with volatile anaesthetics.[16]

Volatile anaesthesia may increase PONV by decreasing serum levels of anandamide, an endogenous cannabinoid neurotransmitter that acts on cannabinoid-1 and transient vanilloid-1 receptors to suppress nausea and vomiting.[16]

Replacing volatile agents with an intravenous anaesthetic like propofol reduces the incidence of nausea and vomiting.[16] This has led to the suggestion that propofol may possess some antiemetic properties, however, there is little evidence to support this claim.

Duration of surgery and operative time also have effects on the incidence of PONV, with more frequent episodes of emesis being reported following longer operations.[13] Since the duration of surgery describes the patient's exposure to emetogenic stimuli, like volatile anaesthetic agents and opioids, this is the most likely cause.

The incidence of PONV is increased in patients with a high level of preoperative anxiety.[16]

The incidence is even higher when anaesthetic agents known to release catecholamines (like ketamine) are used.[16] This suggests that catecholamine release may be a contributory factor. Opioids also cause PONV, by reducing muscle tone and peristaltic activity, delaying gastric emptying, inducing distension and triggering the vomiting reflex.[6,16]

Few multivariable analysis have investigated the effect of general anaesthesia versus locoregional anaesthesia in PONV and the odds ratio associated with general anaesthesia range from 1.3 to 1.6, suggestive that locoregional anaesthesia is associated with less PONV.[16]

Many studies have shown that the type of surgery has an effect on the incidence of PONV; gynaecological, ophthalmological, otological and thyroid surgery can increase the risk of PONV,[2,4,6,13,16] while in children, strabismus surgery has been identified as an independent risk factor.[16]

Dexamethasone, a corticosteroid with a high glucocorticoid and minimal mineralocorticoid activity has a long duration of action. The mechanism of action of dexamethasone as an antiemetic is via prostaglandin inhibition, while others suggest that it acts on glucocorticoid receptors found in the nucleus tractis solitarius, median raphae or area postrema and thereby modulate the nausea and vomiting reflex.[6,7] Another suggestion is based on the anti-inflammatory effects of dexamethasone, it reduces local inflammatory reactions after surgical procedures and this can subsequently reduce inflammation caused by the afferent stimulation of the parasympathetic nervous system to the vomiting center, thereby reducing

PONV.[52] The use of high and repeated doses of dexamethasone in surgical patients can predispose to adverse effects which include difficulties in controlling blood sugar levels, wound infections, delayed wound healing, gastric ulcers and avascular necrosis.[28,47,48]

Glycopyrrolate is an anticholinergic drug, a quaternary ammonium compound with a long duration of action and it acts on the muscarinic receptors, thus it is used in a variety of clinical conditions, ranging from the treatment of respiratory diseases (like asthma) to its use in mitigating the side effects of surgery like bradycardia, excessive saliva secretions and it is also administered with neostigmine in reversing paralysis.[6,52] However, it also produces some unwanted side effects like dryness of the mouth.[6] It prevents nausea and vomiting by blocking antimuscarinic receptors in the vestibular system and halting signaling to the central nervous system and vomiting centre.[14]

Fentanyl is a synthetic opioid and it is100 times as potent as morphine, is lipophilic, and this is thought to reduce its rostral spread to the chemoreceptor trigger zone and vomiting centre when administered intrathecally and therefore reducing the incidence of nausea and vomiting.[6,13] Fentanyl may also reduce the incidence of emesis by improving the quality and duration of analgesia and this is supported by the study done by Idowu et al.[5] Intrathecal administration of low dose fentanyl has been reported to minimize the incidence of PONV intraoperatively and in the early postoperative period during cesarean delivery under spinal anaesthesia, with little side effects.[17]

Four neurotransmitter systems may play important roles in mediating the emetic response:

dopaminergic, histaminic, cholinergic/muscarinic and 5-HT_3. Antiemetic agents are thus directed at these receptors.[13]

Phenothiazines like promethazine and chlorpromazine block receptors in the CTZ, specifically the dopaminergic receptors. However, they produce significant sedation.

Butyrophenones are neuroleptic drugs like haloperidol and droperidol. They are dopamine antagonists and prevent nausea and vomiting by inhibiting the dopaminergic receptors at the CTZ.

On the other hand, antihistamines like cyclizine and diphenydramine act on the vomiting centre and vestibular pathways. Some anticholinergics like scopolamine also have a similar mode of action.[13,14]

Benzamines like metoclopramide have both central and peripheral actions, blocking dopaminergic receptors at the CTZ and increasing lower oesophageal sphincter tone and enhancing gastric emptying.[13]

Serotonin antagonists block the 5-HT_3, Ondansetron is a prototype and it has more anti vomiting than antinausea effects.[13] Ondansetron is the "gold standard" compared with other antiemetics. Ondansetron is as effective as other serotonin antagonists including ramosetron.[51] Other serotonin antagonists can cause QT prolongation and torsade de pointes as side effects.[51]

Nonpharmacologic approaches like trans-cutaneous acupoint stimulation, acupuncture and acupressure have also been used.[13] A meta-analysis of 40 articles showed that the different acupuncture modalities reduce nausea, vomiting and the need for rescue antiemetics.[51]

The incidence of vomiting in pregnant women undergoing cesarean section is high and figures as high as 60% have been reported.[22] However, women who receive antiemetic (metoclopramide) and antacid prophylaxis (ranitidine) have been shown to have a relatively lower incidence of 20%.[7]

In a study by Rudra et al.[17], comparing intrathecal fentanyl and midazolam for the prevention of nausea and vomiting during cesarean delivery under spinal anaesthesia, 120 women were randomly allocated into 3 groups of 40 each. The first group received intrathecal fentanyl with 0.5% bupivacaine, the second intrathecal midazolam and 0.5% bupivacaine, and the third was the placebo-control group. The incidence of PONV in the control group was 75%, statistically significant. The fentanyl group however had a lower incidence of nausea and vomiting than the midazolam group, although there was no significant difference ($P > 0.05$). The study revealed that both fentanyl and midazolam administered intrathecally, lowered the incidence of intraoperative and postoperative nausea and vomiting. Patients who experienced emetic episodes intraoperatively were administered metoclopramide, this could have been a confounding factor in the incidence of postoperative nausea and vomiting in the study.

Vasantha et al.[18] in the pre-operative assessment of ondansetron versus metoclopramide for the prevention of PONV in caesarean section under spinal anaesthesia, randomized 100 women undergoing elective caesarean section into 2 groups (groups I and II). Group I patients received IV metoclopramide 10mg and group II received IV ondansetron 4mg, the study agents were given prior to administration of anaesthesia and the results indicated that both metoclopramide and ondansetron were effective in reducing the incidence of nausea. In

the ondansetron group, the incidence of 13.3%, whilst in the metoclopramide group, it was 26.66%, which was statistically significant (P<0.05). The methodology of the study stated that ondansetron was used as a rescue medication, even though it was one of the study drugs, this would have exposed those patients who received repeated doses of the drug to potential side effects. The patients did not receive antacid prophylaxis and there was no control group in the study.

Studies have been done comparing the efficacy of glycopyrrolate and dexamethasone in the prophylactic management of PONV. Biswas et al.[7] in a comparative study of the control of PONV using dexamethasone, glycopyrrolate and metoclopramide after spinal anaesthesia for caesarean section randomly allocated women into 4 groups of 20 each. Group A was the glycopyrrolate group, B the dexamethasone group, C the metoclopramide group and D the control-placebo group. The incidence of postoperative nausea was not surprisingly highest (40%) in the control-placebo group with a statistically significant P value of < 0.05, 10% in both group A and B (glycopyrrolate and dexamethasone groups) and 20% in group D (metoclopramide group). Interestingly, both groups A and B had similar incidences of nausea. The incidence of vomiting however had a different pattern; it was 15% in the glycopyrrolate group, 20% in the dexamethasone group, 30% in the metoclopramide group and also not surprisingly highest (55%) in the placebo group. In this study, metoclopramide was the least effective in the prevention of PONV. Biswas et al concluded that the administration of glycopyrrolate intravenously before spinal anaesthesia in women undergoing caesarean section is an effective means of reducing the incidence of PONV. One major criticism of this

study would be that the control group received no anti-emetic, putting patients' lives at risk. Also, the assessment of PONV occurrence was only limited to the first 4 hours postoperatively, as such, patients who may have experienced PONV after that period were not included in the result of the study. Another criticism is that the study sample size used (20 per group) was too small, thereby reducing the statistical power of the study.

SuryaSee et al.[20] in their own study, compared 3 groups of drugs in the suppression of PONV in women undergoing elective cesarean section. The first group received IV granisetron (group I), the second IV granisetron+dexamethasone (group II), and the last, IV granisetron+dexamethasone+glycopyrrolate (group III). The incidence of intraoperative nausea was lower in groups II and III, compared to group I. Postoperatively (0-2 hours), very minimal nausea was seen (3.3%) in group I alone, while at 2-24 hours, no incidence of nausea was seen in all 3 groups. Intraoperative vomiting was 0.0% in group II, compared to 3.3% in group I, and 6.67% in group III. Postoperatively, the incidence of vomiting at 0-2 hours was 3.3% in group III compared to 0.0% in groups I and II. At 2-4 hours postoperatively, no vomiting was recorded in all 3 groups. The differences were not statistically significant ($P>0.05$). This prospective study conducted over a 10 month period, showed that the addition of dexamethasone to granisetron was better in reducing nausea and vomiting. Overall, group I had a higher incidence of nausea and group III had a higher incidence of vomiting. It is difficult to read meaning into the conclusion, because of the small sample size of 30 patients in each group and relatively short duration of study. In the methodology of the study, patients who had received opioids perioperatively were not

excluded from the study and this may have potentially been a confounding factor as opioids can cause nausea and vomiting.

Ure et al.[22] studied glycopyrrolate as an agent to reduce nausea during spinal anaesthesia for caesarean section. Glycopyrrolate being a quaternary amine does not cross the placental membrane in significant amounts, and is therefore safer in pregnant women, unlike atropine.[22] He studied 50 women, divided into 2 groups. All women received intravenous ranitidine 150mg prophylaxis. In the glycopyrrolate group, 42% of women experienced nausea during the procedure, compared to 68% in the placebo group (P=0.02). The study concluded that women who received glycopyrrolate experienced less severe and less frequent nausea without deleterious effects on neonatal APGAR scores. The recorded incidence of hypotensive episodes was similar in the 2 groups. However, hypotension may have been underestimated in the placebo group, as it is usually preceded by nausea.[22] The study recruited only 50 patients, which is inadequate to arrive at a scientific conclusion. In the study by Biswas et al[7], glycopyrrolate was compared with other study medications (dexamethasone and metoclopramide) and found to be a more effective prophylaxis for PONV, unlike in this study, where glycopyrrolate was studied alone.

In Nigeria, Orewole et al.[3] compared combined metoclopramide and dexamethasone with dexamethasone only in the prophylactic management of nausea and vomiting in gynaecological surgery. Patients were randomly allocated to two groups, the incidence of PONV in the metoclopramide/dexamethasone group was 11.1% and in the dexamethasone only group, it was 44.4% (P = 0.003). The reduced incidence of PONV in the

metoclopramide group is likely due to the combined effect of dexamethasone. The study result suggests that patients at high risk of PONV should receive special considerations as regards the use of drug combinations as they are more effective in PONV prophylaxis than single drug therapy due to the different sites of action of the antiemetic drugs. It must be noted that this study was on non-pregnant women undergoing gynaecologic procedures. The female gender as an only risk factor to PONV usually has an incidence of 21%[15], while pregnancy can increase this incidence to 60% due to physiological changes in the gastrointestinal tract.[1,2]

Also in Nigeria, Akpan et al.[1] studied IV dexamethasone alone versus IV dexamethasone and IV ondansetron as prophylactic antiemetics in patients receiving intrathecal morphine (0.2mg) with heavy bupivacaine (10-12.5mg) for caesarean section. A total of 116 patients were recruited and randomized into 2 groups. The incidence of nausea and vomiting was significantly lower in patients who received a combination of dexamethasone and ondansetron (9.3%) and higher in patients who received dexamethasone alone (37%), with a P value of 0.003. The study showed that a combination of dexamethasone and ondansetron administered prophylactically significantly reduced the incidence of PONV in pregnant women. It must be noted that in this study, all the patients who experienced nausea or vomiting had it in the first 4 hours, this is probably due to the fact that dexamethasone has a late onset of action and the study design did not take into account the different onsets of action of the study agents before arriving at the conclusion that combining dexamethasone with ondansetron had a greater efficacy than dexamethasone alone. Some patients were

pre-loaded with 500ml of crystalloid, patients who had a low body weight as to require such small volumes should have been excluded from the study. Patients in this study received different doses of intrathecal bupivacaine, ranging from 10mg to 12.5mg. It was not stated if this had any effect on the possible outcomes, considering that hypotension can predispose to PONV. This lack of uniformity is a major flaw of this well-structured study. All patients should have received metoclopramide and ranitidine as standard premedication for patients coming for caesarean section.

Olatosi et al.[23] in a study comparing promethazine and ondansetron as antiemetic prophylaxis in major gynaecological surgery found that nausea occurred in 20%, 40% and 72% of the promethazine, ondansetron and placebo groups respectively (P value=0.001), while vomiting occurred in 12%, 16% and 60% of the promethazine, ondansetron and placebo groups respectively (P=0.001). Patientients who received promethazine had more side effects (drowsiness) compared with ondansetron which had a better safety profile. The study recruited a variety of patients scheduled for major gynaecological surgery ranging from myomectomy, total abdominal hysterectomy to exploratory laparotomies. The duration of surgery of the different procedures varied, translating to varied exposure to anaesthetic and emetogenic stimuli which may have affected the different outcomes. Interestingly, promethazine came out well as an effective prophylaxis of PONV despite its low cost, showing that cheaper alternatives may be as effective as the more expensive drugs.

Nausea, vomiting and retching are usually very different symptoms and can occur independently.[53] Rhodes and Mc Daniel[54] in early 2001 defined each symptom as:

i. Nausea is an unpleasant sensation experienced in the back of the throat and the epigastrum that may or may not result in the expulsion of material from the stomach.
ii. Vomiting involves the actual forceful upward expulsion of contents from the stomach.
iii. Retching is the attempt to expel contents of the stomach without actually bringing anything up.

Due to the wide spectrum of PONV, it is necessary that clinicians have useful and comprehensive tools for its assessment. Such tools should be accurate, easy to use and clinically useful.[53] Three types of scales are commonly used. The visual analogue scale (VAS), the numerical rating scale (NRS) and the verbal categorical scale (VCS).[53] The VAS uses a 0 to 10mm visual line with verbal descriptors. NRSs use a unidirectional line, with evenly spaced markings and VCSs, such as the Likert-type Belville scales.[20,21,53]

The VCSs require patients to convert subjective sensations to a mark provided on an assessment tool. It is difficult to reproduce these results as they subjective, though they are usually easy to administer.

Apfel designed a simplified risk score, calculated for each patient.[3,15] This predictive score of PONV considers four predictors which are: the female sex, history of PONV or motion sickness, non-smoking and expected use of opioids. Patients are allocated one point each for risk factors.[15] Apfel assigned patients with a score of 0 a 10% risk for PONV, those with a score of 1 had a risk of 21%, score of 2 had 39%; score of 3, 61% and a score of 4, a risk factor of 79%.[3,15]

The Society of Ambulatory Anesthesiology published consensus guidelines for the

management of postoperative nausea and vomiting in 2014, which consisted of the most recent data on PONV.[51] The guidelines are:

1. Identification of patients' risk of PONV
2. Reduction of baseline risk factors for PONV
3. Administration of PONV prophylaxis in adults at moderate risk
4. Administration of prophylactic therapy with combination (≥2) interventions/multimodal therapy in patients at high risk for PONV
5. Administration of prophylactic antiemetic therapy to children at increased risk for PONV, as in adults, use of combination therapy is most effective
6. Provision of antiemetic treatment to patients with PONV who did not receive prophylaxis or in whom prophylaxis failed
7. Ensure PONV prevention and treatment is implemented in the clinical setting
8. Use general multimodal prevention to facilitate implementation of PONV policies

These guidelines provide an evidence-based reference tool for the treatment of patients undergoing surgical procedures who may be at risk of PONV.[51]

In conclusion, PONV is an unpleasant side effect of surgery and can result in complications. Many studies[1,7,20,22] have shown both glycopyrrolate and dexamethasone to be effective prophylactic agents in the prevention of PONV, though there is no consensus on the most appropriate agent. This study compares the efficacies of 0.2mg IV glycopyrrolate and 8mg IV dexamethasone for the control of PONV after spinal anaesthesia for caesarean section using intrathecal fentanyl/bupivacaine mixture.

CHAPTER FOUR

METHODOLOGY

PATIENTS' STUDY LOCATION:

The study was carried out on adult females who underwent elective caesarean section under spinal anaesthesia at the University of Nigeria Teaching Hospital (UNTH), Enugu. UNTH is a 700 bedded tertiary hospital located in South East Nigeria.

ETHICAL APPROVAL AND INFORMED CONSENT

Ethical Clearance for the study was obtained from the UNTH Health Research Ethics Committee. Approval and written informed consent of every participating patient was obtained before recruitment into the study.

SAMPLE SIZE:

Sample size calculation was based on reports from previous studies. The incidence of PONV in obstetric surgeries in the study done by Rudra et al.[7] was 25%. For this study, the desired incidence of PONV was 20%. Under the null hypothesis of no difference in the incidence of PONV between groups, the null proportion was 50%.

To calculate the sample size with a significance level of 5% and power of study 90%, the following formula was used.[20]

$$n = \frac{[u\sqrt{\pi(1-\pi)} + v\sqrt{\pi_o(1-\pi_o)}]^2}{(\pi - \pi_o)^2}$$

Where n= the desired sample size

π = proportion of interest = 20% (0.20)

π_o = null hypothesis proportion = 50% (0.5)

u = power of study, 90% = 1.28

v = significance level of 5% = 1.96

$$n = \frac{[1.28x\sqrt{0.20(1-0.20)} + 1.96x\sqrt{0.5(1-0.5)}]^2}{(0.20-0.5)^2}$$

n = 2.226/0.09 = 25

About 25 patients were required in each group, an attrition rate of 5% was used and one additional patient was added to each group. Therefore 26 patients were recruited in each group. The total number was 78 per.

PATIENT SELECTION:

,The study recruited 78 female patients undergoing cesarean section under spinal anaesthesia in a randomized prospective double blind comparative study after approval by the UNTH Health Research Ethics Committee and written and informed consent of the patients were obtained.

INCLUSION CRITERIA:

1. Pregnant women aged 18-40 years
2. ASA I or II patients
3. Women with singleton pregnancy undergoing elective caesarean section under spinal

anaesthesia

EXCLUSION CRITERIA:

1. Patients with ASA classification higher than II
2. Emergency surgery
3. Previous history of PONV
4. Motion sickness
5. Patients who had received anti-emetics, opioids or steroids within the previous 24 hours.
6. Patients with gastrointestinal disease, hepatic insufficiency, mechanical ileus, substance abuse including smoking as well as patients on anticancer treatment
7. Patients' refusal
8. Patient with contraindications to subarachnoid block
9. Patients who are allergic to any of the study drugs

STUDY PROTOCOL

PROCEDURE

Patients aged 18-40 years, scheduled for elective cesarean section under spinal anaesthesia were recruited into the study during preoperative assessment of patients.

Each patient was reviewed a night before the surgery by the investigator and were properly educated on all measuring tools to be used for this study. Adequate history including the biodata was taken. Previous medical history to exclude history of motion sickness, previous

PONV, history of drug therapy and other exclusion criteria were meticulously taken and documented. Vital signs and a thorough systemic examination were carried out. American Society of Anesthesiologists (ASA) physical status classification was determined. The results of the following recent investigations were reviewed: full blood count, serum electrolytes urea, creatinine and urinalysis. At least 2 units of grouped and cross-matched blood were requested. The anaesthetic procedure as well as benefits and possible adverse effects of the study drugs and that of the procedure were all explained to the patients and written informed consent for spinal anaesthesia and voluntary participation in the study was obtained from each patient. Patients were fasted from midnight before surgery day. All patients received ranitidine tablet 150mg a night before and on the morning of surgery, and also received 10mg IV metoclopramide 45 minutes before induction of anaesthesia.

On arrival in the theatre, the anaesthetic machine, suction machine and laryngoscopes (including the different sizes of blades and light source) were all checked. A failed intubation tray (endotracheal tubes, general anaesthesia drugs, and oropharyngeal airway) was provided in case of failed spinal anaesthesia and a need to convert to general anaesthesia. Standard emergency tray containing all the necessary resuscitation drugs (like adrenaline and atropine) was also available in theatre. The patients were asked to randomly pick a ballot paper from a box containing seventy eight (78) ballot papers. A total of 26 papers were labelled G for glycopyrrolate, 26 labelled D for the dexamethasone group and 26 labelled C for the control group (normal saline) all sealed in envelopes. All safety precautions were taken. A Dash 4000 multiparameter monitor (GE Medical Inc. USA) was used for the patients vital signs

monitoring. Parameters monitored included arterial oxygen saturation, systolic blood pressure, diastolic blood pressure, the mean arterial pressure, electrocardiogram and heart rate. Intravenous access was secured with two size 16G cannula and intravenous normal saline infusion connected via a blood giving set.

Study medications were prepared in a double blind fashion in identical 2ml syringes. A pharmacist prepared the drugs while an assistant (resident doctor) administered the medications. The investigator was blinded to the study drugs and monitored the patient, measured and collected the outcome variables data (nausea, vomiting, time and vital signs). Patients received either 0.2mg of IV glycopyrrolate, reconstituted to 2ml with normal saline for group G, 8mg of IV dexamethasone for group D, or 2ml of just saline for group C. All medications were in identical 2ml syringes of the same volume and were administered by the assistant before establishing spinal anaesthesia.

Patients were preloaded with 15ml/kg of normal saline over 20-30 minutes while lying in left lateral position (to avoid aorto-caval compression), after which they were put in a sitting position for the spinal anaesthesia. The patients were requested to flex the back to open the intervertebral spaces. The anaesthetist scrubbed and the back of each patient was cleaned with antiseptic lotion (chlorhexidine) and spirit (70% alcohol) and then draped. The appropriate lumbar inter-space was located at either L4-L5 or L3-L4, with the land mark being an imaginary line drawn between the iliac crest which crosses the L4 vertebral bone or L4-5 interspace. The skin and interspinous ligament were infiltrated with 2ml of 2% lidocaine and the spinal needle was inserted in the midline, with the spinal needle aiming slightly

cranially, using a 25G Whitacre spinal needle with an introducer. Correct placement was confirmed by free flow of cerebrospinal fluid at the hub of the needle. The local anaesthetic agent was administered in each patient using 2.4ml of 0.5% hyperbaric bupivacaine and 25 microgram of fentanyl. Following injection, the patients were repositioned supine with the head supported with a pillow, a wedge placed under the right hip for left uterine displacement by 15^0 and a slight head up tilt to limit the cephalad spread of the spinal agent. The vital signs (pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation and respiratory rate) were recorded every 3 minutes for the first 15 minutes and then every 5 minutes till the end of surgery. At fifteen minutes mark after the injection of spinal anaesthesia, the level of maximum sensory block height was established by using sensation to light touch and cold temperature with cotton wool soaked in methylated spirit. The maximum level of block was then noted.

Hypotension (defined as reduction in systolic blood pressure >30mmHg or diastolic blood pressure >15mmHg from baseline)[3] was treated by increasing the rate of normal saline and where necessary with IV ephedrine 3-6 mg boluses. Normal saline was used for intraoperative fluid management and whole blood was transfused whenever blood loss was more than the calculated allowable blood loss.

Patients were be given supplemental 100% oxygen by a face mask whenever SaO_2 was < 95%. Patients pulse rate, blood pressure and arterial oxygen saturation were monitored intraoperatively every 5 minutes.

At the end of the procedure, patients were transferred to the recovery room where monitoring of patients was continued for one hour. When cardiorespiratory values were stable, they were transferred to the ward.

Rescue antiemetic ondansetron 4 mg IV bolus was administered to patients who vomited and patients who complained of nausea and/or vomiting intraoperatively were excluded from the study. Postoperative pain relief was managed with 100 mg of rectal diclofenac suppository 12 hourly, IV tramadol 100mg, 6-8 hourly and IV paracetamol 1g 8 hourly. Each patient was monitored for 24 hours and while data were collected by the investigator.

In this study, nausea is defined as a subjective unpleasant sensation associated with awareness of the urge to vomit, while vomiting is the forceful expulsion of gastric contents from the mouth. Nausea and vomiting were assessed immediately after surgery and at 30 minute intervals in the recovery room for one hour. In addition, nausea and vomiting were evaluated at 4 hour, 12 hour, 18 hour and 24 hour by direct questioning and by spontaneous complaint of the patients. PONV was therefore assessed from the immediate postoperative period to the first 24 hours of surgery.

Patient's level of satisfaction was assessed using Likert's scale[21], it was expressed as satisfied, dissatisfied and very dissatisfied

Nausea and vomiting were evaluated using the Belville's score[20] (0= none, 1= nausea and 2= vomiting). In this study, no distinction was made between vomiting and retching.

1. Primary outcome measures: incidence of PONV and no administration of rescue antiemetic medication for 24 hours postoperatively
2. Secondary outcome measures: include the proportion of patients who experienced episodes of nausea, retching or vomiting, and the number of patients who needed antiemetic rescue. The incidence of adverse effects throughout the study (0-24 hours after anaesthesia) was assessed each time PONV was assessed. Patient's satisfaction was assessed using the psychometric Likert scale.[21]

A simplified risk score was calculated for each patient.[3,15] This predictive score of PONV considers four predictors, which are: the female sex, history of PONV or motion sickness, non-smoking and expected use of opioids. Patients were allocated one point each for risk factors.

STATISTICAL ANALYSIS:

Data collected were analysed with the aid of statistical package for social sciences (SPSS version 17 Inc Chicago Illinois). Descriptive statistics which includes frequency and percentages were used to summarize categorical variables (e.g incidence of nausea, vomiting and requirement of rescue medication, patient satisfaction e.t.c) while means and standard deviations were obtained for continuous variables (e.g age, scores of Bellville, weight, height e.t.c). Association between categorical variables were done using chi square and logistic regression. Means of continuous variables were compared using ANOVA. A P value of less than 0.05 was accepted as statistically significant. Results were presented in tables and charts.

CHAPTER FIVE

RESULTS

The study duration spanned a period of two years and a total of 78 women who underwent elective caesarean section were recruited into this study. There were 26 patients for group G (glycopyrrolate), 25 for group D (dexamethasone) and 25 for group C (control-placebo group). One patient in group D refused spinal anaesthesia after the study drug had been given and was withdrawn from the study and given general anaesthesia and also a patient in group C was excluded following inadequate intraoperative analgesia and the procedure was converted to general anaesthesia. Therefore, only 76 patients were available for analysis, 26 for group G, 25 for group D and 25 for group C.

The demographic characteristics and mallampati scores are shown in Table I. The ages of the patients in the glycopyrrolate group (group G) range from 18 to 40 years with a mean age of 32.62 ± 4.23, 33.27 ± 4.85 for the dexamethasone group (group D) and 34.84 ± 3.57 for the control group (group C). The mean ages and all other demographic data (weight, height and BMI) did not show any significant statistical difference, (with P values of 0.168, 0.725, 0.424 and 0.882 respectively). All patients recruited for the study had similar mallampati scores (P=0.521).

Tables II and III show the mean heart rates and mean respiratory rates of the three study groups. Patients who received IV glycopyrrolate had higher baseline mean heart rates of 93.96±9.23; group D patients had a mean heart rate of 92.04±11.92 and the control-placebo group had heart rates of 92.96±11.23 as baseline (P=0.819). Over the course of the intra-operative period, glycopyrrolate had the highest mean heart rates (105.67±4.93)

compared with group D and C patients and this was statistically significant with a P value of 0.046. In Table III, groups G, D and C had similar mean values for the respiratory rates and there was no statistical difference in any of the groups.

The mean systolic blood pressures of groups G, D and C are shown in Table IV. The mean values of the three groups were similar apart from the third minute, the twelfth minute and the sixty fifth minute of surgery which showed that glycopyrrolate had statistically significantly higher values of mean systolic blood pressures of (127.62±20.64, 123.27±15.09 and 108.75±5.96 respectively) with P values of 0.024, 0.048 and 0.038 respectively. The dexamethasone group recorded the highest mean systolic pressures when compared with groups G and C, with no statistical significance (P=0.295).

In Table V, the mean diastolic blood pressures of all the groups (groups G, D and C) were outlined. The diastolic mean values were identical, but at the third minute of surgery, the control-placebo group (group C) had the lowest mean diastolic pressure of all the groups (65.44±13.12). This was statistically significant, with a P value of 0.038.

Table VI shows the mean arterial blood pressures (MAP) of patients in groups D, G and C. At the third minute, the MAP of patients in group D was 91.60±14.39, group G was 91.00±17.59 and group C, 81.28±12.47. Group D patients had the highest mean MAP values and this was statistically significant (P=0.028). The pattern was similar all through the surgery durations.

In Table VII, The intraoperative oxygen saturation was 95.88 ± 17.90 in the dexamethasone group (group D), 98.80 ± 1.12 in the glycopyrrolate group (group G) and 99.40 ± 0.76 in the control group (group C). Even though the dexamethasone group had lower oxygen saturation values, there no was statistical difference (p=0.442).

Table VIII shows the incidence of PONV in groups G, D and C. 26 patients were analyzed in group G. Within the first 30 minutes, 1 patient experienced nausea (3.8%) and at the first hour, another 3 patients (11.5%) also experienced nausea. A total of 4 patients experienced naused in group G. No patient vomited within the first 30 minutes and by the first hour, 1 patient vomited (3.8%). Only 1 patient vomited in group G.

While in the group that received 8mg of intravenous dexamethasone (group D), 25 patients were analyzed and of the 25, 1 person experienced nausea by the first 30 minutes, making the incidence of nausea 4%, while at the first hour, 1 person also experienced nausea and the incidence was also 4%. A total of 2 patients experienced nausea in group D. No one vomited in group D. Finally, the control group (group C), out of 25 patients, 1 experienced nausea at 30 minutes (incidence of 4%), another 3 also experienced nausea by 1 hour (incidence of 12%) and 1 by the fourth hour (incidence of 4%), making a total of 5 patients who experienced nausea. 1 patient vomited at 30 minutes (incidence of 4%) and 2 by the first hour (incidence of 8%). A total of 3 patients vomited in group C. All the data were analyzed with chi square and there was no statistical difference between the groups by the thirtieth minute, first hour and fourth hour, with P values of 0.410, 0.448 and 0.356 respectively.

Table IX shows the association between the incidence of PONV and the use of 0.2 mg IV glycopyrrolate and 8mg IV dexamethasone. The Table shows that in the control group, a total of 8 patients, with an incidence of 53.4% experienced PONV. In the glycopyrrolate group, a total of 5 patients experienced PONV, with an incidence of 33.3%, while in the dexamethasone group, a total of 2 patients experienced PONV (incidence 13.3%). The Table shows that the use of 8mg dexamethasone was significantly associated with a lower incidence

of PONV.

Table X shows the level of patient satisfaction during the duration of the procedure. In group G, 1 patient (3.8%) was undecided, 3 patients (11.5%) were somewhat satisfied and 22 patients (84.6%) were very much satisfied. In the dexamethasone group, 1 patient (3.8%) was somewhat satisfied and 25 patients were very much satisfied. Group C had 5 patients (19.2%) who were somewhat satisfied and 21 patients (80.8%) who were very much satisfied. All the patients who were somewhat satisfied in group C, had experienced nausea or vomiting during the surgery. There was no statistical significance ($\chi 2 = 5.049$, $P = 0.282$).

Figure 1 shows the distribution of patients who experienced PONV, while Figures 2, 3, 4, 5, 6 and 7 graphically displays the mean heart rates, respiratory rates, systolic blood pressures, diastolic blood pressures, mean arterial blood pressure and arterial oxygen saturation respectively of the three study groups (groups G, D and C).

In this study, 23 patients (90%) in the glycopyrrolate group complained of dryness of the mouth, there were no other side effects reported during the study and there was no incidence of PONV between 4 and 24 hours postoperatively.

Table I: Demographic and ASA characteristics of the study population

	Agent used				
	G	D	C	F/χ^2	P value
	Mean ± SD	Mean ± SD	Mean ± SD		
Age (years)	32.62 ± 4.23	33.27 ± 4.85	34.84 ± 3.57	1.829	0.168
Weight (kg)	86.17 ± 10.46	84.08 ± 8.30	84.18 ± 12.59	0.323	0.725
Height (m)	1.66 ± 0.07	1.64 ± 0.06	1.66 ± 0.07	0.867	0.424
BMI (kg/m^2)	31.17 ± 3.86	31.24 ± 2.59	30.74 ± 4.89	0.126	0.882
Mallampati score n (%)		n (%)	n (%)		
I	16 (61.5)	19 (76.0)	16 (64.0)	3.226	0.521
II	9 (34.6)	5 (20.0)	6 (24.0)		
III	1 (3.8)	1 (4.0)	3 (12.0)		

**Group G = Glyccopyrolate, Group D = Dexamethasone, Group C = Control*

Table II: Mean heart rate of patients

Time (mins)	Mean Heart rate			F	P value
	Group G	Group D	Group C		
	Mean ± SD	Mean ± SD	Mean ± SD		
Baseline (0)	93.96 ± 9.23	92.04 ± 11.92	92.96 ± 11.23	0.201	0.819
3	91.31 ± 11.84	89.96 ± 13.19	92.60 ± 20.62	0.178	0.837
6	89.58 ± 13.09	88.80 ± 13.43	91.48 ± 20.90	0.182	0.834
9	90.62 ± 13.93	93.04 ± 12.79	95.36 ± 11.68	0.869	0.424
12	91.31 ± 11.45	93.04 ± 12.22	92.66 ± 11.11	0.307	0.737
15	93.96 ± 12.33	93.68 ± 13.54	95.20 ± 9.54	0.115	0.891
20	92.19 ± 11.81	92.76 ± 11.53	93.92 ± 8.71	0.169	0.845
25	92.35 ± 12.76	91.72 ± 12.55	90.68 ± 17.59	0.086	0.918
30	94.92 ± 12.18	93.44 ± 11.63	92.76 ± 8.02	0.269	0.765
35	93.58 ± 12.56	92.60 ± 12.69	93.68 ± 12.83	0.055	0.946
40	93.58 ± 14.62	92.04 ± 13.38	92.92 ± 10.40	0.090	0.914
45	93.50 ± 15.22	93.56 ± 14.67	92.80 ± 9.89	0.025	0.976
50	92.88 ± 14.18	91.88 ± 12.63	92.88 ± 9.12	0.056	0.946
55	92.50 ± 12.99	92.40 ± 11.43	92.96 ± 10.79	0.016	0.985
60	91.27 ± 13.02	91.11 ± 12.41	90.67 ± 9.54	0.013	0.987
65	105.67 ± 4.93	82.60 ± 16.39	83.50 ± 11.44	3.944	0.046
70	91.00 ± 11.23	55.00 ± 14.21	85.00 ± 12.73	2.444	0.412

**Group G = Glyccopyrolate, Group D = Dexamethasone, Group C = Control, SD= Standard Deviation*

Table III: Mean respiratory rate of patients

Time (mins)	Respiratory rate			F	P value
	Group G Mean ± SD	Group D Mean ± SD	Group C Mean ± SD		
Baseline (0)	17.32 ± 1.25	17.12 ± 1.05	16.84 ± 2.62	0.456	0.636
3	17.19 ± 1.49	17.04 ± 1.06	16.84 ± 1.70	0.381	0.685
6	17.04 ± 1.56	17.08 ± 1.08	16.76 ± 1.69	0.353	0.704
9	17.12 ± .48	17.00 ± 1.08	16.72 ± 1.59	0.532	0.590
12	17.04 ± 1.46	17.05 ± 1.08	16.64 ± 1.68	0.728	0.486
15	17.00 ± 1.44	17.08 ± 1.08	16.84 ± 1.84	0.109	0.845
20	16.88 ± 1.45	17.08 ± 1.08	16.92 ± 1.61	0.140	0.869
25	17.04 ± 1.48	17.04 ± 1.06	21.08 ± 18.63	1.189	0.310
30	17.12 ± 1.48	17.08 ± 1.08	17.12 ± 2.15	0.005	0.995
35	17.04 ± 1.48	17.08 ± 1.08	17.12 ± 1.81	0.019	0.981
40	17.04 ± 1.48	17.04 ± 1.09	17.12 ± 1.67	0.027	0.974
45	16.96 ± 1.48	17.08 ± 1.08	17.08 ± 1.73	0.057	0.945
50	17.08 ± 1.57	17.08 ± 1.08	17.17 ± 1.52	0.032	0.969
55	17.12 ± 1.58	17.04 ± 1.06	17.13 ± 1.48	0.028	0.973
60	17.25 ± 1.44	17.05 ± 1.13	16.86 ± 1.77	0.321	0.727
65	16.00 ± 2.31	16.20 ± 1.48	16.25 ± 1.98	0.019	0.981
70	14.00 ± 1.51	14.00 ± 1.08	16.00 ± 2.83	0.250	0.816

**Group G = Glyccopyrolate, Group D = Dexamethasone, Group C = Control, SD= Standard Deviation*

Table IV: Mean SBP of patients

Time (mins)	SBP			F	P value
	Group G Mean ± SD	Group D Mean ± SD	Group C Mean ± SD		
Baseline (0)	129.38 ± 17.23	127.76 ± 11.67	125.12 ± 14.27	0.572	0.567
3	127.62 ± 20.64	125.40 ± 15.65	115.12 ± 13.33	3.943	0.024
6	113.54 ± 18.25	116.52 ± 18.04	110.96 ± 12.54	0.710	0.495
9	117.08 ± 10.82	117.68 ± 12.03	110.44 ± 12.71	2.880	0.063
12	123.27 ± 15.09	124.44 ± 17.92	114.20 ± 14.17	3.160	0.048
15	119.12 ± 16.28	121.24 ± 14.79	116.44 ± 11.14	0.711	0.495
20	116.85 ± 10.89	115.24 ± 21.06	116.32 ± 12.31	1.034	0.361
25	116.88 ± 12.91	118.24 ± 12.88	114.56 ± 16.07	0.441	0.645
30	120.15 ± 14.78	122.12 ± 11.43	117.36 ± 10.54	0.927	0.400
35	120.50 ± 15.64	120.64 ± 12.75	117.96 ± 13.06	0.296	0.745
40	122.27 ± 15.97	123.76 ± 15.98	117.64 ± 8.13	1.322	0.273
45	120.85 ± 16.67	121.36 ± 15.61	118.72 ± 7.89	0.251	0.779
50	119.15 ± 13.99	122.96 ± 14.83	120.46 ± 6.96	0.605	0.549
55	122.65 ± 11.86	122.76 ± 13.66	119.67 ± 6.69	0.602	0.551
60	119.69 ± 9.47	124.89 ± 12.74	120.33 ± 6.55	1.540	0.224
65	108.75 ± 5.96	131.60 ± 19.57	116.38 ± 8.47	4.152	0.038
70	112.00 ± 10.14	168.00 ± 12.33	117.00 ± 14.14	5.243	0.295

**Group G = Glyccopyrolate, Group D = Dexamethasone, Group C = Control, SD= Standard Deviation, SBP = systolic blood pressure*

Table V: Mean DBP of patients

Time (mins)	DBP			F	P value
	Group G Mean ± SD	Group D Mean ± SD	Group C Mean ± SD		
Baseline (0)	77.04 ± 12.09	77.96 ± 9.14	73.68 ± 8.99	1.221	0.301
3	74.23 ± 16.07	75.00 ± 13.71	65.44 ± 13.12	3.427	0.038
6	68.69 ± 16.76	69.68 ± 16.39	62.44 ± 14.72	1.512	0.227
9	72.38 ± 9.96	72.48 ± 12.74	62.40 ± 12.53	6.072	0.004
12	73.65 ± 10.56	74.88 ± 12.07	63.44 ± 10.75	7.985	0.001
15	67.65 ± 11.68	70.68 ± 10.95	66.48 ± 9.98	0.989	0.377
20	66.15 ± 8.73	69.64 ± 9.64	67.48 ± 11.31	0.797	0.455
25	66.50 ± 10.71	67.80 ± 11.20	66.48 ± 10.49	0.123	0.884
30	69.62 ± 12.49	72.48 ± 10.21	65.92 ± 10.87	2.136	0.125
35	69.50 ± 12.14	71.48 ± 11.09	65.92 ± 10.57	1.557	0.218
40	71.58 ± 13.32	72.56 ± 13.95	65.96 ± 11.05	1.929	0.153
45	71.04 ± 11.83	71.36 ± 13.21	66.76 ± 8.98	1.257	0.291
50	72.19 ± 8.15	72.48 ± 10.66	69.25 ± 8.29	0.942	0.395
55	71.85 ± 10.05	72.28 ± 12.79	70.00 ± 8.27	0.321	0.726
60	69.63 ± 12.47	76.21 ± 10.14	70.00 ± 8.00	2.479	0.093
65	61.75 ± 9.91	80.00 ± 14.95	66.63 ± 11.69	2.796	0.095
70	60.00 ± 8.31	70.21 ± 10.67	67.65 ± 43.35	0.539	0.694

**Group G = Glyccopyrolate, Group D = Dexamethasone, Group C = Control, SD= Standard Deviation, DBP = Diastolic blood pressure*

Table VI: Mean MAP of patients

Time (mins)	MAP			F	P value
	Group G	Group D	Group C		
	Mean ± SD	Mean ± SD	Mean ± SD		
Baseline (0)	93.80 ± 12.58	92.65 ± 10.42	91.00 ± 9.55	0.360	0.699
3	91.00 ± 17.59	91.60 ± 14.39	81.28 ± 12.47	3.743	0.028
6	83.62 ± 17.43	85.24 ± 17.18	78.32 ± 13.54	1.255	0.291
9	85.77 ± 17.43	87.08 ± 11.98	77.80 ± 12.95	4.440	0.015
12	88.62 ± 11.92	91.52 ± 14.61	80.48 ± 11.30	5.101	0.008
15	83.31 ± 13.56	83.96 ± 20.96	82.32 ± 9.38	0.072	0.930
20	82.42 ± 10.89	85.52 ± 10.38	85.28 ± 8.73	0.753	0.475
25	81.54 ± 12.98	84.32 ± 11.43	83.36 ± 9.43	0.393	0.676
30	85.08 ± 14.25	88.60 ± 10.04	82.72 ± 10.78	1.554	0.218
35	85.35 ± 14.72	87.76 ± 11.87	82.76 ± 11.21	0.965	0.386
40	87.12 ± 15.89	89.60 ± 15.12	82.96 ± 9.40	1.476	0.235
45	86.27 ± 15.12	88.04 ± 3.46	83.80 ± 12.54	0.716	0.492
50	85.62 ± 11.33	89.40 ± 12.39	85.87 ± 7.07	1.003	0.372
55	86.65 ± 13.69	89.36 ± 13.43	86.08 ± 7.00	0.540	0.585
60	85.75 ± 11.28	92.33 ± 10.64	86.71 ± 6.16	2.545	0.088
65	75.75 ± 7.09	96.80 ± 16.12	86.25 ± 3.65	5.405	0.018
70	67.00 ± 11.11	76.81 ± 12.45	80.00 ± 25.46	0.174	0.749

**Group G = Glyccopyrolate, Group D = Dexamethasone, Group C = Control, SD= Standard Deviation, MAP = Mean arterial blood pressure*

Table VII: Mean SPO2 of patients

Time (mins)	SPO2			F	P value
	Group G Mean ± SD	Group D Mean ± SD	Group C Mean ± SD		
Baseline (0)	98.80 ± 1.12	95.88 ± 17.90	99.40 ± 0.76	0.825	0.442
3	98.50 ± 1.30	99.08 ± 1.12	98.76 ± 1.67	1.129	0.329
6	98.58 ± 1.24	99.28 ± 1.14	98.68 ± 0.95	2.925	0.060
9	98.58 ± 1.45	99.20 ± 1.15	98.24 ± 1.33	3.414	0.038
12	98.46 ± 1.58	99.24 ± 1.05	98.44 ± 1.42	2.780	0.069
15	98.50 ± 1.68	99.36 ± 0.86	98.44 ± 1.19	3.970	0.023
20	98.54 ± 1.58	99.12 ± 0.97	98.52 ± 1.33	1.678	0.194
25	98.50 ± 1.48	99.20 ± 1.04	98.36 ± 1.32	3.034	0.054
30	98.62 ± 1.36	99.20 ± 1.04	98.40 ± 1.41	2.607	0.081
35	98.58 ± 1.30	99.12 ± 1.09	98.44 ± 1.36	2.056	0.135
40	98.65 ± 1.26	99.12 ± 1.13	98.88 ± 0.88	1.134	0.327
45	98.65 ± 1.38	99.20 ± 0.91	98.92 ± 1.04	1.481	0.234
50	98.73 ± 1.08	99.16 ± 0.89	98.33 ± 2.32	1.755	0.180
55	98.81 ± 1.13	99.32 ± 0.90	98.29 ± 2.12	3.019	0.055
60	98.75 ± 1.57	99.32 ± 1.11	98.48 ± 1.57	1.764	0.181
65	96.50 ± 2.89	99.20 ± 0.84	98.75 ± 1.28	3.310	0.067
70	96.00 ± 1.45	99.00 ± 0.93	99.10 ± 1.36	1.567	0.199

**Group G = Glyccopyrolate, Group D = Dexamethasone, Group C = Control, SD= Standard Deviation, SPO2 = Arterial blood oxygen saturation levels*

Table VIII: Shows the Incidence of PONV in groups G, D and C

	Incidence			χ^2	P value
	Group G f/n (%)	Group D f/n (%)	Group C f/n (%)		
30 mins					
None	25/26 (96.2)	24/25 (96.0)	21/25 (84.0)	3.970	0.410
Nausea	1/26 (3.8)	1/25 (4.0)	3/25 (12.0)		
Vomiting	0/26 (0.0)	0/25 (0.0)	1/25 (4.0)		
1 hour					
None	22/26 (84.6)	24/25 (96.0)	22/25 (88.0)	3.699	0.448
Nausea	3/26 (11.5)	1/25 (4.0)	1/25 (4.0)		
Vomiting	1/26 (3.8)	0/25 (0.0)	2/25 (8.0)		
4 hours					
None	26/26 (100.0)	25/25 (100.0)	24/25 (96.0)	2.067	0.356
Nausea	0/26 (0.0)	0/25 (0.0)	1/25 (4.0)		

**f = frequency, n = total no. of patients, Group G = Glyccopyrolate, Group D = Dexamethasone, Group C = Control*

Table IX: Association between incidence of PONV and use of 0.2mg glycopyrrolate and 8mg dexamethasone

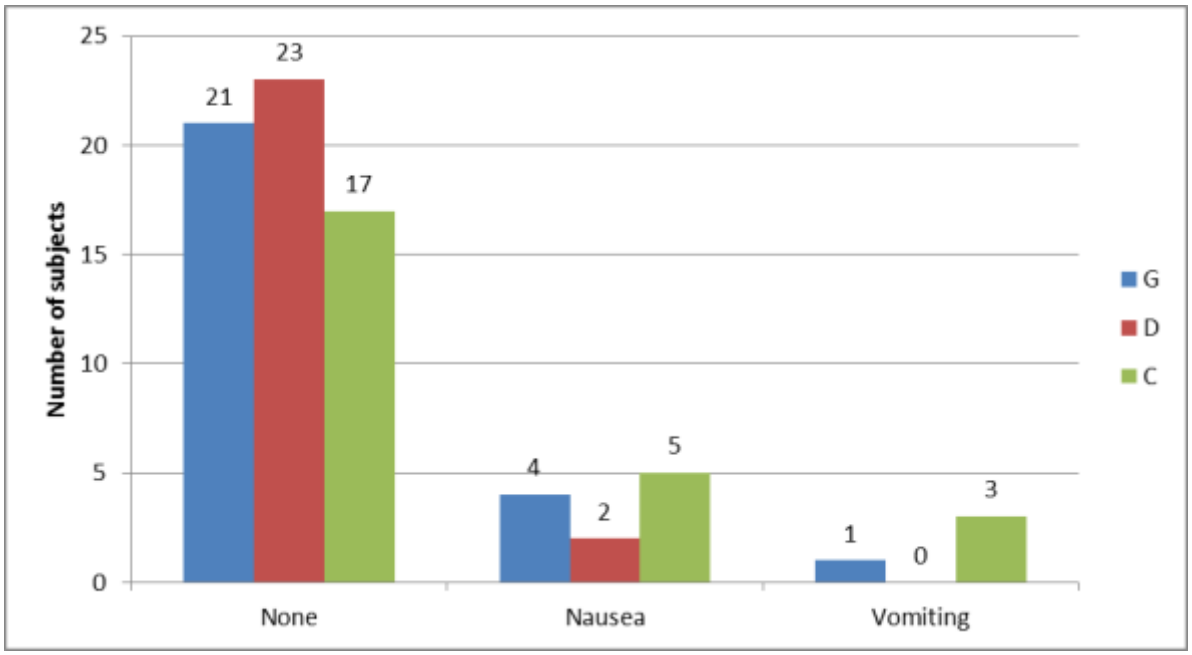
Agent used	PONV incidence		P value	OR	95% C.I for OR
	Yes f/n (%)	No f/n (%)			
Control	8/25 (32.0)	17/25 (68.0)			
0.2mg glycopyrrolate	5/26 (19.2)	21/26 (80.8)	0.300	0.506	0.140 – 1.833
8mg dexamethasone	2/25 (8.0)	23/25 (92.0)	0.048	0.185	0.035 – 0.983

**f = frequency, n = total no. of patients*

Table X: Shows the patients' satisfaction in the three groups

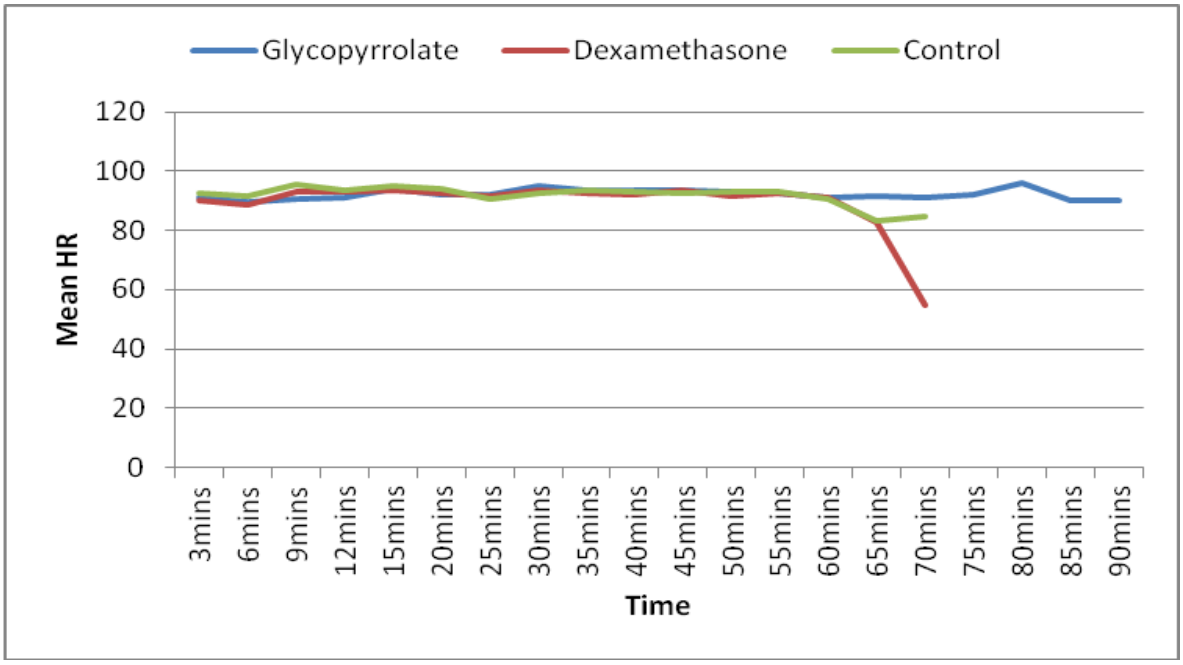
	Agent used		
Satisfaction	G	D	C
	n (%)	n (%)	n (%)
Undecided	1 (3.8)	0 (0.0)	0 (0.0)
Somewhat	3 (11.5)	1 (4.0)	5 (20.0)
Very much	22 (84.6)	24 (96.0)	20 (80.0)

χ^2 = 5.019, P = 0.285



Group G: Glycopyrrolate Group, Group D: Dexamethasone Group, Group C: Control Group.

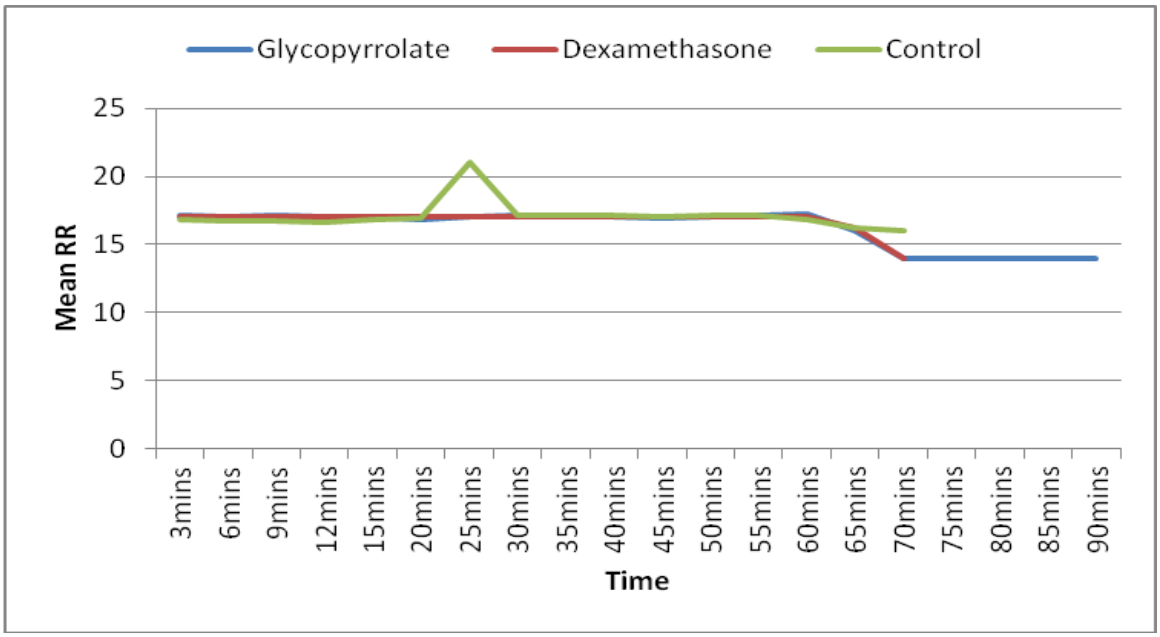
Fig 1: Distribution of patients showing the incidence of PONV



Group G: Glycopyrrolate Group, Group D: Dexamethasone Group, Group C: Control Group

HR: Heart Rate

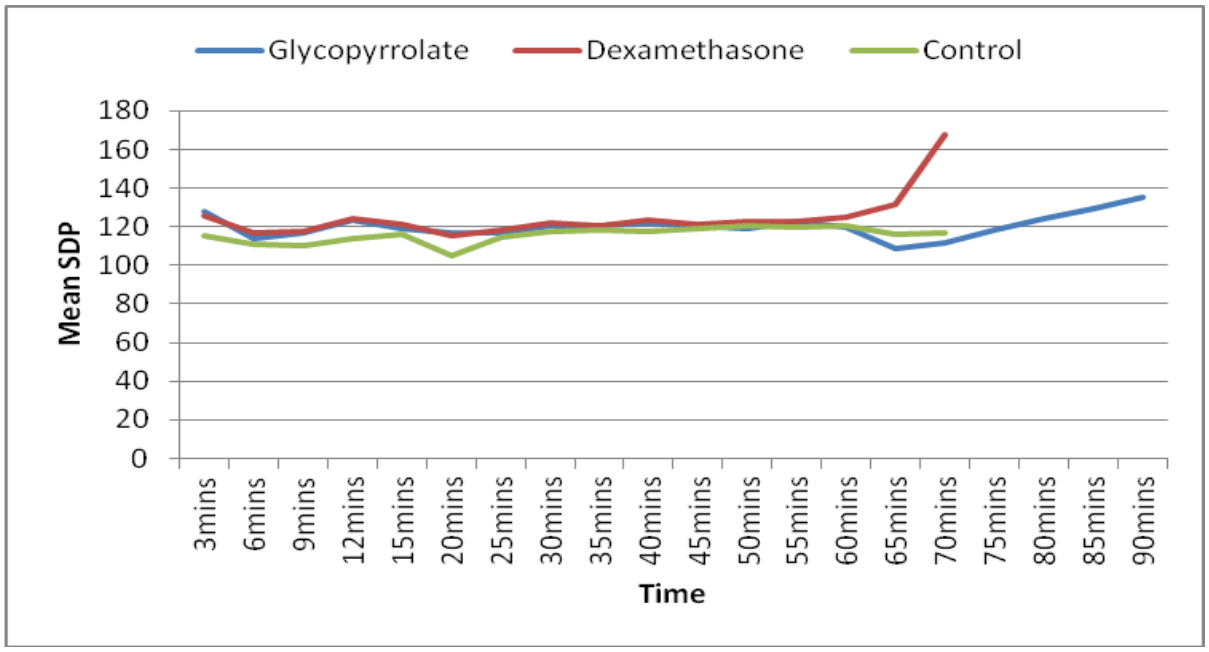
Fig 2: Distribution of patients showing the mean heart rates



Group G: Glycopyrrolate Group, Group D: Dexamethasone Group, Group C: Control Group

RR: Respiratory Rate

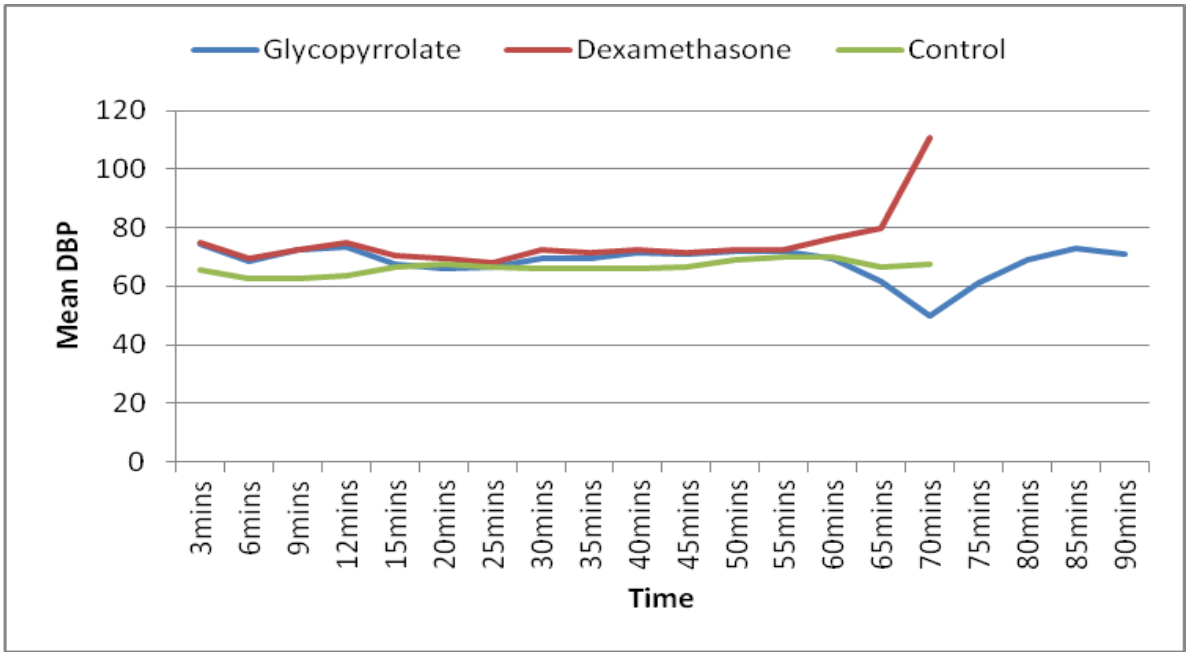
Fig 3: Distribution of patients showing the mean respiratory rates



Group G: Glycopyrrolate Group, Group D: Dexamethasone Group, Group C: Control Group

SBP: Systolic Blood Pressure

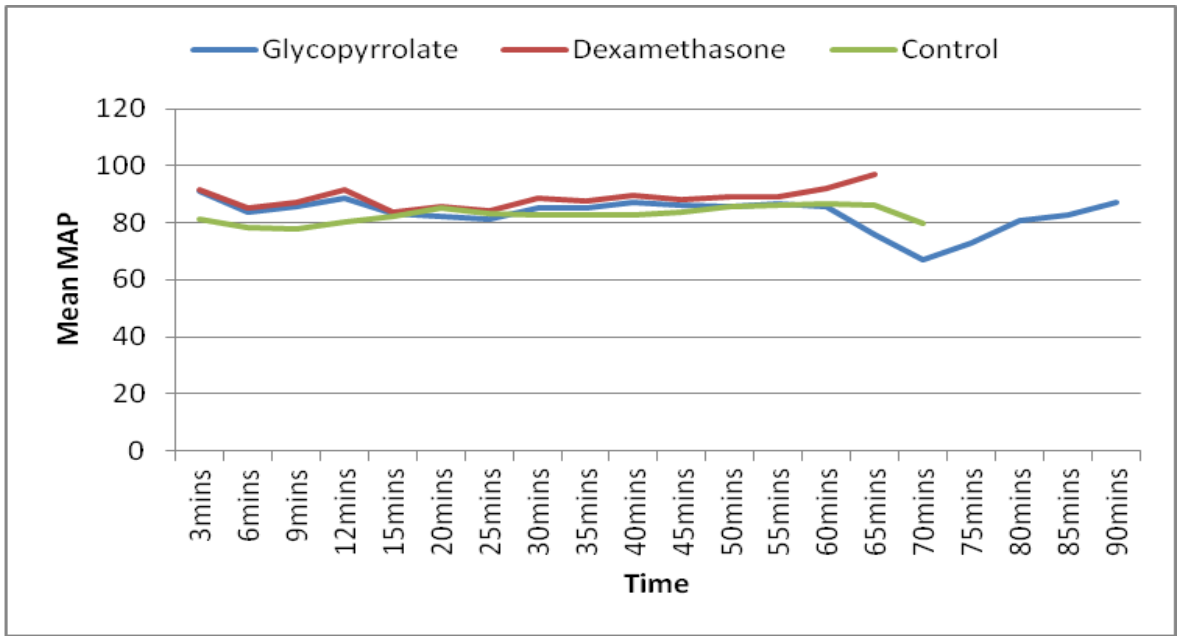
Fig 4: Distribution of patients showing the mean systolic blood pressures



Group G: Glycopyrrolate Group, Group D: Dexamethasone Group, Group C: Control Group

DBP: Diastolic Blood Pressure

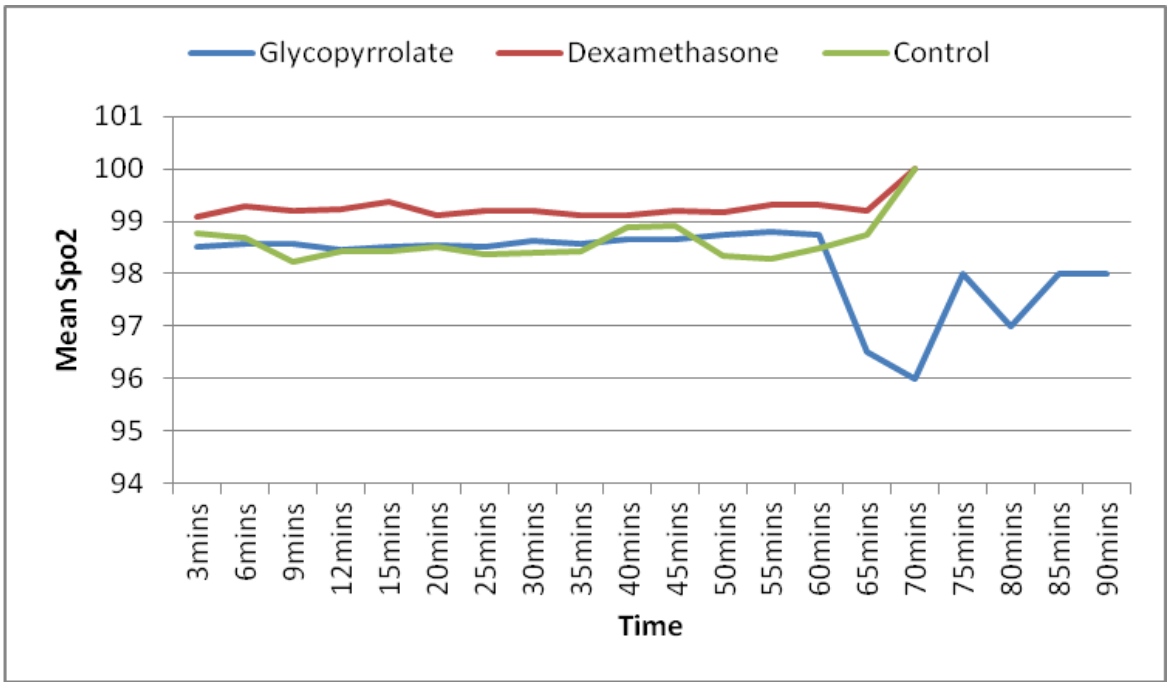
Fig 5: Distribution of patients showing the mean diastolic blood pressures



Group G: Glycopyrrolate Group, Group D: Dexamethasone Group, Group C: Control Group

MAP: Mean Arterial Blood Pressure

Fig 6: Distribution of patients showing the mean arterial blood pressures



Group G: Glycopyrrolate Group, Group D: Dexamethasone Group, Group C: Control Group

SPO2: Arterial Oxygen Saturation

Fig 7: Distribution of patients showing the arterial oxygen saturations

CHAPTER SIX

DISCUSSION

The results of this study showed that intravenous dexamethasone 8mg administered before establishing spinal anaesthesia reduced the incidence of postoperative nausea and vomiting when compared to patients who received intravenous glycopyrrolate 0.2mg and the control group (normal saline placebo). The main findings in this study were similar to other studies done previously which found dexamethasone effective in reducing the incidence of PONV in adult patients undergoing major surgeries.[28,29] The mechanism of action of dexamethasone is not well established, but it is widely used due to its antiemetic properties.[55] It is proposed that dexathasone acts by antagonizing prostaglandin or it releases endorphins that elevate mood.[55,56] Carlisle and Stevenson[57] in a Cochrane Review, calculated a risk ratio for dexamethasone of 0.48 (95% CI 0.43-0.54) for the prevention of PONV, similar to ondansetron [RR 0.56 (95% CI 0.50-0.62)]. The IMPACT Group had similar findings and found that when combined with other antiemetics, dexamethasone had an additive effect and therefore was more effective.[59] Dexamethasone also has other beneficial effects.[58] It has the capacity to relieve laryngeal oedema due to its anti-inflammatory effects and it has been shown to reduce inflammation and tissue damage hence, it is effective in reducing pain after surgery.[60,61] However, dexamethasone has potential side effects and they include increased risk of postoperative infection, impairment of glucose homeostasis and psychiatric disturbances.[58] None of the patients in this study experienced any of these side effects. This is most likely because they all received them as single boluses.

Jain and Sharma[62] studied the effects of glycopyrrolate and ondansetron on nausea and vomiting in cesarean section and they found no significant difference in nausea and vomiting between the two groups. Also, there was significantly less bradycardia in patients who received glycopyrrolate, compared to dexamethasone (P=0.027). Glycopyrrolate acts as an antiemetic by inhibiting central muscarinic and cholinergic receptors.[63,64] It is a quaternary ammonium and unlike atropine, which is a tertiary amine, does not cross the placental barrier hence, it is safe for use in pregnant women.[62] The action of glycopyrrolate on muscarinic receptors in the gut inhibits acetylcholine which decreases the volume and free acidity of gastric secretions apart from its decrease of pharyngeal, tracheal and bronchial secretions.[65,66] In this study, those who experienced side effects complained of dryness of the mouth, and this could be a draw-back to the routine use of glycopyrrolate. Patients who received glycopyrrolate also experienced less bradycardia, even though there was no difference in hypotension between groups. These findings were supported by those done in other studies.[67,68,69] Patel et al[70] in a meta-analysis assessed the effect of glycopyrrolate in the incidence of hypotension and vasopressor requirement during spinal anaesthesia for cesarean delivery. A total of 311 patients were studied, 153 received glycopyrrolate and the rest got placebo. There was no difference in the incidence of spinal-induced hypotension between the glycopyrrolate group and the control group (P=0.59).

The most common symptoms following surgery and anaesthesia are pain and emesis.[24,25] The female gender, sex hormones, young age and increased body fat, all found in pregnant women increases the risk of PONV.[26] Regional anaesthesia with intrathecal opioids as adjuncts has gained popularity in obstetrics and opioids are among the most important drugs

related to PONV.[5,24] PONV during regional anaesthesia for Caesarean section still remains a significant problem for the patient, surgeon and anaesthesiologist.[27] Studies exploring different approaches to reducing the incidence of PONV have been done.[1,6,7,22] In the methodology of this study, all patients in the 3 groups received metoclopramide in addition to the study drugs, so the study in essence compared combination therapies of dexamethasone and metoclopramide, glycopyrrolate and metoclopramide and metoclopramide and normal saline for the control of PONV following the spinal anaesthesia for Caeserean section, just like it was done in this study. Frikha et al[27] in a study which compared the use of combined metoclopramide and dexamethasone versus dexamethasone alone found that the incidence of nausea during both intra and postoperative periods was not different between the two groups, even though intraoperative nausea and vomiting was not assessed in this study. A quantitative systematic review of metoclopramide in the prevention of PONV found no evidence of dose responsiveness with oral, intramuscular or intravenous metoclopramide in children or adults. There was also no significant anti-nausea or anti-vomiting effect.[30]

There was no difference between the groups with regards to age, weight, height BMI or ASA classification. All patients were classified as ASA II as the current definitions and new examples of the last approved ASA House of delegates on October 15, 2014 classified pregnancy as ASA 2.[31] It has been found that a low ASA physical status (I–II) has been associated with an increased risk of PONV.[16] Studies have detailed demographic factors that increase the incidence of PONV.[16,26,32] Stadler et al[33] in their study showed that the female gender was the most important predictor of an increased incidence of nausea and vomiting. All patients in this study were female and all had low ASA classification scores and therefore

were all equally had increased risk of PONV.

This study compared the efficacy of glycopyrrolate and dexamethasone for the control of PONV following spinal anaesthesia for Caeserean section and found that the control group (normal saline) had a 53.4% incidence of PONV, while the glycopyrrolate group had a 33.3% incidence and the dexamethasone group had the lowest incidence of 13.3%. The findings in this study were statistically significant (P=0.048). Anticholinergic agents antagonize muscarinic and histaminic receptors in the vestibular and vomiting centres and have been shown to decrease the incidence of nausea and vomiting.[34] Ure et al[22] studied the efficacy of glycopyrrolate as a prophylaxis against nausea in pregnant women and showed that patients given glycopyrrolate prophylactically showed a reduction in the frequency (P=0.02) and severity (P=0.03) of nausea and it showed no adverse neonatal effects. Even though this study showed that glycopyrrolate reduced the incidence of nausea in the study group significantly, other studies like that done by Thakur et al[35] who studied the combined use of metoclopramide and glycopyrrolate as prophylactic antiemetic in elective cesarean section under spinal anaesthesia and recruited 78 patients. The incidence of nausea was 3.84% and there was no incidence of vomiting. The observed differences in this study were statistically insignificant and showed that glycopyrrolate did not reduce the incidence of nausea and vomiting. Other studies have been done showing that the administration of anticholinergics via the neuraxial route can reduce the incidence of PONV.[36,37] Contrary to the study done by Jain et al[38] who found glycopyrrolate and ondansetron equally as effective as ondansetron in reducing intraoperative and postoperative nausea and vomiting, this study showed dexamethasone more effective than glycopyrrolate.

Studies have been done to assess the efficacy and effective dose of dexamethasone for the prevention of PONV. Lee et al[39] compared the efficacy of dexamethasone 8mg and dexamethasone 5mg in the prevention of PONV in female patients undergoing thyroidectomy. The study demonstrated that the prophylactic administration of dexamethasone 8mg was significantly superior to dexamethasone 5mg ($P<0.001$) in reducing the incidence of PONV. In this present study, 8mg of dexamethasone was also used and it was shown to be adequate. Chiu-Ming et al[40] noted the low cost of dexamethasone as an advantage of its use, coupled with its longer duration of action. It has been found that the use of dexamethasone for the prevention of PONV caused by intravenous or epidural opioid for pain control offers good therapeutic control.[40] Liu and co[41] in the study of the control of PONV in high risk patients showed that dexamethasone was effective in reducing the overall incidence of vomiting from 63.3% to 20.0% ($P<0.01$). In patients who received chemotherapy, Aapro et al[42] in a double-blinded crossover study which compared the antiemetic properties of dexamethasone versus metoclopramide showed that the 2 drugs protected against more than 5 episodes of emesis in 48% of those who received dexamethasone and 40% of patients who got metoclopramide. Nausea lasted for less than six hours in 45% of patients who received dexamethasone and 37% in the metoclopramide group. Side effects were minimal with dexamethasone and 33% of patients experienced unacceptable extrapyramidal side effects with metoclopramide. More patients preferred dexamethasone (70%) as against 22% who preferred metoclopramide due to minimal side effects. In another study, Ping-Heng and co[43] evaluated the effect of dexamethasone on postoperative pain and emesis after intrathecal neostigmine. Sixty ASA physical status I patients were recruited and divided into two groups.

One group received intravenous dexamethasone 10mg, while another received normal saline (the control group). The duration and severity of analgesia and the incidence of PONV did not differ significantly between the two groups. Intravenous dexamethasone therefore, did not reduce the incidence of emesis. The result of this study could be attributed to the fact that all the patients recruited for the study were males, who are generally known to have a lower incidence of PONV.[44,45]

Biswas et al[7] compared glycopyrrolate, dexamethasone and metoclopramide for the control of postoperative nausea and vomiting after spinal anaesthesia for caesarean delivery. The incidence of postoperative nausea was 10% in the glycopyrrolate group, 10% in the dexamethasone group and 20% in the metoclopramide group. The incidence of vomiting was however much lower in the glycopyrrolate group at 15%, 20% in the dexamethasone group and 30% in the metoclopramide group. The study concluded that glycopyrrolate could be better than dexamethasone and metoclopramide. In this present study, a total of 4 patients (15%) experienced nausea in the glycopyrrolate group, 2 patients experienced nausea in the dexamethasone group (8%), and 5 patients (20%) experienced nausea in the normal saline group. One patient vomited (3.8%) in the glycopyrrolate group, none in the dexamethasone group, and 3 patients (12%) vomited in the normal saline group.

Tobi et al[46] studied the effects of dexamethasone and metoclopramide on early and late postoperative nausea and vomiting in women undergoing myomectomy under spinal anaesthesia. Ninety patients were recruited for the study, and were divided into 3 groups, the DM group (dexamethasone and metoclopramide), the MO group (metoclopramide only) and the DO group (dexamethasone only). Dexamethasone only group had the highest incidence of

early PONV (40%) with a P value of 0.003, but not for late, metoclopramide alone group had an incidence of 29.97% for early PONV and the DM group had the lowest incidence of both early and late PONV. The study concluded that dexamethasone protects against the incidence of late PONV without any effect on early PONV, while metoclopramide on the other hand has comparable effect on both. It is very similar to the results of this present study, considering that all patients received metoclopramide.

The sequelae of adverse effects from dexamethasone administration are not usually immediate, and they could range from difficulty in controlling blood sugar levels, delayed wound healing, wound infections, gastric ulcers and avascular necrosis.[28,47,48] However, these potential side effects usually occur following long term use and not after single doses.[40] In this present study, there were no immediate complications following dexamethasone administration, all patients received single doses of 8mg dexamethasone and it was beyond the scope of the study to follow up patients for possible long term complications. Dexamethasone is cheap, readily available, safe and is therefore considered an ideal antiemetic.[40] Glycopyrrolate is a quaternary amine and penetrates biological membranes slowly (placental membrane) and incompletely, making it an ideal drug for obstetric patients.[49,50] In this study, the only side effect reported following the administration of glycopyrrolate was dryness of the mouth and this is consistent with the findings in other studies.[71,72]

CONCLUSION

Postoperative nausea and vomiting (PONV) is a common and unpleasant side effect of anaesthesia and surgery. Complications include dehydration, electrolyte imbalance, bleeding, wound dehiscence and rarely, pulmonary aspiration of gastric contents.[3] In pregnant women undergoing caesarean section, the incidence can be as high as 60%.[1,2] Intravenous dexamethasone and glycopyrrolate have been proven as effective prophylaxis in the prevention of PONV in obstetric surgery.[1,7] This prospective, randomized, double-blinded placebo controlled study demonstrated that IV 8mg dexamethasone administered before the induction of spinal anaesthesia for elective caesarean section, significantly decreased the incidence of PONV, when compared to IV 0.2mg glycopyrrolate and the control (normal saline). The only side effect reported in the study was dryness of the mouth, found in 90% of patients in the glycopyrrolate group. The use of 8mg intravenous dexamethasone is being encouraged as it is cheap, safe, readily available and effective.[40] This study has confirmed that dexamethasone is more effective than glycopyrrolate for the control of PONV after intrathecal fentanyl and bupivacaine for caesarean section.

RECOMMENDATIONS

From this study, the following recommendations can be made:

1. Parturients undergoing caesarean section should in addition to receiving standard premedication with metoclopramide, also receive 8mg intravenous dexamethasone as antiemetic prophylaxis against PONV.
2. A combination of two antiemetics should be used for PONV prohylaxis to the different mechanisms of action of different drugs. Parturients will benefit from a reduced incidence of PONV.
3. Intravenous dexamethasone is preferred to intravenous glycopyrrolate since it is more effective and has minimal side effects as a single dose in the prevention of PONV.

LIMITATIONS

1. Blood sugar levels could not be checked intraoperatively and postoperatively, to monitor the possible side effects of dexamethasone as regards delayed wound healing and wound infections.
2. There were few articles that studied the use of glycopyrrolate as an antiemetic agent.
3. All patients, including the control group (normal saline) had to receive metoclopramide as part of the standard premedication of parturients going for caesarean section.

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APPENDIX 2

PATIENT INFORMED CONSENT

To the patient,

You have been selected to take part in a research which is proposed to compare glycopyrrolate and dexamethasone in the control of postoperative nausea and vomiting (PONV) after intrathecal fentanyl and bupivacaine for caesarean section.

Approval for this study has been obtained from the ethical committee of the hospital.

Information/Voluntary Nature of Participation:

In order to decide whether to be part of the study or not, you have to understand what the study is about and give informed consent. Participation is completely voluntary, and you are free to withdraw from it at any stage of the study without any consequences. There will be no additional cost to you for being part of the study.

Purpose of the study

The purpose of the study is to see to what extent, glycopyrrolate and dexamethasone will prevent or reduce the incidence of PONV and to assess the side effect profile of each of the drugs on patients selected for the study

Description of study procedure:

Before the surgery is carried out, you will be premedicated. To enable surgeons carry out the surgical operation on you, we (anaesthetist) will administer a spinal anaesthetic at your lower back. In this state, the surgeon will be able to carry out the procedure while you are awake.

Like every surgical procedure, there are inherent side effects that may occur which include failure of agent to take (pain) in which case you may have to be put to sleep. Other possible side effects which may occur from the drug administered include blurred vision, dryness of the mouth and reduced sweating. All the complications mentioned above occur very rarely.

Confidentiality

The information you give and your participation in the study will be kept confidential. If the study is published no data will reveal the individual participants.

Benefits from the study

Results from the study will help enhance knowledge about the subject matter. This will help advance patient care which you may benefit from.

You will get treatment services at no additional cost to you during the study.

Every effort will be made to give you the best expert attention during the study.

Risk during study

During the research, you will not be exposed to any drugs or procedure that is not indicated. You will not be exposed to any additional risk.

Feedback

In case you have any enquiries or concern regarding the research, you can contact; Dr Okonkwo IP, Department of Anaesthesia UNTH, Enugu Nigeria. Tel + (234)-7069399834.

Response from the patient

I have read the above information. I have fully understood the procedure, the benefits and the risks have been well explained to me. All my doubts and worries have been clarified. I hereby give consent freely to participate in the research.

Name and signature of subject Name and signature of researcher

Date ---------- Date----------

Name and signature of witness

Date----------

APPENDIX 1

Date collection form

Study title: A Comparative Study Of Glycopyrrolate And Dexamethasone In The Control Of PONV After Intrathecal Fentanyl And Bupivacaine For Caesarean Section.

Date…….

A. Patient Demographic Data

1) Patient's Initials
2) Hospital number…….
3) Date of birth- Age (yrs)…….
4) Weight (kg)……
5) Height (m)……
6) BMI (kg/m^2)……..

B. Preanaesthetic Information

1. ASA physical status …….
2. Mallampati score……
3. Baseline vital signs:

   HR…. RR…… SBP…. DBP…. MAP …… SPO2….

Agent used [G]… [D]…[C]…

TIME OF ADMINISTRATION OF DRUG.

Timeline	**HR** bpm	**RR** cpm	**SDP** mmHg	**DBP** mmHg	**MAP** mmHg	**SPO2** %
3 min						
6min						
9 min						
12 min						
15 min						
20 min						
25 min						
30 min						
35 min						
40 min						
45 min						
50 min						
55 min						
60 min						
65 min						
70 min						
75 min						
80 min						

85 min						
90 min						

Incidence of Intraoperative Nausea and Vomiting please tick (√)

i) 0 ☐ (ii) 1 ☐ (iii) 2 ☐

C. <u>Postoperative Evaluation.</u>

PONV	**30 MIN**	**1 HR**	**4 HRS**	**12 HRS**	**18HRS**	**24HRS**
0						
1						
2						

2. Need for antiemetic rescue: Yes… No…

3. If yes, agent used……..…..

4. Were you satisfied with the care you received.

Very Much	**Somewhat**	**Undecided**	**Not Really**	**Not at all**

5	4	3	2	1

5. Side effects :

   i) Pruritus ☐

   ii) Respiratory Depression ☐

   iii) Dry Mouth ☐

   iv) Blurred Vision ☐

6. Comments:

7. Management of Side Effects if any…….....

   …….

8. Outcome of management.

   i. Good ☐

   ii. Bad ☐

   iii. Death ☐

   iv. Transfer ☐