COMPARATIVE STUDY OF ONDANSETRON, GLYCOPYRROLATE, METOCLOPRAMIDE PLUS DEXAMETHASONE IN PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING FOR CAESAREAN DELIVERY UNDER SPINAL ANAESTHESIA

A study of 160 cases

Dissertation submitted for the Degree of

Doctor of medicine

(Branch – X) Anaesthesiology

September - 2006

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI.

DEPARTMENT OF ANAESTHESIOLOGY

MADURAI MEDICAL COLLEGE

MADURAI

CERTIFICATE

This is to certify that the dissertation entitled **"COMPARATIVE STUDY OF ONDANSETRON, GLYCOPYRROLATE, METOCLOPRAMIDE PLUS DEXAMETHASONE IN PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING FORCAESAREAN DELIVERY UNDER SPINAL ANAESTHESIA",** is a bonafide record work done by **DR. S.M. SENTHIL NATHAN**, in the Department of Anaesthesiology, Government Rajaji Hospital, Madurai Medical College, Madurai.

Professor and Head,

Department of Anaesthesiology,

Government Rajaji Hospital,

Madurai Medical College, Madurai.

ACKNOWLEDGEMENT

I am deeply indebted to all the patients for submitting themselves for this study and I express my heartfelt gratitude to all of them.

If not for my Professor **DR.S.SUBBIAH,** MNAMS, DA., M.D., DCH., Chief and Head of Department of Anaesthesiology, Madurai Medical College, Madurai who gave invaluable guidance and inspiration, this study would not have consummated to its logical conclusions. I sincerely thank him for his encouragement and support at every stage of this study.

I express my profound thanks to **DR.I.CHANDRASEKHARAN,** MD., DA., Additional Professor of Anaesthesiology for his constant support and guidance to perform this study.

I express my gratitude to **DR.S.P.MEENAKSHI SUNDARAM**, MD., DA., Professor of Anaesthesiology, for his able assistance and guidance in doing this project work.

I am greatly thankful to all my Assistant Professors for their support and guidance rendered towards me for this dissertation.

My profound thanks to **THE DEAN**, Madurai Medical College, Madurai for permitting me to utilize the clinical materials of this hospital.

DECLARATION

I, ***DR .S.M. SENTHIL NATHAN,*** solemnly declare that the dissertation titled***"COMPARATIVE STUDY OF ONDANSETRON, GLYCOPYRROLATE, METOCLOPRAMIDE PLUS DEXAMETHASONE IN PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING FOR CAESAREAN DELIVERY UNDER SPINAL ANAESTHESIA",*** has been prepared by me.

This is submitted to The Tamil Nadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the requirements for the award of M.D. Degree Examination (Branch X) Anaesthesiology to be held in SEPTEMBER 2006 .

Place: Madurai.

Date :

DR. S. M. SENTHIL NATHAN

TABLE AND CONTENTS

INTRODUCTION

The most common and distressing symptoms, which follow anaesthesia and surgery are pain and emesis. Sometimes nausea and vomiting may be more distressing especially after minor and ambulatory surgery, delaying the hospital discharge. Yet it may be a major factor in upsetting the post-operative convalescence.

It is common after spinal anaesthesia for caesarian section with reported incidence as high as 66%. Available large number of agents which prevent emesis indicate the magnitude of the problems and lack of satisfactory results.

Nausea and vomiting has been associated for many years in use of general anaesthesia (i.e.) ether and chloroform. Extensive description of postoperative nausea and vomiting has been given by Sir John Snow in 1948 within 18 month of chloroform introduction.

In pregnancy, there is always an increased frequency of nausea and vomiting due to various possibilities. These factors added to the spinal anaesthesia, and effects of sympathetic block, and the anxiety may increase the frequency of nausea and vomiting in the post operative period starting from the intra operative period.

Though there are many drugs available in treating the nausea and vomiting, we are more concerned in prevention of the problem with the help of pharmacological

agents.

The purpose of this double blind randomised study was to assess the efficacy of the following drugs such as ondansetron, glycopyrrolate, metoclopramide + dexamethasone combination in prevention of nausea and vomiting in pregnant women undergoing caesarean section under spinal anaesthesia, by using the drugs prophylactically.

This study is undertaken with atmost care and the results are discussed.

AIM OF THE STUDY

To compare the efficacy of ondansetron, metoclopramide plus dexamethasone and glycopyrrolate as a prophylactic antiemetic agent in prevention of postoperative nausea and vomiting after spinal anaesthesia for caesarean delivery.

REVIEW OF LITERATURE

1] A comparative study of glycopyrrolate, dexamethasone and metaclopramide in control of post-operative nausea and vomiting after spinal anaesthesia for caesarean delivery [Dr. Biswas et al – Indian J Anaesthesia) 2003 47.3]

The study was conducted in 80 women – allocated into 4 groups of 20 each. A-Inj glycopyrrolate 0.2 mg, B – Inj Dexamethasone 8mg, C-Inj – Metoclopramide 10mg, D – normal saline 2ml (control). The incidence of nausea and vomiting was less in the glycopyrrolate group. P value <0.05. The incidence was 40% in the placebo group, 10% in the glycopyrrolate group, 10% in the dexamethasone group and 20% in the metoclopramide group.

2] Double blind cross over study of comparison of antiemetic efficacy of dexamethasone 8mg versus high dose metaclopramide in caesarean section under spinal anaesthesia [Ms. Aapro et al – Journal of clinical gynecology vol. 2 2003].

Two group of 50 each were compared and there was reduction in post operative nausea vomiting in the metaclopramide group. (P <0.05)

3] Combination of granisetron and dexamethasone decreases post operative nausea vomiting in regional anaesthesia in lower limb surgeries [Fujii et al, Dept. of Anaesthesiology, Toridl Gen Hospital, Tokyo 2003).

Granisetron 20μ/kg + Dexamethasone 8mg has reduced incidence of nausea vomiting by 27% compared to the control group.

4] Comparison of Ondansetron versus placebo for nausea and vomiting in caesarean section under subarachanoid block - EI Abouliesh et al [Journal of Anaesthesia – Association of Anaesthetists of Great Britain and Ireland, Vol. 54].

Seventy four patients were divided into 2 groups. The drug was given (Ondansetron 4mg) before induction during preloading.

The incidence of nausea vomiting was reduced in the Ondansetron group.

The incidence of nausea, vomiting was 85% in placebo group and 34% in ondansetron group ($p<0.028$).

5] Prospective double blind study – comparison of ondansetron, ondansetron plus dexamethasone, dexamethasone as prophylaxis for post operative nausea vomiting for day care gynaecology surgeries – Thomas et al (Dept. of Anaesthesia, South Hampton Gen Hospital, UK 2002).

The study was conducted in 150 females 50 in each group. The dexamethasone plus ondansetron group was superior in reduction of post operative nausea vomiting among the three groups ($p<0.05$).

6] Double blind study – comparison of efficacy of metoclopramide and ondansetron – for prophylaxis for post operative nausea and vomiting for caesarean section under spinal anaesthesia – F.J. Horea – Mignel MD et al, Hospital General de Sogoria [2001].

This was a double blind placebo controlled study 50 women in each group.

Nausea and vomiting was seen in 11.5% of total cases. 91.8% of ondansetron group had no vomiting and 91.6% of metoclopramide had no vomiting. Increased emetic symptoms were noted during umbilical cord clamping. There was no statistically significant difference between ondansetron and metoclopramide group ($p<0.01$).

7] Double blind prospective study – evaluating efficacy of 200µ of glycopyrrolate iv before induction for caesarean patients using 2.5ml isobaric bupivicaine spinal anaesthesia – BJ of Anaesthesia 1995 Sep. Ure – D James KS et al.

This study was done in 50 women coming for caesarean section under spinal anaesthesia. Glycopyrrolate decreased frequency of vomiting and ephedrine requirement in pregnancy patients ($p<0.02$).

8] Prophylactic single dose intravenous administration of ondansetron in the prevention of postoperative – emetic symptoms during spinal anaesthesia for caesarean delivery – Dr. A.K. Pan, Dr.A. Rend. [2002]

In a placebo controlled study 40 women were studied, 4mg of ondansetron was administered iv before spinal anaesthesia. The frequency of nausea was 75% after placebo and 10% after ondansetron. The corresponding frequency of retching and vomiting were 60% after placebo and 5% after ondansetron.

HISTORICAL ASPECTS IN POSTOPERATIVE NAUSEA AND VOMITING

During ether era, reported incidence of post operative nausea and vomiting was as high as 75-80%. Various techniques including olive oil and glucose insulin injection were reported to be effective as reported by Robert Ferguson in 1912. The effect of atropine was appreciated by Brown Sequard as early as 1883.

In second half of the century the incidence of post operative nausea and vomiting decreased to about 50% due to the use of non opoid, non-ether, regional anaesthetic techniques, refinement of surgical techniques and identification of patient's predictive emetogenic factors. There are 3 kinds of vomiting, the first of which is attributed to anaesthetics such as ether, second due to the reflex responses, third due to the medication used intraoperatively. Subsequent investigation unfolded a spectrum of non-anaesthetic factors in the pathogenesis of post operative nausea and vomiting.

Over years numerous of drugs have been used in the management of post operative nausea and vomiting. Phenothiazines were synthesized in late 19th century by chemists in dyeing industry. Promethazines were found in 1930 to have good anti-emetic property. However sedative action of it, limited its use. Phenothiazine derivatives

have been exclusively used in the treatment of post operative nausea and vomiting.

The recent introduction of the $5HT_3$ antagonists such as ondansetron and granisetron have reached good heights in the treatment of nausea and vomiting.

There are new antiemetics like neurokinin-1, (substance-P antagonists) in development.

The reason for the magnitude of the problem of **PONV** persisting inspite of the various drugs in use can be assessed by four factors.

1. **Complexity of the problem:** The variables are many that it becomes difficult to assess the effects of an intervention as it requires considerable number of patients of well controlled trials.
2. **Inadequate qualification of phenomena:** The phenomena has been poorly qualified i.e. nausea, vomiting, retching etc.
3. **Inadequate antiemetic regimen:** Unable to identify a good drug which can prevent nausea and vomiting.
4. **Animal Model:** A lack of model to study the physiology and pharmacology of mechanism of **PONV**, though monkey and dogs are available they don't suffer from pregnancy induced vomiting and motion sickness and post operative and post anesthetic emesis.

THE ANATOMY OF VOMITING CONTROL

There two areas which control or take part in the modulation of vomiting process.

i) The vomiting centre

ii) The chemoreceptor trigger zone.

The vomiting centre

The vomiting centre is located in the reticular formation of the medulla oblongata. These take part in the initiation of vomiting when they are stimulated by certain circulating chemical agents.

The chemoreceptor trigger zone

This centre is in or near the area postrema a 'V' shaped tissue in the lateral wall of the 4^{th} ventricle near the obex. It's a circumventricular organ. This shows response to gastric radiation sickness, uremia, morphine and other emetic agents.

PHYSIOLOGY OF VOMITING

DEFINITIONS

1. Nausea

Its an unpleasant sensation referred to a desire to vomit, not associated with expulsive muscular movement.

2. Retching

When no stomach contents are expelled even with expulsive muscular efforts.

3. Vomiting

It is the forceful expulsion of even small amount of upper gastrointestinal contents through mouth.

There are three major components of vomiting reflex, emetic detectors, integrative mechanism and motor output.

The main sensors of somatic stimuli are located in the gut and chemoreceptor trigger zone.

The emetic stimuli are detected from gut by 2 types of vagal afferent fibres.

a) **Mechanoreceptor:** Located in muscular wall of the gut and are activated by contraction and distension of the gut, on physical damage and manipulation during surgery of proximal gut may induce vomiting in over eating.

b) **Chemoreceptors:** They are situated in the mucosa of upper gut and are sensitive to noxious stimuli.

The CTZ (Chemoreceptor Trigger Zone) lies in the area postrema, which is able to detect the circulatory toxins in the CSF and activates the vomiting centre in the medulla. Afferent impulses from other areas of vestibular labrynthine (morning sickness, input from limbic system and visual cortex) can stimulate it.

The vomiting reflex is divided into two phases.

i) The pre-ejection phase

This is characterised by a sensation of nausea associated with cold, sweating, pupil dilatation, salivation and tachycardia mediated by sympathetic and para sympathetic nerves.

ii) The ejection phase

This consists of retching and vomiting with expulsion of gastric contents.

Causes of vomiting

- Pharyngeal Stimulation
- Gastrointestinal distension
- Abdominal surgery
- Anaesthetic agents
- Pain
- Opiod medication
- Hypoxia – hypotension

- Hypertension
- Vestibular disturbances
- Psychological factors
- Pregnancy / Hormones

Factors influencing post operative emesis

1. Patient factors
2. Pre operative factors
3. Intra operative factors
    a. Anaesthesia factors
    b. Anaesthesia techniques
    c. Surgical factors
4. Post operative factors

Vestibular cardiac afferents can also stimulate the vomiting centre as in myocardial infarction.

The vomiting centre in medulla is also in close proximity to other visceral centres like respiratory and vasomotor centres. Four types of receptors are involved in vomiting.

- Cholinergic receptors (M)
- Dopaminergic receptors (D_2)
- Histamine receptors (H_1)
- Serotonergic receptors (HT_3)

Integrative mechanism

Its a co-ordination between many physiological systems and autonomic and somatic components of nervous system – which occurs in brain stem.

The motor component of vomiting reflex is mediated by both autonomic and somatic senses, and is coordinated by the vomiting system in the brain stem. The vagal neurons that supply the gut and the heart originate in the dorsal motor vagal nucleus and nucleus ambigus. The dorsal and ventral respiratory group which regulate the phrenic nerve output from the cervical spine, are parasympathetic neurons. The output of these nuclei are coordinated to produce the physiologic pattern associated with vomiting.

1. PATIENT FACTORS

a. **Age:** The incidence of nausea and vomiting is 5% in infants, 25% below 5 yrs, 42-51% in 6-16 group and 42-51% in adults.
b. **Gender:** Adult women have 2-4 times greater incidence than men due to female hormones.
c. **Obesity:** Increased frequency of nausea and vomiting is seen because adipose tissue store anaesthetic agents excessively and may also produce excess estrogen.
d. **H/o motion sickness:** Increased risk of PONV in this group.
e. **Delayed gastric emptying:** In patients with intra abdominal pathology pregnancy, diabetes mellitus, hypothyroidism, increased ICT, H/o swallowing blood, full stomach have increased risk of nausea and vomiting.

f. **Smokers:** Non smokers are more prone to than smokers.

2. PREOPERATIVE FACTORS

a. **Food:** Prolonged pre-operative fasting or recent intake of food can both increase the incidence.

b. **Anxiety:** Both psychological stress and anxiety predisposes to emesis.

c. **Reasons for surgery:** Surgery associated with increased ICT, GIT obstruction, pregnancy, abortion or cancer patients on chemotheraphy, have increased risk of emesis.

d. **Premedication:** Atropine delays gastric emptying and lowers the oesophageal tone, opiods like morphine and pethidine decreases gastric motility and gastric emptying. This enhances the release of 5HT from chromaffin cells and releases ADH, also stimulates CTZ.

3. INTRAOPERATIVE FACTORS

1. Anaesthesia factors

a. **Intubation:** Stimulation of pharyngeal mechanoreceptor afferents lead to emesis.

b. **Anaesthetics:** Deeper plane of anaesthesia or gastric inflation during mask ventilation may be a causative factor.

c. **Anaesthesia:** Head movement of patient after awakening leads to sudden vestibular change and increase incidence of PONV.

d. **Anaesthetic drugs:** Opiods, etomidate, and methohexital are associated with high rates of PONV.

e. **Inhalational agents:** Ether and cyclopropane increase the risk of PONV Nitrousoxide too has a significant role in causing nausea. The proposed mechanism of N_2O emesis is its action on opiod receptors, changes in middle ear pressure, sympathetic nerve stimulation and gastric distension.

2. Anaesthetic techniques

The incidence is said to be lower in spinal than in general anaesthesia. Regional anaesthesia is associated with lower incidence.

3. Surgical factors

Ophthalmic surgery, ENT surgery, abdominal surgery, gynecological surgery are associated with increased incidence.

4. Post operative factors

Pain, dizziness, early ambulation, early intake of food increases the incidence.

FACTORS WHICH INCREASE THE RISK OF PONV IN REGIONAL ANAESTHESIA PATIENTS

Patient factors

1. **Age:** Younger age has an increased risk of postoperative nausea and vomiting compared to middle age groups. Age >60yrs also have increased incidence.
2. **Gender:** Increased risk of nausea and vomiting in the female sex than in males. There is also relation of to the menstrual cycle.
3. **Other factors:**
    - H/o motion sickness
    - Non smokers > smokers
    - Obesity

    All the factors have increased risk of PONV.

Systemic anaesthetic factors

1. **Premedication:** The role of premedication in regional anaesthesia remains largely uninvestigated. No conclusion can be drawn from various premedications given except the opiods which remain at risk.
2. **Intraoperative sedation:** Many patients may receive intraoperative sedation to supplement the regional anaesthesia, to improve patient acceptability and comfort, and to reduce the stress and anxiety, while clonidine, propofol and midazolam have no effect on PONV, other drugs like methohexital γ-hydroxy

butyrate and etomidate have increased risk.

3. **Hydration:** Another factor that has been implicated is dehydration. If there is dehydration, there is increased risk of PONV. Probably this effect of dehydration in equated to blood pressure.
4. **Intrathecal medications:** Increased risk of PONV in patients where intrathecal opiods, are used with local anaethetics.

Post – operative factors

There is increased risk of PONV when there is increased post operative pain. This post – operative pain if treated by opiods may therefore increase the risk of PONV.

THE FACTORS WHICH LEAD TO INCREASED RISK OF PONV IN PREGNANCY PATIENTS DURING CAESAREAN SECTION

PATIENT FACTORS

1. There is always increased anxiety stress and pain when the female is coming for caesarean section which itself increases the risk of PONV.
2. The retardation of gastro-intestinal motility and the condition of the stomach fullness has an independent risk of nausea and vomiting.
3. Increased compression of the stomach due to the gravid uterus may cause a problem.
4. Decreased lower oesophageal tone due to the hormone progesterone has an increased risk of vomiting.
5. The presence of female hormones oestrogen, progestrone, human chorionic gonadotropin in increased levels, add to the risk of nausea and vomiting.
6. Anatomical changes in esophageal gastic junction increases the risk of vomiting.
7. The addition of any opiods or other analgesics in the labour room or ward may intern increase the risk of nausea and vomiting.

INTRAOPERATIVE FACTORS

1. **Intraoperative hypotension:** Intra operative hypotension has a greater influence

in the issue of nausea. When there is a greater deal of hypotension, there is increased risk of nausea and vomiting.

2. **Intraoperative O_2 supplementation:** It has been found out that O_2 supplementation during the caesarean section have reduced the incidence of PONV.
3. **Intraoperative sedation:** Avoidance of intraoperative opiod sedations and use of benzodiazepenes such as midazolam to allay the anxiety have reduced the incidence of PONV.
4. **Intraoperative medications:** Intra operative medications given systemically such as prostoglandins, methergine have increased the incidence of postoperative nausea and vomiting.

5. **Surgical factors:**
    i. The compression of uterus from outside the abdominal cavity to deliver the baby, has an increased roll to play in the risk of nausea and vomiting.
    ii. The manual delivery of placenta by compression of uterus and pulling the umbilical cord, is one of the important periods, where the patient complains of nausea.
    iii. The exteriorization of the uterus to secure the bleeding points and compressing of the uterus to prevent post partum hemorrhage, pull the peritoneal attachments and have increase release of vagal discharge, which

is a critical period of nausea and vomiting.

POST OPERATIVE FACTORS

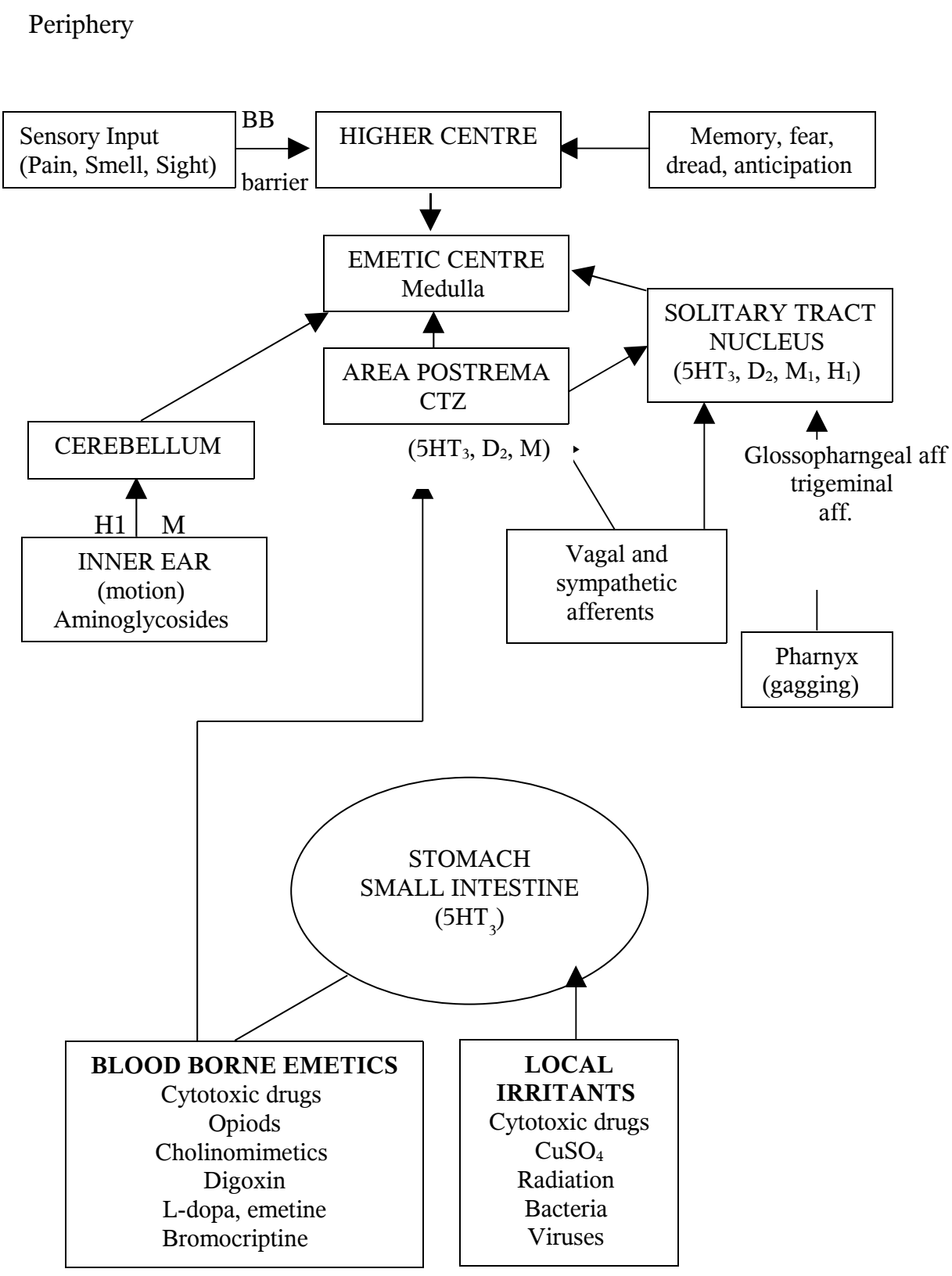
i) The anxiety plays an important role in the post operative period.

ii) The quick decent of the local anaesthetic, and if the patient experiences pain, it may increase the risk of post-operative nausea and vomiting.

iii) Early ambulation may have an important role to play in PONV.

iv) Early oral feeds may also cause increased incidence of PONV.

PHARMACOLOGIST VIEW OF EMETIC STIMULI



RECEPTOR SPECIFIC ANTI EMETIC EFFECTS OF DRUGS, OTHER THAN STUDY DRUGS

Group and drugs	Mechanism of action				Side effects
	D_2	M	H2	5HT	
PHENOTHIAZONES 1. Fluphenazine 2. Chloropramazine 3. Prochlorperazine 4. Promethazine	++++ ++++ +++	+ ++	++ ++++	- +	• Sedation • Extra pyramidal side effects • Cholestatic jaundice • Hemolytic abnormality • Skin sensitization • Hypotension
ANTI-HISTAMINES 1. Diphenhydramine 2. Promethazine 3. Cyclizine 4. Meclizine 5. Hydroxyzine	+ ++	++ ++	++++ ++++	- -	• Sedation • Drowsiness • Depression • Dry mouth
BUTYRO- PHENONES 1. Haloperidol 2. Droperidol 3. Domperidone	++++ ++++ ++++	- - -	+ +	+ -	• Drowsiness • Restlessness • Extrapyranidal side effects
ANTI-					

CHOLINERGICS Hyoscine/Scopalamine Atropine	+	++++	+	-	Dryness of mouth, tachycardia, mydriasis retention of urine
PROKINETICS 1. Benzamides (Metaclopramide) 2. Thiobenzamides 3. Benzimidazole derivative (Domperidone) 4. Benzamide 5. derivatives cisaprid 6. Substituted benzamides. Batanopride/ Zacropride	+++	-	+	++	Dysrrhythmias galactorrhoea. Gynecomastia Amenorrhorea Constipation Diarrhoea Extrapyramidal side effects
$5HT_3$ ANTAGONISTS Ondansetron Granisetron Tropisetron Dolasetron	-	-	-	++++	Allergic reactions Dysarrythmia Bronchospasm Blurred vision

Non – pharmacologic approach

- Acupuncture
- Acupressure

Manual electric stimulation of the P_6 Acupuncture point by needle results in decrease in incidence of PONV upto 6 hrs. Application of pressure on P-6 patient every

2 hrs is reported to produce effect for 24 hrs.

The vomiting reflex

The act of vomiting is a complex, almost convulsive reflex maneuver involving both visceral and striated muscle. Vomiting begins with deep inspiration, elevation of the soft palate to occlude the naso pharynx and glottic closure. Then the proximal area of the stomach relaxes and a giant contraction of the small intestine forces the previously ingested contents to the stomach diluting and buffering the gastric acid. Finally the contraction of the oesophagus muscles pull the stomach into the thorax forming an oesophageal funnel and food is forced out of the stomach by contraction of the abdominal muscles against the lowered diaphragm. If glottis is closed only retching occurs, if the pharynx is relaxed the content is exited through the mouth.

Several autonomic signs precede vomiting. The warning signs include excessive salivation, dilated pupils, tachypnoea, swallowing, pallor, sweating and tachycardia. If nausea proceeds to retching bradycardia may replace tachycardia.

PEPTIDES IMPLICATED IN CAUSING NAUSEA AND VOMITING

Nor – epinephrine

ACTH

Vasopressin

Human chorionic gonadotropin

Angiotensin – II

Bombesin

Thyrotropin releasing hormone

Peptide 77

Leu-Enkephalin

Met. Enkephalin

Cholecystokinin

Insulin

Gastrin

Oxytocin

Neurotensin

Vasoactive intestinal peptide

PHYSIOLOGICAL COMPLICATIONS OF VOMITING

There are several physiological complications of nausea and vomiting that are of concern to the anaesthetist. Possible complications include the following:

1. Aspiration pneumonitis

In an unanaesthetized patient laryngeal reflexes accompany the vomiting reflex, preventing aspiration of the gastric contents. If the laryngeal reflexes are blunted however vomiting can result in regurgitated gastric contents entering the trachea with attendant risk of aspiration pneumonitis.

2. Visceral and wound dehiscence

The act of vomiting causes a considerable increase in both intrathoracic and intra abdominal pressure. If the pharyngeal sphincter is incompletely relaxed at this time, oesophageal rupture can occur. Severe retching and vomiting can lead to a syndrome called Mallory – Weiss lear. In post surgical setting the rise in intraabdominal pressure

can stern visceral anastomosis as well as dehiscence of wound closures. It may also initiate post surgical bleeding secondary to raised intravascular pressure.

3. Electrolyte disorders

Severe prolonged vomiting such as that seen in children with pyloric stenosis causes electrolyte depletion, dehydration and gastric acid loss. The predominant resultant disorder is metabolic alkalosis. Hypokalemia and hyponatremia can occur as well and are exacerbated by renal exerction of K^+ and Na^+ in an effort to conserve H^+.

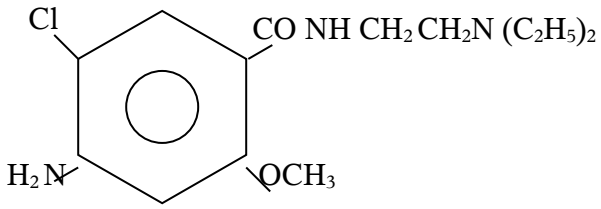
PHARMACOLOGY

Metoclopramide

Metoclopramide comes under the group of substituted benzamides. They are the derivatives of para-amino benzoic acid and are structurally related to procainamide.

The chemical structure of metaclopramide is shown below

Metoclopramide



Metoclopramide is one of the oldest true prokinetic agents. Its administration results in coordinated contractions that enhance transit. Its effects are confined largely to upper digestive tract where it increases lower oesophageal sphincter tone and stimulates antral and small intestinal contractions. Despite having invitro effects on the contractility of colonic smooth muscle, the drug has no significant effect on the motility of the large bowel.

Mechanism of action

The mechanism of action of metoclopramide is complex. In general agents of this class facilitate Ach release from the enteric neurons, an action that may be mediated indirectly by several different mechanisms, which include suppression of $5HT_3$ receptors

and stimulation of excitatory neurons via $5HT_4$ receptors. In addition metoclopramide is distinguished from agents such as cisapride by having both central and peripheral antidopaminergic effects. The former is responsible for its anti-nausea and anti emetic effects, whereas the latter contributes to the prokinetic activity by concentrating the inhibitory effects of dopamine mediated via D_2 dopaminergic receptors on cholinergic enteric neurons.

Pharmacokinetics

Metoclopramide is absorbed rapidly after oral ingestion. Undergoes sulfation and glucronide conjugation in the liver and is excreted principally in the urine with a half life of 4 to 6 hrs. Peak concentration occur with about half an hour thereafter single oral dose with a duration of action that last to 1-2 hrs.

Therapeutic use

Metoclopramide has been used in patients with gastroesophagial reflux disease (GERD). It can produce symptomatic relief without necessarily promoting healing of the associated oesophagitis. Its clearly less effective than the modern day and suppressive medications like the proton pump inhibitors or even H_2-receptor antagonists. And now metoclopramide is rarely used for treatment in GERD.

Metoclopramide is indicated more often in patients with gastroparesis, in whom it may cause moderate improvement in gastric empting.

Metoclopramide injections can be used as an adjunctive measure in medical or diagnostic measures such as intestinal inhibition or contrast radiography of gastrointestinal tract.

Although it has been used in postoperative ileus. Its effect on improving transit time in disorders of small bowel motility is limited.

In general its greatest utility lies in its ability to ameliorate nausea and vomiting that often accompanies gastrointestinal dysmotility syndromes. The effect is mediated by dopamine receptor antagonism within chemoreceptor trigger zone.

Metoclopramide has also been used in persistent hiccups. But its efficacy in this condition is equivocal at best.

Metoclopramide is available at oral dosage forms and has parental preparation for intramuscular and intravenous use. The oral dose ranges from 10-20mg three times daily, 30 minute before meals. The onset of action within 30 to 60 minutes after an oral dose. In patients with severe nausea and vomiting 10 mg can be given intramuscularly (onset of action 10-15 minutes) or intravenously (onset of action 1-3 minutes). Intravenous dosing for patients undergoing chemotherapy can be given as infusion 1.2mg/kg of body weight administered over at least 15 minutes, beginning 30 minutes before chemotherapy and repeated if needed after 2-3 hours. The usual pediatric dose for gastroparesis is 0.1 to 0.2 mg per kg of body weight per dose given 30 minutes before meals and at bed time.

Drug interactions

It hastens the absorption of many drugs example: aspirin, diazepam by facilitating gastric emptying. It reduces the extent of absorption of digoxin by allowing less time for it. Bioavailability of cimetidine is also reduced. By blocking DA receptors in basal ganglia, it abolishes the therapeutic effect of levodopa.

Adverse effects

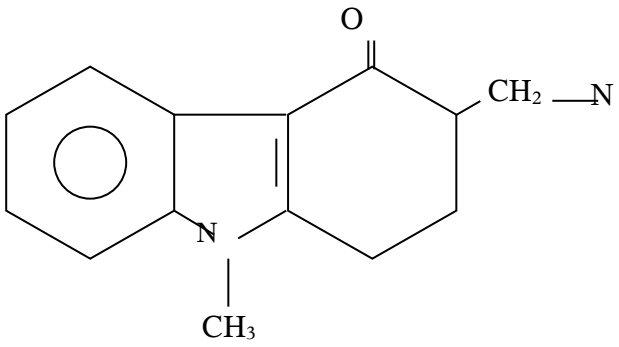
The major side effects of metoclopramide, although rare can be serious and include extrapyramidal effects such as those seen with phenothiazines. Dystonias usually occurring acutely after intravenous administration and parkinsonism like symptoms which may occur several weeks after initiation of therapy. These generally respond to treatment (with an anti-cholinergic or anti-histamine) and are reversible after discontinuation of the drug.

Tardive dyskinesia can also occur with chronic treatment (months to years) but may be irreversible. Extrapyramidal side effects appear to occur more commonly in children and young adults, particularly at high doses. Like domperidone and other dopamine antagonists, metoclopramide can also cause galactorrhea, but this is infrequent.

Methemoglobinemia has been reported occasionally in premature and full term neonates receiving metoclopramide.

ONDANSETRON

CHEMICAL STRUCTURE



CHEMISTRY, PHARMACOLOGICAL EFFECTS AND ACTION

Ondansetron is the prototypical drug of the group of the class of $5HT_3$ antagonists. It was introduced in the year 1990. It was a widely used drug in the chemotherapy induced emesis. The difference to the other drugs in its class such as granisetron, dolasetron, tropisetron is mainly by its chemical structure.

Whether the main site of action of this drug is peripheral or central is not clear. There is evidence that effects at both the location contribute to their efficacy. $5HT_3$ receptors are present in several sites related to emesis, including vagal afferents, the NTS-Nucleus of tractus solitarius (which receive signals from vagal afferents) and the area postrema itself. Serotonin is released by the enterochromafin cells of the small intestine in response to the chemotherapeutic agents and may stimulate vagal afferents

(via $5HT_3$ receptors) and initiate the vomiting reflex. Experimentally vagotomy has shown to prevent cisplatin induced emesis. However the highest concentration of $5HT_3$ receptors in the CNS are found in NTS and CTZ. Antagonists of $5HT_3$ receptors may also suppress vomiting by acting on these sites.

Pharmacokinetics

The difference in plasma half lives of different $5HT_3$ receptor antagonists are not very meaningful in practice as antiemetic effects persists long after these drugs disappear from the circulation. This suggests their continuing interaction at the receptor level. In fact all of these drugs can be administered effectively once a day.

Ondansetron is well absorbed from the gastrointestinal tract. It is extensively metabolized in the liver by cytochrome P450 pathway, followed by glucuronide and sulfate conjugation. Patients with liver dysfunction have a reduction in plasma clearance and some adjustment in dosage is advisable. Some reduction in ondansetron clearance is seen in elderly patients but no dosage adjustment is advised.

Therapeutic use

Ondansetron is effective in treating chemotherapy induced nausea and in treating nausea secondary to upper abdominal irradiation, were all the $5HT_3$ antagonists are efficacious.

Ondasetron is also effective in hyperemesis of pregnancy and to post operative nausea, but not to motion sickness.

Ondansetron is available as tablets, oral solution and intravenous preparation for

injections. For patients on cancer chemotherapy, this drug can be given in a single intravenous dose or as a continuous infusion over 15 minutes beginning 30 minutes before chemotherapy or in 2 to 3 divided doses, with the 1st dose given 30 minutes before and subsequent doses at various intervals in drug chemotherapy.

For post operative nausea and vomiting, this drug can be given intravenously during the intra operative period. Reports of efficacy in vomiting associated with drug over dosage, side effect of cotrimoxazole and fluvoxamine, uremia and certain neurological injuries are also available.

Adverse effects

In fact, ondansetron is well tolerated with the most adverse effects being constipation or diarrhea, headache and light headedness. A class of these agents have shown to induce minor electrocardiographic changes. But these are not felt clinically significant in most number of cases. Rashes and allergic reactions can occur specially after it injections.

DEXAMETHASONE

Dexamethasone is a very potent and highly selective glucocorticoid. It is a long acting drug.

PHARMACOLOGICAL ACTIONS

1. Carbohydrate and protein metabolism

Glucocorticoids promote glycogen deposition in the liver (They are analysed in the basis of this action) by inducing hepatic glycogen synthetase and promoting glyconeogenesis. It inhibits glucose utilisation in peripheral tissues. This along with increased glucose release causes insulin resistance and a diabetes like state. It causes protein breakdown and amino acid mobilization from peripheral tissues, responsible for side effects like muscle wasting. The amino acids are funneled into the liver and used for glyconeogensis. Excess urea is produced and these cause negative nitrogen balance.

Fat metabolism

This action is primary permissive in nature. It promotes lipolysis due to glucagon, growth hormone, adrenaline and thyroxine. Cyclic adenosine mono phosphate (CAMP) induced breakdown of triglycerides are enhanced. Fat areas in various sites respond differently and redistribution of fat occurs. More fat is deposited in the face, neck, shoulder – (moon face, fish mouth and buffalo hump), and there is loss of subcutaneous

fat over the extremities. The explanation to this is because the peripheral adipocytes are less sensitive to insulin, and corticosteroid enhanced lipolytic action of adrenaline and growth hormone predominates.

Calcium metabolism

It inhibits the intestinal absorption of calcium and increase renal excretion of calcium. There is also loss of Ca from bone indirectly due to loss of osteoid in chronic use. Spongy bones (vertebra, ribs etc) are more sensitive.

Water excretion

Effect on water excretion is independent of action on Na transport, in maintaining GFR.

In adrenal insufficiency the capacity to excrete a water load is considerably reduced.

Glucocorticoid enhances the secretory capacity of renal tubules.

Cardiovascular system

Glucocorticoids restrict capillary permeability and maintain tone of arteries and myocardial contractility. It has permissive effect on pressor action of adrenaline and angiotensin. They also play a role in development of hypertension and should be cautiously used in hypertensives.

Skeletal muscles

Optimal level of corticosteroids are needed for normal muscular activity,

weakness may occur in both hypo and hypercortism but the effects may be different.

Hypocortism – weakness due to hypodynamic circulation

Hypercortism – excess glucocorticoid action → muscle wasting → myopathy → weakness.

Central nervous system

Mild euphoria is common with pharmacological doses of glucocorticoids. This is due to a direct effect on brain, independent of relief of disease symptoms, sometimes progresses to cause increased motor activity, insomnia, anxiety or depression. It also maintains the level of sensory perception and normal level of excitability of neurons. High doses, lower seizure threshold in epileptics.

Stomach

Secretion of gastric acid and pepsin is increased and may aggravate peptic ulcer.

Lymphoid tissue and blood cells

Glucocorticoid drive can raise the rate of destruction of lymphoid cells (T cells are more sensitive than B cells). However a marked lytic response is shown by malignant lymphatic cells – usually in lymphomas.

Corticosteroid increases the number of RBCs, platelets and neutrophils in the circulation. They decrease lymphocytes, basophils and eosinophils. These are due to sequestration of cells. The count becomes normal in 24 hrs.

Inflammatory responses

Irrespective of type of injury or insult, the attending inflammatory response is

suppressed by glucocorticords. This is the basis of most of their clinical uses. It lowers all stages of inflammation. The action are direct and even local application is possible. The cardinal signs of inflammation such as redness, heat, swelling and pain are suppressed.

Corticosteroids are only palliative, the underlying disease processes continues while manifestations are dampened.

Immunological and allergic response

They cause greater suppression of cell mediated immunity in which T cells are primarily involved example: delayed hypersensitivity and graft rejection. It decreases the release of interleukin-1 and interleukin -2.

Pharmacokinetics

Dexamethasone is a water soluble ester, in the form of dexamethasone sodium phosphate. It has an oral, intramuscular or intravenous preparation. It acts rapidly and attain high concentration in tissue fluids.

Dexamethasone is mainly metabolized in the liver by hepatic microsomal enzymes.

The t ½ of dexamethasone in greater than 36 hrs, its action starts within 30 minute of injection and action persists even after the drug disappears from the circulation.

Drug interaction

Phenobarbitone and phenytoin induce metabolism of dexamethasone to decrease its therapeutic effect.

USES

1. **Arthritis:** Used in rheumatoid arthritis in conjunction with NSAIDs, arthritis in rheumatic fever and in gouty arthritis.
2. **Collagen diseases:** In disease like systemic lupus erythematosus, polyarteritis nodosa, dermatomyositis, this drug may be life saving.
3. **Severe allergic reactions:** Used in anaphylaxis for short periods, in angioneurotic edema, urticaria, serum sickness.
4. **Autoimmune diseases:** Autoimmune hemolytic anemia, thrombocytopenia, active chronic hepatitis respond to corticosteroids.
5. **Bronchial asthma:** Used intravenously in status asthmaticus.
6. **As an adjunct to drug in nausea and vomiting:** As it prevent the release of inflammatory mediators and prostoglandins, they modulate neuronal activity and have a membrane stabilising action. It has a minimal action in nausea and vomiting. It increases the efficacy of the drug which is co-administered.
7. **Eye disease:** Allergic conjuctivitis, iridocyclitis, keratitis
8. **Intestinal disease:** In diseases like crohns, ulcerative colitis, celiac disease with remissions and exacerbations.
9. **Cerebral edema:** In cerebral edema due to meningitis and tumours. dexamethasone is preferred because, it does not have Na retaining capacity. Large

doses given in spinal injury can reduce neurological sequalae.

10. **Malignancies:** As a component of chemotherapy, in ALL, Hodgkin's and other lymphomas.
11. **In organ transplantations and skin allograft:** To prevent rejection.
12. **To test adrenal** – Pituatary axis function.

Contraindications for chronic use

These are only relative contraindications since, the steroid dexamethasone is a life saving drug they are, peptic ulcer, diabetes mellitus, hypertension, viral and fungal infections, tuberculosis and other infections, osteoporosis, herpes simplex keratitis, psychosis, epilepsy, congestive heart failure, renal failure.

GLYCOPYRROLATE

Glycopyrrolate is a semisynthetic preparation of belladona and is a quartenary ammonium derivative. It is potent than any other anticholinergic compound but lacks CNS activity.

Mechanism of action

All the anticholinergic drugs including glycopyrrolate combine reversibly with cholinergic muscuranic receptor and prevent the access of acetylcholine to these sites.

Molecular cloning of muscuranic receptors and its site

M1 – CNS, stomach

M2 – Heart, CNS

M3 – CNS, salivary glands, airway smooth muscles

M4 – CNS, Heart

M5 – CNS

Muscuranic receptors are example of protein coupled receptors.

Muscuranic cholinergic receptors that control salivary and bronchial secretions are inhibited by lower doses of glycopyrrolate, which can also cause effects on heart.

Comparative effect of glycopyrrolate with other anticholinergic drugs

	Glycopyrrolate	**Atropine**	**Scopolamine**
Sedation	0	+	+++
Antisialogogue	++	+	+++
Increased heart rate	++	+++	+
Smooth muscle relaxation	++	++	+

Mydriasis	0	+	+
Decreased gastric secretion	+	+	?
Alteration of fetal heart rate	0	0	

- The variable antisialogogue dose of glycopyrrolate is 5 to 8µg/kg body weight.
- Glycopyrrolate may increase metabolic oxygen consumption.
- Glycopyrrolate has increased potency in inhibiting the salivary and tracheal secretions compared to atropine.
- It does not cross the blood - brain barrier so it has no action on the central nervous system.

But it has increased vagal inhibitory action of vagal afferents from the intestine and blocks the vagal stimulation during anaesthesia and surgery, hence used to minimize the effect of handling during surgery.

MATERIALS AND METHODS

This is a prospective, double blind study conducted at Government Rajaji Hospital attached to Madurai Medical College.

After approval by the ethical committee, 160 women of ASA grade I & II who came for caesarean delivery under spinal anaesthesia, were entered in this study.

Women with history of hepatic dysfunction, history of previous post operative nausea and vomiting, diabetes patients, hypertensive patients, history of allergies to local anaesthetics, and patients with inadequate starvation <6 hrs were excluded from the study. Patients were randomised to receive one of the combination of drugs intravenously during induction. Only injection ranitidine 50mg IV was given as premedication.

On arrival to the operation theatre, intravenous access was established and oxygen saturation by pulseoximeter was estimated continuously. Non invasive blood pressure monitor was attached to monitor the BP manually. Pulse rate and oxygen saturation was monitored by the pulseoximeter.

The patients were preloaded with 500ml of crystalloids.

Group MD (Metoclopramide plus dexamethasone)

These patients will receive injection metoclopramide 10 mg plus injection dexamethasone 8 mg intravenously during preloading.

Group OD (Ondansetron)

These patients will receive injection ondansetron 4 mg intravenously during preloading.

Group G (Glycopyrrolate)

These patients will receive injection glycopyrrolate 0.2 mg intravenously during preloading.

Group C (the control group)

This is the group which will receive 2ml of normal saline IV during preloading.

Then the patients would by made to lie down in the right lateral position. After strict aseptic precautions subarachanoid block will be performed in L_3 L_4 space using 23 gauge quinke spinal needle. The drug used was 1.8ml of 0.5% hyperbaric bupivicaine.

After spinal anaesthesia, patients were put in supine position and draped. Then the surgery was proceeded. Pulse and the blood pressure were monitored continuously. If hypotension arised and if systolic BP reduces more than 20 percent from the baseline, injection ephedrine 6 mg intravenous was given.

Injection methergine 0.2mg IV and injection oxytocin 10 mg in drip was routinely given after umbilical cord clamping of the baby.

The patients were continuously monitored intraoperatively and post operatively for any nausea, retching or vomiting. The follow up was done upto 4 hours postoperatively.

Rescue antiemetic in the postoperative and intraoperative period will be injection ondansetron .4 mg IV,

The patients sedation was also noted and graded.

The nausea and vomiting response was graded as follows:

Emesis score

0 - No nausea

1 - Mild nausea

2 - Severe nausea

3 - Retching

4 - One episode of vomiting

5 - Vomiting greater than 1 episode

Parameters which were also observed were duration of surgery, pulse rate, systolic BP, sedation of the patient and APGAR of the baby.

The sedation was graded as follows by Ramsay sedation score

1 – Anxious

2 - Co-operative and oriented

3 – Responds to commands

4 – Patient asleep – responds only to loud sound

5 – Sluggish response

6 – No response

The study ends after 4 hours of surgery.

STATISTICAL METHOD

Results were established on mean ± standard deviation statistical significance was determined by students t test.

OBSERVATION

In our study totally 160 patients were studied – Four groups of 40 each. One group was the control group (group-C), and the other three group were designated as Group – G (glycopyrrolate group), Group – MD (Metoclopramide and Dexamethasone group), Group – OD (Ondansetron group). As in table I and II in the control group of 40, 8 cases had intraoperative nausea and vomiting, 11 cases had intraoperative fall in BP, and 26 cases had postoperative nausea and vomiting. Rescue antiemetic injection ondansetron was given to 7 cases intraoperatively and 26 cases postoperatively totally. The occurrence of PONV was about 65% in the control group. In those 26 cases which had nausea and vomiting postoperatively, 6 cases had mild nausea, 8 cases had severe nausea, 8 cases retching and the remaining cases vomited once.

In the G-group (glycopyrrolate) out of the 40 cases, 12 cases had intraoperative fall in BP, 6 cases had intra-operative nausea and vomiting and 16 cases had postoperative nausea and vomiting. Rescue anti-emetic injections ondansetron was given to 7 cases intraoperatively, who did not have PONV later. The occurrence of PONV was 40%, ie., 16 cases out of 40. Out of them 6 cases had mild nausea, 3 cases had severe nausea, 4 cases had retching and the remaining cases vomited once.

In the group-MD (Metoclopramide plus dexamethasone group) the fall in blood

pressure was present in 13 cases. 4 cases had intraoperative nausea and vomiting. Post-operative nausea and vomiting was seen in 7 cases out of the 40 cases. In those seven cases 6 cases had mild nausea and 1 case had retching. The occurrence of PONV in this group was 17.50 percent.

In the O-group (Ondansetron group), 14 cases had intraoperative fall in BP, 4 cases had intraoperative nausea, 8 cases had postoperative nausea and vomiting. Out of the 8 cases of PONV, 5 cases had mild nausea, 1 case had severe nausea and 2 cases had retching. The occurrence of PONV was 20 percent.

The observation are represented in the tables I, II and III.

DISCUSSION

In our study the occurrence of post operative nausea and vomiting was 65% in the control group. In the study conducted by A.K. Pan et al the occurrence of PONV was in 75% in the placebo group of caesarean delivery under spinal anaesthesia and in the study conducted by Biswas et al the occurrence of PONV in placebo group was 40%

In the glycopyrrolate group the occurrence of post operative nausea was 40% in our study. Out of them 22% had nausea, 10% had retching and 7% had vomiting. In the study conducted by Biswas et al the occurrence of nausea was 10%.

In the ondansetron group the occurrence of nausea and vomiting was 20% in our study. Out of the 15% had nausea and 5% had retching. In the study conducted by Dr. A.K. Pan et al 2003. the ondansetron group had an incidence of 10% PONV. Versus 75% in the placebo group. In his study there were cases of vomiting reported. But in our study no case had vomiting, only nausea and retching were reported.

In the metoclopramide plus dexamethasone group the incidence of PONV was 17.5%. Out of those, 15% had nausea and 2.5% had retching. There was no report of vomiting. In the study conducted by Biswas et al using metoclopramide alone the incidence of PONV was 30%, whereas in our study by combining metoclopramide with dexamethasone,the incidence of PONV has been reduced to 17.5%.

Though in all the cases a little correlation between the fall in blood pressure and

intraoperative and postoperative nausea vomiting, all the cases who had hypotension did not get nausea of vomiting. The correlation was not statistically significant. (P>0.05).

The intraoperative rescue drug was also taken into account in our calculation. The Null hypothesis was framed as there will be no nausea and vomiting postoperatively in the cases where the drugs were administered pre-operatively.

The P value was 0.9760 (P>0.05) Hence null hypothesis accepted.

Comparing the individual group, first comparing the glycopyrrolate group with the ondansetron group, (OD group versus G group) and applying the student 't' test , the P value obtained was 0.015,(P value <0.05). So there was significant difference between the drug ondansetron and glycopyrrolate for prevention of PONV. Moreover in the ondansetron group there were only 8 cases of PONV compared to 18 cases in the glycopyrrolate group.

While comparing the metoclopramide plus dexamethasone group with the glycopyrrolate group, the group MD had only 7 cases of PONV compared to 18 cases in the glycopyrrolate group (G). The test of significant value was 0.0068 (P<0.05). Hence the two groups were statistically significant.

When comparing the two groups metoclopramide plus dexamethasone group (MD) and ondansetron (group – OD), 7 cases out of 40 cases had nausea and vomiting

in the MD group and 8 cases out of 40 cases in the ondansetron group (OD).

The test of significance value between these two groups was 0.77 (P-Value) (P>0.05). Hence there two groups showed no statistical difference between them in control of postoperative nausea and vomiting. Though in the patients who received metaclopramide and dexamethasone, out of 7 cases only 1 case had retching and 6 cases had only mild nausea post operatively.

In the patients who received ondansetron out of 8 cases who had PONV, 5 cases had mild nausea, 1 case had severe nausea and 2 cases had retching, showing that metoclopramide dexamethasone combination is slightly more advantageous than ondansetron group.

In the aspect of sedation, the metaclopramide plus dexamethasone group had average sedation score of 2.87, most of the people had the sedation score of 2 (co-operative and oriented), 8 people had the sedation score of 4 (patient asleep, responds to loud sound).

In the ondansetron group all the patients had a sedation score of 2, (Cooperative and oriented).

In the glycopyrrolate group the patients had an average sedation score of 1.8% where as most of the patients had a score of 2(Cooperative and oriented).

SUMMARY AND CONCLUSION

The occurrence of postoperative nausea and vomiting in caesarean delivery under spinal anaesthesia can occur upto 67% without usage of prophylactic antiemetic drugs.

In fact in my study the occurrence of PONV was about 65%. The occurrence of peripartum emetic episodes are infact distressing to the patient and disturbing to the surgeons. Our main aim of the study was to find out a good prophylactic anti-emetic agent to prevent the postoperative emesis of caesarean delivery patients under spinal anaesthesia.

One hundred and sixty patients were allocated into four group of forty each and they received glycopyrrolate 0.2m.gIV, injection ondansetron 4 mg, injection metoclopramide plus dexamethasone 5 mg, and 2 ml normal saline randomly. The drug was given before spinal anaesthesia during preloading.

The occurrence of PONV in the control group was nearly 65% without any antiemetics.

In the comparing the other three groups, the incidence was 45% in glycopyrrolate. Though glycopyrrolate had reduced incidence of PONV it has not completely reduced it in a significant level.

In the metoclopramide plus dexamethasone group, the occurrence of PONV was 17.5% and in the ondansetron group the occurrence was 20%. Both the drugs significantly reduced the incidence of postoperative nausea and vomiting in the caesarean patients. There was no statistical difference between these groups. But comparing the severity of nausea in the patients of these two groups , the metoclopramide group patients showed less severity compared to the ondansetron group in number and emesis score.

Comparing their cost effectiveness, the combination of dexamethasone and metoclopramide is cost effective than the drug ondansetron and hence can be used as good anti-emetic combination. Though there was mild sedation in certain patients where metoclopramide was administered, it did not create any problem but infact kept the patient calm and cool.

BIBLIOGRAPHY

1. Anesthesia and Postoperative complication – Jonathan L. Benumof
2. Current management of postoperative nausea and vomiting Br. J. Anaesthesia 1992 – (69).
3. Good man and Gillman's textbook of Pharmacology – 10^{m} edition.
4. Physiology of nausea and vomiting – Br. J. Anesthesia = 1992 (69)
5. Post operative nausea and emesis – Watcha MF. Anaesthesia clinic. North America
6. Postoperative nausea and vomiting (PONV) – A review article – Dr. Saeeda Islam et al. Ind.J. Anesthesia 2004 (August).
7. Prophylactic single dose administration of ondansetron for caesarean patients for spinal anaesthesia – A.K. Dan et al. Ind. J. Anaesthesia 2003 (47).
8. Surgical and patient factors involved in postoperative nausea and vomiting. – Lerman J et al.
9. Text book of Pharmacology – K.D. Tripathy – 6^{m} edition.
10. Un anticipated admission to hospital following ambulatory surgery – ISMA 1989.

11. Administration of metoclopramide for prevention of nausea and vomiting during epidural analgesia for elective caesarean delivery – Chest nut et al Anaesthesiology – 1987.

12. Single dose ondansetron in the prevention of post operative nausea and vomiting - Anaesthesia – 1994(49-11-15) .

13. Physiology and pharmacology of post operative nausea and vomiting - Anaesthesia – 1994.

14. Comparative study of glycopyrrolate, dexamethasone and metoclopramide in control of post operative nausea and vomiting for caesarean delivery under spinal anaesthesia – Biswas et al Indian journal of Anaesthesia 2003.

15. Comparison of ondansetron versus placebo for nausea, vomiting for caesarean delivery under spinal anaesthesia – Association of anaesthetists GB and Ireland Volume 54.

PROFORMA

DEPARTMENT OF ANAESTHESIOLOGY
MADURAI MEDICAL COLLEGE

Dr.S.M.Senthilnathan, MDPG

PROPHYLACTIC ANTI-EMETICS IN PREVENTION OF PONV IN CAESAREAN SECTION UNDER SAB

Name of the patient : Date : ASA Risk – I/II

Age : IP.NO :

Premedication : Inj Ranitidine 50 mg IV Indication:

Group

A – Inj glycopyrrolate 0.2mg IV

B – Inj ondansetron IV

C – Inj Metaclopramide + Dexmethasone 8 mg IV

D – Control

Intra operative period

Time	PR	SBP	SPO_2
5 Min			
10 Min			
20 Min			
30 Min			
45 Min			
1 Hr			

Duration of Surgery

Intra operative → Nausea / Vomiting / Retching

Rescue anti-emetic → yes / No

APGAR OF BABY →

POST – OPERATIVE PERIOD FOR 4 HRS

Emesis score →

Sedation Score →

EMESIS SCORE

0 – No Nausea

1 - Mild nausea

2 - Severe nausea

3 – Retching

4 - Vomiting once

5 – Vomiting >1 time

Ramsay Sedation Score

1 – Anxious, agitated or restless

2 – Co-operative but oriented

3 – Responds to commands

4 – Pt. asleep – responds to loud sound (Brisk response)

5 – Sluggish response

6 – No response