"COMPARISON OF THREE GROUPS OF ANTIEMETIC DRUGS FOR PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING AFTER MIDDLE EAR SURGERY "

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

INSTITUTE OF ANAESTHESIOLOGY AND

CRITICAL CARE

MADRAS MEDICAL COLLEGE

CHENNAI- 600003

MAY 2018

CERTIFICATE

This is to certify that the dissertation titled **"COMPARISON OF THREE GROUPS OF ANTIEMETIC DRUGS FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING AFTER MIDDLE EAR SURGERY"** submitted by DR.M.KASI in partial fulfilment for the award of the degree of DOCTOR OF MEDICINE IN ANAESTHESIOLOGY by The Tamilnadu Dr.M.G.R MEDICAL UNIVERSITY, CHENNAI is a bonafide record of work done by him in the INSTITUTE OF ANAESTHESIOLOGY& CRITICAL CARE, Madras Medical College, during the academic year 2015 -2018 .

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CERTIFICATE OF THE GUIDE

This is to certify that the dissertation titled **"COMPARISON OF THREE GROUPS OF ANTIEMETIC DRUGS FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING AFTER MIDDLE EAR SURGERY "** in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamil Nadu Dr. M.G.R. Medical University, Chennai., is a bonafide record of the work done by him in the INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE, Madras Medical College and Rajiv Gandhi Government General Hospital, during the academic year 2015-2018.

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Place:

DECLARATION

I hereby declare that the dissertation titled **"COMPARISON OF THREE GROUPS OF ANTIEMETIC DRUGS FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING AFTER MIDDLE EAR SURGERY"** has been prepared by me under the guidance of **PROF.DR.VELLINGIRI,MD,DA,** Professor of Anaesthesiology, Institute of Anaesthesiology & Critical care, Madras Medical college, Chennai, in partial fulfilment of the regulations for the award of the degree of M.D (Anaesthesiology),examination to be held in April 2018.

This study was conducted at Institute of Anaesthesiology & Critical care, Madras Medical College, Chennai.

I have not submitted this dissertation previously to any journal or any university for the award of any degree or diploma.

Date:

Place: Chennai **DR.M.KASI**

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CERTIFICATE OF APPROVAL

To
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Dear Dr.M.Kasi,

The Institutional Ethics Committee has considered your request and approved your study titled **"COMPARISON OF THREE GROUPS OF ANTIEMETIC DRUGS FOR PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING AFTER MIDDLE EAR SURGERY" - NO.15022017 (II)**

The following members of Ethics Committee were present in the meeting hold on **21.02.2017** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.M.K.Muralidharan,MS.,M.Ch.,Dean, MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD., Prof.of Pharmacology.,MMC,Ch-3	: Member
5.Prof.K.Ramadevi,MD.,Director,Inst.of Bio-Che,MMC,Ch-3	: Member
6.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
7.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
8.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
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PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"COMPARISON OF THREE GROUPS OF ANTIEMETIC DRUGS FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING AFTER MIDDLE EAR SURGERY"** of the candidate **Dr. KASI. M.** with registration number **201520006** for the award of **M.D.** in the branch of **ANAESTHESIOLOGY.** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion 78 pages and the result shows **9 percentage** of plagiarism in the dissertation.

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ABSTRACT

BACKGROUND:

The incidence of postoperative nausea and vomiting (PONV) after middle ear surgery is 30 to 40 % and higher in high risk individuals. In this study we want to compare the antiemetic effects and efficacy of three groups of drugs, intravenous Ramosetron with Dexamethasone, Ondensetron with Dexamethasone and Metoclopramide with Dexamethasone as a prophylatic administered before surgery in patients undergoing middle ear surgeries.

MATERIALS AND METHODS:

We enrolled 120 patients that were randomly divided into four groups of 30 in each. Group I received 2ml distilled water with Dexamethasone IV 8mg one hour before end of surgery ;

Group II received Ramosetron 0.3mg with Dexamethasone 8mg IV given one hour before end of surgery.

Group III received Ondensetron 4mg with Dexamethasone 8mg IV given one hour before end of surgery

Group IV received Metoclopramide 10mg with Dexamethasone 8mg IV given one hour before end of surgery

Incidence and severity of PONV were recorded in each group for 24 hours in the post-anesthesia care unit (PACU) .The duration after which the rescue antiemetic was given was also recorded for each group. Dose of Rescue antiemetic drug usage also noted. The severity of pain intensity was assessed by visual analogue scale (VAS) after repeated intervals .The side effects of the study drug like headache , dizziness , allergic reaction etc ., if any were assessed and recorded.

RESULT:

The incidence of nausea is least in first few hours (6 hours) in group R+D compared to other groups . Incidence of nausea and vomiting at different time intervals in Groups R+D and Group O+D were remains same and not statistically significant. There was no significant difference in the incidence of side effects like respiratory depression,headache , extra pyramidal disorders, drowsiness, dizziness, vertigo and allergic in all the groups . Need of Rescue antiemetic need was substantially reduced in R+D and O+D group .

Key Words:

$5HT_3$ receptors, Ramosetron , Ondansetron, Metoclopramide , post operating nausea and vomiting (PONV), Efficacy

INTRODUCTION

It is now very well understood that post operative nausea and vomiting (PONV) is no longer just a discomfort , but it is a significant cause of postoperative morbidity. It has psycological, physiological and economic implications for both the patient and health care providers. Every effort should therefore be made to prevent it. Like pain, PONV is no longer acceptable in modern day anaesthetic practice.

Post operative vomiting results in complications which affect the success of the surgery or procedure . It also affects patient safety because it alters hemodynamic parameters and it rises chance of aspiration significantly . It is also a distressing side effect associated with esophageal rupture, dehydration, pulmonary aspiration, electrolyte imbalances, raised intracranial and intraocular pressure. Wound complications such as rebleeding and hematoma formation, wound dehiscence, increased pressure on suture lines and venous hypertension in skin flaps can also occur. Recovery is always delayed in patients with persistent PONV and also cost of hospital stay increases substantially . Amelioration of PONV has become even more important in day care surgery , an essential part of modern health care.. PONV also prolongs hospital stay and unplanned overnight admission after day care surgery. Return to normal daily activities is delayed by PONV and so is employment . It creates a negative impact on patients towards day care surgery.

More resources are spent on PONV as this disrupts patient comfort and psychology . More nursing time and care is required, extra drugs and intravenous fluids are needed to correct dehydration , hospital bed stay is increased and care to other patients is adversely affected . PONV is feared by most patients and is the yard stick by which they judge the efficency of their anaesthetist .

There are many factors associated with PONV and these can be related to the patient, the surgery, anesthestic procedure , perioperative drug usage and other perioperative events .There is also considerable difference among patients: females are three times more susceptible to PONV than males under the same surgical conditions. Patients with a previous history of PONV have a threefold increased risk of PONV .

PONV has equally been noted to be increased in some disease conditions and certain surgical procedures. It is increased in abdominal laparoscopic surgeries and also in head and neck surgeries. Among various surgeries middle ear surgery is notorious for Post Operative Nausea and Vomiting. Various antiemetic drugs and interventions have been proposed to overcome this problem. It is more common following general anaesthesia occurring in 30 to 40% of all patients .PONV is considered as the most troublesome side effect which occurs 24 to 48 hrs after surgery. It can be prevented to some extent by changing anaesthetic technique or drugs and relieving patient anxiety preoperatively.

Antiemetic prophylaxis is not routinely recommended for all patients undergoing general anaesthesia . It is reserved only for surgeries that have high risk for Post Operative Nausea and Vomiting. Various classes of drugs are used to prevent PONV like anti-dopaminergic, anti-cholinergic, phenothiazines and butyrophenones . These drugs have prominent side effects like dry mouth, sedation and extra pyramidal symptoms. The introduction of 5 HT3 receptor antagonists in 1990 , it revolutionised antiemetic therapy .

In this study we are evaluating the antiemetic effect and efficacy of three groups of drugs after middle ear surgery , Ramosetron (0.3 mg) with Dexamethasone (8mg) Vs Ondensetron (4mg) with Dexamethasone(8mg) Vs Metoclopramide (10mg) with Dexamethasone(8mg).

AIM AND OBJECTIVES

The aim of our study is to compare the antiemetic efficacy of prophylactic intravenous administration of a combination of antiemetic drugs Ramosetron ,Ondensetron and Metoclopramide with Dexamethasone for prevention of Post operative nausea and vomiting after middle ear surgery

Secondary objectives

- To evaluate the need for rescue antiemetic after surgery
- To assess post operative pain intensity using Post operative visual analogue scale pain score.
- Side effects and complication rates.
- To evaluate post operative opioid dosage.

NEURO PHYSIOLOGY OF NAUSEA AND VOMITING

NAUSEA:

Nausea is the subjective sensation of an urge to vomit, in the absence o f expulsive muscular movements; when severe, it is associated with increased salivary secretion, vasomotor disturbances, and sweating.

VOMITING:

Vomiting or emesis is defined as forcible expulsion through the mouth of the gastric contents. Vomiting results from coordinated activity of the abdominal, intercostal, laryngeal and pharyngeal muscles, including retrograde giant contraction of the intestines, relaxation of the gastric fundus, closure of the glottis and elevation of the soft palate..

RETCHING:

It is defined as laboured rhythmic activity of the respiratory musculature that usually precedes or accompanies vomiting.

PHASES OF VOMITING:

There are two primary phases involved in emesis:

1. The prodromal phase,
2. The vomiting phase.

PRODROMAL PHASE:

1. It may be accompanied by nausea

2. Stimulation of sympathetic system leads to increase in heart rate , my driasis and cutaneous vasoconstriction.

3. Stimulation of parasympathetic system leads to salivation and gastro-intestinal motor activity.

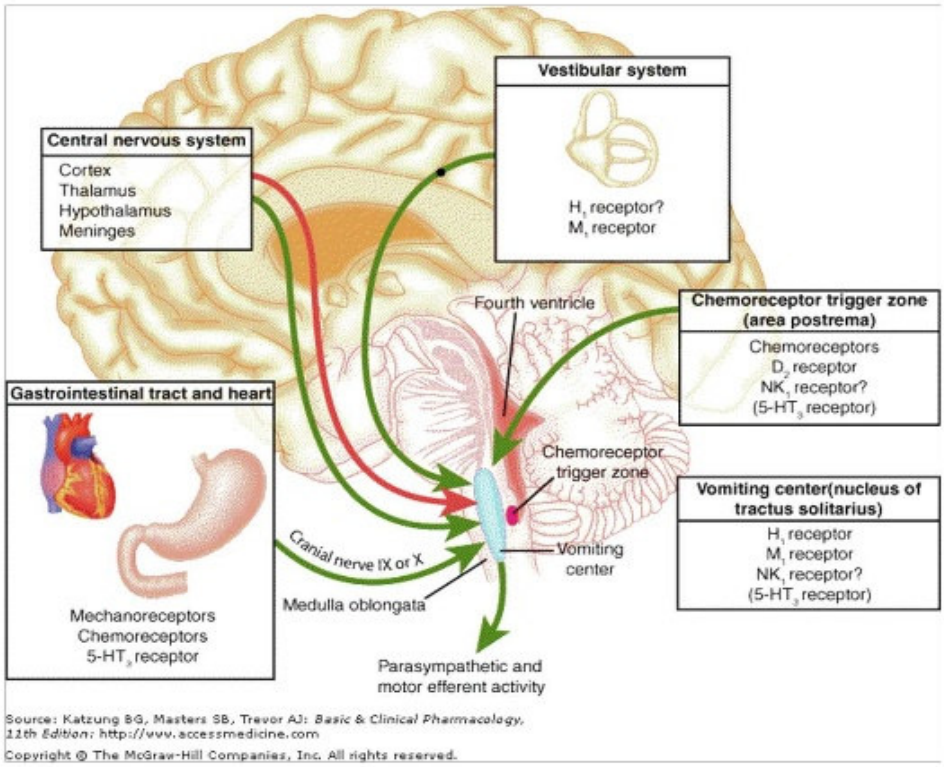
VOMITING PHASE:

The first effects after stimulating vomiting centre are

- A deep breath is taken, the glottis is closed and the larynx is raised to open the upper esophageal sphincter.
- The soft palate is elevated to close off the posterior nares.
- The diaphragm is contracted sharply downward to create negative pressure in the thorax, which facilitates opening of the esophagus and distal esophageal sphincter.
- Simultaneously with downward movement of the diaphragm, the muscles of the abdominal walls are vigorously contracted, squeezing the stomach contents and thus elevating intragastric pressure. With the pylorus closed and the esophagus relatively open, the route of exit is clear

VOMITING CENTRE:

It is located in the medulla oblongata in close proximity to the respiratory centre, salivation nuclei, vestibular nuclei, vasomotor nuclei. It receives stimulus from various regions like chemoreceptor trigger zone(CTZ) nucleus Tractus solitarius(NTS), afferents from the abdomen , vestibular system and from certain higher centres.



CHEMORECEPTOR TRIGGER ZONE:

The chemoreceptor trigger zone is a bilateral set of centers in the brainstem lying under the floor of the fourth ventricle. Electrical stimulation of these centers does not induce vomiting, but application of emetic drugs does - if and only if the vomiting centers are intact. The chemoreceptor trigger zones function as emetic chemoreceptors for the vomition centers - chemical abnormalities in the body (e.g. emetic drugs, uremia, hypoxia and diabetic ketoacidosis) are sensed by these centers, which then send excitatory signs to the vomition centers. Many of the antiemetic drugs act at the level of the chemoreceptor trigger zone.The blood brain barrier is poorly developed in this region.

Vomiting may be triggered through a variety of different input mechanisms including PONV, pregnancy sickness, radiation-induced emesis.

cancer chemotherapy-induced emesis, food poisoning, psychogenic vomiting, motion sickness, and blood poisoning. Afferent sources for emesis to vomiting centre include the abdominal viscera, heart, vestibular system, brain stem area postrema chemoreceptor trigger zone(CTZ), and higher brain centres.

ABDOMINAL VISCERAL AFFERENTS:

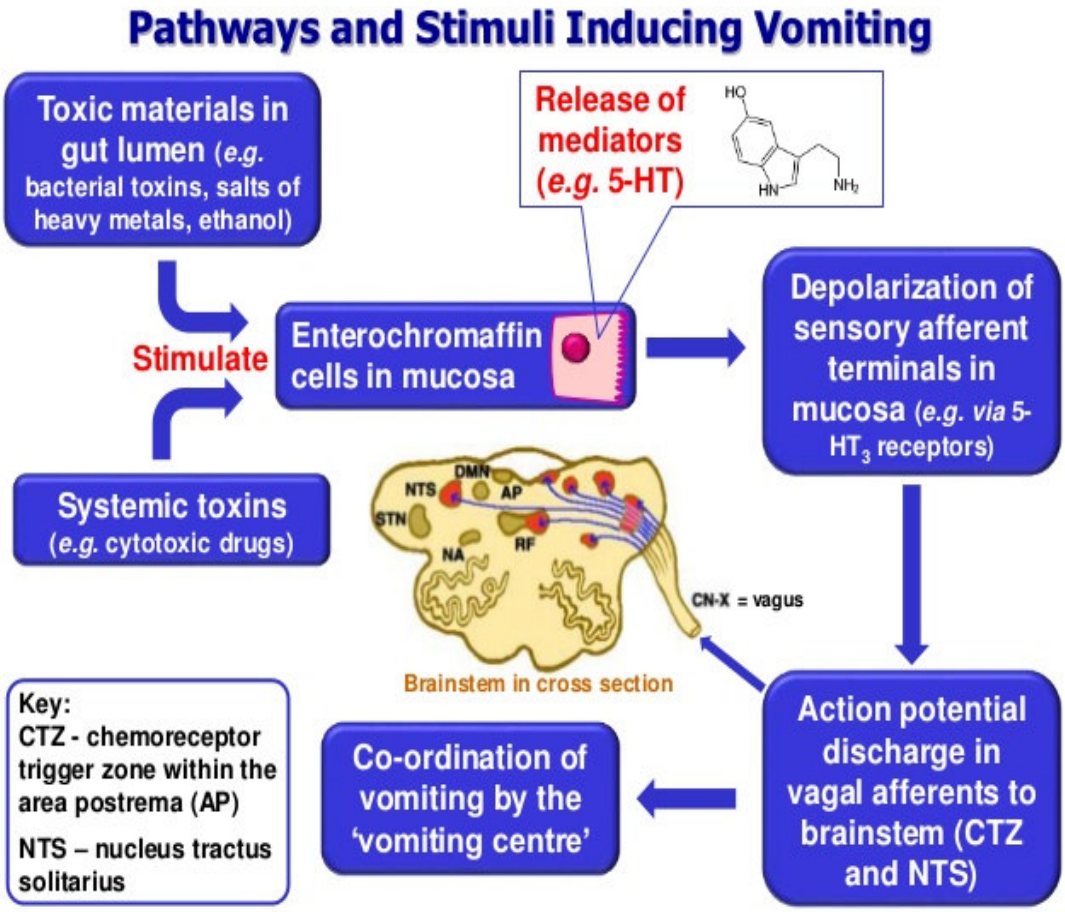
Signals from the peripheral afferent input may also trigger vomiting. For PONV, enterochromaffin cells in the gastrointestinal (GI) tract release serotonin, which binds to visceral receptors (5-hydroxytryptamine type 3 [5 -HT3]), causing stimulation of vagal afferents in the GI tract to conduct impulses that reach the CTZ, also known as the area postrema through the nucleus of Tractus solitarius(NTS)

HIGHER CENTRES:

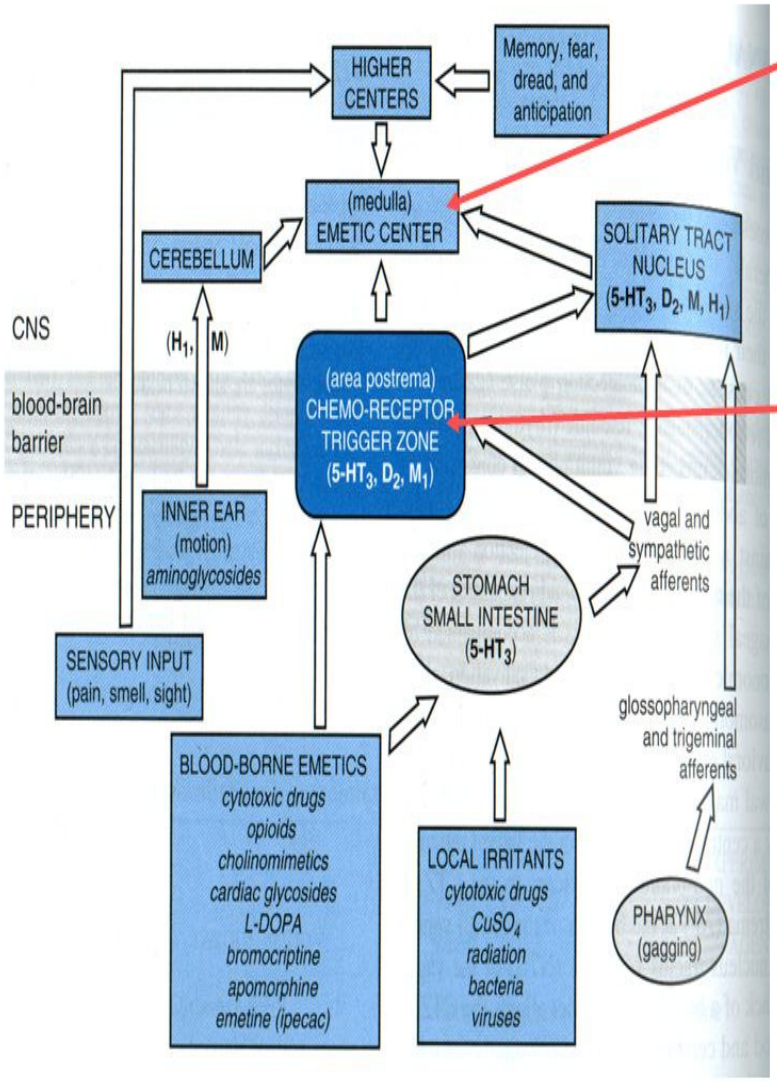
Vomiting can also be induced by unpleasant smell, pain, taste and sight.

VESTIBULAR SYSTEM:

Activation of vestibular receptors due to motion sickness which in turn stimulates labyrinth of inner ear, send signals to vestibular nuclei in the cerebellum which stimulates chemoreceptor trigger zone triggers the vomiting centre that leads to emesis.



Sensory Inputs to the Emetic (Vomiting) Center



Emetic center in the medulla, a CNS component

II. Chemo-receptor trigger zone (CTZ), a sensory component outside the blood-brain barrier

Hardman, et al, *Goodman & Gilman's The Pharmacologic Basis of Therapeutics*, 10th ed., 2001, McGraw-Hill, p. 1030.

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MOTOR COMPONENTS OF VOMITING REFLEX :

The motor components are mediated through somatic and autonomic nerves of GIT. Sensory impulses from pharynx , oesophagus, stomach are carried to the vomiting centre.

Sensory signals sent from pharynx, oesophagus, upper part of small intestine

Via Vagal and sympathetic afferent nerve fibres

Vomiting centre(multiple nuclei in the brainstem)

Efferent via 5^{th},7^{th},9^{th},10^{th},12^{th} cranial nerves

Through vagal and sympathetic nerves to lower tract and through spinal nerves to respiratory and abdominal muscles.

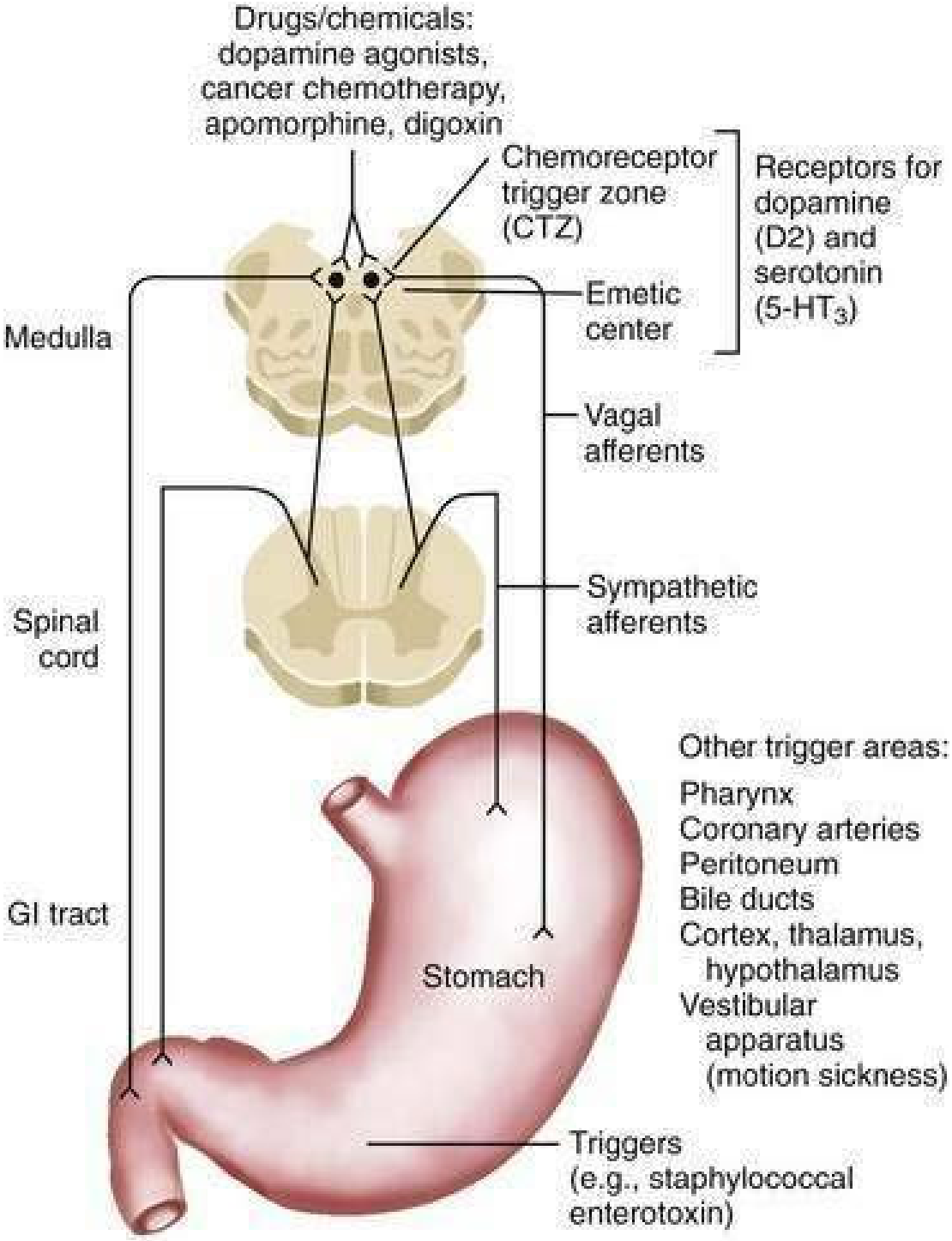
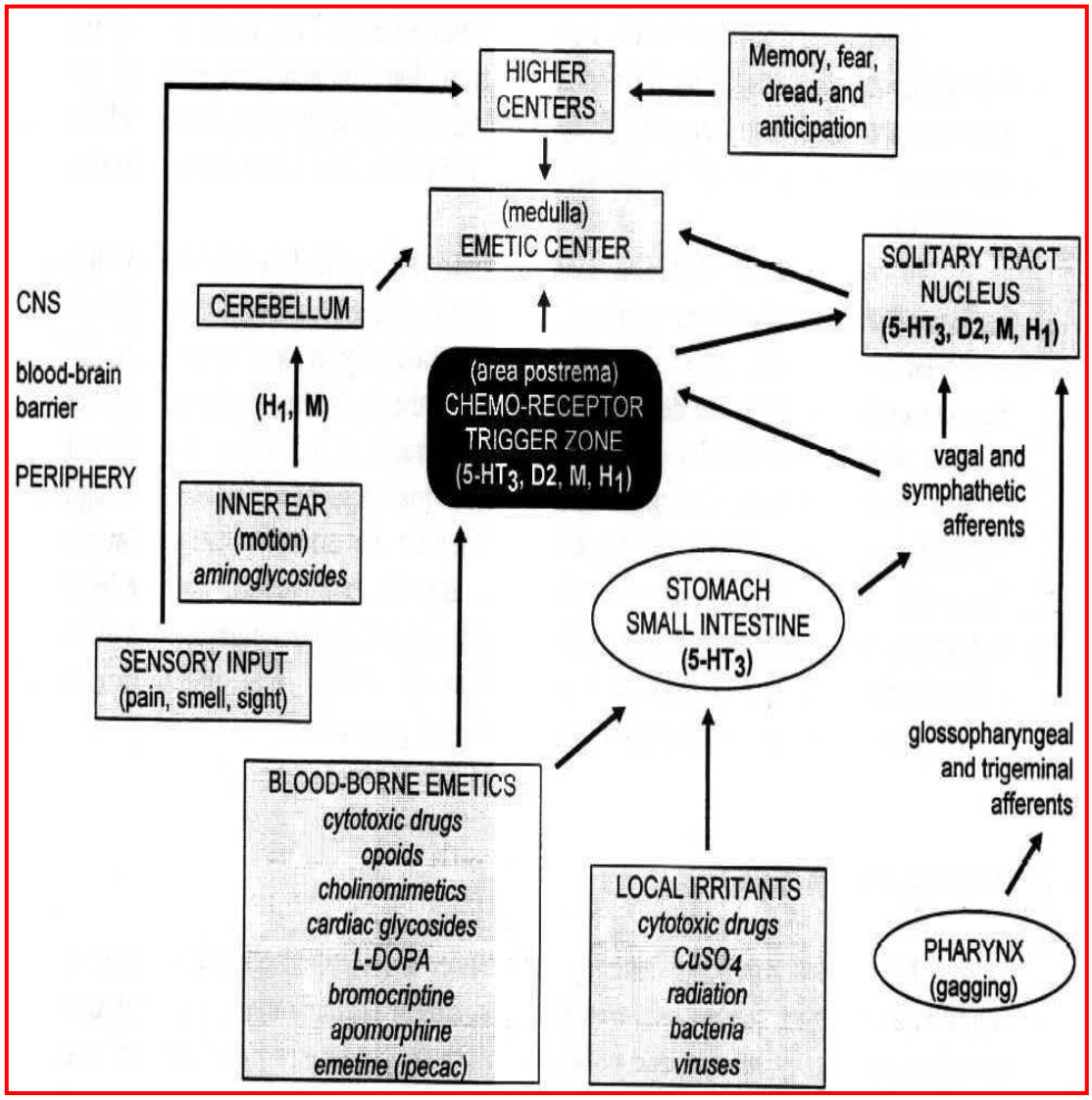


Figure : Motor Components of vomiting reflex

EMETIC PATHWAYS AND CENTRES RESPONSIBLE FOR EMESIS



COMPLICATIONS /CONSEQUENCES OF POST OPERATIVE NAUSEA AND VOMITING

Patient :

Emesis or nausea results in postoperative pain and discomfort after surgery especially after high risk surgeries and abdominal and thoracic sugeries .The fluid and food intake is often delayed.

Physiological:

Dehydration ,Sweating , increase in heart rate, salivation , abnormal cardiac rhythms and even haemetemesis rarely

Medical:

Electolyte imbalance like hypokalemia , metabolic alkalosis due to hyponatremia , dehydration , orthostatic hypotension and interuption of diet.Increases ICU or hospital stay and results in economic burden to family .

Surgical:

Wound dehiscence and bleeding over the suture site , oesophageal tears while retching , increased intracranial and intraocular pressure results in GCS drop in neurosurgery patients. It also causes anastamotic graft disruption and chances of herniation later on .

Anaesthesia:

High potential for causing aspiration pneumonia since patients may be drowsy soon after surgery.

Hospital stay / cost:

Unexpected hospital admission in day care surgery patients and delay in discharge

RISK FACTORS ASSOCIATED WITH POSTOPERATIVE NAUSEA AND VOMITING

Although the many new available antiemetic drugs have been proven safe in clinical trials, no agent is without its side-effects. Side-effects of antiemetics range from mild (e.g. headache for ondansetron) to potentially severe (e.g. QT prolongation with palanosetron). To reduce the incidence of PONV without increasing the risk of unnecessary side-effects, prophylactic antiemetic regimens should be tailored to the patients most likely to experience PONV. To identify patients at risk , it is critical to accurately identify strong and reliable independent risk factors using multivariable analysis. Some risk factors, like abdominal and gynaecological surgery, are associated with a high incidence of PONV. However, this correlation is likely due to confounding factors inherent to the surgery type, like female gender.

Well-established risk factors

Patient-related

Female gender is consistently the strongest risk factor for PONV with an odds ratio (OR) of 3, which indicates that females are on average three times more likely to suffer from PONV than males.

Non-smoking status, with an Odds ratio equal to 2, roughly doubles the patient's risk of PONV. The mechanism underlying smoking's protective effect is unknown. One of the most commonly believed hypothesis is that polycyclic aromatic hydrocarbons in cigarette smoke will induce cytochrome P450 enzymes, thereby increasing the metabolism of emetogenic volatile anaesthetics. However, there is currently little evidence to support this theory.

A history of motion sickness,previous history of PONV, or both, also with an Odds ratio of 2, indicates a general susceptibility to PONV .

For adult patients, age is a statistically, though not clinically, relevant risk factor, with the incidence of PONV decreases as patients age advances. For paediatric patients, however, age increases the risk of postoperative vomiting , such that children older than 3 yrs have been shown to have an increased risk compared with children younger than 3.

Anxiety :

Infants and children are more anxious before surgery because of that they swallow large volumes of air and anaesthetic gases during induction which results in bowel distension and so are prone to develop vomiting after surgery. Anxiety also delays gastric emptying.

Body habitus:

Obese patients are more likely to develop Post Operative Nausea and Vomiting than asthenic patients probably due to increased abdominal pressures and decreases lower oesophageal sphicter tone.

Menstruation :

Studies have reported that women have more chances for Post Operative Nausea and Vomiting during first seven days of menstrual cycle . Reason not demonstrated and statistically insignificant

Anaesthesia-related

General anesthesia with volatile anaesthetics is associated with a two-fold increased risk of PONV, with risk increasing in a dose-dependent manner, and no significant difference in incidence with different volatile anaesthetics. In fact, the use of volatile anaesthetics is the single most important factor for predicting PONV in the first few postoperative hours. Volatile anaesthesia may increase PONV by decreasing levels of anandamide, an endogenous cannabinoid neurotransmitter that acts on cannabinoid-1 and and vanilloid-1 receptors to suppress nausea and vomiting. Because replacing volatile anaesthetics with total intravenous anaesthesia with an agent like propofol reduces the incidence of PONV, some have suggested that propofol itself has antiemetic properties; however, these mechanism are doubtful and many studies proved antiemetic effects of propofol .

Nitrous oxide increases the risk of PONV by 1.4 ,Probably due to the high incidence of gastric and bowel distention.

Intraoperative and postoperative opioid like ketamine and tramadol use increases the risk of PONV in a dose-dependent manner. Opioids also reduces muscle tone and peristaltic activity, thereby delaying gastric emptying, inducing distension, and triggering the vomiting reflex.

The Duration of surgery, can help predict the patient's risk of PONV, since the duration of anaesthesia increases the patient's exposure to emetogenic stimuli like volatile anaesthetics and intraoperative opioid usuage like morphine etc.

Potential risk factors

Patient-related

ASA physical status (I–II),previous history of migraine, and preoperative anxiety have all been associated with an increased risk of PONV, although the strength of association varies from study to study.

Anaesthesia-related

Few randomized controlled trial or study and few multivariable analyses have investigated the effect of general *vs* regional anaesthesia on

PONV, and Odds ratio associated with general anaesthesia range from 1.3 to 10.6. It appears that regional anaesthesia is associated with less PONV except in hypotension.

The use of facemask ventilation causing PONV are conflicting, And no study suggest significant risk factor for PONV

There is insufficient evidence to conclude that neostigmine increases the risk of PONV.

Surgery-factors

Middle ear surgery:

Due to increased middle ear pressure secondary to nitrous oxide , the incidence of PONV increases and the mechanism is the activation of vestibular system afferent pathway especially if the system is sensitized by use of opiods. Another pathway is the nerve supplying the tympanum , called auricular branch of vagus nerve- Arnold`s Nerve ,its activation leads to emesis.

Adenotonsillectomy :

The irritation of trigeminal nerve during surgery and the irritant effect of blood swallowed on the oesophago-gastric chemoreceptors results in higher incidence of Post Operative Nausea and Vomiting.

Abdominal surgery:

The direct effect of vagal afferents and stimulation of receptors due to the release of 5HT from the enterochromaffin cells due to surgical manipulation of intestine stimulates vomiting centre which results in emesis.

Post Operative Nausea and Vomiting incidence over 24 hours was 42%

for abdominal sugery compared with other surgical procedures(36%)[26].

Gynaecological surgery

Laproscopic surgeries like abdominal hysterectomy is associated with increased incidence of Post Operative Nausea and Vomiting due to abdominal insuffulation due to CO2 (upto 65 -77%).

Opthalmic surgery

Strabismus surgery is commonly associated with high incidence of Post Operative Nausea and Vomiting

Duration of anaesthesia

Increase in the duration of the surgery is associated with higher incidence and severity of postoperative nausea and vomitting probably due to prolongation of exposure to volatile anesthesia and intraoperative opiod usuage

Anaesthesia-related

According to various trials in over 5000 patients, the use of a short-acting opioid-like remifentanil instead of fentanyl does not decrease the incidence of PONV. The use of supplemental oxygen during regional does not reduce the incidence of PONV. While the use of nasogastric tubes may increase the incidence of nausea, gastric tube decompression has no effect on PONV. Therefore, the major risk factors for PONV appear to be patient-specific and anaesthesia-related.

Table 2. Factors Contributing to the Incidence of PONV.

Preexisting Conditions
****Age***
****Gender***
****History of PONV or Motion Sickness***
****Preoperative Anxiety***
****Obesity***
Site of Surgery/Type of Surgical Procedure
Anesthetic Agents and Technique
Duration of Surgery
Postoperative Conditions
****Pain***
****Movement***
****Hypotension, hypoxemia, or hypoglycemia***
from fasting
****Premature intake of fluids and foods.***

Postoperative Factors in the Etiology of PONV

Finally, postoperative considerations involved in increasing the risk of developing PONV include pain and the use of opioids, movement or early ambulation, hypotension, hypoglycemia, hypoxemia and premature oral intake. Additionally, several studies have shown that the relief of pain is commonly associated with the relief of nausea.

As mentioned previously regarding the use of intraoperative opioids, sudden motion or changes in position of patient , including the transport from the operating room to the postanesthesia care unit, can precipitate nausea and vomiting especially in patients who have received opioids suggesting that opioids sensitize the vestibular system to motion-induced nausea and vomiting. PONV is also increased in patients experiencing giddiness and dizziness, mostly in association with postural hypotension and/or hypovolemia. Postural hypotension is often an early sign of unrecognized hypovolemia . Patients will experience giddiness when first trying to stand up postoperatively, which may lead to nausea and vomiting. This is believed to be due to decrease in medullary blood flow to the CTZ and is most often relieved with adequate hydration and/or sympathomimetics.

The timing of the oral intake postoperatively may also influence the incidence of PONV. Multiple studies have shown variations with some demonstrating that restriction of oral intake in the early postoperative period does not decrease the overall incidence of vomiting but only delays its occurrence, while few studies have shown a distinct relationship between restriction of oral intake during the first 8 hours postoperatively and a significantly decreased incidence of PONV.

Apfel *et al.*[36] point out that although many factors have been associated with an increased risk for developing PONV, evidence based on clinical trials is available that correlates with only a few risk factors, namely female gender, previous history of PONV or motion sickness, non-smoking status, volatile anesthetics , nitrous oxide, and opioid usage.

As a result, they conclude that PONV is caused predominantly by intraoperative opioids and volatile anesthetics when administered to susceptible patients. Emphasis is placed on the recommendation that the anesthesiologist should perform a preoperative patient assessment to include a thorough evaluation of pre-existing patient, surgical factors , and anesthesia-related risk factors , method of anesthetic technique for precipitating the incidence of PONV followed by the development of an appropriate anesthesia care plan that takes such risk factors into consideration and the implementation of appropriate therapeutic interventions as necessary.

Interestingly, another factor that may contribute to the incidence of PONV is the skill level of the anesthesiologist in relation to the possible effects on anesthetic administration that may result in gastric distension due to improper mask ventilation prior to induction; the incidence of , hypercapnia,hypoxia or hypotension intraoperatively or postoperatively; instrumentation of the airway gadgets during laryngoscopy, frequent suctioning, or oral airway placement; and vestibular disturbances by rough handling of patients during transfer and transport.

It is important to note that due to the multiple factors and variations among individuals that may contribute to the incidence of PONV, it is recommended that an optimal study regarding anesthesia or surgical implications in the occurrence of PONV requires careful and precise control of perioperative conditions in order to determine that the incidence of PONV can actually be attributed to a specific anesthetic or surgical intervention

ROLE OF 5HT3 IN POST OPERATIVE NAUSEA AND VOMITING

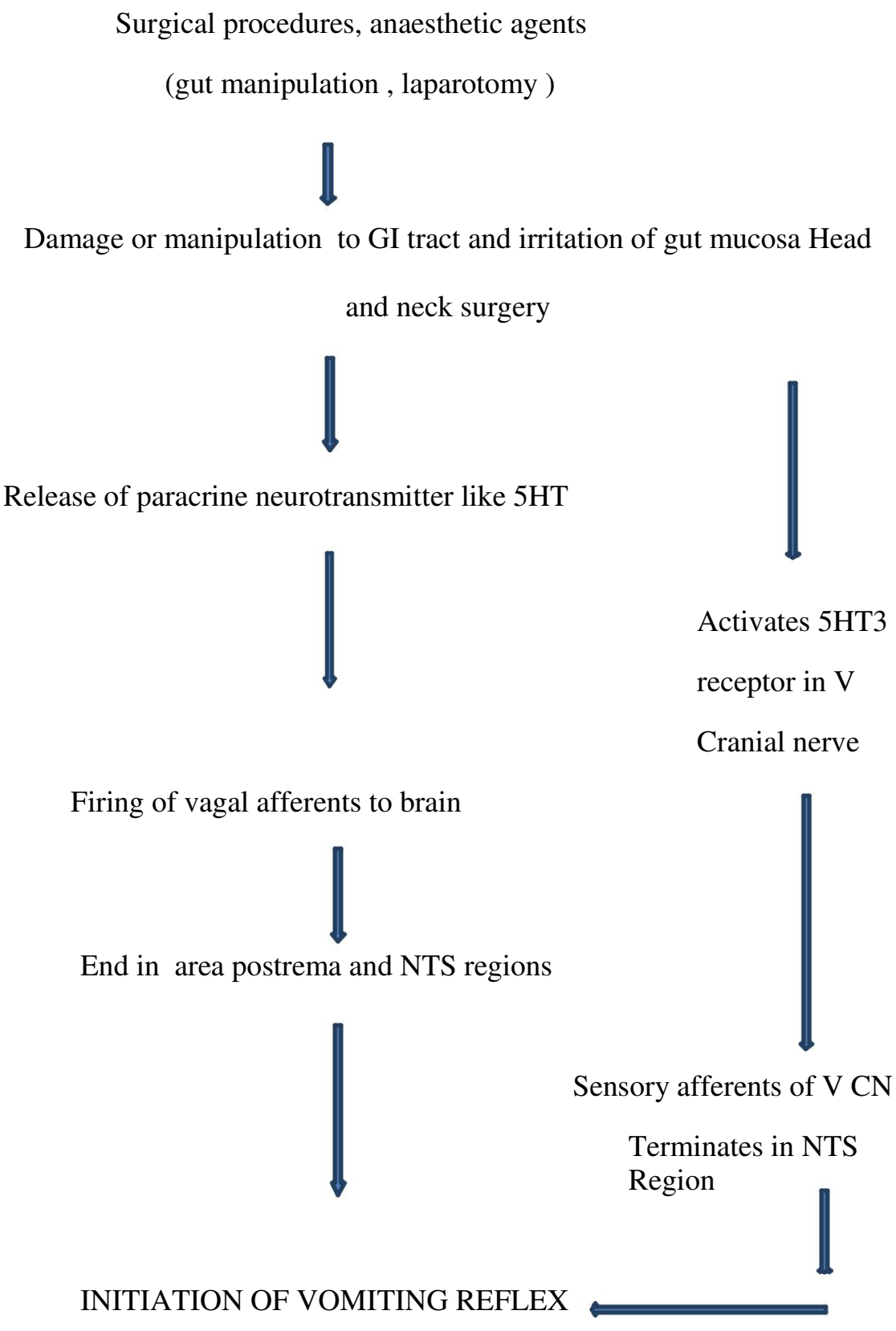
Both peripheral and central mechanisms are involved in the control of vomiting. Role of 5HT3 Receptors have been proven in the animal model

The discovery of $5HT_3$ receptor antagonists in control of chemotherapy and radiotherapy induced emesis has led to the clinical evaluation of Ondensetron in preventing postoperative nausea and vomiting.

In the CNS the $5HT_3$ receptors are more abudant in the Nucleus Tractus Solitarius -Area Postrema regions. The chemoreceptor trigger zone is located in this region.

Most vagal afferents from the periphery enter brain from GIT where the concentration of $5HT_3$ receptors are located.

PERIPHERAL PATHWAYS:



CHANGING TRENDS IN THE MANAGEMENT OF POST OPERATIVE NAUSEA AND VOMITING

Post Operative Nausea and Vomiting is the result of interaction of many factors like type of surgery, age, gender , use of opioids, anaesthetic agents etc. It is apparent that single antiemetic drug will not be effective in all conditions.Sometimes combination of drugs used for desired effect is better than a single drug .

Many pharmacological and non-pharmacological therapies have been evaluated in the treatment of Post Operative Nausea and Vomiting.

PHARMACOLOGICAL PROPHYLAXIS

Acetylcholine Receptor Antagonists

Anticholinergics, among the oldest antiemetic drugs,which block muscarinic cholinergic CNS emetic receptors in the cerebral cortex and pons . Scopolamine , blocks cholinergic transmission from the vestibular nuclei to higher centres in the CNS and from the reticular formation to the central vomiting centre . Common adverse effects associated with anticholinergics include dry mouth and drowsiness, disorientation, memory disturbances, dizziness, and hallucinations

Histamine Receptor Antagonists

Histamine receptors(H1) exert their peripheral effects, including contraction of smooth muscle and dilation and increased permeability of capillaries, as well as stimulation of nausea and vomiting via the NTS. Antihistamines, *i.e.,* H1 receptor blockers, block acetylcholine in the vestibular apparatus and in the NTS. Because antihistamines can effectively treat motion sickness and nausea or vomiting after middle ear surgery, they are thought to act on the central vomiting centre and vestibular system. Antihistamines used to treat emesis include cyclizine, hydroxyzine, meclizine, dimenhydrinate , diphenhydramine and promethazine. More frequent adverse effects include sedation, dry mouth, and constipation, confusion, blurred vision, and urinary retention. The combination of promethazine and opioid in the postoperative period may cause significant sedation and respiratory depression.

Dopaminergic Receptor Antagonists

Dopaminergic receptors may be blocked by D receptor antagonists (D2 receptor antagonist)acting at the CTZ. D2 Receptor antagonist include the phenothiazines *(e.g.,* chlorpromazine, fluphenazine, prochlorperazine), benzamides*(e.g.,* domperidone, metoclopramide), and butyrophenones

Although the phenothiazines, chlorpromazine and promethazine have been used historically to treat PONV, many adverse effects frequently associated with their use *(e.g.,*sedation, lethargy, and skin sensitization) have limited their usefulness. Common adverse effects associated with benzamides include diarrhoea, agitation, and central nervous system (CNS) depression with sedation and restlessness .Less commonly extrapyramidal effects, hypotension, and neuroleptic syndrome also occur with these drugs.

Phenothiazines, particularly droperidol, have been commonly used previously , either as a single agent or in combination with 5-HT3 receptors antagonists.. In a dose o f 1.25 mg. it was more cost-effective than ondansetron 4 mg and was recommended as a first line agent for PONV prophylaxis .

Droperidol received a “black box” warning from the US Food and Drug Administration in December 2001 because it has adverse effects like arrhythmias of the torsades de pointe variety. However, recent studies have shown no significant increase in the incidence of QTc prolongation among patients undergoing prophylaxis for PONV with low-dose droperidol compared with placebo or ondansetron.

5-Hydroxytryptamine Receptor Antagonists

When there is noxious or mechanical stimuli to GIT, the neurotransmitter serotonin (5-hydroxytryptamine [5-HT]) released from enterochromaffin cells of the gastrointestinal tract (and also in the central nervous system), stimulating vagal afferent neurons, which in turn activate the vomiting centre or directly activate the CTZ by binding to receptor sites.

Serotonin has many different receptors, but the most important receptor is subtype 3 (5-HT3). The greatest intensity of 5 -HT3 receptors is in the NTS and CTZ. 5-HT3 Receptor antagonist like Ondansetron ,Palonosetron ,Graniseton and newer one like Ramosetron block the nausea and vomiting cascade mediated by serotonin. As a class, 5 -HT3 Antagonists are considered the most potent antiemetic agents and are effective both for prophylaxis and treatment of PONV. However, their action is potent primarily during the early phase of PONV. They are less efficacious during the delayed phase of PONV.

5 -HT3 antagonists are highly specific for the 5 -HT3 receptor, having little to no affinity for dopamine, muscarinic ,cholinergic, or histamine receptor . These drugs are metabolized by the CYP450 system in the liver. Granisetron, unlike ondansetron or dolasetron, is not metabolized by the CYP2D6 isoform, which may be responsible for

many adverse drug interactions, poor metabolism in patients with CYP2D6 deficiency (leading to accumulation of drug), Frequently observed adverse effects with 5- HT3 antagonist include headache and asymptomatic prolongation of the QTc interval. Less commonly constipation, asthenia, somnolence, diarrhoea, ataxia, lightheadedness, dizziness, and muscle pain may occur.

There is no evidence that there is any difference in efficacy or side-effect profile between the various 5 -HT3 receptor antagonists, when appropriate doses are used for the management of PONV. In a few studies with patients undergoing laparoscopic cholecystectomy, there was no difference in antiemetic efficacy between ondansetron 4mg, Ramosetron 0.3mg before induction of anaesthesia [28]

Dolasetron 12.5mg was also found to have same efficacy to ondansetron 4mg with a similar side effect profile for the prevention o f PONV . In an earlier study, dolasetron 50 mg had similar efficacy to ondansetron 4 mg.

Fujii and colleagues[21] compared the antiemetic efficacy of Granisetron 2.5-3 mg with Ramosetron 0.3 mg in three studies. There was no difference between the two agents in achieving a complete response (no PONV and no antiemetic rescue) during the first 24 hours postoperatively. Between 24 and 48 hours, however, ramosetron provided better prophylaxis

Eberhart et al says that meta-analysis between 5 -HT3 antagonist in combination with droperidol and with dexamethasone (5-HT3RA/dexamethasone) for prevention of PONV. During both the early phase and overall period, it is observed no significant difference in nausea or vomiting rates between 5-HT3RA/droperidol compared to 5 -HT3 antagonist or droperidol monotherapies. On the other hand, Habib et al. Also observed significantly greater prevention of vomiting with 5-HT3 Antagonist /droperidol combination compared to droperidol monotherapy during the early phase and overall period. The same study also observed that combination. therapies of 5-HT3 antagonist with dexamethasone had greater prevention of nausea and vomiting during both the early period and overall.

A more recent meta-analysis by Kovac70 (N = 49; n = 12,752) evaluated the need for rescue medication with 5-HT3 antagonist with dexamethasone compared to placebo, and to 5 -HT3 Antagonist and dexamethasone monotherapies. For each comparison, a significantly less proportion of patients treated with combination 5-HT3 antagonist dexamethasone required rescue medication.

Leslie et al. conducted a large meta-analysis that examined the safety of 5 -HT3 receptor antagonist combination therapies. The proportion of patients experiencing headaches was significantly smaller with 5-HT3 antagonist/droperidol combination therapy than droperidol monotherapy. The drowsiness, dizziness, or any adverse rates of 5-HT3 antagonist /droperidol combination did not significantly differ from 5 -HT3 antagonist or droperidol monotherapies.

However, the efficacy of 5 -HT3 antagonist as monotherapy or in combination with dexamethasone or droperidol, primarily good during the early postoperative period and overall; but little efficacy has been reported during the late postoperative period. Delayed emesis remains a problem. This has led to prompt interest in the use of neurokinin receptor antagonists, which appear to show efficacy during both the early and delayed chemotherapy-induced nausea and vomiting.

Neurokinin Receptor Antagonists

Substance P is a important neurotransmitter in afferent pathways of emesis and pain . Substance P also released from enterochromaffin cells in the stomach and intestine *{e.g.,* postoperative trauma) or from sensory neurons *{e.g.,* radiation, chemotherapeutic agents). Tachykinin peptide activity act on three G -protein-coupled receptor subtype found in the peripheral or central nervous tissue: neurokinin receptor subtype 1 (NK1),

subtype 2 (NK 2), and subtype 3 **(N K3).** The **NK 1** receptors are located intense in the area postrema and are thought to play a particularly important role in vomiting. However, NK1 receptor antagonists (NK1 antagonist) are thought to exert their action on neurons in the "afferent relay station" situated between the medial NTS and the central vomiting centre, although this has not been definitively isolated for humans. The potential NK1 receptor blocking activity located deeper in the brain stem is thought to prevent both acute and delayed emesis, whereas 5 -HT3 Receptor antagonists are more effective only against acute emesis than delayed PONV." This has led to considerable recent interest in the use of NK1 receptor antagonist for prophylaxis of PONV.

Other anti-emetics

Steroids

After successful usefulness of dexamethasone in the prevention and treatment of chemotherapy induced emesis, this drug has been evaluated and found to be effective for the management of PONV . The recommended dose is 5-10 mg in adults and 150 mcg/kg in children. More recently, smaller doses (2.5 - 5 mg) have been found to be effective. Dexamethasone appears to be most effective when it is administered prior to induction of anaesthesia rather than at the end in preventing early PONV (0 - 2 hours).There are no studies of dexamethasone related adverse effects in the doses used for the management of PONV.

Benzodiazepines

Benzodiazepines were found to be effective for the prophylaxis of PONV . The successful use of midazolam in cases of persistent PONV and following failure of other antiemetics has also been described.

Adrenergic agonists

*Central a*drenergic agonists significantly reduced the incidence of PONV in both children and adults. It has been suggested that the antiemetic effect of clonidine might be secondary to a reduction in the use of volatile agents and opioids, or a reduction in sympathetic tone. But direct role of antiemetic effect unknown .

High concentration o f oxygen

Intraoperative usuage of Oxygen supplementation (80%) or both intraoperative and postoperative usuge for two hours have been shown to be effective in reducing the incidence o f PONV compared to patients receiving 30% oxygen. These findings were not confirmed in future studies.

Fluid Administration

Adequate hydration is associated with a significant reduction in the incidence of

PONV. " Liberal fluid regimen (median vol = 4.2 L) is associated with a lower incidence of vomiting and improved pulmonary function in patients undergoing knee arthroplasty compared with fluid restricted regimen (median vol = 1.7 L). In a recent study, a combination of crystalloid and colloid fluid resuscitation was associated with less PONV and less use of rescue antiemetics, compared with the administration of crystalloids alone in patients undergoing major abdominal procedures.Mechanism unknown.

Combination Antiemetic Therapy

It is important to note that despite the lack of conclusive research results to date , it is becoming increasingly popular to use a multimodal or combination of antiemetic drugs approach, in the pharmacologic management of PONV. As mentioned previously, this practice is based upon the complex and multifactorial etiology of nausea and vomiting . It is believed that administering a drug that antagonizes only one of the receptors that may be involved in the etiology of PONV is often ineffective, whereas using combinations of drugs with different mechanisms of action acts synergistically to provide an overall good therapeutic effect. This approach is similar to the concepts of balanced anesthesia and balanced analgesia. The multimodal antiemetic drug approach takes into consideration the fact that each antiemetic agent may

selectively block a specific receptor(s) that may or may not be present in multiple anatomic sites. Combining different drugs may, therefore, help to make a specific receptor blockade more effective and achieve a blockade in a different anatomic site or block multiple receptor sites. In addition, it may also serve to lessen the incidence of side effects of the drugs themselves because of the use of smaller doses of each drug with combination therapy regimens. Corticosteroids, such as dexamethasone, are the drug most commonly used in combination with other antiemetics for combination therapy.In our study we added Dexamethasone to all group of antiemetics .

Additionally, it is often recommended that if an initial antiemetic or combination of antiemetics drugs is ineffective, the preferred choice for additional drug therapy should involve an agent that works at a different receptor site(s) than at same site . Multimodal management of PONV, however, refers not only to a combination of pharmacologic antiemetic drugs alone , but it is also with use of multiple antiemetics in combination with numerous nonpharmacologic techniques that best avoid the incidence of PONV.

With regard to multimodal management of PONV and patients at high risk for experiencing PONV, one study by Scuderi *et al.* demonstrated the ability to significantly decrease the incidence of PONV in a high risk population through the use of multimodal therapy for

PONV that included total intravenous anesthesia with propofol and remfentanil, no nitrous oxide, nil neuromuscular blockade, aggressive IV hydration, the use of ketorolac 30mg, and triple prophylactic antiemetics with Ondansetron 4 mg, droperidol 0.625 mg, and decadran 10 mg. Thus, further emphasis is placed on the importance of controlling PONV through minimizing or avoiding the preventable factors that may lead to nausea and vomiting postoperatively like avoiding hypoxia and hypotension and utilizing those measures that assist in lessening PONV in association with appropriate anitemetic drug therapy.

Non-Pharmacological Methods

Acupuncture

Hypnosis

The baseline risk factors which can be reduced are as follows

1. Use of regional anaesthetic techniques
2. Use of propofol for induction and maintenance of anaesthesia which also as antiemetic property.
3. Avoidance of Nitrous oxide (N2O)
4. Avoidance of volatile anesthetic
5. Reduction of intraoperative and postoperative opioid usuage

PHARMACOLOGY OF RAMOSETRON

Ramosetron hydrochloride, an anti-emetic drug, is prescribed for the treatment of diarrhoea-predominant irritable bowel syndrome in adult men. Ramosetron hydrochloride is also prescribed for the treatment and management of nausea and vomiting associated with carcinostatic drugs including cisplatin. Ramosetron hydrochloride, as injections, is indicated for the management of postoperative nausea and vomiting.

Chemical formula ; C17H17N3O

Molecular mass ; 279.33

MOLECULAR STRUCTURE

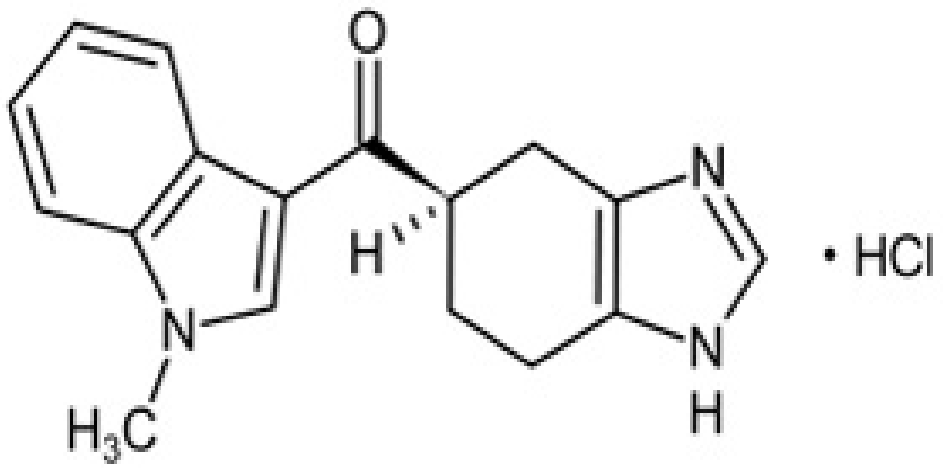


Figure . Molecular Structure of Ramosetron

Pharmacodynamics

Ramosetron hydrochloride selectively blocks serotonin receptors (5-HT3). Serotonin plays a important role in vomiting, serotonin-induced bradycardic reflex and peristalsis of gut. The pharmacological action of Ramosetron hydrochloride is sustained and potent.

Pharmacokinetics

After oral or intravenous administration, Ramosetron hydrochloride achieves Cmax after 2 hours with a plasma half-life of 5 hours to 6 hours. The Cmax and AUC are linear activity in nature and dose-dependent. The oral bioavailability of Ramosetron hydrochloride is about 50%. The drug is widely distributed in the body fluids including breast milk. Ramosetron hydrochloride is excreted via urine as drug metabolites and as unaltered drug.

Precautions

Ramosetron hydrochloride is contraindicated in patients with constipation predominant irritable bowel syndrome ,infectious enteritis, colitis, active diarrhoea, patients unresponsive to conventional therapy and colon cancer. Ramosetron hydrochloride is contraindicated in patients with hypersentivity and its very rare

Other Drug Interactions

Ramosetron hydrochloride may interact with other drugs including CYP1A2 inhibitors, MAOIs, anti-psychotics, phenothiazines, anti-cholinergics and opioid narcotics, tricyclic anti depressants. Co administration of Ramosetron hydrochloride with these drugs results in severe and serious GI disturbances including diarrhoea or constipation.

Dosage

Consider administration of 5 mcg of Ramosetron hydrochloride once daily. The maximum daily dose should not exceed 10 mcg. Dose adjustments can be considered based on clinical response. If severe symptoms persist, the dosage adjustments should not be considered .Ramosetron hydrochloride can be taken before or after food intake

List of Contraindications

Ramosetron hydrochloride and Pregnancy

USFDA pregnancy category C. May be or may not be harmful to fetus.

Ramosetron hydrochloride and Lactation

Ramosetron hydrochloride can pass through the breast milk and harm a nursing infant. Care should be taken in breastfeeding a baby while taking Ramosetron hydrochloride.

PHARMACOLOGY OF ONDANSETRON

INTRODUCTION

Ondansetron was the first of the 5-HT_3 receptor antagonists introduced into practice for the management of nausea and vomiting in 1991. Ondansetron is a carbazalone derivative that is structurally similar to serotonin.

The full chemical name of ondansetron hydrochloride is ±1,2,3,9-tetrahydro-9-methyl-3-[(2-methyl-1H-imidazol-1-yl) methyl]-4H-carbazol-4-one, monohydrochloride, dihydrate and the brand name is

The empirical formula is $C_{18}H_{19}N_3O$-HCL-$2H_2O$

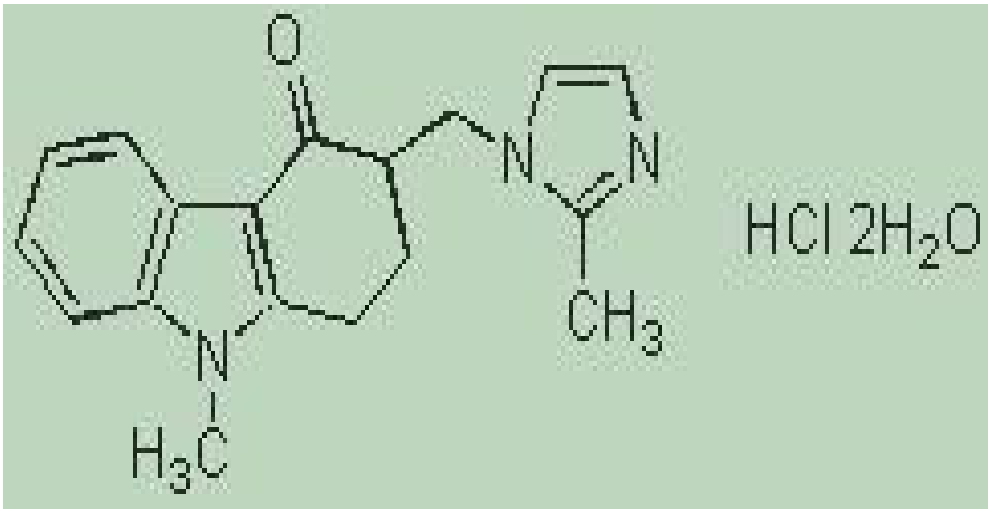


Figure . Molecular Structure of Ondansetron

Pharmacokinetics

Ondansetron is available is available in aqueous solution for intravenous or intramuscular injection as well as available in oral administration in the form of tablets, oral solution, and orally disintegrating tablets. Ondansetron is well absorbed and does not undergo significant first-pass metabolism in liver. The time to peak plasma concentration is approximately 1.7 hours. Ondansetron is extensively metabolized by the liver and has an elimination half-life of three to five hours in a healthy individual with a bioavailability of 56%. In some patients, the antiemetic effects may last for 24 hours. The primary metabolic pathway is hydroxylation of the imdole ring followed by glucuronide and sulfate conjugation and elimination in the urine with only 5% excreted unchanged. In patients over the age of 75 years , the clearance of ondansetron decreases and the elimination half-life increases . In addition, ondansetron is metabolized by cytochrome P-450 enzyme system of the liver, and drugs or metabolites that will induce or inhibit this cytochrome P-450 system will alter the pharmacokinetics of ondansetron. Ondansetron does not appear to affect cardiac or respiratory function.

Side effects

It is most common side effect include headache, fever, constipation or diarrhea, and transient increases in the plasma concentrations of liver transaminase enzymes. Less common side effects are abdominal cramps, dizziness, musculoskeletal pain, chills, dry mouth , fatigue . Most importantly with respect to its use in anesthesia, ondansetron does not cause drowsiness or sedation in patients postoperatively

REVIEW OF LITERATURE

In order to direct the antiemetic prophylaxis to the patients at high risk, several attempts have been made to identify the risk factors for PONV. During the 1990s, several independent models using logistic regression were created for this purpose Koivuranta *et al.* 1997; Apfel *et al.* 1998 [1]

Palazzo and Evans (1993) studied PONV in patients undergoing orthopaedic surgery . The total incidence of vomiting was 27% in their study. They concluded that the history of PONV, female gender, the previous history of motion sickness and history of PONV and interaction between gender, history of PONV and postoperative opioids are fixed risk factors. The relative effects of the factors are summarized in an equation as follows:

Koivuranta *et al.* (1997) surveyed in patients undergoing various types of surgery. The incidence of nausea was around 52% and the incidence of vomiting 25% during the entire 24 hour study period. According to the survey female gender, the history of PONV, the history of motion sickness, and long duration of surgery and nonsmoking are patient-related risk factors[26]

The risk score of Apfel *et al.* (1998) was based on the data of 1137 patients undergoing ear, nose and throat surgery . Only postoperative vomiting was studied, not postoperative nausea. The incidence of vomiting is around 21% and 22% in the sets, respectively. According to the study age, gender, the history of motion sickness and/or POV, nonsmok-ing status and the duration of anaesthesia are independent risk factors. The risk of POV can be estimated from the equation:

Risk (probability of POV) = $1 / (1 + e^{-z})$, where z = 1.28 (female gender) – 0.029 (age) – 0.74 (smoking) + 0.63 (history of PONV or motion sickness) + 0.26 (duration) – 0.92.

The discrimination power of the score was then tested in patients undergoing various types of ophthalmologic and surgical operations under general anaesthesia with use of volatile anaesthetics, and found to be accurate (Apfel *et al.* 1998)[1]

Sinclair *et al*. (1999) studied 17,638 outpatients; they found the incidence of PONV to be 4.6% in the PACU and 9.1% within 24 hour of the surgery . The patient population was divided into a model development set and a model validation set. The logistic regression model for assessing the risk of PONV age, gender, smoking status of patient , history of PONV, type and duration of anaesthesia, and type of surgery were included as indepen-dent factors (Sinclair *et al.* 1999).

The data of Koivuranta and Apfel scores were cross-validated afterwards by the two more centres (Apfel *et al.* 1999), and a simplified risk score was developed without losing dis-criminating power (Table). The simplified risk score included female gender, history of motion sickness or PONV, nonsmoking status, and the use of postoperative opioids. If none, one, two, three, or four of the risk factors were present, the incidence of PONV was 10%, 21%, 39%, 61% and 79%, respectively[26]

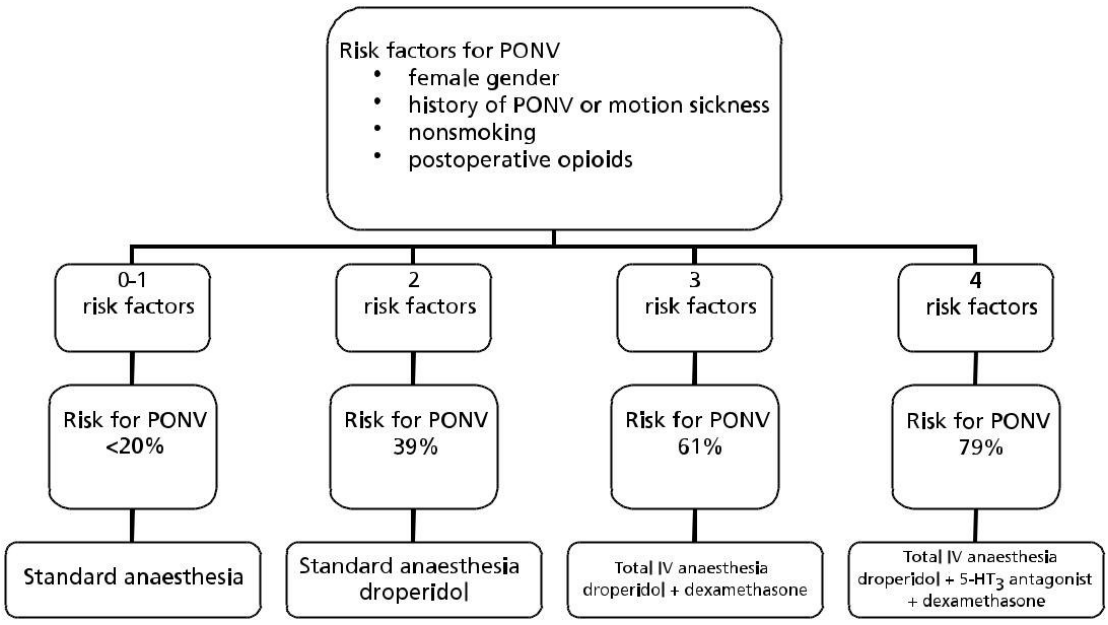


Figure . Flow chart for assessing the individual risk for postoperative nausea and vomiting according to Apfel *et al*. (1999) and suggested anaesthetic and antiemetic regimen

Investigated separately, smoking was shown to reduce the risk of PONV (Chimbira and Sweeney 2000). The effect of smoking in reducing the risk of PONV has been suggested to result from the dopaminergic stimulus (Apfel *et al.* 1998) or the increased metabolism of the anaesthetic agents via induction of the cytochrome P450 enzyme (Chimbira and Sweeney 2000; Sweeney 2002). On the other hand, this study also evalutes obesity as the risk for PONV , it was not found to be a risk factor (Kranke *et al.* 2001). Perioperative gastric emptying appeared not to be a predictor of early PONV in patients undergoing laparoscopic cholecystectomy (Wattwil *et al.* 2002).

MATERIALS AND METHODS

This was a randomised, double blinded study conducted at the Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai. 120 patients between ages of 18 to 60 yrs, who were scheduled to undergo elective middle ear surgeries under general Anaesthesia were included in the study and divided in to four groups ,30 patients in each group .

Written Informed consent regarding the procedure was obtained from all patients. Pre-operatively the patients were educated about the visual analogue scale. They were shown the scale and were taught how to rate the severity of nausea post-operatively. The scale was graded from 0

to 10cm. “0” indicated no nausea at all and “10” was very severe nausea. The scale was divided into 3 equal portions to denote mild, moderate and severe nausea respectively.

Inclusion criteria

ASA-I,II

Age group 18-60 years.

Undergoing any middle ear surgery.

Exclusion criteria

- Not satisfying inclusion criteria
- Patient receiving pre operative anti emetic therapy
- Patient receiving Peri operative steroid for facial nerve damage usuage
- Patients posted for emergency surgery
- Patients with difficult airway
- Lack of written informed consent
- Pregnant female
- H/O seizures and any neurological deficit

- Poor lung compliance such as pulmonary fibrosis
- Allergy to drugs used.
- Patient refusal.
- Patients with severe cardiovascular ,respiratory, renal, hepatic diseases.

MATERIALS :

Drugs–injection Glycopyrolate 0.2mg , injection Fentanyl 2 mcg/kg, injection Thiopentone 5mg/kg, Succinylcholine 2mg/kg , injection Atracurium , Ramosetron 0.3mg , Ondensetron 4mg, Metoclopramide 10mg and Dexamethasone 8mg and normal saline,

- Monitors – ECG, NIBP, SPO2, EtCO2.

Study design

All the patients in the study will be divided into four groups.

120 patients presenting for any middle ear surgery like tympanoplasty and myringoplasty , Chronic suppurative otitis media , cortical mastoidectomy ,modified radical mastoidectomy ., etc were randomly assigned to three groups .

GroupA- Isotonic saline 2cc with Dexamethasone 8mg one hour before end of surgery

Group B- Injection of Ramosetron(0.3mg) with Dexamethasone 8mg one hour before end of surgery

Group C- injection of Ondensetron 4mg with Dexamethasone 8mg one hour before end of surgery

Group D- Injection of Metoclopramide 10mg with Dexamethasone 8mg one hour before end of surgery

Criteria for inclusion in the study consisted of both male and female surgical outpatients, 18-60 years of age, ASA class I and II status, and those patients receiving general anesthesia for their planned middle ear surgery. Demographic data for each patient, including previous history of PONV & motion sickness ,smoking status of patient , history of opiod usage and other risk factors for PONV, were noted.

The patient were premedicated with 0.01mg/kg of Glycopyrolate and 2µg/kg of Fentanyl after connecting the monitors and securing intravenous line. All Patients were induced with thiopentone 5mg/kg body wt and endotracheal intubation was facilitated with succinyl choline 2mg/kg body weight. Maintainence of anesthesia with nitrous oxide 50% and oxygen 50 % , atracurium as muscle relaxant and Sevoflurane as

volatile anesthetic with Minimum alveolar concentration 1-2 % .and patients were monitored hemodynamically during course of surgery .

The patients were randomly allocated to four groups. Group A and Group B, Group C and Group D. Patient was given combination of antiemetic drugs one hour before end of surgery .Patients were extubated after given Neostigmine 50ug/kg body wt and glycopyrolate 10ug/kg body weight . All patients were giving intramuscular injection diclofenac 75 mg for post operative analgesia.

Postoperatively, patients were observed for the incidence of nausea and vomiting. The use of a prophylactic antiemetic was documented and the time of arrival in the postanesthesia care unit (PACU) was noted so that each incidence of nausea and/or vomiting could be assessed in terms of the time, from timing of adminstration of study drug to that the episode of nausea or vomiting . Episodes of nausea and/or vomiting separated by more than 1 minute were considered to be individual incidents. Nausea and vomiting was assessed and rated according to a specific nausea scale (see Table).

Table ;. NAUSEA SCALE (Adapted from WHO)

0 = No PONV, No feelings of nausea, no vomiting.

1 = Mild feelings of nausea, no retching, no vomiting, no treatment needed.

2 = Mild to moderate feelings of nausea, some retching, no vomiting, treatment dose given.

3 = Moderate feelings of nausea, retching, vomiting, treatment dose given.

4 = Moderate to severe feelings of nausea with vomiting, treatment dose given.

5 = Severe nausea/vomiting, treatment given with no relief.

Complete response - no nausea/vomiting for 24 hours

Partial response - one episode of nausea / vomiting

No response/ treatment failure - two or more episode of nausea and vomiting

During an episode of PONV, patient was given rescue antiemetic treatment if scale > 2 or VAS score >5 and a dose of rescue antiemetic ondanseton 4mg (2cc) was given . Patients were observed for 24 hrs and VAS score for pain intensity was monitored for 24 hours and rescue opiod dose was given and dose was calculated .Subjects were assessed throughout their stay and divided into 0-2 hours , 2-6 hours , 6-12 hours and 12 -24 hours. Patients were also asked for any other complaints like headache, dizziness and allergy and recorded appropriate treatment was given. After 24 hours, patients shifted to ENT ward.

INTRA-OPERATIVE MONITORING

Intraoperatively the heart rate, ,non-invasive blood pressure and oxygen saturation monitoring were done. Intraoperative fluid balance was maintained with 10ml/kg/hr of normal saline. Blood loss was assessed using weighing method and blood was replaced if the loss was >10% of patients blood volume.

DATA ANALYSIS

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t test.. Categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS version 17 and Microsoft Excel 2011

OBSERVATION AND RESULTS

Results:

Demographic details:

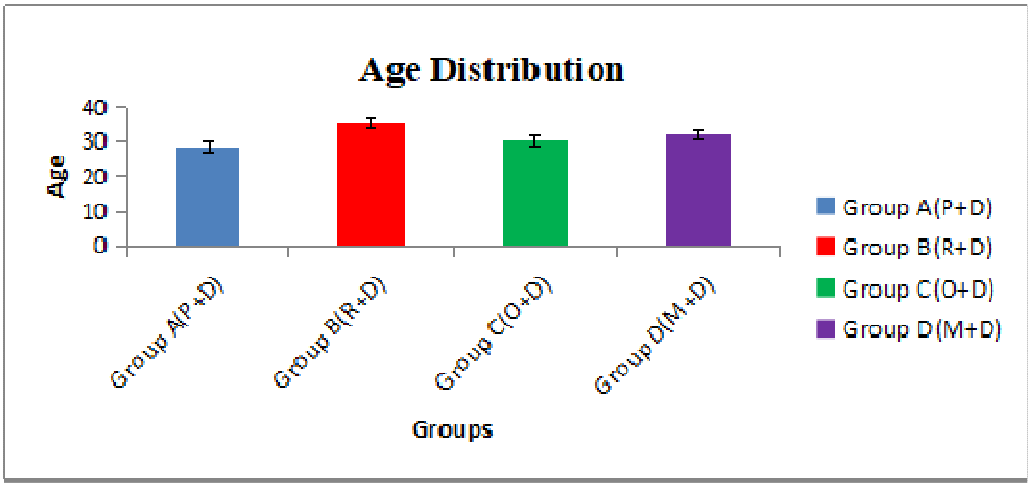
A total of 120 subjects were recruited to the studydivided into four groups GroupI served as (Placebo+Dextrmethasone) , Group II(Ramisetraon + Dextromethasone), Group III (Ondensetron + Dextromethasone) and Group IV(Metoclopromide + Dextromethasone) 30 subjects in each group. Among the 120 participants 65 were male and 55 female. There were 13 male and 17 females in P+D, 17 male and 13 female in R+D , 17 male and 13 female in O+D and 18 male and 12 female in M+D . The study participants were aged mean average 32.5 years in group P+D , 37.3 years in group R+D, 31.93 in group O+D and 32.26 in group M+D.The patients in all four groups were statistically comparable with regard demographic details of age and gender distribution with p value more than 0.05 (Table 1 & 2)

Table 1: Age distribution

Groups	Mean	F Value	P value
Group (P+D)	32.5 ± 10.86	1.262	**0.29(NS)**
Group (R+D)	37.3 ± 12.01		
Group (O+D)	31.93 ± 10.25		
Group (M+D)	32.26 ± 13.86		

Values are expressed as Mean ± SD, $p<0.05$ considered as statistically significant

Figure 1: Age distribution



Physical parameters:

The study participants were averege weight 57.73 kg in group P+D, 55.8 kg in group R+D, 56.06 kg in group O+D and 54.96 kg in group M+D.The height distribution were average 153 cm in group P+D , 152.4cm in group R+D, 151.4 in group O+D and 151cm in group M+D. The patients in all four groups were statistically comparable with physical parameters Weight and Height distribution with p value more than 0.05 (Table 3 & 4)

Table 3 : Weight of the patients

Groups	Mean(kg)	F Value	P value
Group (P+D)	57.73 ± 14.77	0.85	0.25(NS)
Group (R+D)	55.8 ± 10.6		
Group (O+D)	56.06 ± 11.03		
Group (M+D)	54.96 ± 13.64		

Values are expressed as Mean ± SD, $p<0.05$ considered as statistically significant

Figure 3:Wweight of the patients

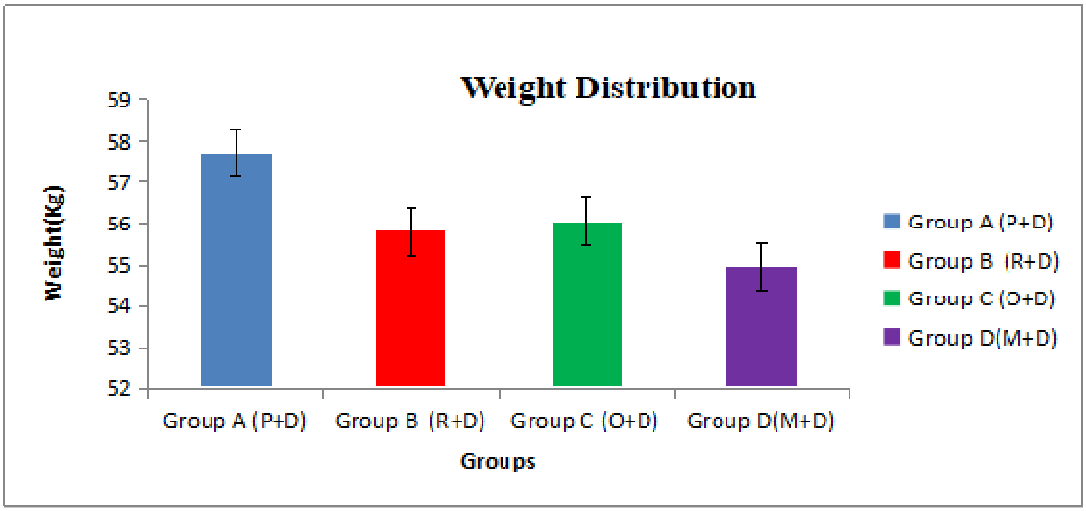
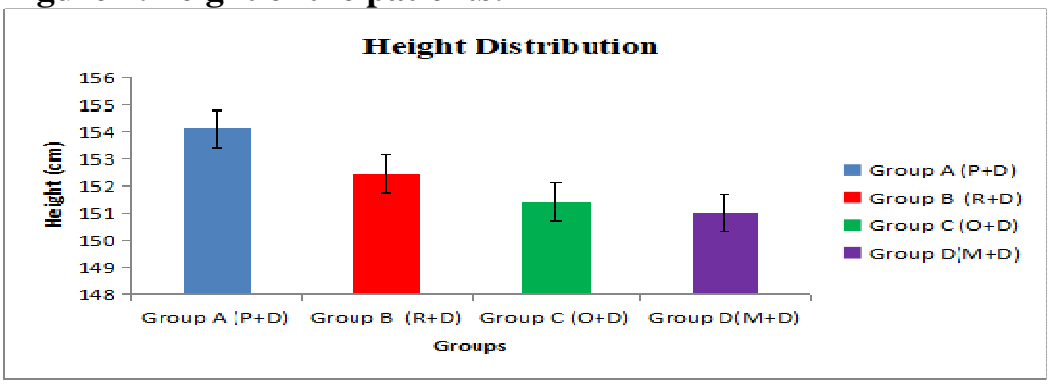


Table 4 : Height of the patients

Groups	Mean(kg)	SD	F Value	P value
Group (P+D)	154.13 ±	10.16	0.85	0.25(NS)
Group (R+D)	152.46 ±	9.43		
Group (O+D)	151.4 ±	10.66		
Group (M+D)	151.03 ±	11.39		

Values are expressed as Mean ± SD, $p<0.05$ considered as statistically significant

Figure 4:Height of the patients:



Patient response to anti emetics:

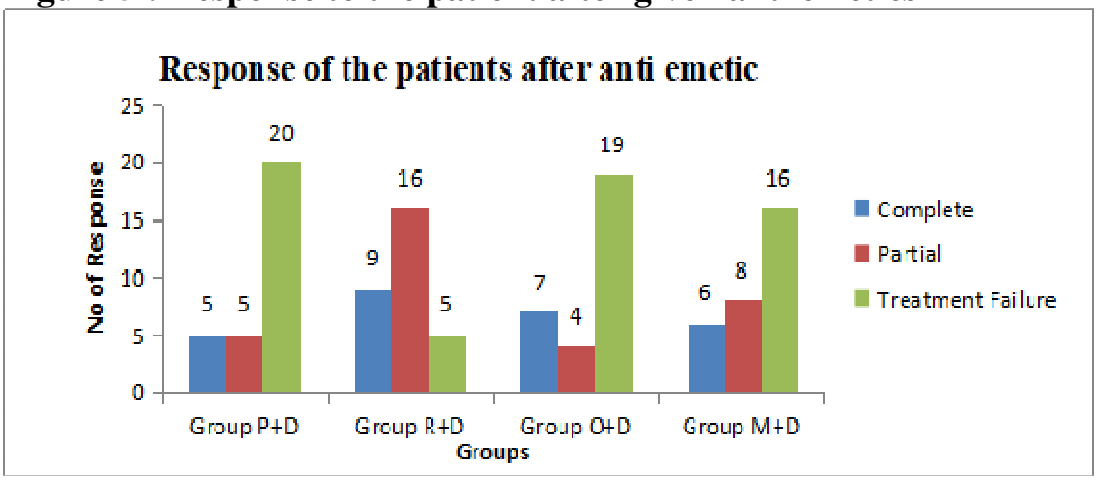
Out of 120 patients in the study, a total of 27 patients (22.5%) were completely relieved from PONV and did not required any rescue anti emetic drug for first 24 hrs after post operatively. Majority of the patients belonged to Group R+D 9 patients (30%) with less no of patients in Group P+D.

A total of 33 patients (27.5%) came under partial responponders, experiencing a single episode of PNOV in the post operative period. The maximum number of patients seen in the category of treatment failure with 60 patients(50%) who required two or more doses of rescue anti emetic drug post operatively. Maximum number of patients 20(66.66%) who lead treatment failure were in group P+D. Table (5).

Table 5: Response to the patient after given anti emetics

Groups	Response					
	Complete		Partial		Treatment Failure	
	No of patients	Percentage (%)	No of patients	Percentage (%)	No of patients	Percentage (%)
Group P+D	5	16.66%	5	16.66%	20	66.66%
Group R+D	9 (30)	30%	16	53.33%	5	16.66%
Group O+D	7(23.33)	23.33%	4	13.33%	19	63.33%
Group M+D	6(20)	20%	8	26.66%	16	53.33%
Total	27(22.5)	22.5%	33	27.5%	60	50%

Figure 5 : Response to the patient after given anti emetics



Incidence of Nausea:

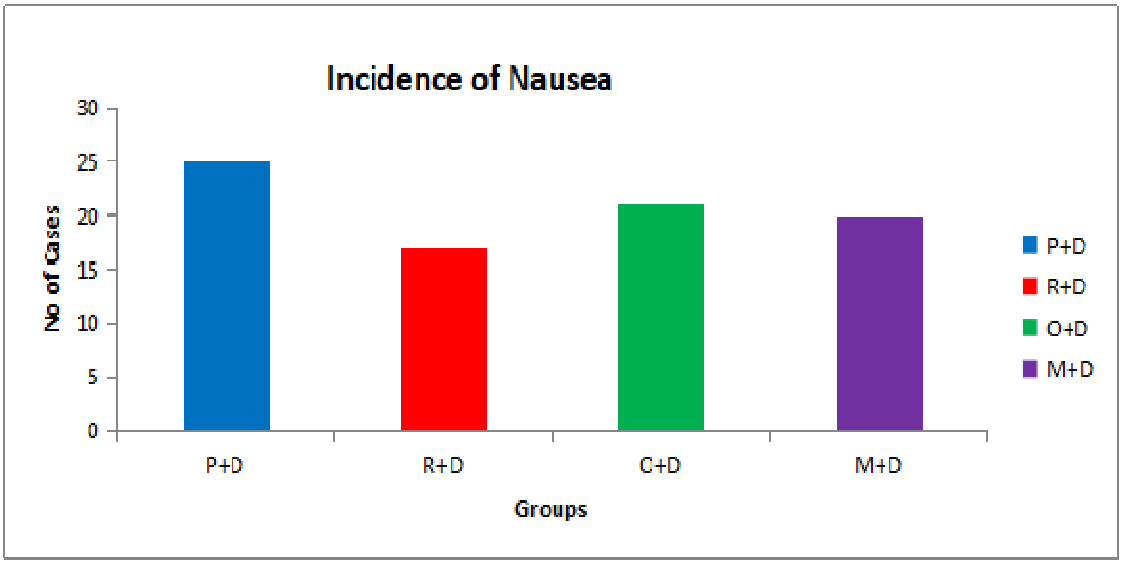
The incidence of nausea is shown in Table 7. Out of total of 120 patients in the study 83 patients experienced nausea. Maximum episodes ocurred in Group P+D 25 patients (83.33%) and minimum in Group R+D 17 patients(56.7%). The incidence of nausea was comparable in all the four groups, with a p value 0.163 which is not significant.

Table 7: Incidence of Nausea

Groups	Incidence of Nausea	X^2	P value
P+D	25 (83.33%)	5.119	0.163(NS)
R+D	17 (56.70%)		
O+D	21 (70.00%)		
M+D	20 (66.70%)		

NS- non significance

Figure 7: Incidence of Nausea



Episodes of nausea according to the duration of onset post operatively. Maximum episodes ocurred in 12-24hrs times span Duration wise incidence of vomiting was comparable in all the four groups. Maximum episode experienced in group P+D. Maximum effectiveness was shown in R+D with least incidence in first 6 hours. Statistics showed a significant difference in 0-2hrs($p<0.054$) and 2-6hrs($p<0.044$) among all the four groups.

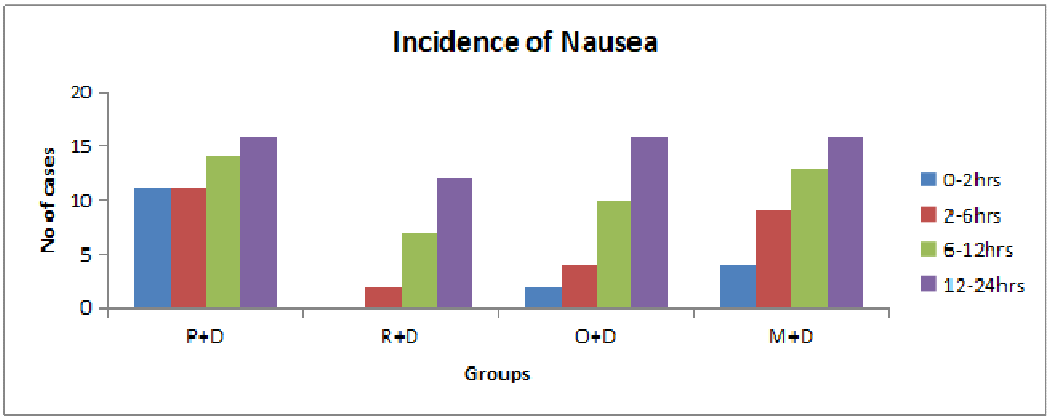
Table 8: Duration wise incidence of Nausea

Duration(Hrs)	Groups				X^2 Value	P Value
	P+D	R+D	O+D	M+D		
0-2hrs	11	0	2	4	5.831	**0.054**
2-6hrs	11	2	4	9	6.24	**0.044**
6-12hrs	14	7	10	13	2.71	0.259
12-24hrs	16	12	16	16	1.26	0.532

P<0.05 considered statistically significant

The statistics showed a significant difference in 0-2hrs(p<0.054) and 2-6hrs(p<0.044) and not a significant difference in 6-12 hrs and 12 - 24 hrs.

Figure 8: Duration wise incidence of Nausea



Incidence of Vomiting

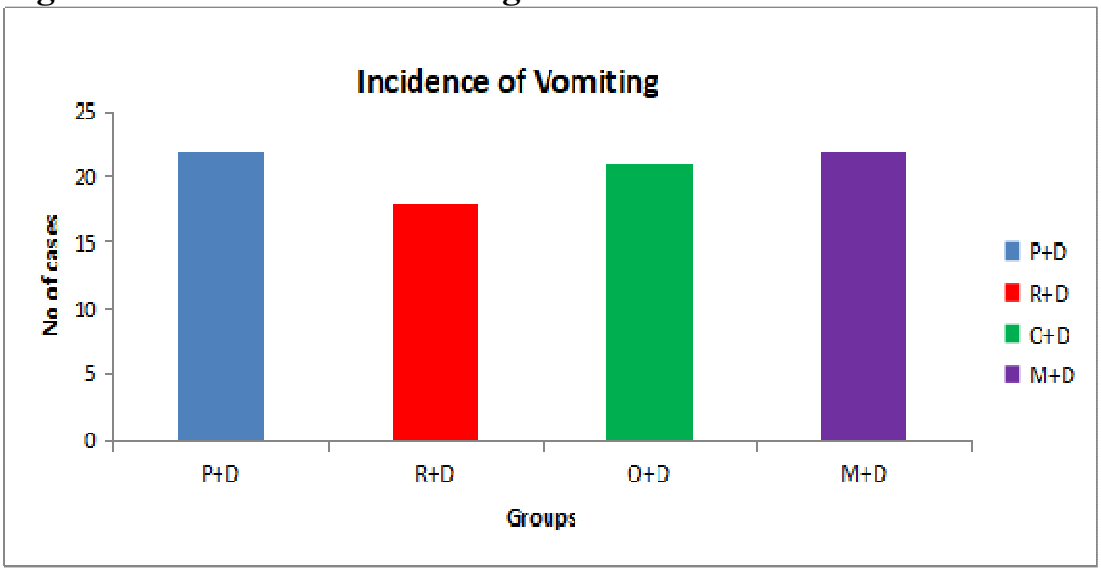
The incidence of vomiting is shown Table 9. Out of total of 120 patients in the study 83 patients experienced with nausea.Maximum episodes ocurred in Group P+D and Group M+D both with 22 patients (73.33%) and minimum in Group R+D 18 patients(60 %). The incidence of vomiting was comparable in all the four groups, with a p value 0.197 which is non significant.

Table 9: Incidence of Vomiting

Groups	Incidence of Vomiting	X^2	P value
P+D	22(73.3%)	1.973	0.373(NS)
R+D	18 (60 %)		
O+D	21 (70.00%)		
M+D	22(73.3%)		

P<0.05 statistically significance. NS- non significance

Figure 9 : Incidence of Vomiting



The episodes of vomiting according to the duration of occurance post operatively. Maximum episodes ocurred in 12-24hrs time span and overall highest incidence in group P+D. The duration wise incidence of vomiting was comparable in all the four groups. Maximum antiemetic effect was observed with least incidence of vomiting in group P+D. The statistics showed significant difference in 0-2hrs(P<0.012)

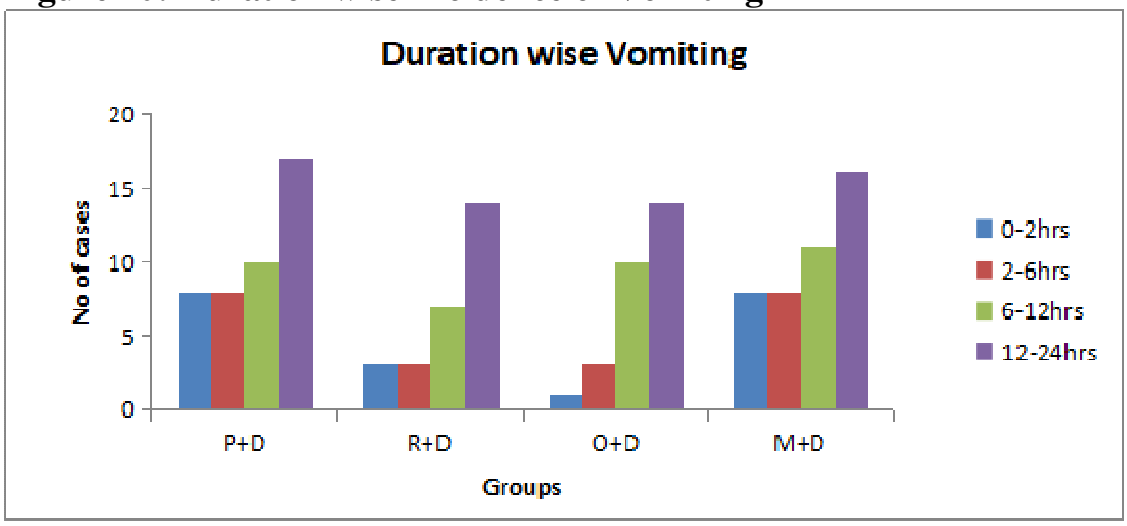
Table 10: Duration wise Incidence of Vomiting

Duration(Hrs)	Groups				X^2 Value	P Value
	P+D	R+D	O+D	M+D		
0-2hrs	8	3	1	8	14.07	**0.012(S)**
2-6hrs	8	3	3	8	4.22	0.121
6-12hrs	10	7	10	11	1.34	0.510
12-24hrs	17	14	14	16	0.913	0.825

S- Significance

Result showed a statistical significance among all the four groups in 0- 2hrs with p value 0.012 and no significant in other durations.

Figure 10: Duration wise Incidence of Vomiting



Total PONV:

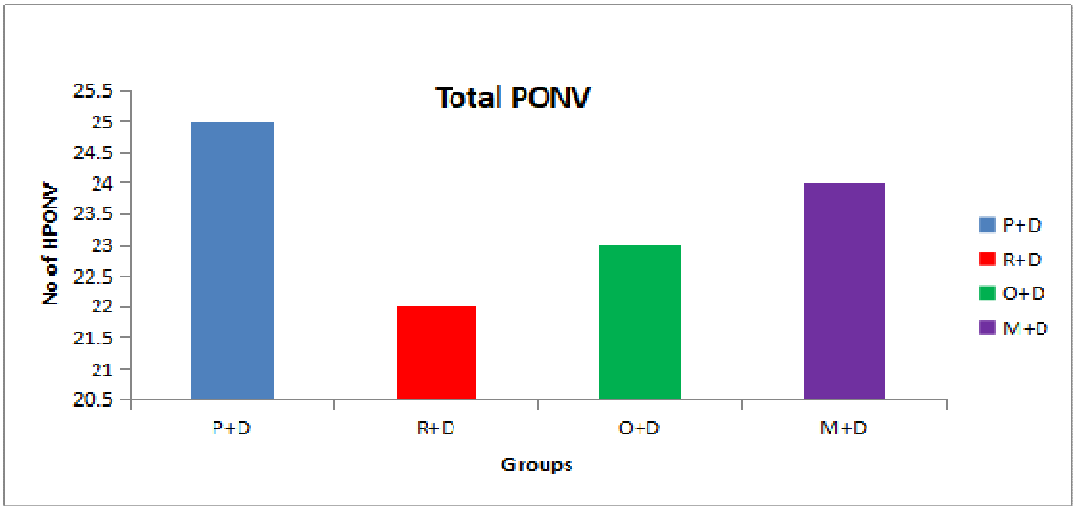
Total of 120 patients in the study , 94 patients experienced PONV. The incidence was highest in group P+D 25 patients (83.33%) and lowest in group R+D 22 patients (73.3%).The maximum preventive effect was observed in group R+D. The total PONV were comparable in all the four groups, with a p value 0.83 which is not significant.

Table 15: PONV in 0- 24 hrs

Groups	No of PONV (0-24hrs)	X^2	P value
P+D	25(83.3.%)	0.373	0.83(NS)
R+D	22(73.3%)		
O+D	23(76.7)		
M+D	24(80%)		

P<0.05 considered statistically significant

Figure 15: PONV in 0-24hrs



Duration after first rescue was given:

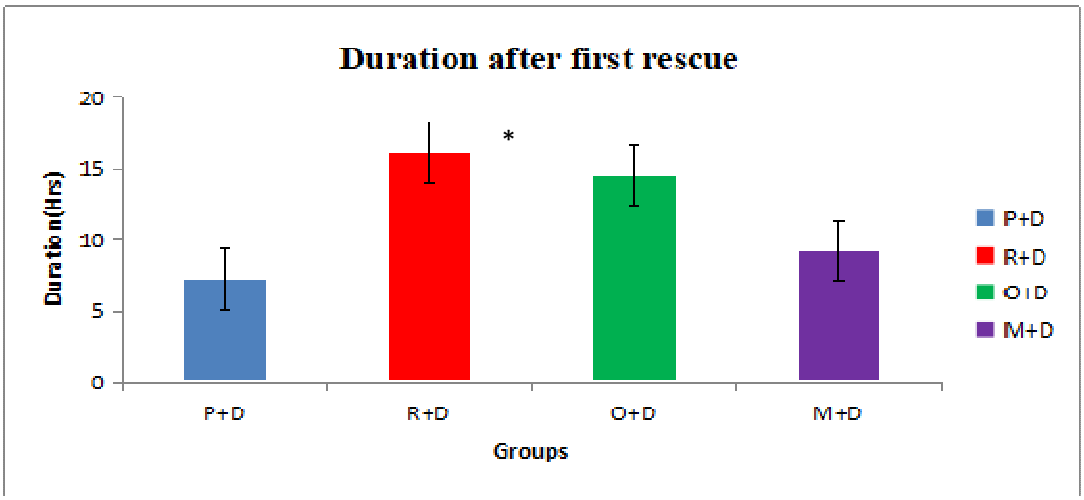
The time at which first dose of rescue anti emetic drug was given to the patients was observed (Table 11).The duration shown was longest in Group R+D (16.12 hrs) and shortest duration experienced in Group P+D(7.25hrs). The longer duration showing its higher efficacy in preventing PONV. It gave an indirect indication of the duration of action of the drugs. The R+D showed longer duration and were found to be statistically significant compared with P+D and M+D.. The p value is 0.019.

Table 11: Duration after first rescue was given

Duration (Hrs)	Groups				F Value	P Value
	P+D	R+D	O+D	M+D		
	7.25±7.67	16.12±8.40*	14.6±8.46	9.23±6.24	4.250	**0.019**

Results were expressed as Mean ± SEM & significant difference between groups was calculated using One-way ANOVA followed by post hoc (Tukey's)test. $p<0.05$ considered as statistically significant. * p value is 0.019 statistically significant in R+D when compared with P+D and M+D.

Figure 11: Duration after first rescue was given



Adverse drug reactions:

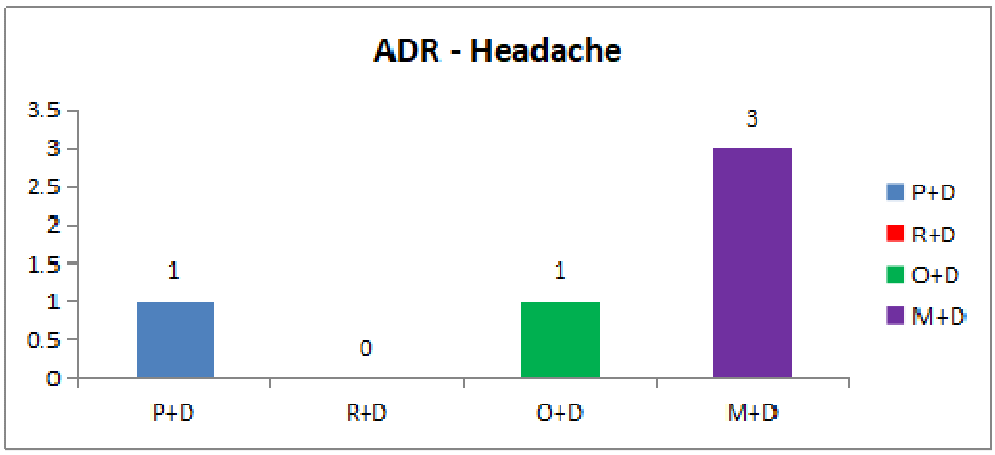
Out of 120 patients in the study, 5 patients experinced adverse drug reactions like headache. The maximum was observed in group M+D 3 patients. The statistics showed p value 0.265 which is non significant.

Table 12: ADR –Headache in each group

Groups	ADR- Headache	X^2 value	P Value
P+D	1	3.96	0.265 (NS)
R+D	0		
O+D	1		
M+D	3		

NS: Non significant

Figure 12: ADR –Headache in each group



ADR – Dizziness

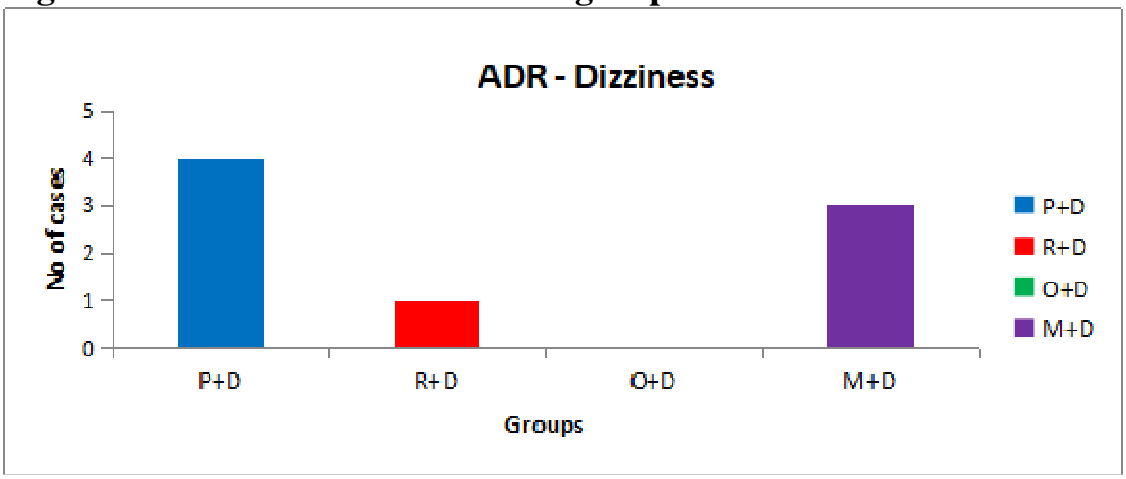
Out of 120 patients in the study, 8 patients experinced adverse drug reactions of dizziness. The maximum was observed in group P+D(4 patients) and Group M+D (3 patients) . The statistics were showed p value 0.265 which is not significant.

Table13 : ADR – Dizziness in each group

Groups	ADR- Heache	X^2 value	P Value
P+D	4	5.357	0.147
R+D	1		
O+D	0		
M+D	3		

NS: Non significant

Figure 13: ADR – Dizziness in each group



VAS score:

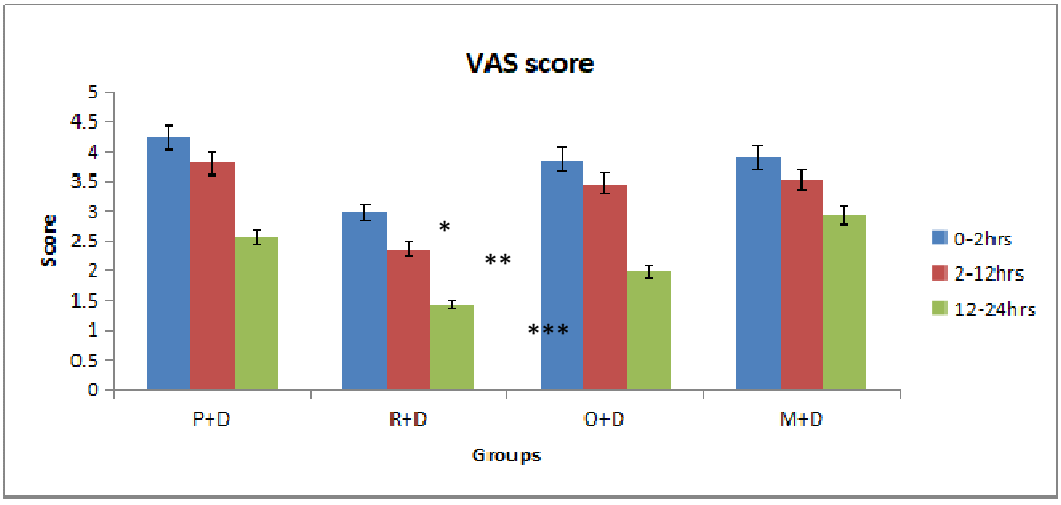
The VAS score difference in groups is shown in table14. The maximum score were in group P+D 4.22 in first 0-2 hrs. The maximum reduction of VAS score was observed in group R+D from 0 to 24hours. The R+D showed maximum reduction and were found to be statistically significant compared with P+D and M+D.

Table 14: VAS score difference in groups

Duration	Groups				F value	P value
	P+D	R+D	O+D	M+D		
0-2hrs	4.22±	2.98±0.71*	3.86±0.86	3.9±1.91	4.39	**0.015**
2-12hrs	3.81±	2.36±1.27**	3.46±1.35	3.53±1.65	5.93	**0.003**
12-24hrs	2.56±	1.43±1.13***	2.01±1.33	2.93±1.92	7.72	**0.001**

Results were expressed as Mean ± SEM & significant difference between groups was calculated using One-way ANOVA followed by post hoc (Tukey's)test. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ considered as statistically significant. * p value 0.015 statistically significant in R+D compared with P+D , O+D and M+D. ** p value 0.003 statistically significant in R+D compared with P+D , O+D and M+D. *** p value 0.001 statistically significant in R+D compared with P+D , O+D and M+D.

Figure 14: VAS score difference in groups



Results were expressed as Mean ± SEM & significant difference between groups was calculated using One-way ANOVA followed by post hoc (Tukey's)test. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ considered as statistically significant. * p value 0.015 statistically significant in R+D compared with P+D , O+D and M+D. ** p value 0.003 statistically significant in R+D compared with P+D , O+D and M+D. *** p value 0.001 statistically significant in R+D compared with P+D , O+D and M+D.

DISCUSSION

The optimal anti – emetic regimen for post-operative nausea and vomiting (PONV) is one which would decrease the incidence of nausea and vomiting without side effects like sedation , extrapyramidal symptoms , dry mouth , hypotension etc. Inspite of much attention paid to Post Operative Nausea and Vomiting the optimal anti-emetic regimen in surgical setting has still has not been established.

Four primary risk factors for PONV identified are: female gender, non-smoking, past history of motion sickness or PONV and use of postoperative opioids. Apfel classified patients with the presence of 0, 1, 2, 3, and 4 risk factors and noted incidence of PONV to be about 10%, 20%, 40%, 60%, and 80%, respectively.[5] In the present study we selected only patients with 2 or more risk factors, which put them in moderate to severe risk for PONV. As per the guidelines, patients with moderate to severe risk for PONV should receive combination therapy with two or more prophylactic drugs from different classes. Due to better side effect profile dexamethasone and 5HT3 antagonist are the commonly used antiemetics.

When ondansetron was the only 5HT3 antagonist available, the combination of dexamethasone and ondansetron was considered best choice for prevention of PONV after middle ear surgery. In a previous studies, they compared antiemetic efficacy of ramosetron to that of dexamethasone and ondansetron combination therapy and noted that combination of ondansetron with dexamethasone was still superior to ramosetron given alone for prevention of PONV following mastoid surgery. This was attributed to the fact that combination antiemetic are more efficacious than any single antiemetic agent, by blocking different receptors involved in the PONV pathway.

PONV occurs frequently in gynaecological, obstetric, breast and middle ear surgeries. PONV is a frequent and distressing complication after middle ear surgeries due to stimulation of vestibular system , with an incidence up to 80% when no antiemetics are used. Dexamethasone was found to be an effective antiemetic in patients undergoing chemotherapy for any carcinoma with limited side effects.The mechanism of action of corticosteroids is not clear but, may be related to inhibition of prostaglandin synthesis, decrease in the 5HT3 levels in the CNS or by an anti inflammatory action at operative sites there by reducing edema and pain. Animal studies suggest that it exerts its antiemetic effects through central inhibition of the nucleus tractus

solitarus but not the area postrema. PONV is multifactorial and combination drug therapy with different mechanisms of action is more effective. For patients at increased risk of PONV, the combination therapy using 5HT3 receptor antagonist with another antiemetic drug having a different mechanism and site of action is recommended.

SAMBA guidelines suggest that adults at moderate to high risk for PONV should receive combination therapy with one or more prophylactic drugs from different classes. It is also found that combinations will act synergistically. Single drug therapy has frequent failure rates in situations with severe and frequent PONV. Combination therapy is superior when compared to monotherapy for PONV prophylaxis. In view of these observations, in the present study combination of antiemetics was employed.

For PONV treatment and prevention , Ondansetron was the first 5HT3 receptor antagonist to become clinically available in market But when compared with other 5HT3 antagonists Ondansetron is less selective for the 5HT3 receptor. It also binds to 5HT1B, 5HT1C alpha adrenergic and opioid receptors with low affinity. It was revealed by a systematic review that Ondansetron's prophylactic effect on nausea was less pronounced when compared to vomiting. The combination of Dexamethasone and Ondansetron was considered as the good choice for preven tion of PONV after middle ear surgery. This was because of the different mechanisms by which the drugs act in controlling PONV.

Ramosetron is a recently developed 5HT3 receptor antagonist with a strong affinity and longer duration of action compared with other 5HT3 receptor antagonists. The elimination half life of Ramosetron (9.3hour) is longer in comparison to Ondansetron (3.5h),Granisetron(4.9h) and Alosetron(3.0h).

Ramosetron has a higher affinity (Ki = 0.091) and slower dissociation rate for 5HT3 receptors compared with other 5HT3 receptor antagonists. The active metabolite M1 maintains a high receptor occupancy and prolongs the duration of action.

In present study, Out of 120 patients in the study, a total of 27 patients (22.5%) were completely relieved from PONV and did not required any rescue anti emetic drug for first 24 hrs after post operatively. Majority of the patients belonged to Group R+D , 9 patients (30%) with less no of patients in Group P+D.

A total of 33 patients (27.5%) comes under partial responders, experiencing single episode of PONV in the post operative period. The maximum number of patients seen in the category of treatment failure with 60 patients(50%) they required two or more doses of rescue anti emetic drug post operatively. Maximum number of patients 20(66.66%) under treatment failure in group P+D. Table (5).

Also there was clinical and statistical significance in the incidence of Nausea in between the groups in the first 6 hours. When compared to other groups , in group II (Ramosetron + Dexamethasone) the incidence of nausea is decreased significantly in first 6 hours. which is statistically highly significant ($p<0.054$). When compared to the group (P+ D) and group (M+D) , in group III (O+D) also the incidence of nausea is decreased which is also statistically significant ($p= 0.044$). When compared to the group I (P+D) , in group IV (M+D), the incidence of nausea was less in the group but it was not statistically significant ($P= 0.532$).

There was no statistical significance in the incidence of PONV in between the groups in 6 -12 hours. When compared to P+D and M+D group the incidence of PONV is decreased in the O+D and R+D group, which is not statistically significant($p= 510$& $p= 0.825$). When compared to the P+D and M+D group has less incidence of PONV but is not statistically significant ($p= 0.825$)

Between 12 -24 hours ,the incidence of vomiting showed in Table 9. Out of total of 120 patients in the study 83 patients experienced with nausea.The maximum episodes ocurred in Group P+D and Group M+D both were 22 patients (73.33%) and minimum in Group R+D 18 patients(60 %). The incidence of vomiting was comparable in all the four groups, with a p value 0.197 which is non significant.

Our study is comparable with Sameer N Desai et al study ^25. Total of 120 patients in the study , 94 patients experienced with PONV. The incidence was higher in group P+D 25 patients (83.33%) and least in group R+D 22 patients(73.3%). The total PONV were comparable in all the four groups, with a p value 0.83 which is non significant.

Our study is also comparable with Younghoon Jeon et al study. They found that PONV rate was significantly lower in the combination group i.e., Ramosetron 0.3mg + Dexamethasone 8 mg than in the Dexamethasone alone Group I P+D . In the current study we observed that PONV rate was significantly lower in the Group II (R+D) when compared to the O+D in the first 6 hours. We also noted that incidence of PONV was lower in O+D when compared to the M+D Group. Our results were also comparable to S. I. Kim et al study who found that the incidence of nausea was less in the Ramosetron and Ondansetron Group Groups in comparison to the placebo group ($p< 0.05$). In addition, the incidence of vomiting was lower in both the Ramosetron and the Ondansetron Groups than in the placebo Group in 24 hours after surgery, but statistically not significant. Only saline was used as placebo in their study whereas we used saline + Dexamethasone in our control group.

Dinesh Govinda Rao et al in their study found complete response in 90% in OD Group and 100%in RD Group in 6-12 hour period and in the 12- 24 hour period complete response was 97% in OD Group and 100% in RD Group. These results were comparable with our study. We found complete response in 30 %in R+D and 23.33 % in R+D group .

Our study is also comparable to Lee et al study in thyroid surgeries under general anaesthesia, they used Ramosetron and Dexamethasone for PONV with ramosetron alone. They concluded that combination therapy is better than single drug therapy for PONV.

The requirement of rescue antiemetics was higher in the P+D Group when compared to O+ D Group and R+D Group . The adverse effects like headache, dizziness, drowsiness, flushing or sedation were very minimal in all the three groups at any time interval during the study period and statistically not significant.

The VAS score difference in groups showed in table14. The maximum score was in group P+D 4.22 in first 0-2 hrs. The VAS score were comparable in all the four groups and showed a highly significant variation with a p value < 0.001 in P+D group , which shows PONV was also associated with pain and discomfort and need of opiod for post operative analgesia also increases. In other groups it was same and no significant results obtained .

CONCLUSION

Combination of Dexamethasone 8 mg with antiemetic 5HT3 receptor antagonists Ramosetron (0.3mg) or Ondansetron (4mg) decreases the incidence of nausea and vomiting and the requirement for rescue antiemetic therapy and rescue analgesia in the first 24 hours post operatively. Dexamethasone and Ramosetron combination has a longer duration of action than Dexamethasone and Ondansetron combination in decreasing PONV after middle ear surgery , but they have same efficacy .Cost effectives of Ondansetron was significant when compared to Ramosetron .

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PROFORMA

DATE: ROLL NO:

AIRWAY DEVICE: NAME:

AGE: SEX: IP NO:

DIAGNOSIS:

SURGICAL PROCEDURE DONE:

Ht: CVS: HB:

Wt: RS:

AIRWAY:MMC -

IID - DENTITION -

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness

H/O Documented Difficult Airway

H/O previous surgeries

MEASURES OF STUDY OUTCOME:

INTUBATION RESPONSE:

Premedication:

induction:

Intubation:

Maintanance:

Positioning;

ANTI EMETIC DRUG GROUPS ;

Drugs

COMPLICATIONS IN INTRA OPERATIVE PERIOD:

COMPLICATIONS POST EXTUBATION:

Hemodynamics: intra operative

Events	Time	Systolic BP (mmHg)	Diastolic BP (mmHg)	MAP	Heart rate Beats/min	SPO2
Baseline						
Induction						
Incision						
End of procedure						
Extubation						

TIME(MIN	0	5	10	15	20	25	3 0	45	60	75	90	105	120	135	150	165	180
HR																	
SBP																	
DBP																	
MAP																	
SPO2																	
ATRACURIUM																	
FENTANYL																	

POST OPERATIVE

TIME(hrs)	0	**0.5**	**1**	**1.5**	**2**	**2.5**	**3**	**3.5**	**4**	**4.5**	**5**	**5.5**	**6**	**10**	**14**	**18**	**22**	**24**
VAS																		
HR																		
SBP																		
DBP																		
MAP																		
SEDATION SCORE																		
Resque antiemetics																		

INFORMATION TO PARTICIPENTS

Investigator **:** Dr. M.KASI

Name of the Participant:

"**COMPARISON OF THREE GROUPS OF ANTIEMETIC DRUGS FOR PREVENTION OF PONV AFTER MIDDLE EAR SURGERY** ".

(A Prospective, randomized, double blinded , placebo controlled study for evaluating the antiemetic effect and efficacy of ramosetron (0.3 mg)with dexamethasone Vs Ondensetron(4mg) with dexamethasone Vs metoclopramide (10mg) with dexamethasone)

You are invited to take part in this research study. We have got approval from the IEC. You are asked to participate because you satisfy the eligibility criteria. We want to compare three anti emetic drug groups for prevention of post operative nausea and vomiting after middle ear surgery

(A Prospective, randomized, double blinded , placebo controlled study for evaluating the antiemetic effect and efficacy of ramosetron (0.3 mg)with dexamethasone Vs Ondensetron(4mg) with dexamethasone Vs metoclopramide (10mg) with dexamethasone)

What is the Purpose of the Research:

For Thyroid surgeries, superficial and deep cervical plexus block performed using ultrasound after general anaesthesia to study

1. **To evaluate the need of rescue antiemetic after surgery**
2. **To assess an post operative pain intensity using Post operative visual analogue scale pain score.**
3. **Complication rate.**
4. **To evaluate post operative opioids dosage**

The Study Design:

All the patients in the study will be divided into four groups.

120 patients presenting for thyroid surgery were randomly assigned to three groups .

GroupA-Isotonic saline 2cc with dexamethasone 8mg one hour before end of surgery

Group B- Injection of ramosetron(0.3mg) with dexamethasone 8mg one hour before end of surgery

Group C- injection of ondensetron 4mg with dexamethasone 8mg one hour before end of surgery

Group D – Injection of metoclopramide 10mg with dexamethasone 8mg one hour before end of surgery

Benefits

To know which is effective antiemetic drug to prevent post operative nausea and vomiting after middle ear surgery which is most common complication .

Discomforts and risks

This intervention has been shown to be well tolerated as shown by previous studies. And if you do not want to participate you will have alternative of setting the standard treatment and your safety is our prime concern.

Time : Date : Place :

Signature / Thumb Impression of Patient

Patient Name:

Signature of the Investigator : _____

Name of the Investigator : _____

PATIENT CONSENT FORM

Study title "**COMPARISON OF THREE GROUPS OF ANTIEMETIC DRUGS FOR PREVENTION OF PONV AFTER MIDDLE EAR SURGERY** ".

(A Prospective, randomized, double blinded , placebo controlled study for evaluating the antiemetic effect and efficacy of Ramosetron (0.3 mg)with Dexamethasone Vs Ondensetron(4mg) with Dexamethasone Vs Metoclopramide (10mg) With Dexamethasone)

Study center: **INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE,**

RAJIV GANDHI GOVT. GENERAL HOSPITAL,

MADRAS MEDICAL COLLEGE,

CHENNAI-0 3.

Participant name: Age: Sex: I.P.No:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Time:

Date: Signature / thumb impression of patient

Place: Patient name:

Signature of the investigator:

Name of the investigator:

Master Chart

Group - A

MASTER CHART														FIRST 2 HRS			
NAME	AGE	SEX	IP NO	WT(KG)	HT(CM)	DIAGNOSIS	OSSICULOPLASTY	SMOKER/NS	H/OPONV	APFEL S	ANES DUR	SUG DUR	DOF	NAUSEA	VOMITING	RESCUE	H/OPONV
KUMARAN	25	M	16454	48	150	R AURAL POLYP	N	NS	S	2	140	120	140	N	N	N	N
LAKSHMI	36	F	12453	49	155	R CSOM CP	S	NS	N	3	120	110	100	N	N	N	N
PREMA	40	F	18452	72	162	R COM CP	S	NS	S	3	140	120	140	Y	Y	Y	Y
YOGESHWARI	13	F	56933	24	120	R CSOM CP	N	NS	N	2	110	100	120	N	N	N	N
RAMANI	44	F	8834	50	155	L COM AAD	S	NS	S	3	180	160	140	Y	Y	Y	Y
VELAN	44	M	18582	100	164	LCSOM CP	N	S	N	0	180	140	180	N	N	N	N
BHARATHI	28	F	22763	64	154	L COM CP	N	NS	S	3	160	110	140	N	N	N	N
RAJKUMAR	24	M	23769	50	154	L CSOM CP	N	NS	S	2	140	120	100	Y	Y	Y	Y
KARTHICK	28	M	153302	70	160	R CSOM CP	N	NS	S	2	120	100	140	N	N	N	N
SANKARLINGAM	14	M	58505	38	140	R COM AAD	S	NS	S	2	190	170	100	N	N	N	N
SUBA	23	F	67823	53	153	L AURAL POLYP	N	NS	N	2	190	150	130	N	N	N	N
YOGESHWARI	21	F	52142	42	160	R CSOM AAD	S	NS	N	2	210	190	100	Y	Y	Y	Y
KIRUBA	49	F	12308	64	160	L CSOM CP	N	NS	N	2	200	180	120	N	N	N	N
RENKI DEVI	30	F	16917	70	154	R COM CP	S	NS	S	4	180	160	140	N	N	N	N
APAAJITHA	26	F	16383	54	154	L COM CP	N	NS	N	2	190	170	140	N	N	N	N
SIKKATHAI	52	F	10517	72	154	L COM CP	N	NS	N	2	180	160	160	N	N	N	N
INDRAJITH	22	M	18557	47	155	R COM CP	N	NS	S	3	160	130	140	Y	Y	Y	Y
ANBARASI	33	F	13723	54	162	R CSOM CP	N	NS	S	3	160	120	140	N	N	N	N
PERIYASAMY	47	M	14399	72	165	R COM CP	N	S	N	0	160	140	140	Y	N	Y	Y
SANKAMMAL	47	F	57041	62	140	L COM AAD	S	NS	S	4	210	190	160	Y	Y	Y	Y
SIVA	32	M	63228	60	168	L CSOM CP	N	NS	N	1	190	170	130	N	N	N	N
BAKKIYARAJ	36	M	23443	45	161	L COM CP	N	S	N	0	145	130	130	N	N	N	N
SELVI	23	F	14578	68	160	L COM CP	N	NS	N	2	165	130	140	Y	N	Y	Y
MOORTHY	20	M	19034	39	135	L CSOM CP	N	NS	N	0	130	110	130	N	N	N	N
BAKKIYAM	27	F	17834	70	150	R CSOM CP	N	NS	N	2	120	100	140	Y	Y	Y	Y
HAFIES	26	M	12300	65	150	L COM CP	N	NS	N	1	160	135	150	N	N	N	N
CHITHRA	37	F	15200	45	165	L COM CP	S	NS	N	3	150	130	150	Y	Y	Y	Y
PONNUSAMMY	47	M	15686	56	147	R CSOM CP	S	NS	N	1	135	120	170	N	N	N	N
BABY	46	F	14586	75	152	R COM CP	S	NS	N	2	180	150	140	Y	N	Y	Y
SOLAI	35	M	10032	54	165	R COM CP	N	S	N	0	160	140	140	N	N	N	N

GROUP A ISOTONIC SALINE+ DEXAMETHASONE																				
2-6 HRS				6-12 HRS				12-24 HRS				0-24 HRS PON	RESCUE DOSE	T DURATION	VAS SCORE			OPIOD DOS	SIDE EFFECTS	
NAUSEA	VOMITING	RESCUE	H/OPON	NAUSEA	VOMITING	RESCUE	H/OPON	NAUSEA	VOMITING	RESCUE	H/OPONV				2HRS	2-12 HRS	12-24 HRS		HEADACH	DIZZINES	ALLERGY
Y	N	Y	Y	N	N	N	N	N	N	N	N	Y	4MG	4HRS	8	3	2	50MG	N	N	N
Y	N	Y	Y	Y	N	Y	Y	Y	N	Y	Y	Y	12MG	2HRS	6	4	4	50MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	0HRS	8	5	1	100MG	N	N	N
Y	N	N	N	Y	Y	Y	Y	N	Y	Y	Y	Y	8MG	2HRS	3	5	5	100MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	0HRS	3	2	1	0MG	N	N	N
Y	N	Y	Y	N	N	N	N	Y	N	Y	Y	Y	8MG	4HRS	3	3	3	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	8MG	6HRS	2	4	4	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	1HRS	4	4	3	0MG	N	N	N
Y	N	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	12MG	3HRS	4	3	3	0MG	N	Y	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24HRS	3	3	0	0MG	N	N	N
Y	Y	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	8MG	4HRS	2	5	3	50MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	Y	4MG	1HRS	4	3	3	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24HRS	3	3	0	0MG	N	Y	N
Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	12MG	2 HRS	5	1	1	50MG	N	N	N
N	N	N	N	N	N	N	N	Y	N	Y	Y	Y	4MG	12HRS	3	2	1	0MG	Y	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24HRS	3	3	2	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	N	N	N	N	Y	8MG	0HRS	8	5	4	100MG	N	N	N
Y	N	Y	Y	Y	N	Y	Y	Y	N	Y	Y	Y	12MG	4HRS	3	5	5	100MG	N	N	N
N	N	N	N	Y	N	Y	Y	Y	Y	Y	Y	Y	12MG	1HRS	5	3	3	50MG	N	Y	N
Y	Y	Y	Y	N	N	N	N	N	N	N	N	Y	8MG	1HRS	6	5	0	100MG	N	N	N
N	N	N	N	N	Y	N	Y	Y	N	N	N	Y	4MG	8HRS	4	8	4	50MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24HRS	2	2	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	N	Y	Y	Y	8MG	1HRS	10	6	5	150MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	8MG	8HRS	3	3	2	0MG	N	Y	N
N	Y	Y	Y	N	N	N	N	N	Y	Y	Y	Y	12MG	0HRS	3	3	0	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	8MG	8HRS	3	4	4	0MG	N	N	N
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	0HRS	8	6	0	100MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24HRS	1	1	0	0MG	N	N	N
N	Y	Y	Y	N	N	N	N	N	N	N	N	Y	8MG	0HRS	4	6	6	100MG	N	N	N
Y	Y	Y	Y	N	N	N	N	N	N	N	N	Y	4MG	3HRS	2	4	4	0MG	N	N	N

Group – B

MASTER CHART

NAME	AGE	SEX	IP NO	WT(KG)	HT(CM)	DIAGNOSIS	OSSICULOPLASTY	SMOKER/NS	H/OPONV	APFEL S	ANES DUR	SUG DUR	DOF	FIRST 2 HRS			
														NAUSEA	VOMITTING	RESCUE	H/O PONV
SATHISH	28	M	21868	56	156	L CSOM CP	Y	NS	N	1	200	180	140	N	N	N	N
MADHU	46	M	3150	50	158	L CSOM CP	N	S	S	1	150	130	120	N	N	N	N
KALPANA	33	F	3814	48	150	R CSOM CP	Y	NS	S	3	154	140	120	N	N	N	N
KUMAR	48	M	38155	70	162	R CSOM CP	Y	NS	N	1	120	90	140	N	N	N	N
RANI	35	F	8405	52	150	L CSOM CP	Y	NS	N	3	130	120	100	N	N	N	N
USHA	32	F	4689	42	156	R CSOM CP	N	NS	N	2	90	80	100	N	N	N	N
MURUGAN	23	M	7484	50	135	R CSOM CP	N	NS	N	1	110	100	120	N	N	N	N
KALPANA	45	F	16484	62	140	R ATTIC RET	Y	NS	S	4	200	180	150	N	N	N	N
NARASIMMAN	16	M	32860	38	135	R AURAL POLYP	N	NS	S	2	160	140	120	N	N	N	N
VENDA	26	F	36441	48	152	L CSOM CP	N	NS	N	2	160	140	120	N	N	N	N
ANJALI	35	F	1977	54	154	L CSOM CP	N	NS	N	2	210	190	140	N	N	N	N
CHITHRA PANDI	47	M	37968	64	160	L CSOM CP	Y	S	S	1	130	100	140	N	N	N	N
DURGA	20	F	5454	42	142	R CSOM CP	N	NS	N	2	140	120	100	N	N	N	N
MUTHUPANDIYAN	55	M	32811	70	164	L CHOLESTE	S	S	N	1	210	180	180	N	N	N	N
KUMAR	43	M	10823	64	156	R CSOM CP	N	NS	S	2	130	120	140	N	N	N	N
KARTHICK	19	M	46132	50	146	L CSOM CP	N	NS	S	2	145	130	140	N	N	N	N
SEKAR	55	M	3537	80	164	L CSOM CP	N	S	N	1	140	120	160	N	N	N	N
LOGANAYAKI	36	F	178190	70	158	L CSOM CP	N	NS	S	2	110	90	140	N	N	N	N
PARIMALA	30	F	14745	46	162	L COM CP	N	NS	N	1	150	120	140	N	N	N	N
MALLIKA	45	F	9223	56	152	R COM TTD	S	NS	S	3	175	150	150	N	N	N	N
KAMALA	23	F	34456	60	148	L CSOM CP	N	NS	S	3	150	130	140	N	N	N	N
RAM	40	M	15173	62	152	R CSOM CP	N	S	N	0	130	110	150	N	N	N	N
GOPINATH	34	M	13456	46	145	L CSOM CP	S	NS	N	1	150	130	150	N	N	N	N
MULLAI	23	F	13245	60	167	L ATTIC PER	S	NS	S	4	190	170	160	N	N	N	N
BASKAR	43	M	10567	45	156	L CSOM CP	N	S	N	0	130	100	100	N	N	N	N
SABARI	56	M	10876	67	160	R CSOM CP	N	S	N	0	120	100	140	N	N	N	N
RUPA	46	M	10345	56	134	L CSOM CP	N	NS	N	2	135	120	130	N	N	N	N
SENTHIL	35	M	10879	56	165	R ATTIC RET	S	NS	N	1	200	170	150	N	N	N	N
CHOCKALINGAM	40	M	1789	40	139	L CSOM CP	N	NS	N	0	100	80	100	N	N	N	N
PACHAIAMMAL	62	F	13224	70	156	L CSOM CP	N	NS	S	3	140	120	160	N	N	N	N

Group B RAMOSETRON+DEXAMETHASONE																					
2-6 HRS				6-12 HRS				12-24 HRS				0-24 HRS PON	RESCUE DOSA	T DURATION	VAS SCORE			OPIOD DOSAG	SIDE EFFECTS		
NAUSEA	VOMITING	RESCUE	H/OPONV	NAUSEA	VOMITING	RESCUE	H/O PONV	NAUSEA	VOMITING	RESCUE	H/O PONV				2HRS	2-12 HRS	12-24 HRS		HEADACH	DIZZINES	ALLERGY
N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	4MG	14	3	3	3	0MG	N	N	N
Y	Y	Y	Y	N	N	N	N	N	N	N	N	Y	4MG	4	3	4	2	0MG	N	N	N
N	N	N	N	N	Y	Y	Y	N	N	N	N	Y	4MG	12	4	2	0	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0 MG	24	3	3	1	0MG	N	N	N
N	N	N	N	Y	N	Y	Y	Y	N	Y	Y	Y	8MG	8	4	2	1	0MG	N	N	N
N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	4	2	2	2	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0 MG	24	2	0	0	0MG	N	N	N
N	N	N	N	Y	N	N	Y	N	N	N	N	Y	4MG	8	3	5	2	50MG	N	N	N
N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	4MG	12	3	3	0	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	4	4	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	4MG	15	4	2	1	0MG	N	N	N
Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	8	2	4	4	0MG	N	N	N
N	N	N	N	N	N	N	N	N	Y	Y	N	Y	4MG	13	3	3	3	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	3	0	0	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	3	0	0	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	3	2	1	0MG	N	Y	N
N	N	N	N	N	N	N	N	Y	N	Y	Y	Y	4MG	18	4	3	1	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	4MG	12	3	2	2	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	2	3	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	4MG	15	3	2	2	0MG	N	N	N
N	Y	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	4MG	5	3	4	1	0MG	N	N	N
N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	4MG	15	2	3	1	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	3	1	0	0MG	N	N	N
N	N	N	N	Y	Y	N	Y	N	N	N	N	Y	4MG	10	4	1	0	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	4MG	12	2	1	0	0MG	N	N	N
N	N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	8MG	10	2	2	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	4MG	14	4	2	3	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	N	N	N	N	Y	4MG	8	3	2	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	N	N	N	Y	0MG	24	4	2	3	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	8MG	6	3	4	2	0MG	N	N	N

Group –C

MASTER CHART														FIRST 2 HRS			
NAME	AGE	SEX	IP NO	WT(KG)	HT(CM)	DIAGNOSIS	OSSICULOPLASTY	SMOKER/NS	H/OPONV	APFEL S	ANES DUR	SUG DUR	DOF	NAUSEA	VOMITING	RESCUE	H/OPONV
SARAVANA KUMAR	30	M	46946	62	160	R CSOM AAD	Y	NS	N	1	120	100	160	N	N	N	N
SHANMUGAM	49	M	46165	60	168	R COM CP	Y	S	S	1	134	120	140	N	N	N	N
REVATHY	19	F	23056	40	148	R COM CP	N	NS	N	2	120	110	120	N	N	N	N
TAMIL SELVI	23	F	3523	52	148	L COM POLYP	N	NS	N	2	110	90	140	N	N	N	N
SALIM	28	M	1873	60	154	L COM CP	N	NS	N	1	140	120	120	N	N	N	N
SURESH	44	M	47939	72	164	L AURAL POLYP	N	S	N	1	160	140	140	N	N	N	N
MADHAVI	15	F	47936	40	130	L COM CP	N	NS	S	3	100	90	100	N	N	N	N
KUMARAN	42	M	28109	70	154	L CSOM CP	N	NS	N	1	150	130	140	N	N	N	N
LINGESH	17	M	13297	46	140	R CSOM CP	S	NS	N	1	140	120	120	N	N	N	N
MURALI	41	M	17973	70	162	OTOSCLEROSIS	S	NS	N	1	210	190	160	N	N	N	N
RAMYA	17	F	11253	56	135	R CSOM CP	N	NS	S	4	160	140	140	N	N	N	N
NASIRA	45	F	39413	64	146	R CSOM CP	N	NS	N	3	140	110	140	Y	Y	Y	Y
LAKSHMI DEVI	43	F	49633	68	160	R CSOM CP	N	NS	S	3	160	140	140	N	N	N	N
BHAVANI	30	F	32364	54	148	L COM CP	N	NS	N	2	160	140	120	N	N	N	N
THIRUNAVUKKARASU	15	M	12471	38	138	R COM CP	S	NS	N	2	120	100	100	N	N	N	N
SARITHA	30	F	2663	50	160	R COM CP	N	NS	N	2	130	100	120	N	N	N	N
RAMAMOORTHY	47	M	182706	52	156	R COM CP	N	NS	S	2	140	120	140	N	N	N	N
HONESRAJ	23	M	12460	40	140	R COM CP	N	NS	S	2	110	90	100	N	N	N	N
KALAIMANI	34	F	10988	52	162	R CSOM CP	S	NS	S	4	160	130	140	N	N	N	N
SUBRAMANI	42	M	22912	72	160	R CSOM CP	N	NS	N	1	130	120	140	N	N	N	N
BRINDA	28	F	9228	60	145	L COM CP	N	NS	N	2	120	90	140	N	N	N	N
RENGA	34	M	33212	54	160	L CSOM CP	N	NS	N	1	130	110	140	N	N	N	N
RAMESH	23	M	12456	45	135	R COM AP	S	NS	N	1	180	140	120	N	N	N	N
GIRI	45	M	13453	67	167	L COM	N	S	N	0	140	130	140	N	N	N	N
MURALI	32	M	1443	53	150	L CSOM CP	N	S	N	0	120	100	120	N	N	N	N
GANESH	31	M	12346	57	162	R AURAL POLY	N	NS	N	1	145	120	150	N	N	N	N
FREEDA	23	F	14567	38	135	L CHOLEST	S	NS	S	4	220	200	140	N	N	N	N
BINDU	36	F	12490	50	145	R COM CP	N	NS	N	2	135	120	120	Y	N	Y	Y
DEEPA	40	F	13456	65	156	L COM CP	N	NS	N	2	140	120	140	N	N	N	N
SIDDHATH	32	M	4529	75	154	L COM CP	N	S	N	0	140	110	140	N	N	N	N

GROUP C ONDENSETRON+DEXAMETHASONE

2-6 HRS				6-12 HRS				12-24 HRS				0-24 HRS PON	RESCUE DOSE	T DURATION/H	VAS SCORE			OPIOD DOSE	SIDE EFFECTS		
NAUSEA	VOMITING	RESCUE	H/OPON	NAUSEA	VOMITING	RESCUE	H/OPON	NAUSEA	VOMITING	RESCUE	H/OPONV			2HRS	2-12 HRS	12-24 HRS			HEADACH	DIZZINESS	ALLERGY
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	16MG	8	5	4	3	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	5	4	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	8MG	10	5	5	3	0MG	N	N	N
Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	16MG	4	5	4	3	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	4	4	4	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	8MG	12	5	5	4	0MG	N	N	N
N	N	N	N	Y	N	Y	Y	N	N	N	N	Y	8MG	6	5	3	1	0MG	N	N	N
N	N	N	N	N	Y	Y	Y	N	N	N	N	Y	8MG	8	3	5	2	0MG	N	N	N
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	24MG	4	5	4	3	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	4	4	0	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	8MG	14	4	5	3	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	24MG	1	4	3	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	8MG	12	3	4	0	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	4	4	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	8MG	14	4	4	2	0MG	Y	N	N
Y	N	Y	Y	N	N	N	N	N	N	N	N	Y	8MG	4	3	5	4	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	4	4	4	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	16MG	6	4	4	0	0MG	N	N	N
N	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	Y	16MG	2	4	4	0	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	8MG	12	4	4	3	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	16MG	8	4	0	0	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	3	2	0	0MG	N	N	N
Y	Y	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	16MG	4	3	1	1	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	8MG	12	3	1	1	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	Y	Y	8MG	14	3	2	2	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	8MG	16	2	2	2	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	N	N	N	N	Y	8MG	6	3	2	1	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	N	N	N	N	Y	16MG	1	5	5	3	50MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	3	3	2	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	16MG	6	3	2	1	0MG	N	N	N

Group –D

MASTER CHART

NAME	AGE	SEX	IP NO	WT(KG)	HT(CM)	DIAGNOSIS	OSSICULOPLASTY	SMOKER/NS	H/OPONV	APFEL S	ANES DUR	SUG DUR	DOF	FIRST 2 HRS NAUSEA	VOMITING	RESCUE	H/OPONV
PRIYA	18	F	20861	48	150	L CSOM CP	N	NS	N	2	130	120	140	N	N	N	N
SATHYA	27	F	12846	54	150	R CSOM CP	N	NS	S	4	160	140	140	N	N	N	N
PRIYA	27	F	10861	56	160	L CSOM CP	N	NS	S	3	140	120	140	N	Y	Y	Y
BANU	62	F	12518	62	148	L CSOM CP	S	NS	N	2	140	130	120	N	N	N	N
DIVYA	20	F	16208	40	140	R CSOM CP	N	NS	N	3	120	110	130	N	Y	Y	Y
MALAR	37	F	15627	70	154	L CSOM CP	N	NS	S	2	140	120	120	N	N	N	N
ETHIRAJ	35	M	18490	72	162	L CSOM CP	S	NS	N	1	160	140	120	N	N	N	N
NAVEEN KUMAR	19	M	12812	47	150	L COM CP	N	NS	S	2	110	90	100	N	N	N	N
ROSY	30	F	23537	38	140	R CSOM CP	N	NS	S	3	120	110	120	Y	Y	Y	Y
MURUGAN	25	M	20498	48	150	L CSOM CP	S	NS	N	3	140	120	140	Y	Y	Y	Y
SUMITHRA	14	F	51252	30	125	L CSOM CP	S	NS	N	3	140	120	120	N	N	N	N
REETHALAKSHMI	64	M	1980	70	164	R CSOM CP	S	NS	N	2	180	160	140	N	N	N	N
SARASWATHI	34	F	53320	62	154	L COM CP	S	NS	N	2	160	140	140	N	N	N	N
KALAIVANI	30	F	3829	58	160	L CSOM CP	S	NS	S	4	160	140	140	N	Y	Y	Y
KARTHICK	30	M	38292	50	150	R CSOM AP	S	NS	S	3	150	130	120	N	N	N	N
SHANTHI	45	F	53472	56	162	L CSOM CP	S	NS	N	2	150	120	120	N	N	N	N
RANI	45	F	51539	64	160	L CSOM CP	N	NS	S	3	150	110	140	Y	Y	Y	Y
RAVI	52	M	54210	56	154	L CSOM CP	N	S	N	1	190	160	160	N	N	N	N
HAMIDAS	16	M	16815	40	140	L CSOM CP	N	NS	S	2	120	90	100	N	N	N	N
KATHIRAVAN	15	M	54799	40	136	R CSOM CP	N	NS	N	1	110	90	100	N	N	N	N
GURUMOORTHY	47	M	21123	54	145	L AURAL POLY	N	S	N	0	170	150	150	N	Y	Y	Y
SANTHOSH	35	M	21234	65	165	L ATTIC RETRAC	S	S	N	0	200	180	160	N	N	N	N
SURIYAN	48	M	29067	80	159	L CSOM CP	N	NS	N	1	190	170	170	N	N	N	N
SELVAM	34	M	67890	90	165	R COM CP	N	NS	N	1	175	125	180	N	N	N	N
KARTHIKEYAN	23	M	34565	45	140	L COM CP	N	NS	N	1	130	100	100	Y	Y	Y	Y
SARAVANAN	36	M	24567	56	145	OTOSCLEROSIS	S	NS	N	1	200	180	140	N	N	N	N
SHANKARLINGAM	56	M	34278	65	167	L COM CP	N	S	N	0	130	100	140	N	N	N	N
KISHORE	20	M	12450	34	130	R COM CP	N	NS	N	1	160	140	90	N	N	N	N
KRISHNAN	20	M	15678	54	138	L COM CP	N	NS	N	1	130	110	100	N	N	N	N
BALA	34	M	14009	45	168	L COM CP	N	S	N	0	180	160	100	N	N	N	N

GROUP D METOCLOPRAMIDE+ DEXAMETHASONE																						
2-6 HRS				6-12 HRS				12-24 HRS				0-24 HRS PON	RESCUE DOSE	T DURATION H	VAS SCORE			OPIOD DOS	SIDE EFFECTS			
NAUSEA	VOMITING	RESCUE	H/OPON	NAUSEA	VOMITING	RESCUE	H/OPON	NAUSEA	VOMITING	RESCUE	H/OPONV				2HRS	2-12 HRS	12-24 HRS		HEADACH	DIZZINES	ALLERGY
Y	Y	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	8MG	3	5	5	3	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	8MG	6	5	7	5	50MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	0	3	3	2	0MG	N	N	N
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	2	3	3	3	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	1	3	5	5	100MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	2	2	1	0MG	Y	N	N
Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	4	3	3	3	0MG	N	N	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	4MG	12	4	4	8	50MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	1	8	4	4	50MG	N	N	N
Y	Y	Y	Y	N	N	N	N	N	N	N	N	Y	4MG	1	4	4	2	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	8MG	6	4	5	5	50MG	N	N	N
Y	Y	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	8MG	2	5	6	3	100MG	N	N	N
N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	4MG	12	3	3	5	50MG	Y	Y	N
N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	1	5	3	3	50MG	N	N	N
N	Y	Y	Y	N	N	N	N	N	N	N	N	Y	8MG	4	4	4	0	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	2	1	0	0MG	N	N	N
N	N	N	N	Y	Y	Y	Y	N	N	N	N	Y	8MG	0	7	3	3	50MG	N	N	N
Y	Y	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	8MG	4	3	3	3	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	3	3	0	0MG	N	Y	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	3	2	2	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	Y	4MG	1	5	3	3	50MG	N	N	N
N	N	N	N	Y	Y	Y	Y	N	N	N	N	Y	4MG	6	3	3	3	0MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	2	1	1	0MG	N	N	N
Y	N	Y	Y	N	N	N	N	N	Y	N	N	Y	8MG	4	4	3	4	0MG	N	N	N
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	12MG	0	10	8	3	100MG	N	N	N
N	N	N	N	Y	N	Y	Y	N	N	N	N	Y	4MG	6	4	5	5	100MG	Y	Y	N
N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	4MG	12	4	4	5	50MG	N	N	N
N	N	N	N	N	N	N	N	N	N	N	N	N	0MG	24	0	0	0	0MG	N	N	N
N	N	N	N	Y	N	N	N	Y	N	Y	Y	Y	4MG	14	4	4	0	0MG	N	N	N
Y	Y	Y	Y	N	N	N	N	Y	N	Y	Y	Y	8MG	4	2	2	4	0MG	N	N	N