" INTRATHECAL FENTANYL VERSUS INTRAVENOUS ONDANSETRON FOR PREVENTION OF NAUSEA-VOMITING DURING CAESAREAN SECTION UNDER SPINAL ANAESTHESIA – A RANDOMIZED CONTROLLED TRAIL"

DISSERTATION

BY

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ABBREVIATIONS

ASA American Society of Anaesthesiologist

BP- Blood pressure

CNS- Central nervous system

CSF- Cerebrospinal fluid

CTZ- Chemoreceptor trigger zone

CVS- Cardio vascular system

ECG- Electrocardiogram

EEG- Electroencephalogram

GABA-Gama amino butyric acid

Hist- Histamine

HR- Heart rate

Hr- Hour

Inj- Injection

IONV-Intraoperative nausea and vomiting

IV- Intravenous

Kg- Kilograms

mg - Milligrams

min - Minute

NTS- Nucleus of tactus solitarius

PONV-Postoperative nausea and vomiting

RR- Respiratory rate

SAB- Subarachnoid block

ABSTRACT

Objective: To compare the efficacy of intrathecally administered fentanyl in preventing intraoperative nausea and vomiting with that of intravenous ondansetron in patients undergoing elective caesarean deliveries under spinal anaesthesia.

Study design: A randomized controlled trial.

Methods: One twenty healthy parturients posted for elective caesarean section under spinal anaesthesia using hyperbaric 0.5% bupivacaine were randomly allocated into two groups of sixty each. Group-F received 12.5µg of fentanyl intrathecally along with 2 ml of hyperbaric bupivacaine. Group-O received 4 mg of intravenous ondansetron. Intraoperatively, an anaesthesiologist blinded to the study recorded the presence or absence of nausea, retching and vomiting. The frequencies for nausea, retching and vomiting were compared using test of proportion for the two samples. The level of significance was taken as 0.05.

Results: The incidence of nausea, retching and vomiting in fentanyl group is 11.67%, 5% and 3.33% respectively where as in ondansetron group the incidence is 26.67%, 20% and 18.33%. There is significant difference between two groups with the P values 0.037, 0.013 and 0.08 for nausea, retching and vomiting respectively.

Conclusion: From our study we conclude that administration of fentanyl as adjuvant to spinal anaesthesia during caesarean section reduces the incidence of intraoperative nausea and vomiting.

Key words: Spinal anaesthesia, intrathecal fentanyl, Nausea vomiting, Ondansetron

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF PHOTOGRAPHS

INTRODUCTION

Nausea and vomiting remains as "Big little problem" in caesarean delivery under spinal anaesthesia and poses major problem.[1] This common side effect can be distressing to the patient and may increase the risk of aspiration of gastric contents.

Intraoperative nausea and vomiting occurs as many as 66% of the caesarean deliveries performed under regional anaesthesia.[2] In day today practice several drugs like metoclopramide, ondansetron, droperidol, dexamethosone, propofol, etc have been tried to reduce the incidence of nausea vomiting.[3,4] But none have been proved to be effective without exhibiting significant adverse side effects. During past decade, anaesthesiologists have been modifying their anaesthetic techniques to reduce the incidence of nausea and vomiting. However in spite of these modifications incidence of nausea and vomiting is continue to be high in caesarean deliveries.

Recently intra-thecal administration of benzodiazepines like midazolam have been tried to minimise intra operative nausea and vomiting.[5] Reduced incidence of nausea and vomiting has been observed when intrathecal lipophilic opioids like fentanyl and sufentanyl were administered to enhance post operative analgesia.[6] Fentanyl being inexpensive with fewer side effects makes it an attractive drug for the prophylaxis of intra operative nausea and vomiting.

Although both intravenous ondansetron and intrathecal fentanyl have been demonstrated efficacy in preventing nausea and vomiting during caesarean delivery, no direct comparative studies have been performed. Therefore we designed a randomized

controlled trial comparing intrathecal fentanyl with intravenous ondansetron for the prevention of nausea and vomiting during elective caesarean delivery under spinal anaesthesia.

OBJECTIVES

Aim of the study is to compare the efficacy of intrathecally administered fentanyl in preventing intraoperative nausea and vomiting with that of intravenous ondansetron in patients undergoing elective caesarean deliveries under spinal anaesthesia.

REVIEW OF LITERATURE

Nausea and vomiting is one of the most common perioperative complications in clinical practice. Its incidence varies widely from 20% to 60% in the perioperative period.[7, 8, 9] Nausea and vomiting commonly occurring during caesarean delivery performed under spinal anaesthesia is attributed to manipulation of uterus or at the time of peritoneal closure.

Lussos et al showed that the incidence of intra operative nausea vomiting in caesarean section can be as high as 66%.[2]

Simpson and colleagues compared buprenorphine and morphine extradurally after caesarean section and found that patient treated with morphine and buprenorphine experienced highest nausea and vomiting.

Prevention of intra operative nausea and vomiting in caesarean delivery, under regional anaesthesia, has been a continual challenge for an anaesthesiologist. Hence several pharmacological and non pharmacological methods have been tried in prevention and treatment of nausea and vomiting.[10]

Kotelko DM et al in the year 1989 found that transdermal scopolamine patch was effective in reducing nausea and vomiting.[11]

Bader and colleagues studied the anti emetic efficacy of prophylactic metoclopramide for caesarean delivery under spinal anaesthesia and found that emetic episodes were significantly less with its use.[2]

Ho et al advocates the prophylactic use of acupuncture bands bilaterally on the P-6 acupoint to reduce the incidence of nausea and vomiting after the administration of epidural morphine for post caesarean analgesia.[12]

Leeser and Lip by their study concluded that the pre operative administration of ondansetron 16 mg orally reduces the incidence of nausea and vomiting from 52% and 40% to 17% and 12% respectively.[13]

Alan Santos and sanjay dutta in the year 1994 studied the use of prophylactic droperidolamine for control of nausea and vomiting during caesarean section under spinal anaesthesia and found that the incidence of nausea reduced to 12% from 40% in the saline group.[14]

Studies done by Yaksh and colleagues have demonstrated the use of intrathecal opioids is safe.[15]

Randall et al in the year 1991 conducted a study for comparison of four subarachnoid solutions for elective caesarean sections.[16] The four different solutions were: 0.5% bupivacaine alone, or with adrenaline, fentanyl or adrenaline and fentanyl. The conclusion of the study was that addition of fentanyl to bupivacaine resulted in minimal nausea and good intra operative and post operative analgesia.

Gunnar D et al compared the effect of intrathecal sufentanyl, fentanyl and placebo when administered together with bupivacaine for caesarean section.[17] The study concluded that addition of sufentanyl and fentanyl reduced the need for intra operative anti emetic medications.

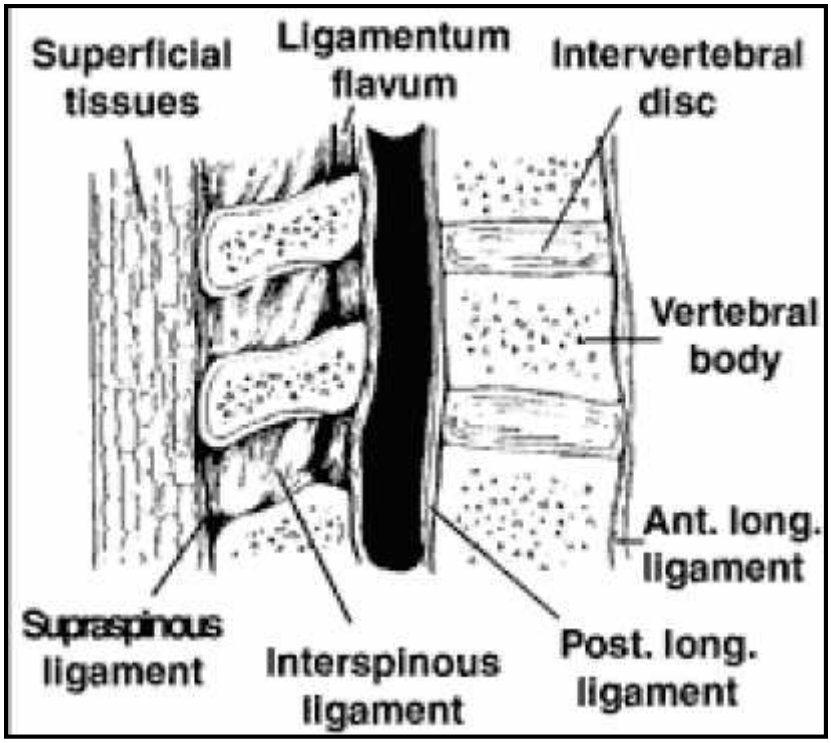
Biswas BN and Rudra have compared intrathecal fentanyl with intravenous dexamethosone combination for prevention of intra operative and early post operative emesis.[18] The results revealed that 90% of the women were emesis free with dexamethosone and ondansetron combination in comparison with 85% of the women with intrathecal fentanyl group.

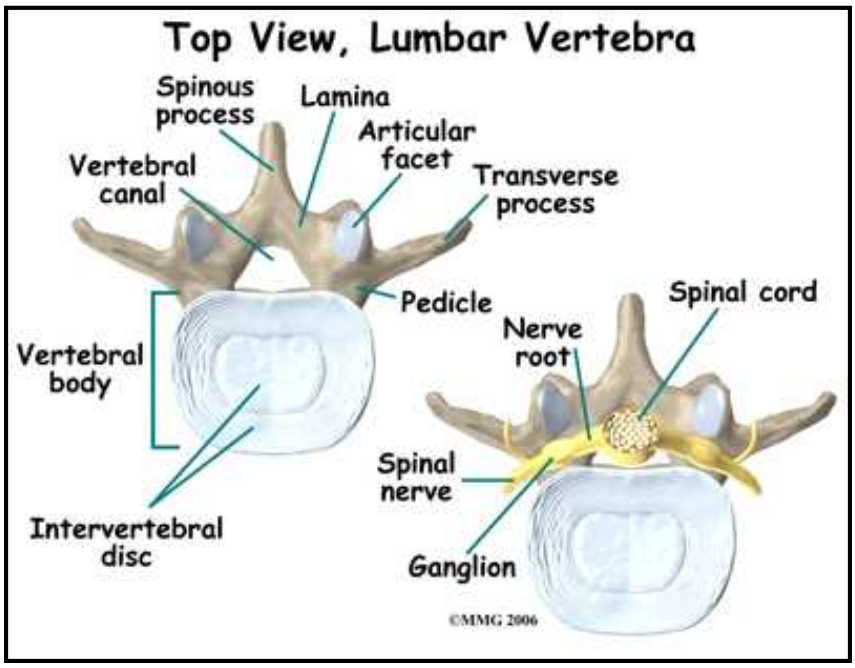
Pallab Rudra compared intrathecal fentanyl with intrathecal midazolam for prevention of nausea and vomiting during caesarean delivery.[19] They found that there was an incidence of nausea and vomiting of 40% in the midazolam (2 mg) group and 25% with fentanyl (12.5 mcg) group during intra operative and early post operative period.

Biswas et al conducted a study to know the analgesic efficacy of addition of fentanyl to bupivacaine for spinal anaesthesia during caesarean delivery. [20] The addition of fentanyl in this study improved the analgesia both intra and post operatively. It was also a coincidental finding that addition of fentanyl reduces the incidence of nausea and vomiting.

Halder R and colleagues tried low dose propofol for control of emetic episodes during caesarean deliveries under spinal anaesthesia.[21] 86% of the patients were emesis free with propofol in comparison with 40% in the placebo group.

ANATOMY


Superficial tissues
Ligamentum flavum
Intervertebral disc
Vertebral body
Ant. long. ligament
Supraspinous ligament
Interspinous ligament
Post. long. ligament


Top View, Lumbar Vertebra
Spinous process
Lamina
Articular facet
Vertebral canal
Transverse process
Pedicle
Spinal cord
Nerve root
Vertebral body
Spinal nerve
Intervertebral disc
Ganglion
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Sound knowledge of anatomy of vertebral column and its contents is essential to all the anaesthesiologists for safe and successful administration of spinal anaesthesia, not only in terms of performance but also in terms of spread of drug in CSF and level of block achieved.

Vertebral column

The vertebral column comprises total of 33 vertebrae and includes 7 cervical, 12 thoracic, 5 lumbar 5 fused sacral and 4 coccygeal vertebrae. The vertebral column has 4 curves which have significant effect on spread of drugs in sub arachnoid space. Cervical and lumbar curves are convex anteriorly whereas thoracic and sacral curves are convex posteriorly. The highest point of cervical and lumbar curves in supine position are at C5 and L5; lowest points of thoracic and sacral are at T5 and S2 respectively. Main function of vertebral column is to protect the spinal cord.

Vertebral ligaments

Vertebral column is bound together by following ligaments which give stability and elasticity.

Supraspinous ligament**:** This is strong fibrous cord connects apices of spinous processes from sacrum to C5 where it is continued as the ligamentum nuchae.

Interspinous ligament**:** This is thin membranous ligament connects spinous processes blending anteriorly with ligamentum flavum and posteriorly with supraspinous ligament.

Ligamentum flavum**:** This ligament comprises yellow elastic fibres and connects adjacent lamina. Laterally this ligament begins at the root of articular processes and extends posteriorly and medially to the point where laminae join to form spinous process.

Longitudinal ligaments**:** There are 2 longitudinal ligaments (anterior and posterior) that binds vertebral bodies together.

Lumbar vertebrae

A typical lumbar vertebrae consists of

1. A kidney shaped body.
2. Two pedicles directed backwards from the upper part of the body.
3. Two transverse processes which are slender
4. Two laminae meeting posteriorly and enclosing the triangular vertebral foramen.
5. Spinous processes which are thick broad and quadrilateral in shape.
6. Two upper and lower articular processes which prevent rotation but allow limited flexion and extension between contiguous vertebrae.

Vertebral canal

Vertebral canal is bounded posteriorly by spinous processes and interspinous ligaments, laterally by the pedicles and posterolaterally by the laminae and ligamentum flavum. This ends superiorly in the foramina magnum and inferiorly in the sacral hiatus. The vertebral canal consists of spinal cord, spinal membranes, adipose tissue, blood vessels, CSF and the roots of the spinal nerves.

Spinal cord

The spinal cord which is the extension of central nervous system into the vertebral canal begins at the level of foramen magnum and ends below as conus medullaris. At birth spinal cord ends at the level of L3 but rises as the age progresses and reaches to lower border of L1 in adults. It measures about 42-45 cm.

The spinal cord receives blood supply from three arteries, one anterior and two posterior spinal arteries.

Anterior spinal artery is single vessel lying in the substance of pia matter overlying the anterior median fissure. It receives communications from intercostals, lumbar and other small arteries and supplies the lateral and anterior columns, comprising three quarters of substance of the cord. Thrombosis of this artery causes anterior spinal artery syndrome.

There are two pairs of posterior spinal arteries one pair on each side arises from posterior inferior cerebellar arteries at the level of foramen magnum. They supply posterior columns of the cord.

Spinal meninges

Along with the bony vertebral column spinal cord is also protected with three connective tissue coverings called meninges.

Dura mater: This is the tough outermost fibro elastic covering consisting of outer endosteal layer and inner meningeal layer. Fibres of dura run longitudinally, thus it is important to insert the spinal needle so as to split these fibres not to cut them. Dural sac ends at lower border of S2, where it is pierced by filum terminale.

Arachnoid mater: It is the delicate, non vascular, middle covering and is closely attached to the dura. There is a capillary interval or potential space between dura and arachnoid mater called subdural space and contains serous fluid.

Pia mater: It is the delicate highly vascular covering closely investing the spinal cord and brain.

Subarachnoid space

The space between the arachnoid and pia is called subarachnoid space and is filled with cerebrospinal fluid and contains numerous arachnoid trabaculae which form delicate sponge like mass. This space has three divisions which are free communication to each other: cranial (surrounding the brain), spinal (surrounding the spinal cord) and root (surrounding the dorsal and ventral nerve roots). In the spinal cord these nerve roots are covered only by pia and bathed in CSF. As these spinal nerve roots pass beyond the spinal dura and traverse the epidural space, they carry with them all the three meningeal layers and have a distinct epidural, subdural, subarachnoid and subpial spaces. The subarachnoid space extends separately along both the dorsal and ventral roots to the level of dorsal root ganglion, where arachnoid and pia continue as perineural epithelium of peripheral nerve.

Cerebrospinal fluid

It is a clear colourless fluid found in the cranial and spinal subarachnoid spaces and in the ventricles. CSF is mainly formed by either secretion or ultrafilteration from the choroids arterial plexus of lateral ventricles. CSF flows from the lateral ventricles into the third ventricle through the foramina of Monro into the fourth ventricle through the aqueduct of Sylvius into the cerebromedullary cisterna (cisterna magna) through foramen of Magendie and foramina of Luschka. From the cisterna magna, CSF enters subarachnoid space circulating around brain and spinal cord before being absorbed into the arachnoid granulations over the cerebral hemispheres.

Composition of cerebrospinal fluid:

Specific gravity: 1.003-1.009 at 37 c.

Volume: 120 ml-150 ml (25 ml-35ml in spinal space).

CSF pressure: 60-80 mm of Hg in lumbar space.

pH: 7.27- 7.37

PCO_2: 48 mm of Hg

HCO_3:23 mEq/L

Sodium-135-145 mEq/L

Calcium:2-3 mEq/L

Phosphorous:1.6 mg/dl

Magnesium: 2-2.5 mEq/L

Chloride: 15-20 mEq/L

Proteins: 23-38 mg/dl

It is important to know that certain drugs alter the rate of formation of CSF. Carbonic anhydrase inhibitors like acetazolamide reduce the rate of CSF formation by as much as 50%. Furosemide in large doses may reduce the CSF formation where as steroids have an inconsistent effect. Inhalational anaesthetics like isoflourane and vasoconstrictors decrease the CSF formation. CSF formation is decreased when the serum osmolality is increases and increased when the serum is made hypotonic. During equllibrium rate of formation equals the rat of formation (500 ml/day).

PHYSIOLOGY OF SUBARACHNOID BLOCK

Physiological responses to intra and extra dural blockade results from autonomic blockade with its effects on both vascular beds and cardiac action from addition of somatic pain and the reflex responses associated with it and from the effects of blockade of motor fibres.

1) Autonomic blockade

Order of blocking nerve fibres,

a) Autonomic pre ganglionic B fibres.

b) Temperature fibres.

c) Pin prick fibres.

d) Fibres conveying pain greater than pin prick.

e) Touch fibres.

f) Deep pressure fibres.

g) Somatic motor fibres.

h) Fibres conveying vibratory sense and proprioceptive impulses.

During recovery return of sensations in the reverse order assumed, but it has been suggested that sympathetic activity returns before sensation.

In SAB sympathetic fibres are blocked two to three segments higher than sensory fibres and sensory block is two segments higher than motor block.

2) Effects of SAB on cardiovascular system

Spinal block can influence CVS in various ways.

a. Vasodilatation of resistance and capacitance vessels.

b. Block of cardiac efferent sympathetic fibres from T1-T4 resulting in loss of chronotrophic and inotropic drive and fall in cardiac output.

c. Bainbridge reflex causing bradycardia.

d. Depression of vascular smooth muscle and beta adrenergic blockade of myocardium with fall in CO following systemic absorption of local anaesthetic drug.

Block extending above T4 is associated with fall in BP, slowing of HR is caused if any of anterior roots carrying sympathetic cardiac accelerator fibres are blocked as may happen in high spinals above T4-T5. Bradycardia may also be due to lowering of BP in the right atrium consequent to diminished venous return.

Theories of causation of fall in BP.

a. Diminished cardiac output due to reduction of venous return to cardia and lack of muscular propulsive force in veins.

b. Dilatation of post arteriolar capillaries and small venules due to paralysis of vasoconstrictors.

c. Paralysis of sympathetic nerve supply to heart.

d. Paralysis of sympathetic nerve supply to adrenal glands with consequent catacholamines depletion.

e. Ischemia and hypoxia of vital centres.

f. Compression of great vessels in abdomen by pregnant uterus or abdominal tumours.

3) Effects of SAB on respiratory system

Due to motor blockade and deafferentation with reduction of sensory input to respiratory centre breathing quiet during spinal anaesthesia. Intercostal paralysis is compensated by descent of diaphragm which is made easier by lax abdominal wall. This is not accompanied by hypoxia or hypercapnia although the ability to cough forcibly to expel secretions is impaired. Spinal anaesthesia as such does not interfere significantly with gas exchange.

4) Effects of SAB on gastrointestinal system

SAB up to T5 results in,

a) Narrowing of gut.

b) Active peristalsis.

c) Increase in intraluminal pressure.

d) Relaxation of sphincters.

e) Enlargement of spleen.

f) Nausea and vomiting.

5) Effects of SAB on endocrine system

The stress response to surgery results in rise in blood sugar, cortisol and catecholamine level sufficiently high and prolonged spinal blockade can minimise or even prevent these changes.

6) Effects of SAB on genito urinary system

Kidney function is not affected unless severe hypotension is present. The urinary bladder is relaxed and its spincter is contracted leading to retention of urine. Post spinal

injury retention may be moderately prolonged as L2-L3 contains small autonomic fibres and their paralysis lasts longer than that of larger sensory and motor fibres.

The engorgement of flaccid penis due to paralysis of nervigentis is often the first sign of successful block. The tone of uterus is not greatly altered after spinal anaesthesia in pregnancy.

Factors affecting height of analgesia in SAB

a) Specific gravity of solution.

b) Position of patient during and after injection.

c) Volume of solution.

d) Concentration of drug.

e) Rate force of injection.

f) The site of injection.

g) Pregnancy and intraabdominal tumours.

PHYSIOLOGY OF NAUSEA AND VOMITING

Definitions:

The terms nausea, vomiting and retching are not synonymous. Nausea, derived from Greek word for "ship" is an unpleasant sensation in the epigastrium and throat associated with urge to vomit, where as vomiting is the forceful expulsion of gastric contents from the mouth.[22]Retching is the rhythmic labored contractions of respiratory muscles, including diaphragm and abdominal muscles without expulsion of gastric contents.[23]

In contrast to vomiting, regurgitation is the passive reflux of the gastric contents that occurs when the lower oesophageal sphincter relaxes as in comatose patients or in infants.[24] The complex muscular activation is not seen with regurgitation. Emesis may be divided into three phases:

1) pre ejection phase
2) ejection phase
3) post ejection phase

Pre ejection phase: is dominated by nausea and associated autonomic and gastrointestinal changes. Prodromal symptoms include heavy salivation, swallowing, sweating, pallor and tachycardia. It has been suggested that low level stimulation of vomiting pathways may result in nausea without vomiting. Pre ejection phase may last minutes, hours, or even days, as seen with pregnancy, chemotherapy and space sickness.

Autonomic manifestations often precede active vomiting and may result from the proximity of vomiting centres to vagal and regulatory nuclei.

Gastrointestinal changes in this phase include relaxation of proximal stomach and changes in gut motility. A retrograde giant contraction originates in the mid-small intestine and travels towards the stomach. This anti peristaltic wave travels backward up the intestine at a rate of 2 to 3 cm/sec, then as the upper portion of the gastro-intestinal tract, especially the duodenum become over distended. The distension is the main exciting factor that initiates the actual vomiting act. Strong intrinsic contractions occur in both the duodenum and stomach, along with the beginning of relaxation of lower oesophageal sphincter. This allows the vomitus to begin moving into the oesophagus.

Ejection phase: consists of retching and vomiting. The esophagus and stomach do not eject gastric contents; they have a passive role in the emetic reflex and emesis achieved by the action of the diaphragmatic, thoracic and abdominal muscles.[25]

Retching is the act of rhythmic inspiratory movements against a closed glottis. Identical to vomiting, inspiratory movements of chest wall and diaphragm with expiratory efforts of the muscle of abdominal wall are seen during retching. The “thoracic suction pulse” is created due to efforts to expand the thoracic cage and contract the diaphragm while keeping the glottis closed. [26]

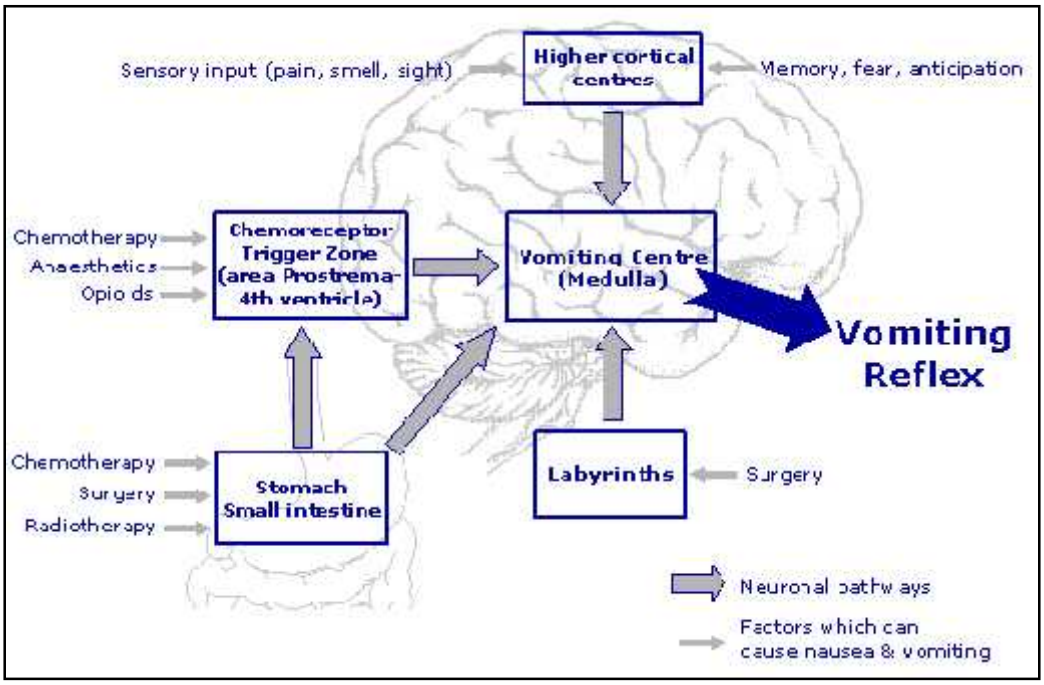
In vomiting the contraction of the rectus abdominis and external oblique muscles overlying the stomach expels the gastric contents. In contrast to retching, vomiting is accompanied by diaphragmatic ascent and a positive thoracic pressure wave. The upper oesophageal sphincter and oesophagus relax, the abdominal muscles and diaphragm

contract, and the intra-thoracic and intra-abdominal pressures both increase to about 100 mm Hg. The relaxation of the hiatal portion of diaphragm during vomiting allows transmission of the abdominal pressure up into the thorax and expulsion of the gastric contents. This relaxation is also seen during eructation and regurgitation but not during retching.[27]

The Vomiting Reflex: The act of vomiting is a complex, almost convulsive, reflex manoeuvre involving both visceral and striated muscle vomiting begins with deep inspiration, elevation of the soft palate to occlude the nasopharynx, and glottic closure. Then the proximal area of the stomach relaxes and a giant contraction of small intestine forces previously ingested contents orad into the relaxed stomach, diluting and buffering the gastric acid. Finally, contracture of the oesophageal muscles pulls the stomach into thorax, forming an oesophageal funnel, and food is forced out of the stomach by contraction of abdominal muscles against the lowered diaphragm. If the glottis closed only retching results: if the pharynx is relaxed, the contents exit through the mouth. During vomiting, animals observe a characteristic posture that permits maximal compression of the stomach by abdominal musculature. Characteristically, a wide opened mouth, spine held in flexion and the forceful expulsion of upper gastro intestinal contents are observed.

Post ejection phase: This phase is characterised by recovery from emesis and the sequelae of vomiting. Emesis may occur again and again, cycling through the pre-ejection and ejection phases. It consists of autonomic and visceral responses that return the body to a quiescent phase with or without residual nausea.[23]

Control of vomiting:



A. The chemoreceptor zone

There are two anatomic sites for CNS control of vomiting: the chemoreceptor triggers zone (CTZ) and the vomiting centre. The CTZ is located in the area postrema (AP), a spongiform vascular body protruding into the fourth ventricle. In 1950 Borison and Wang identified it as the major chemosensory area for inducing vomiting. Blood vessels supplying the area postrema leak injected dye into the underlying tissue; the area postrema also exchanges solutes directly with the cerebrospinal fluid. These properties could represent a countercurrent mechanism for concentrating blood-borne toxins, bypassing the blood-brain barrier.

The CTZ is rich in enkephalins, opiate receptors, and dopamine receptors. Stimulation of the CTZ by injection of apomorphine, L-dopa, and numerous other

substances leads to vomiting. The CTZ is believed to be responsible for the vomiting associated with opiates, cardiac glycosides, and the dopaminergic agonists.

Ablation of the CTZ prevents the vomiting associated with uremia, motion sickness, and radiation therapy. There is afferent input to the area postrema from the vagal and glossopharyngeal nerves, which can provide information on blood pressure, arterial gas composition, lung volume, and gut content.

B. The vomiting center

The CTZ acts only as a sensor; it induces vomiting by signaling the vomiting center, located deep in the medulla in the lateral reticular formation. Electrical stimulation of the vomiting center leads to emesis through both visceral and somatic efferents. These include the fifth, seventh, ninth, tenth, and twelfth cranial nerves as well as spinal nerves that innervate the diaphragm and abdominal muscles. Nearby nuclei associated with vasomotor and bulbar activity, respiration, and salivation are often activated in concert with the vomiting center and lead to the autonomic prodromes of vomiting. Input to the vomiting center comes from the CTZ, the cerebral cortex, the vestibular nucleus, and the nucleus of the tractus solitarius (NTS).

C. The nucleus of the tractus solitarius

The NTS is the terminus in the lower medulla for all general and special visceral afferent fibers of the cranial nerves. Although vagal fibers predominate, fibers from the seventh, ninth~ and possibly spinal nerves end there as well. The NTS' could tl1erefore serve as the pathway whereby pharyngeal stimulation, gut irritation or distension, distension of the renal pelvis, testicular injury, or cervical dilatation leads to nausea and vomiting.

D. The vestibular nucleus

The vestibular nucleus is the relay station for spatial and motion input, and through its action on the CTZ it can mediate the nausea and vomiting of "motion sickness" or "seasickness." Bursts of acceleration or deceleration set the endolymph in the inner ear into motion and generate impulses that are conducted centrally via the eight cranial nerve. Cortical activity can sometimes override and destruction of the CTZ can eliminate the vomiting response to motion.

E. The cerebral cortex

The role of the cerebral cortex in nausea and vomiting is not well described; however, it is clear that the sensation of nausea involves conscious perception. Nausea often precedes or accompanies vomiting, but it is not a necessary concomitant. For example, the vomiting seen with intracranial hypertension is rarely associated with nausea. Psychologic factors are well known to modulate the nausea and vomiting associated with chemotherapy and cancer; perception of pain is believed to play a role in nausea and vomiting. Temporary staying of the vomiting reflex can occur through voluntary effort, though a strong enough stimulus cannot be voluntarily overridden.

F. Hormonal influences

The NTS, vestibular cortex, and cerebral cortex are well established as furnishing important input to the vomiting center or CTZ. A large number of hormones are also suspected of having such an impact. The prominent emetic effects of the sympathomimetic anesthetics, ether and cyclopropane, have led to the investigation of catecholamines as causes ofnausea and vomiting. In cats, even when blood pressure is controlled, intraventricular injection of alpha-adrenergic receptor agents leads to

vomiting.- and the emesis is blocked by alpha-blockers but not beta-blockers. Beta-adrenergic receptor stimulation is associated with deactivation of the vomiting response. Numerous other peptide hormones, like norepinephrine, ACTH, vasopressin, HCG etc, have been implicated in causing nausea and vomiting, but the search for a circulating "emetic" substance continues. A recently discovered hormone, peptide YY, has been isolated from animal ileum and is a very potent emetic in dogs and ferrets. However, most evidence indicates tl1at nausea and vomiting in humans is influenced by numerous pathways, hormonal action being only one of them.

G. The antiemetic center

Work in the cat has led to postulation of an antiemetic center. It has been noted that opiates at low doses may have antiemetic effects but at higher doses stimulate the CTZ. An antiemetic center with different types of opiate receptors from those of the CTZ could explain some of these bimodal results.

Physiologic complications of nausea and vomiting

There are several physiologic complications of nausea and vomiting that are of concern to the anesthetist. Significant complications include possible acid aspiration, visceral or wound dehiscence from the steep rise in intrathoracic and intra-abdominal pressure, and electrolyte disorders from prolonged vomiting.

1. Aspiration pneumonitis.

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

2. Visceral and wound dehiscence.

The act of vomiting causes a considerable increase in both intrathoracic and intra-abdominal pressure. If the pharyngeal sphincter is incompletely relaxed at this time, esophageal rupture can occur. Severe retching or vomiting also can lead to small esophageal tears, known as "MalloryWeiss tears." In the postsurgical setting, the rise in intra-abdominal pressure can stress visceral anastomoses as well as dehisce wound closures. There may also be an initiation of postsurgical bleeding secondary to raised intravascular pressures.

3. Electrolyte disorders.

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

PREOPERATIVE STATES PREDISPOSING TO NAUSEA AND VOMITING

Hormonal or neural imbalances, central nervous system diseases, and gastrointestinal disturbances can lead to nausea and vomiting. These disorders, when present in the preoperative period, increase the likelihood of nausea and vomiting. Specific conditions that make nausea and vomiting more likely include diabetes mellitus, uremia, intracranial hypertension, pregnancy, motion sickness, and abdominal disorders. In addition, perioperative pain, certain medications, or even anxiety can increase the incidence of intra-operative nausea-vomiting. Factors such as female sex, young age, emergency operation, and obesity seem to predispose to nausea-vomiting as well.

A. Pregnancy

Vomiting commonly occurs in the first 14 to 16 weeks of pregnancy; nausea occurs in 50% to 90% of pregnancies and vomiting in 25% to 55%.13. Nausea and vomiting are more frequent in primigravidas, younger women, nonsmokers, the obese, and those with a prior history of nausea and vomiting. Nausea and vomiting have no known adverse effects on the fetus and, in fact, a lower rate of spontaneous abortion has been noted among women with nausea. Severe vomiting, known as "hyperemesis gravi-darum," occurs in 3.5 of 1000 pregnancies and results in significant fluid and electrolyte losses requiring hospitalization. Some suspect a hormonal cause for the nausea of pregnancy and human chorionic gonadotropin (hCG) is often implicated. hCG is elevated not only in pregnancy, but also in the third to fourth week of me menstrual cycle, when a higher incidence of has been nausea-vomiting observed. Molar pregnancy and multiple gestations are also associated with nausea and elevated hCG.

B. Diabetes mellitus

Impaired gastric motility without anatomic obstruction can lead to nausea and vomiting. This commonly occurs in diabetics who have an autonomic neuropathy involving visceral as well as cardiac fibers. The visceral neuropathy can lead to delayed gastric emptying, early satiety, and nausea and vomiting, and it can predispose diabetic patients to aspiration after induction of anesthesia.

C. Uremia

Uremia appears to act through the CTZ because ablation of this area eliminates uremic vomiting. Some have suggested that the inciting agent is the elevated level of vasopressin seen in uremic patients. Intravenous infusion of vasopressin in humans

causes nausea and vomiting and increases the firing of neurons in the area postrema. Several other disorders of fluid balance, such as water intoxication, intracranial hypertension, and acute severe hyponatremia, also elevate vasopressin levels. This may explain the high incidence of nausea and vomiting observed in these disorders. Whether delayed gastric emptying occurs in uremia is controversial; if present, it too could contribute to nausea.

D. Intracranial hypertension

The vomiting associated with raised intracranial pressure typically occurs in the morning, without preceding nausea, and can be projectile. It presumably results from direct pressure on the vomiting center but also may be related to high levels of vasopressin.

E. Abdominal disorders

Irritation or distension of viscera can lead to emesis; this is seen in multiple abdominal disorders including peritonitis, bowel or gastric outlet obstruction, and viral gastroenteritis. Distension of the ureter by renal calculi, testicular pain, or cervical dilatation will also induce nausea and vomiting. These stimuli are carried by splanchnic and vagal afferents to the area postrema and the vomiting center. Vagotomy eliminates vomiting caused by these stimuli; ablation of the area postrema does not.

F. Motion sickness

Motion sickness is caused by excitation of vestibular afferents by movement and is eliminated by destruction of the vestibular apparatus or the CTZ. In humans, motion sickness causes a pronounced antidiuresis and the magnitude of vasopressin secretion is closely related to the degree of nausea and vomiting. However, emesis also occurs in

patients with diabetes insipidus, making the significance of vasopressin questionable. Opiates predispose humans to by nausea-vomiting sensitizing the vestibular apparatus to movement.

Anticholinergics have been successful in treating motion sickness. Sensorial cells for motion are not cholinergic; therefore the anticholinergics must act at the level of the vestibular nucleus or the area postrema, which both contain cholinergic neurons. Histamine blockers are also useful in treating motion sickness through their effect on sensorial cells.

G. Perioperative pain

Clinical studies show that pain is a stimulus to nausea and vomiting and that pain relief, regardless of analgesic used, can decrease nausea and vomiting. In a study of 104 postoperative patients, complete cessation of pain relieved nausea in 80% of episodes and only 10% of patients experienced nausea without pain. Naloxone itself does not cause nausea, but nausea often accompanies the pain occurring after a naloxone overdose. Whether activation of the sympathetic nervous system plays a role in the nausea of pain is not known.

H. Medications

There are numerous pathways whereby medications may affect nausea and vomiting. Two of the most notorious classes of medications encountered in preoperative patients are the opiates and the chemotherapeutic agents.

1. Opioids

Many patients take opioids before surgery. Opioids can cause nausea and vomiting by stimulating the CTZ, by sensitizing the vestibular system, and by delaying gastric emptying. The CTZ has a high concentration of enkephalins and opiate receptors, and the opioids probably induce vomiting through stimulation of these receptors. This differs from the action of apomorphine, which acts through dopanunergic receptors in the CTZ. Pain relief and possible stimulation of an antiemetic center may moderate the nausea and vomiting response to opioids.

Opioid effects on the vestibular system are prominent in patients with nausea-vomiting. In a study of 411 patients given morphine, the ambulatory group experienced significantly more nausea than the bedridden patients did. In almost every instance, one could relieve the nausea by lying down. Other studies have corroborated the relationship of movement to opiate-induced nausea and vomiting increasing dose is an additional risk factor.

2. Chemotherapeutic agents

The most potent emetics encountered in the preoperative setting are chemotherapeutic agents, particularly cisplatin. Animal studies have shown that cisplatin produces vomiting through stimulation of the CTZ. Since ablation of the area postrema does not entirely eliminate drug-induced emesis, there also may be peripheral drug effects. Metabolic intermediates having indirect as well as direct effects on the CTZ and vomiting center could explain the delayed emetic response seen with some cytotoxic agents.

The incidence and severity of vomiting after chemotherapy are related to the particular agent used, the dose, and the rapidity of administration. Additional risk factors are a propensity to develop motion sickness, female sex, and youth.

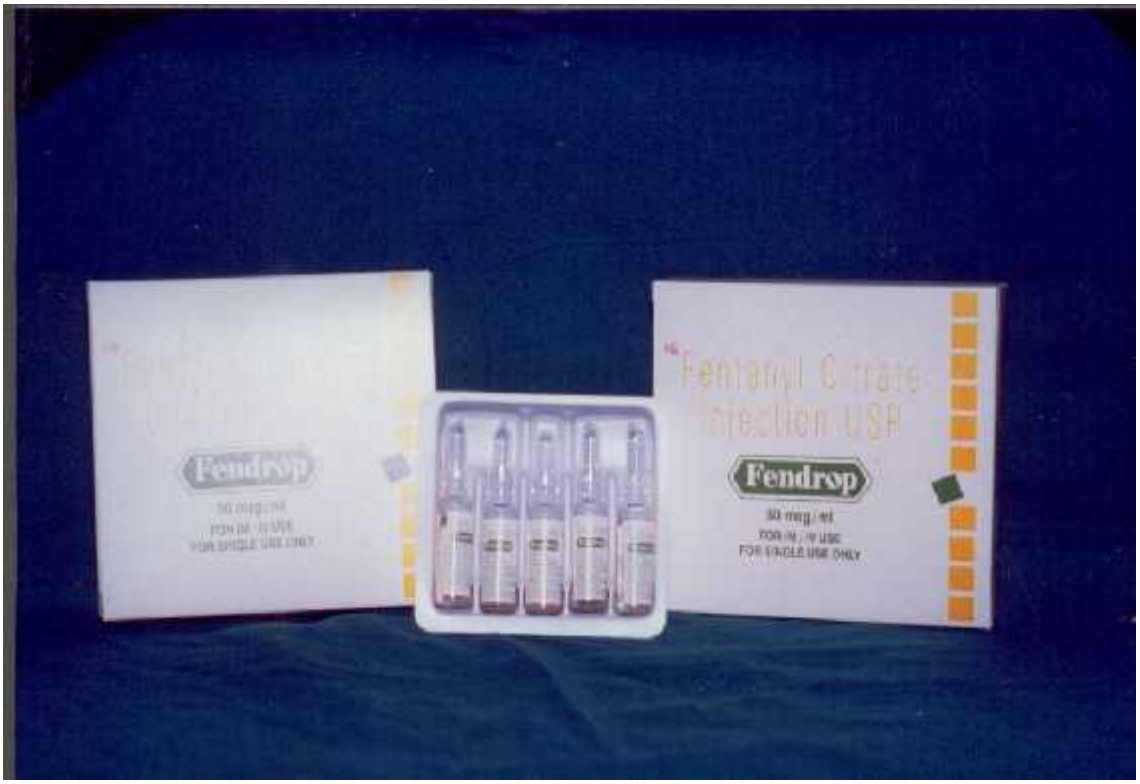
Treatment of chemotherapy-induced emesis often requires much higher doses of antiemetics than those given for nausea and vomiting. Dopamine receptor antagonists and 5-hydroxytryptamine-3 antagonists work well, but antihistamines are relatively unsuccessful. It is possible that the high dose antiemetic combination regimens used for chemotherapy might be helpful in the recovery room as well. The obvious disadvantage in the nausea and vomiting context is that sedation may delay recovery and discharge. Further discussion on treatment is covered in the section on therapy fornausea and vomiting.

I. Miscellaneous risk factors

Female sex, youth, obesity, type of surgery, and history of previous postanesthetic nausea and vomiting are risk factors for nausea-vomiting. Even the skill of the anesthesiologist has been known to influence the incidence of vomiting.

Regional anaesthesia and vomiting

The quoted incidence of nausea and vomiting under spinal anaesthesia ranges from 11% to 21%. The postulated causes include an effect on the vomiting center through a reduction in cerebral blood flow or an increase in gastrointestinal peristalsis from pre ganglionic sympathetic blockade. Hypotension is the one of the most common cause implicated in the etiology of nausea and vomiting. Blood pressure may be maintained by preoperative infusion of 1 to 1.5 litres of crystalloid, by ephedrineinjection preoperatively or by ephedrine infusion.

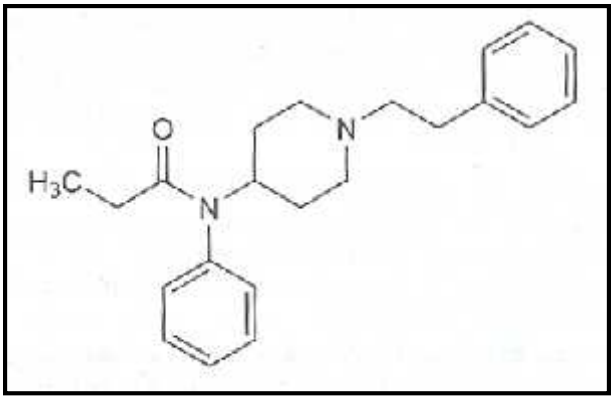


Fentanyl

FENTANYL

Fentanyl was synthesized by Janseen Pharmaceutica in the year 1960 with the emphasis on potency and safety.

CHEMISTRY:



Fentanyl citrate is a synthetic phenyl piperidine opioid analgesic and a chemical congener of the reversed ester of pethidine (meperidine).

PHYSICO-CHEMICAL PROPERTIES:

The drug occurs as a white crystalline powder. It is highly lipid soluble, sparingly soluble in water and soluble in alcohol. The commercially available injections have a pH of 7-7.5. It is 50-100 times more potent than morphine on weight basis.

The injections should be protected from light and stored at 15-30^{0}C. It is hydrolysed in acidic medium and is reportedly physically incompatible with methohexital sodium, phenobarbital sodium and thiopentone sodium. In some countries, it is also available as intrabuccal, transdermal and aerosolized preparations.

MECHANISM OF ACTION:

Fentanyl is primarily a μ receptor agonist. μ receptors are present in the brain, spinal cord, and other tissues like intestine and also in peripheral nerves. Analgesia is produced principally through interaction with μ receptors of supra spinal sites. It does not alter the threshold of responsiveness of afferent nerve endings to noxious stimuli nor the conduction of impulses along peripheral nerves. Instead it appears to prevent the release of β-endorphin possibly by altering the patient's perception of pain at the spinal cord and other higher CNS centers. It also alters the patients emotional response to pain.

Fentanyl also binds to a lesser extent to K receptors within the spinal cord and mediates sedation and miosis. In addition to analgesia, it causes depression of cough reflex, respiratory depression, drowsiness, sedation, changes in mood (euphoria and dysphoria), mental clouding, nausea and vomiting and EEG changes.

Fentanyl causes respiratory depression by direct effect on the respiratory center in the brainstem resulting in decreased sensitivity and responsiveness to increase in serum CO2 tension.

It depresses the pontine and meduallary centers which regulate respiratory rhythm and may also alter voluntary control of respiration.

Fentanyl causes stimulation of the chemoreceptor trigger zone in the medulla oblongata and also an increase in vestibular activity in ambulatory patients thereby causing nausea and vomiting.

The gastric, billary and pancreatic secretions are decreased and digestion is delayed. Ultimate result is constipation. Generally opioids increase smooth muscle tone in the antral part of the stomach, small intestine, large intestine and sphincters to the point of spasm. Opioids normally increase billiary tract pressure and especially at the sphincter of Oddi, but fentanyl does not.

The urinary tract smooth muscle tone is increased and induces spasm. In the urinary bladder, the tone of detrussor muscle is increased resulting in urinary urgency. The ultimate effect is urinary retention.

Fentanyl when used as part of the anaesthetic regime, abolishes the hyperglycemic response to surgery and decreases surgery elicited increases in plasma cortisol and growth hormone. The mechanism of action of decreased endocrine response is not known. Decreased levels of stress hormones will have a positive effect on the patients recovery rate, especially as increase in catecholamines are deleterious to a patients myocardium. Thus fentanyl produces cardiovascular stability.

The magnitude of histamine release is very less with fentanyl when compared to other opioids.

ABSORPTION:

After intravenous administration, the onset of action of fentanyl is much more prompt and its duration of action much as prolonged compared with other opioids. Similar patterns are observed following epidural administration of fentanyl and morphine.

DISTRIBUTION:

A highly lipid soluble drug, fentanyl distributes widely throughout the body. The drug initially distributes rapidly in highly vascular organs, such as the heart, lungs and brain, then in skeletal muscles and finally in deeper fat compartments. The short duration of action of fentanyl is due to its rapid redistribution, which also accounts for the drugs relatively long elimination half life and for its potential to accumulate with repeated or continuous administration.

The volume of distribution of fentanyl after intravenous administration is reportedly 4.0±0.4 l/kg. Fentanyl is 79% to 87% protein bond is plasma.

METABOLISM:

Fentanyl is eliminated is eliminated from the body predominantly by transformation in the liver and is metabolized primarily by oxidation to norfentanyl; and hydrolysed to 4-N-anilinopiperidine and proprionic acid. All known fentanyl metabolites are believed to be pharmacologically inactive or minimally active.

ELIMINATION:

Fentanyl is excreted mainly in the urine, mostly as metabolites; less than 8% is excreted as unchanged drug. The mean clearance of fentanyl after intravenous administration has been reported to range between 34 and 53 l/hr or approximately 13 ml/min/kg. Mean fentanyl terminal half-lives of between 2.5 and 8 hours have been reported after single intravenous doses in surgical patients.

DRUG INTERACTIONS:

Fentanyl may potentiate the effects of other CNS depressants including other opiate agonists, general anaesthetics, tranquilizers, sedatives and hypnotics, alcohol and other CNS drugs such as tricyclic antidepressants and monoamine oxidase inhibitors (MAO). Hence fentanyl should be used with great caution and in reduced dosage when used in conjunction with such drugs. Fentanyl is contraindicated in patients receiving MAO inhibitors.

Some tranquilizers, especially phenothiazines, may antagonize opiate agonist analgesia; dextroamphetamine may enhance opiate agonist analgesia. Opiate agonist may enhance the neuromuscular blocking action of skeletal muscle relaxants. Opiate agonists have been reported to potentiate the anticoagulant activity of coumarin anticoagulants. They may decrease the effect of diuretics in patients with congestive heart failure.

PLASMA PROTEIN BINDING:

Approximately 80% of fentanyl is bound plasma proteins, and significant amounts (40%) are taken up by red cells. Approximately half of fentanyl binds to $\alpha 1$ acid glycoprotein. Fentanyl has a high pKa (8.4) at physiological pH and hence it exists mostly in the ionized form (>90%).

ADVERSE REACTIONS:

As with other narcotic analgesics, the most common serious adverse reactions reported to occur with fentanyl are respiratory depression, apnoea, muscular rigidity and

bradycardia. If these are untreated, respiratory arrest, circulatory depression of cardiac arrest could occur.

Other adverse reactions reported are hypertension, hypotension, dizziness, blurred vision, nausea, emesis, diaphoresis, pruritis, urticaria, laryngospasm and anaphylaxis.

Ondansetron

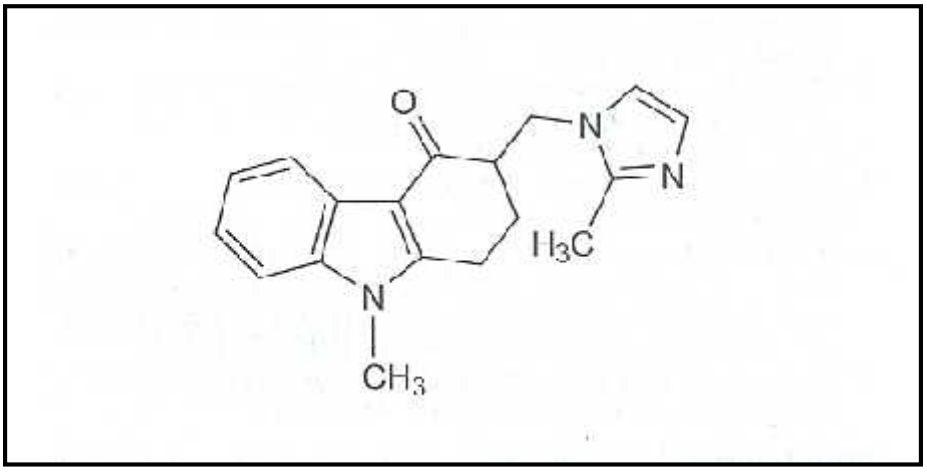
ONDANSETRON

Ondansetron is the first of a new class of drugs useful in preventing nausea & vomiting associated with cancer chemotherapy & radiotherapy.

It has also proved useful in treatment of postoperative nausea & vomiting.

Ondansetron hydrochloride is the first compound which has been demonstrated to be highly selective & highly effective anti emetic, superior to metachlopramide & devoid of undesirable extra pyramidal actions.

CHEMISTRY: Ondansetron is a synthetic structurally novel carbazole derivative.



Pharmacology: Ondansetron is a potent, reversible and competitive antagonist of 5- HT3 receptor.

Antiemetic action: Antiemetic action is believed to be mediated via antagonism of 5-Ht type3 receptors located centrally (in the CTZ in the area postrema of brain) and peripherally (on vagal efferents in upper gastrointestinal tract). In established animal models of radiotherapy and chemotherapy induced emesis, ondansetron completely

controls emesis at a dose of 0.5 mg/kg body weight intraperitoneally and 0.01mg/kg intravenously up to 4 hrs.

Selectivity: Ondansetron has been reported to have very weak affinity at 5-HT 3C, alpha 1 and opiod binding sites. It has no action on other 5- HT receptors, alpha 2 and beta adrenoreceptors, muscarinic and nicotinic cholinergic receptors, GABA A receptors, H1 and H2 histamine receptors, dopamine D2 receptors and NK1, NK2 and NK 3 neurokinin receptors.

Other actions: Ondansetron prolongs colonic transit time in healthy volunteers. It also enhances gastric emptying time. From animal models there is good evidence that 5-HT 3 receptor may be involved in anxiety, schizophrenia , cognitive dysfunction and drug dependency states .

Drug interactions: Ondansetron does not affect the cytotoxic activity of many cytotoxic drugs like Doxarubicin, Methotrexate, Cyclophosphamide, 5- Fluorouracil, Cisplatin and Cytosine arabinoside. Studies in animals have shown that Ondansetron (0.5mg base/kg) subcutaneously has no effects on the pharmacological actions of morphine, diazepam, pentobarbitone and ethanol. No effect on acute inflammatory action of predinosolone was observed in rats and there is no interaction with other anti- emetics which might be co-administered with ondansetron. Studies in healthy volunteers have shown that ondansetron does not antagonize the analgesic effect of alfentanil.

Pharmacokinetics:

Absorption and distribution.

In healthy volunteers, oral administration of ondansetron 8 mg produces a peak plasma concentration of approximately 30ng/ml one to one and half hours post administration.

An intravenous infusion of 8 mg ondansetron over five minutes gives peak plasma values of 80-100ng/ml. plasma levels fall steadily over the subsequent 15 hours.

The bioavailability of the drug following oral administration to healthy volunteers is about 60%. It is 70-76% protein bound. Protein binding does not seem to influence significantly the elimination of ondansetron.

Animal studies have shown the drug to be widely distributed. The apparent volume of distribution is 160 L.

Metabolism and Elimination:

Ondansetron undergoes exentsive hepatic metabolism. It is metabolized by hepatic cytochrome P -450 drug metabolizing enzyme. 40% of a single dose is oxidized to B- hydroxyl ondansetron and 20% to 7 hydroxy ondansetron. Minor roots of metabolism include oxidation to 6- position to produce 6-hydroxy ondansetron and N – dimethyl alkylation.

The mean elimination half life is three hours. Renal clearance accounts for less than 5% of total ondansetron clearance. Less than 10% of the parent drug is excreted unchanged in urine.

Ondansetron clearance is reduced in elderly patients. The half life of Ondansetron in these patients tends to increase to about 5 hours (range 4.3- 5.8 hrs). But dosage reduction does not appear to be necessary in this patient group.

Tolerability and safety profile:

Evidence from animal pharmacology and toxicology has indicated that ondansetron has a wide therapeutic index, no interaction with commonly co-prescribed drugs and no dependence liability.

Clinical experience has shown that ondansetron is well tolerated. In normal volunteers and patients the commonest adverse effects were headache, diarrhea and constipation. Ondansetron related headache occurs with both the oral and IV routes. It is mild and responsive to treatment with simple analgesics.

Transient elevation of the aminotranferases and bilirubin was observed with ondansetron. The elevation in aminotranseferase levels were 2-3 times the upper limit of normal and usually occurred 24 hours after anti- emetic treatment, values returned to normal one week later.

Other adverse reactions include bronchospasm, hypotension, urticaria, tachycardia, angina, ECG alteration, transient blurred vision, xerostomia. Sedation and extra pyramidal effects like acute dystonic reaction are seen very rarely.

Contraindications:

Ondansetron is concentrated in patients known to have hypersensitivity to the drug.

Precautions;

Pregnancy: Animal studies have revealed no evidence of impaired fertility or harm to the fetus due to ondansetron. However no adequate and well controlled studies in pregnant women are available. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Lactation: It is not known whether ondansetron is excreated in human milk. Because many drugs are excreted in human milk, caution should be exercised when ondansetron is administered to nursing mother.

PHARMACEUTICAL INFORMATION

Ondansetron injection is aqueous isotonic solutions of 2 mg/ml ondansetron base as the hydrochloride dehydrate. The injection is maintained at pH 3.5 with citrate buffer and isotonicity is maintained by inclusion of sodium chloride.

Availability: Tablets→ 4 mg and 8 mg

Injections→ 1 ml= 2 mg.

2 ml and 4 ml ampoules available.

The injections have shelf life of 2 years. Several infusion fluids are compatible with ondansetron injection, viz, sodium chloride 0.9%, dextrose 5%, mannitol 10%, ringer lactate, potassium chloride 0.3%.

Dosage: In children→ 0.1 to 0.15 mg/kg/day.

In adults→ 4mg or 8 mg OD or TDS.

METHODOLOGY

Materials:

The material of the study consisted of 120 parturients of ASA grade I and II posted for elective caesarean section under spinal anaesthesia. The study was carried out at KLE Hospital and Medical Research Centre, Belgaum.

Study Design: A randomized controlled trial.

Sample size: 120 parturients

Sample size calculation: Percentage of patients with nausea and vomiting in ondansetron group is 48%. 50% reduction in nausea and vomiting in fentanyl group is taken as clinically significant.

$P_1 = 48\%$, $P_2 = 24\%$,

$P = P_1 + P_2 / 2 = 36$

$\alpha = 0.05 \qquad \beta = 0.2$

Power of the study is 80%

$Z\alpha = 1.65$ and $Z\beta = 0.84$

Sample size is calculated using the formula

$$n = \frac{2 (Z\alpha + Z\beta)^2 P (1-P)}{(P_1 - P_2)^2}$$

Inclusion Criteria: Parturients of ASA Grade I and II aged between 20-35 years scheduled for elective caesarean section under spinal anaesthesia were included.

Exclusion Criteria: Parturients with history of hyperemesis gravidarum, contraindications to spinal anaesthesia and those who have received antiemetics 24 hours prior to surgery were excluded.

The equipment of the study consisted of

1. A sterile tray consisting of two disposable syringes(2 ml and 5 ml), adequate sponges, sponge holding forceps and hole towel.
2. 23 G disposable Quinke spinal needle, 0.5% (H) bupivacaine and study drug.
3. Emergency drugs like atropine, ephedrine, adrenaline, dopamine etc.

Methods:

The thorough pre anesthetic evaluation was carried out in all the patients on the day before surgery. Investigations like Hb% and urine routine were performed to all patients. The height and weight of the patients were also noted. The procedure of the study was explained to all the patients.

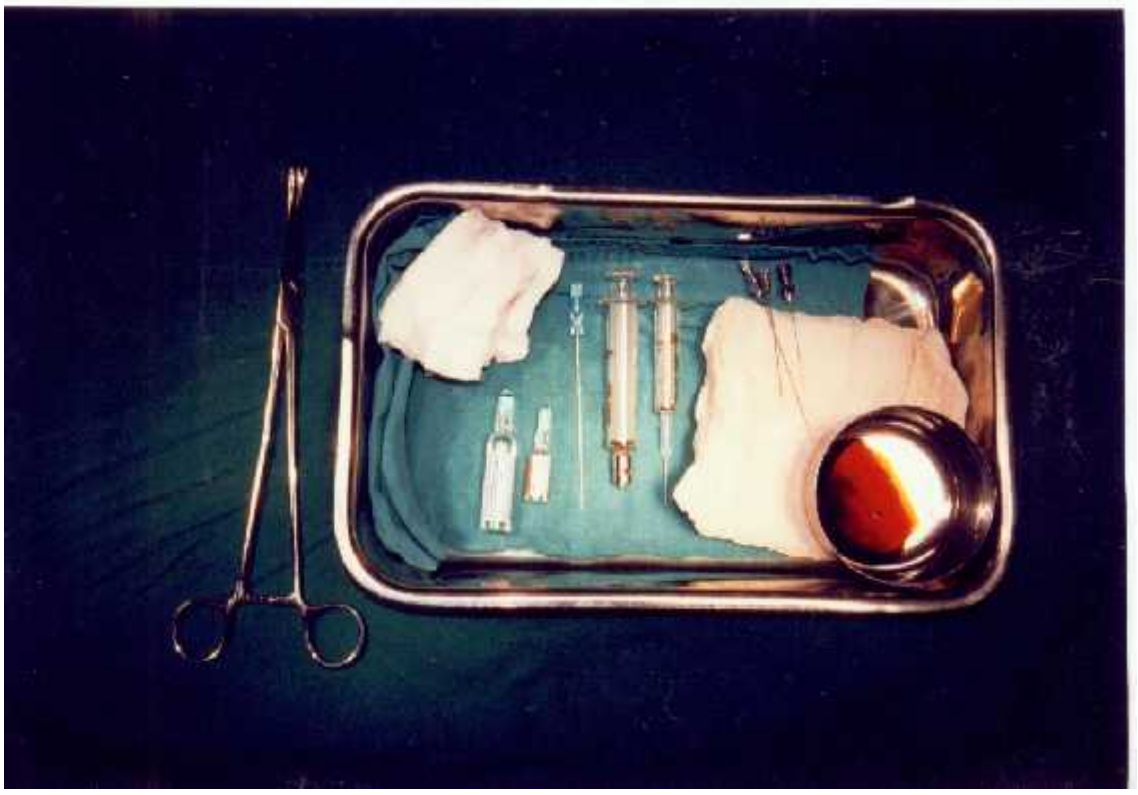
After having met all the inclusion and exclusion criteria and obtaining written informed consent, parturients were randomized into two groups of 60 using computer generated randomization table. Study drugs were prepared and dispensed in unlabelled syringes by an anaesthesiologist not involved in this study. The patients belonging to Fentanyl group (group F, n=60) received 2ml of 0.5% hyperbaric bupivacaine, 12.5μg fentanyl (0.25 ml) intrathecally and 2ml of normal Saline IV. The patients belonging to Ondansetron group (group O, n=60) received 2ml of 0.5% hyperbaric bupivacaine, 0.25ml of normal saline intrathecally and 4mg of (2ml) ondansetron IV.

Parturients were preloaded with 20ml/kg of Ringer lactate solution before spinal anaesthesia. The drug to be administered intravenously was given 15 min prior to surgery. On arrival to the operating room baseline blood pressure, pulse rate, pulse oxymetry values were recorded using routine monitoring devices.

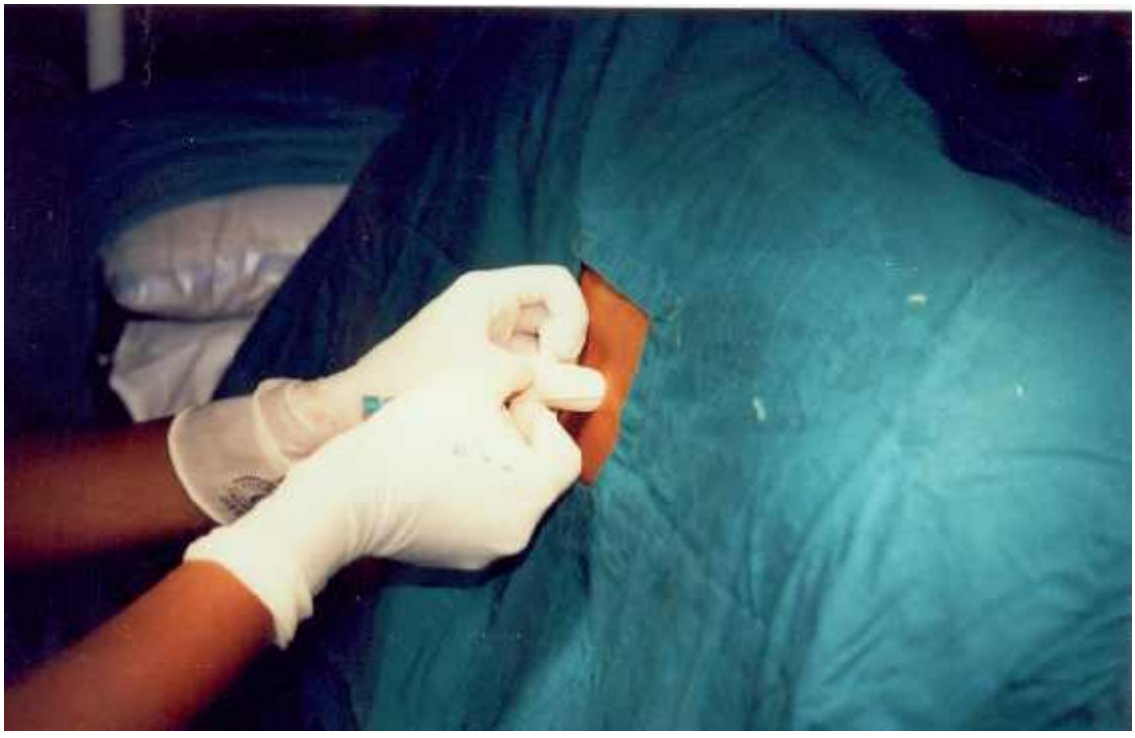
Dural puncture was performed at L_3-L_4 interspace using 23G spinal needle with patient in left lateral decubitus position. Following free flow of CSF, 2ml of bupivacaine and 0.25ml of study agent was injected intrathecally. Immediately after the injection patient was placed on supine position. Blood pressure measurements performed at 2min interval for initial 10min and 5mins interval thereafter till completion of surgery. Any hypotension is treated by intravenous fluids alone or by injecting 5-15mg of ephedrine intravenously. Bradycardia is treated with atropine. Oxygen administered through face mask throughout the surgery .

Intra operative episodes of nausea, vomiting were recorded by direct questioning by an anesthesiologist blinded to which study drug the patient had received. Ondansetron 4mg was administered as rescue anti-emetic with the occurrence of two or more emetic episodes.

Statistical analysis: The quantitative variables like age, height, weight and duration of surgery were compared between two groups using students unpaired‘t’ test. The percentages for different indications for cesarean section were compared using the test of proportion for the two samples. The frequencies for nausea, retching and vomiting were compared using test of proportion for the two samples. The level of significance was taken as 0.05. Statistical analysis was done by using Microsoft Excel and GenStat version 9.1



Spinal Tray



Sub arachnoid block

RESULTS

The present study consisted of 120 parturients posted for elective caesarean section under spinal anaesthesia. The parturients were divided randomly into two groups of sixty each using computer generated randomisation table,

Group O consisted of sixty patients who had received ondanesetron 4 mg intravenously 15 minutes before surgery.

Group F consisted of sixty patients who had received fentanyl 12.5 µg intrathecally with 2 ml of heavy bupivacaine.

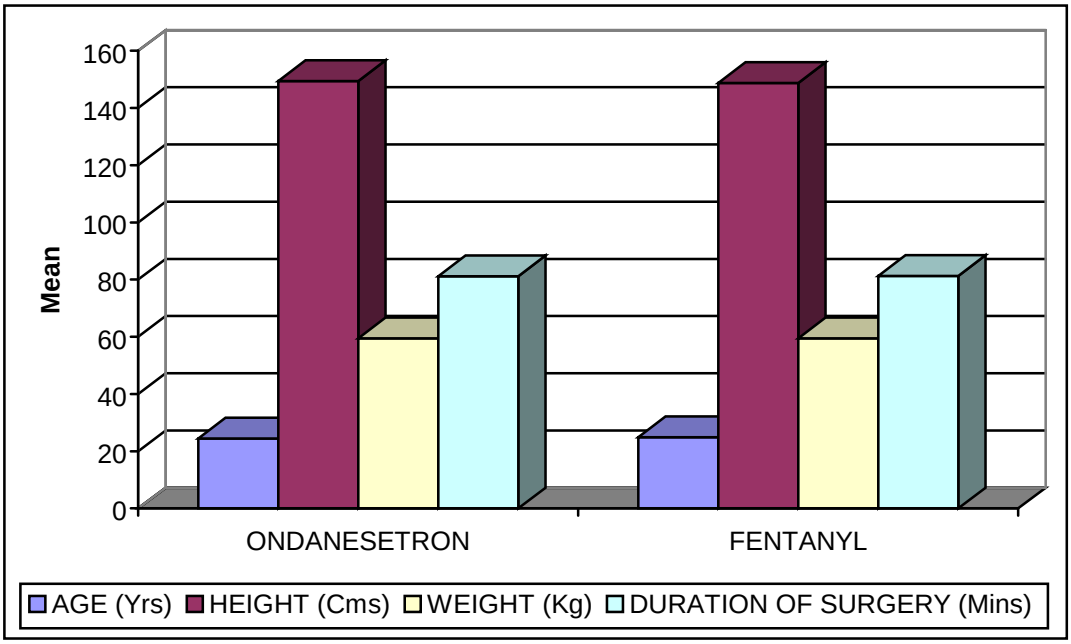
The demographic data of both the groups were as follows.

Table 1 : Shows the demographic data in both the groups.

	ONDANESETRON		FENTANYL			
	MEAN	S.D.	MEAN	S.D.	p VALUE	Inference
AGE	24.48	3.91	24.93	3.75	0.5216	NS
HEIGHT	149.38	3.69	148.73	2.66	0.2704	NS
WEIGHT	59.45	5.67	59.50	5.62	0.9614	NS
DURATION OF SURGERY	81.17	15.63	81.25	16.76	0.9776	NS

NS = Not significant

The demographic data were compared using students unpaired‘t’ test and observations from the above table shows that the demographic data in both the groups are comparable and the difference is not statistically significant. The mean duration of surgery in ondansetron group is 81.17 minutes and in fentanyl group is 81.25 minutes which is not statistically significant.



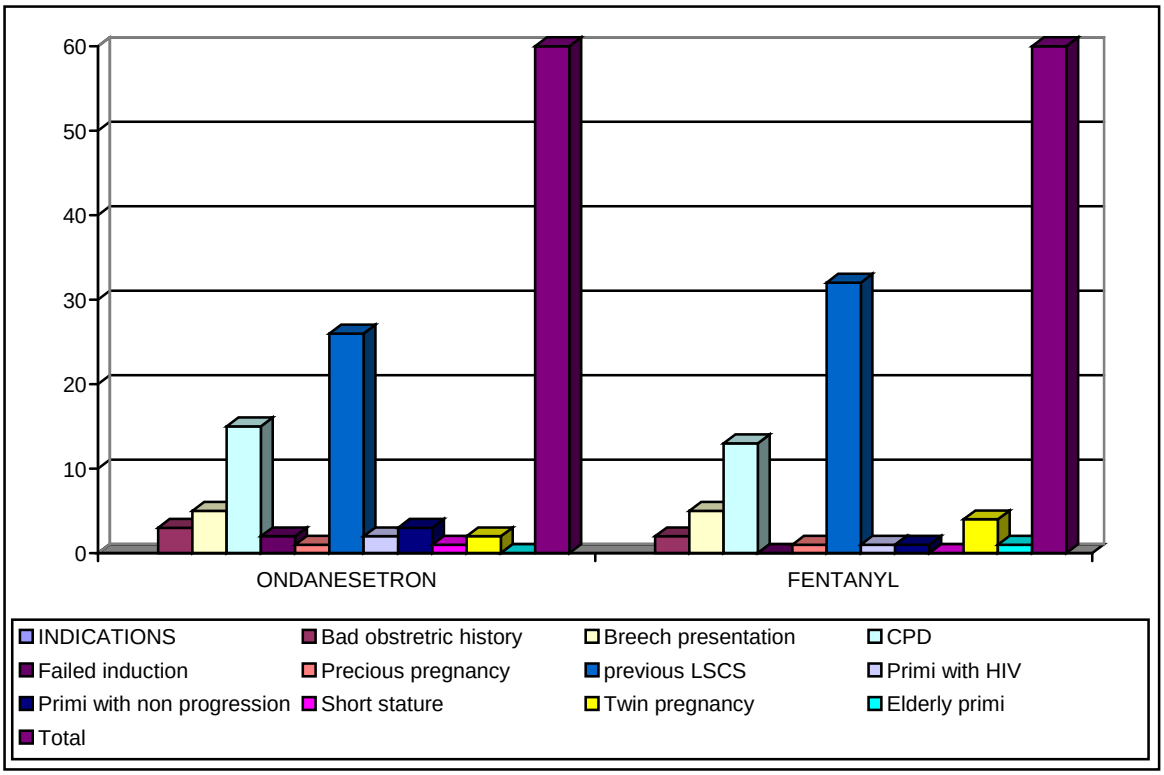
Graph 1 shows the demographic data in both the groups.

Table 2 shows frequency of indications for elective caesarean section.

	ONDANESETRON		FENTANYL			
INDICATIONS	**Frequency**	**Percent**	**Frequency**	**Percent**	**p Values**	**Inference**
Bad obstretric history	3	5.00	2	3.33	0.648	NS
Breech presentation	5	8.33	5	8.33	1.000	NS
CPD	15	25.00	13	21.67	0.666	NS
Failed induction	2	3.33	0	0.00	0.154	NS
Precious pregnancy	1	1.67	1	1.67	1.000	NS
previous LSCS	26	43.33	32	53.33	0.273	NS
Primi with HIV	2	3.33	1	1.67	0.559	NS
Primi with non progression	3	5.00	1	1.67	0.309	NS
Short stature	1	1.67	0	0.00	0.315	NS
Twin pregnancy	2	3.33	4	6.67	0.402	NS
Elderly primi	0	0.00	1	1.67	0.315	NS
Total	60	100.00	60.00	100.00		

NS = Not significant

The percentages of the indications for caesarean section were compared using the test of proportion for the two samples. Observations from above table and graph shows that there is no statistical difference in indications for elective caesarean section between the two groups.

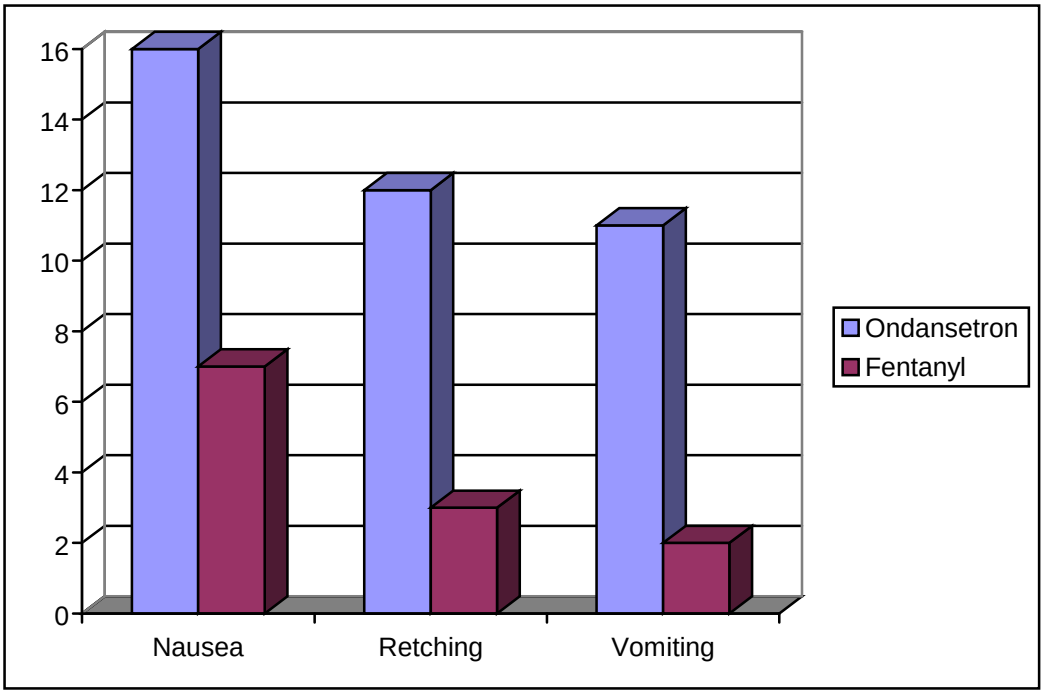


Graph 2 shows frequency of indications for elective caesarean section.

Table 3 shows the distribution of nausea retching and vomiting in two groups.

	Ondanesetron	Fentanyl	P value
Nausea	16(26.67%)	7(11.67%)	0.037
Retching	12(20%)	3(5%)	0.013
Vomiting	11(18.33%)	2(3.33%)	0.008

The frequencies for nausea retching and vomiting were compared using the test of proportion for the two samples. From the above table it is observed that the incidence of intraoperative nausea, retching and vomiting is 26.67%, 20% and 18.33% respectively in ondanesetron group where as the incidence is 11.67%, 5% and 3.33% in fentanyl group. There is reduction in the incidence of nausea, retching and vomiting in the fentanyl group as compared to ondansetron group and this difference is statistically significant($p<0.05$) with the P values 0.037, 0.013 and 0.008 respectively.



Graph 3 shows the distribution of nausea retching and vomiting in two groups.

DISCUSSION

Spinal anaesthesia is an easy, rapid and safe technique for caesarean section.[28] it is considered the procedure of choice for elective or emergency caesarean section in countries such as United States, where it is used in up to 41% of the cases.[29]

The effects of subarachnoid block on parturients are different from those observed in non obstetric patients. The distribution of the anaesthetic drug in the subarachnoid space is less predictable in parturients not only because of increased spinal canal pressure, but also as a consequence of changes in CSF acid base balance and protein content.[30, 31] Above all, side effects including nausea and vomiting, hypotension and high spinal are common and more pronounced in pregnancy.

Nausea and vomiting are very common and unpleasant events during caesarean section under spinal anaesthesia. The incidence of intraoperative nausea and vomiting being more than 66% is distressing to the parturients and disturbing to the surgeons.[32] The abrupt diaphragmatic contractions accompanying nausea and vomiting are uncomfortable to the patients and may cause protrusion of the abdominal viscera, rendering surgery more difficult and increase the risk of visceral injuries. In patients with stomach, aspiration is an additional hazard.

Intraoperative emetic symptoms during caesarean section under spinal anaesthesia have a multifactorial origin such as psychological changes (anxiety) arterial hypotension, hypoperfusion of the central nervous system, abrupt visceral movements. Additionally, there is a higher predisposition to intraoperative nausea and vomiting among patients at

the end of their pregnancies, as a consequence of increased intra abdominal pressure and hormonal changes. Therefore it is preferable to prevent nausea and vomiting during cesarean section under spinal anaesthesia.

Numerous intervention methods have been studied for the prevention of nausea and vomiting during cesarean section. Non pharmacological methods include acupuncture, electropuncture, transcutaneous electrical nerve stimulation, acupoint stimulation and acupressure. Pharmacological methods include dopamine receptor antagonists (phenothiazines, buterophenones and benzamides), histamine receptor antagonists (dimenhydrinate), muscarinic receptor antagonists (scopolamine), and serotonin receptor antagonists (ondanesetron). Miscellaneous drugs like dexamethosone, propofol, clonidine, and ephedrine are also tried for the prevention of nausea and vomiting. All the above drugs are effective in reducing nausea and vomiting with varying efficacy. They are also associated with unwanted side effects and also are less cost effective. None of the available interventions are entirely effective, perhaps because most of them act through the blockade on one type of receptor. So the search for the novel antiemetic is still going.

There are many studies regarding the effect of intrathecally administered opioids as adjuvants. In 1995, Palmer CM et al conducted a study to determine the effect of intrathecally administered fentanyl on the duration of postoperative analgesia in patients scheduled for caesarean section.[33] Coincidentally they observed significantly less nausea and vomiting in patients who received intrathecal fentanyl. Randall et al compared the effect of intrathecally administered epinephrine alone with that fentanyl and epinephrine and observed significant association between the incidence of nausea and groups

receiving epinephrine with p=0.033. None of the patient in the bupivacaine had nausea and vomiting.[16]

Cooper et al administered 25µg of fentanyl intrathecally with heavy bupivacaine and observed decreased incidence of intraoperative nausea and vomiting.[34] Rasooli S et al in their study reduced the dose of fentanyl to 20µg and administered intrathecally with 6 mg of bupivacaine. Out of 22 patients in fentanyl group, no patient had vomiting.[35]

However in the above studies, the antiemetic efficacy of different doses of fentanyl was just the coincidental finding. So we designed a direct comparative study between intravenous ondanesetron and reduced dose of intrathecal fentanyl, i.e. 12.5µg. We reduced the dose of fentanyl to find out the optimal dose for the prevention of nausea and vomiting when it is administered intrathecally.

We conducted the study on 120 parturients scheduled for elective caesarean section. Patients were randomised using computer generated randomisation table. The demographic data in both the groups were comparable (Table 1) and the difference is not significant.

The mean age in ondanesetron group is 24.48 years with S.D of 3.91,where as in fentanyl group it is 24.93 years with S.D of 3.75 (P=0.5216). The mean height in ondanesetron group is 149.38 cm with S.D of 3.69, where as in fentanyl group it is 148.73 with S.D of 2.66(P=0.2704). The mean weight in ondanesetron group is 59.45kg with S.D of 5.67, where as in fentanyl group it is 59.50 kg with S.D of 5.62 (P=0.9614). The mean duration of surgery in ondanesetron group is 81.17 minutes with S.D of 15.63 where as in fentanyl group it is 81.25 minutes with S.D of 16.76 (P= 0.9776). The

indications for elective caesarean section in the two groups were also similar, CPD and previous LSCS being more common indications. The difference is not significant (Table 2).

In present study, we observed significant decrease in intraoperative nausea, retching and vomiting in fentanyl group when compared with ondanesetron group (Table 3). The incidence of nausea in ondansetron group 26.67% and in fentanyl group is 11.67 % (P=0.037). The incidence of retching in ondanesetron group is 20% and in fentanyl group is 5% (P=0.013). The incidence of vomiting in ondanesetron group is 18.33% and in fentanyl is 3.33% (P=0.008) and the difference is highly significant. No side effect was observed in either of the groups.

The results observed in our study agree with the results of following studies.

Randall et al compared four different subarachnoid solutions: 0.5% heavy bupivacaine alone, or with adrenaline, fentanyl or adrenaline and fentanyl, they observed no nausea and vomiting in bupivacaine-fentanyl group.[16] There was a significant association between the incidence of nausea and the groups receiving adrenaline (P=0.033).

In a study conducted by Biswas BN et al the incidence of nausea and vomiting is 5% in patients receiving intrathacal fentanyl where as it is 40% in control group.

Dan B et al conducted a study to compare the analgesic efficacy and side effects of hyperbaric bupivacaine alone or combined with clonidine or with clonidine- fentanyl

group.[36] They observed intraoperative nausea and vomiting in 13% of the patients in bupivacaine-clonidine –fentanyl group, where as it is 41% inbupivacaine alone group.

Intraoperative nausea and vomiting during caesarean section is frequently related to peritoneal traction and exteriorisation of uterus.[37] This is accompanied by visceral pain despite adequate dermatomal blockade that stimulate vagal afferents. Intrathecal administration of fentanyl provides improved analgesia and thereby decreases the discomfort from intraoperative peritoneal manipulations which initiate emetic episodes could be the possible reason for reduced incidence of nausea and vomiting.

Lussos et al concluded that intraoperative nausea and vomiting is rather related to surgical manipulation of the uterus, abdominal viscera and peretonium even in the presence of adequate sensorimotor blockade.[2] Therefore antiemetic treatment may be effectively administered to a group of surgical patients submitted to a certain procedure, but not for another group having different surgical procedure or anaesthetic techniques.

Hence from our study we conclude that administration of fentanyl as adjuvant to spinal anaesthesia during caesarean section avoids intraoperative discomfort while peritoneal traction and exteriorisation of uterus and therby reduces the incidence of intraoperative nausea and vomiting.

CONCLUSION

From our study we conclude that, the administration of fentanyl intrathecally as an adjuvant to hyperbaric 0.5% bupivacaine reduces the incidence of intraoperative nausea and vomiting compared to intravenous ondanesetron in parturients posted for elective caesarean section under spinal anaesthesia.

SUMMARY

Nausea and vomiting during spinal anaesthesia for abdominal surgeries is distressing to the patient and unpleasant aspect of anaesthesia contributing to the patients morbidity.

The present study was conducted to compare the efficacy of intrathecal fentanyl in preventing nausea and vomiting with that of intravenous ondanesetron. This study was consisted of 120 parturients of ASA grade I and II between 20 to 35 years of age posted for elective caesarean section under spinal anaesthesia. Parturients were randomly allocated into two groups of sixty each.

Sixty patients belonging to fentanyl group received 12.5µg fentanyl intrathecally with 2ml of heavy bupivacaine. Sixty patients belonging to ondanesetrn group received ondanesetron 4 mg intravenously 15 minutes before surgery. Patients were observed for intraoperative nausea, retching and vomiting and the incidence was compared.

Results were analysed using test of proportion for the two samples and $p< 0.05$ was considered to be significant. The incidence of intraoperative nausea, retching and vomiting is 26.67%, 20% and 18.33% respectively in ondanesetron group where as the incidence is 11.67%, 5% and 3.33% in fentanyl group. The results were clinically and statistically significant.

So to conclude, the incidence of intraoperative nausea and vomiting in parturients posted for elective caesarean section under spinal anaesthesia is less in patients who had received intrathecal fentanyl 12.5µg in comparison to those who had received intravenous ondanesetron 4 mg.

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Ref. No. : JNMC/IECHSR/2515 Date : 5-12-2006

To,

Dr. Gangadhara Gowda K.G.,
Postgraduate student in
Department of Anaesthesiology,
J.N.Medical College,
Belgaum.

Dear Dr. Gangadhara Gowda K.G.,

The JNMC – Institutional Ethics Committee on Human Subjects Research met on 28th November, 2006 to consider your application for approval of the research project **"Intrathecal fentanyl versus intravenous ondansetron for prevention of nausea-vomiting during caesarean section under spinal anaesthesia –A Randomized Controlled Trial".**

After review of the documents submitted by you and satisfactory explanations provided to the members, the committee has provided approval date through November 27th, 2007 at which time the study will be reviewed by the committee.

If you have any questions concerning the above, please feel free to contact the committee office.

Sincerely,

(Dr.V.D.Patil)
Chairman,
JNMC Institutional Ethics Committee on
Human Subjects Research

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mrs. _____ we are requesting you to enroll yourself in study titled **"INTRATHECAL FENTANYL VERSUS INTRAVENOUS ONDANSETRON FOR PREVENTION OF NAUSEA-VOMITING DURING CAESAREAN SECTION UNDER SPINAL ANAESTHESIA - A RANDOMIZED CONTROLLED TRAIL"** conducted by Dr. Gangadhara Gowda K.G., Post Graduate in M.D. Anaesthesiology under the guidance of Dr. M.G. Dhorigol M.D., Associate Professor, Department of Anaesthesiology, J.N. Medical College, Belgaum under KLE Academy of Higher Education and Research, Belgaum.

Respected Sir/Madam we request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to participate you are free to withdraw at any time.

The purpose of research is to ascertain the efficacy of intrathecally administered fentanyl in preventing intraoperative nausea and vomiting during caesarean delivery under spinal anaesthesia.

Procedure Involved:

If you agree to enroll yourself in my study, I will ask your present past and family history. Then you will be clinically examined in detail and investigations like Hb% urine analysis for albumin, sugar and microscopy will be done.

Risks and Benefits:

Fentanyl rarely may cause pruritis, respiratory depression, urinary retention and bradycardia. If you agree to enroll in my study the incidence of intraoperative nausea and vomiting will be reduced and you will receive adequate intraoperative and post operative analgesia..

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality:

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Compensation:

In the event of injury related to the study, treatment will be made available through KLESH & MRC, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact Dr. Gangadhara Gowda K.G. PG MD Anaesthesiology, KLESH and MRC, Belgaum Phone No.9844119282.

Questions:

In case you have any questions related to the study, you can contact Dr. Gangadhara Gowda K.G. Mob: 9844119282.

In case you have any question about your rights as a study participant, you can contact Dr. V.D. Patil (0831-2471350).

Consent for participation in research trial:

I, Mrs _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject : _____

Witness Name : _____ Signature : _____

Investigators Name: _____ Signature : _____

Date : _____

Place : _____

PROFORMA

"INTRATHECAL FENTANYL VERSUS INTRAVENOUS ONDAN-SETRON FOR PREVENTION OF NAUSEA-VOMITING DURING CAESAREAN SECTION UNDER SPINAL ANAESTHESIA – A RANDOMIZED CONTROL TRAIL".

Investigator: Dr. Gangadhara Gowda K.G. **Guide: Dr. M. G. Dhorigol** **M.D.**

Name & Address of the patient: _____

_____

Age of the Patient: _____ Years IP. No. _____

Anaesthesiologist: _____ Surgeon : _____

PREANAESTHETIC EVALUATION:

Chief Complaints:

Past History:

1. History of hyperemesis gravidarum
2. Contraindications to spinal anaesthesia
3. Those who have received antiemetics 24 hours prior to surgery.

Family History:

General Physical Examination:

Weight: Height: Temperature: Pallor:

Cyanosis: Pedal Edema: Clubbing:

Pulse : BP: RR:

SYSTEMIC EXAMINATION:

Respiratory System:

Cardiovascular System:

Central Nervous system:

Per Abdomen:

Air way and spine assessment:

INVESTIGATIONS:

Hb% Urine : Albumin

Sugar

Microscopy

Diagnosis:

Proposed Surgery:

Inclusion Criteria:

1. Parturients of ASA Grade I and II aged between 20-35 years.
2. Posted for caesarean section delivery under spinal anaesthesia.

Exclusion Criteria:

1. History of hyperemesis gravidarum
2. Contraindications to spinal anaesthesia
3. Those who have received antiemetics 24 hours prior to surgery.

Date of Surgery : _____

From: _____ To : _____

After having met all the inclusion and exclusion criteria and obtaining written informed consent, parturients will be randomized into two groups of 60 using computer generated randomization table. Study drugs will be prepared and dispensed in unlabelled syringes by an anaesthesiologist not involved in this study. Fentanyl group (group F, n=60) will receive 2ml of 0.5% hyperbaric bupivacaine, 12.5μg fentanyl intrathecally and 2ml of normal Saline IV. Ondansetron group (group O, n=60) will receive 2ml of 0.5% hyperbaric bupivacaine, 0.25ml of normal saline intrathecally and 4mg of (2ml) ondansetron IV.

Each patient will receive 20ml/kg of Ringer lactate solution before spinal anaesthesia. 2ml of study drug will be administered intravenously 15 min prior to surgery. On arrival to the operating room baseline blood pressure, pulse rate, pulse oxymetry values will be recorded using routine monitoring devices.

Dural puncture will be performed at L_3-L_4 interspace using 23G spinal needle with patient in left lateral decubitus position. 2.5ml of study agent will be injected intrathecally. Immediately after the injection patient will be placed on supine position. Blood pressure measurements performed at 2min interval for initial 10min and 5mins

interval thereafter. Any hypotension is treated by intravenous fluids or by infecting 5-15mg of ephedrine IV. Oxygen administered through face mask.

Intra operative episodes of nausea, vomiting will be recorded by direct questioning by an anaesthesiologist blinded to which study drug the patient had received. Nausea is defined as subjective unpleasant sensation associated with awareness of the urge to vomit. Retching is defined as the laboured, spasmodic, rhythmic contraction of respiratory muscles without expulsion of gastric contents. Vomiting is defined as the forceful expulsion of gastric content from the mouth. Ondansetron 4mg was administered as rescue antiemetic with the occurrence of two or more emetic episodes.

Observations:

Nausea: Yes / No

Retching : Yes / No

Vomiting : Yes / No

Mins	2	4	6	8	10	15	20	25	30	35	40	45	50	55	60
BP															
Pulse															
SPO_2															

Introduction

Objectives

Review of Literature

Methodology

Results

Discussion

Conclusion

Summary

Bibliography

Annexures

Master Chart

Ondanesetron Group | **Fentanyl Group**

Sl No.	Name	Age	Height (cm)	Weight (kg)	Nausea	Retching	Vomiting	Complications	Diagnosis	Duration (min)	Sl No	Name	Age	Height (cm)	Weight (kg)	Diagnosis	Duration (min)	Nausea	Retching	Vomiting	Complications
1	Deepa Desai	26	149	63	Absent	Absent	Absent	Nil	Primi with non progression	75	1	Jayashree Dinesh	32	146	64	Previous LSCS	70	Absent	Absent	Absent	Nil
2	Kalavathi	23	147	48	Absent	Absent	Absent	Nil	Previous LSCS	85	2	Gayathri	25	152	57	CPD	70	Absent	Absent	Absent	Nil
3	Jyothi patil	20	150	54	Absent	Absent	Absent	Nil	Previous LSCS	90	3	Manjula modagi	29	150	64	CPD	60	Absent	Absent	Absent	Nil
4	Dilshad Umadh Khan	20	146	56	**Present**	**Present**	**Present**	Nil	Primi with non progression	60	4	Roopa	30	148	56	CPD	90	Absent	Absent	Absent	Nil
5	Shaila	26	150	57	Absent	Absent	Absent	Nil	Previous LSCS	65	5	Vidya	22	146	59	CPD	100	Absent	Absent	Absent	Nil
6	Bhaveshwari	22	148	58	**Present**	**Present**	**Present**	Nil	Primi with breech, non progression	100	6	Suvarna	35	154	60	Elderly primi	70	Absent	Absent	Absent	Nil
7	Maneesha	28	148	55	Absent	Absent	Absent	Nil	Previous LSCS	120	7	Rajashree	28	150	55	Previous LSCS with HTN	80	Absent	Absent	Absent	Nil
8	Annapurna	24	144	59	Absent	Absent	Absent	Nil	Previous LSCS	90	8	Smitha	24	148	72	Previous LSCS	60	Absent	Absent	Absent	Nil
9	Yashodha	22	145	62	**Present**	**Present**	**Present**	Nil	Primi with breech, non progression	85	9	Anisha	25	154	70	Twin pregnancy	120	Absent	Absent	Absent	Nil
10	Nirmala	18	150	62	Absent	Absent	Absent	Nil	Previous LSCS with CPD	65	10	Nirmala	24	146	58	Previous LSCS	65	Absent	Absent	Absent	Nil
11	Lakshmi	24	150	65	Absent	Absent	Absent	Nil	CPD	75	11	Sangeetha	28	146	58	Primi with CPD	75	Absent	Absent	Absent	Nil
12	Shakunthala	23	149	72	Absent	Absent	Absent	Nil	Failed induction	80	12	Bhagyashree	24	149	54	Previous LSCS	80	Absent	Absent	Absent	Nil
13	Rajalakshmi	31	148	57	Absent	Absent	Absent	Nil	CPD	90	13	Sonali	20	150	59	Breech presentation	90	Absent	Absent	Absent	Nil
14	Yallawwa	25	148	54	Absent	Absent	Absent	Nil	Previous LSCS	85	14	Sujatha	28	147	61	Previous LSCS	70	**present**	Absent	Absent	Nil
15	Thangawwa	24	149	53	**Present**	**Present**	Absent	Nil	Bad obstretric history	85	15	Jayashree	20	145	67	Twin pregnancy	110	Absent	Absent	Absent	Nil
16	Asmiya musthaq	20	147	60	Absent	Absent	Absent	Nil	CPD	90	16	Shivaleela	28	151	57	Previous LSCS	100	Absent	Absent	Absent	Nil
17	Latha	28	154	59	Absent	Absent	Absent	Nil	Previous LSCS	75	17	Sangeetha	30	148	54	Two Previous LSCS	70	Absent	Absent	Absent	Nil
18	Manjula	25	155	56	Absent	Absent	Absent	Nil	Previous LSCS	60	18	Bharathi	21	143	57	Primi with CPD	50	Absent	Absent	Absent	Nil
19	Lalitha	19	140	68	**Present**	**Present**	**Present**	Nil	Short stature	75	19	Neelamma mutwad	23	149	58	Previous LSCS	60	Absent	Absent	Absent	Nil
20	Savitha	20	149	62	Absent	Absent	Absent	Nil	Primi with non progression	75	20	Renuka	21	147	56	Previous LSCS	90	Absent	Absent	Absent	Nil
21	Lakshmi	36	152	55	Absent	Absent	Absent	Nil	Previous LSCS	80	21	Shilpa	20	146	53	CPD	80	Absent	Absent	Absent	Nil
22	Shantha	22	148	51	**Present**	Absent	Absent	Nil	CPD	90	22	Vidya	25	146	62	Previous LSCS	70	Absent	Absent	Absent	Nil
23	Nandini	21	150	59	Absent	Absent	Absent	Nil	Primi with breech	85	23	Hema	24	151	59	Twin pregnancy	100	Absent	Absent	Absent	Nil
24	Anusuya	25	149	69	Absent	Absent	Absent	Nil	Previous LSCS	70	24	Nusrath	25	154	55	Previous LSCS	70	Absent	Absent	Absent	Nil
25	Rekha	30	150	64	Absent	Absent	Absent	Nil	Precious pregnancy	70	25	Bharathi	23	153	56	Previous LSCS	75	**present**	Absent	Absent	Nil
26	Roopa umesh	34	147	72	**Present**	**Present**	**Present**	Nil	Previous LSCS	70	26	Bharathi	25	148	55	Previous LSCS	75	Absent	Absent	Absent	Nil
27	Chaya	25	147	70	Absent	Absent	Absent	Nil	Previous LSCS	80	27	Kasthuri	28	148	54	Previous LSCS	80	Absent	Absent	Absent	Nil
28	Nirmala	22	149	64	Absent	Absent	Absent	Nil	Previous LSCS	90	28	Renuka	26	147	63	Primi with CPD	90	Absent	Absent	Absent	Nil
29	Lakshmi	21	153	55	**Present**	**Present**	**Present**	Nil	CPD	70	29	Sakshi	22	146	70	Breech presentation	100	**present**	Absent	Absent	Nil
30	Asma	22	155	59	**Present**	**Present**	**Present**	Nil	Three Previous LSCS	90	30	Karthika	19	150	59	Bad obstretric history	90	Absent	Absent	Absent	Nil
31	Prema	28	146	57	Absent	Absent	Absent	Nil	Bad obstretric history	80	31	Renuka	30	152	49	Precious pregnancy	90	Absent	Absent	Absent	Nil
32	Girijawwa	19	145	66	Absent	Absent	Absent	Nil	CPD	80	32	Shabia	29	149	64	Previous LSCS	90	Absent	Absent	Absent	Nil
33	Manjula	20	149	57	Absent	Absent	Absent	Nil	Primi with HIV	80	33	Suvarna	23	148	57	Previous LSCS	80	Absent	Absent	Absent	Nil
34	Shwetha	32	150	58	Absent	Absent	Absent	Nil	Two Previous LSCS	70	34	Channamma	22	148	59	Primi with CPD	70	**Present**	**Present**	**present**	Nil
35	Sunanda	21	151	53	Absent	Absent	Absent	Nil	CPD	90	35	Prabhavathi	31	147	55	Two Previous LSCS	70	Absent	Absent	Absent	Nil
36	Sujatha	25	147	54	**Present**	Absent	Absent	Nil	Previous LSCS	95	36	Shaila	20	147	66	Twin pregnancy	110	Absent	Absent	Absent	Nil
37	Savitha	20	147	60	Absent	Absent	Absent	Nil	CPD	110	37	Sridevi	20	152	74	Breech presentation	120	Absent	Absent	Absent	Nil
38	Jyothi	26	149	56	Absent	Absent	Absent	Nil	Bad obstretric history	110	38	Vidya	24	150	65	Previous LSCS	50	Absent	Absent	Absent	Nil
39	Lalitha	25	152	50	Absent	Absent	Absent	Nil	Previous LSCS	95	39	Sangeetha	22	156	68	Breech presentation	100	Absent	Absent	Absent	Nil
40	Sudha	22	150	58	**Present**	Absent	Absent	Nil	CPD	60	40	Lakshmi	23	152	58	Previous LSCS	80	Absent	Absent	Absent	Nil
41	Shanthawwa	23	155	57	Absent	Absent	Absent	Nil	CPD	60	41	Rekha	20	149	59	CPD	90	**present**	Absent	Absent	Nil
42	Shobhana	28	152	56	**Present**	**Present**	**Present**	Nil	Primi with HIV	70	42	Preethi	20	148	55	Breech presentation	120	Absent	Absent	Absent	Nil
43	Revathi	28	152	60	Absent	Absent	Absent	Nil	Two Previous LSCS	75	43	Mahadevi	23	146	57	Previous LSCS	80	Absent	Absent	Absent	Nil
44	Kavitha	28	149	64	Absent	Absent	Absent	Nil	Previous LSCS	75	44	Kalpana	25	152	54	Previous LSCS	75	Absent	Absent	Absent	Nil
45	Thabassum	25	147	59	Absent	Absent	Absent	Nil	Previous LSCS	75	45	Kavitha	23	150	56	Previous LSCS	65	Absent	Absent	Absent	Nil
46	Sujatha	23	146	59	Absent	Absent	Absent	Nil	CPD	65	46	Vanitha	26	148	52	CPD	70	**Present**	**Present**	Absent	Nil
47	Sugandhi	33	150	70	Absent	Absent	Absent	Nil	CPD	50	47	Ashwini	29	150	55	Primi with HIV	115	Absent	Absent	Absent	Nil
48	Sumangala	25	152	58	Absent	Absent	Absent	Nil	CPD	65	48	Annapurna	26	148	55	CPD	70	Absent	Absent	Absent	Nil
49	Mamatha	24	150	55	Absent	Absent	Absent	Nil	Previous LSCS	75	49	Ruchitha	25	145	77	Previous LSCS	70	Absent	Absent	Absent	Nil
50	Fathima	22	147	65	Absent	Absent	Absent	Nil	Previous LSCS	120	50	Kasthuri	22	147	65	Previous LSCS	70	Absent	Absent	Absent	Nil
51	Sandhya	22	152	61	**Present**	**Present**	**Present**	Nil	Breech presentation	100	51	Bharathi	22	146	61	Previous LSCS	60	Absent	Absent	Absent	Nil
52	Sujatha	22	149	58	Absent	Absent	Absent	Nil	CPD	90	52	Suma	28	151	62	Previous LSCS	90	Absent	Absent	Absent	Nil
53	Jayashree	22	168	76	**Present**	Absent	Absent	Nil	Breech presentation	100	53	Saroja	22	147	58	CPD	80	**Present**	**Present**	**present**	Nil
54	Irawwa	30	152	63	Absent	Absent	Absent	Nil	Twin pregnancy	60	54	Kanchan	26	147	58	Previous LSCS	70	Absent	Absent	Absent	Nil
55	Sushma	23	151	59	Absent	Absent	Absent	Nil	previous LSCS	70	55	Gangamma	30	147	56	Non progression with shou	100	Absent	Absent	Absent	Nil
56	Shobhana	22	147	55	Absent	Absent	Absent	Nil	CPD with previous LSCS	70	56	Shivabasawwa	24	149	60	previous LSCS	80	Absent	Absent	Absent	Nil
57	Mangala	24	147	55	**Present**	**Present**	**Present**	Nil	Primi with failed induction	70	57	Renuka	25	146	56	previous LSCS	80	Absent	Absent	Absent	Nil
58	Ujwala	25	146	58	Absent	Absent	Absent	Nil	previous LSCS with incisional hernia	110	58	Philomina	35	152	57	Bad obstretric history	80	Absent	Absent	Absent	Nil
59	Geetha	28	149	54	**Present**	**Present**	**Present**	Nil	previous LSCS	70	59	Gayathri	24	150	65	previous LSCS	70	Absent	Absent	Absent	Nil
60	Madhuri	28	150	58	Absent	Absent	Absent	Nil	Twin pregnancy	110	60	Ashwini	23	147	55	previous LSCS	70	Absent	Absent	Absent	Nil
	MEAN	####	149.38	59.45	16	12	11			81.17			24.93	148.73	59.50		81.25	7	3	2	
	S.D.	3.91	3.69	5.67	44	48	49			15.63			3.75	2.66	5.62		16.76	53	57	58	
	P VALUE	####	0.2704	0.9614	0.037	0.013	0.008			0.9776											
			NS	NS	NS	S	S	S		NS											

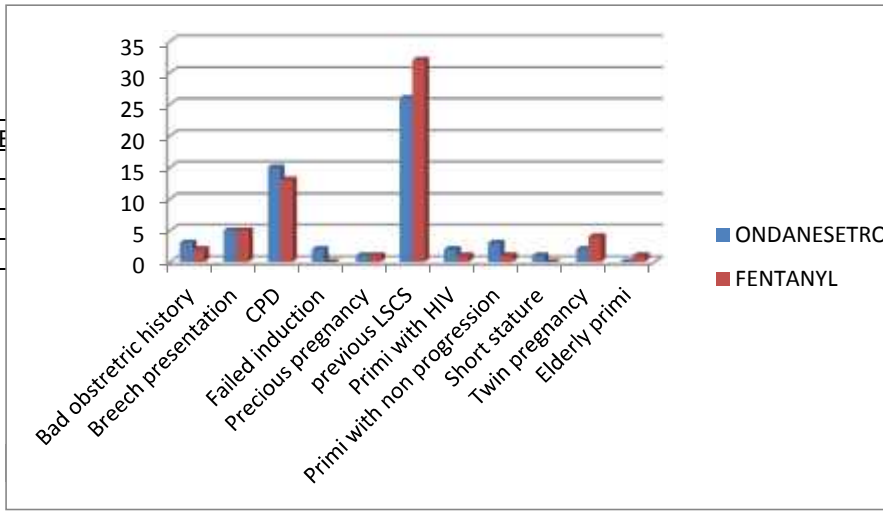
VAR00001		ONDANESETRON		FENTANYL	
	INDICATIONS	Frequency	Percent	Frequency	Percent
Valid	Bad obstretric history	3	5.00	2	3.33
	Breech presentation	5	8.33	5	8.33
	CPD	15	25.00	13	21.67
	Failed induction	2	3.33	0	0.00
	Precious pregnancy	1	1.67	1	1.67
	previous LSCS	26	43.33	32	53.33
	Primi with HIV	2	3.33	1	1.67
	Primi with non progression	3	5.00	1	1.67
	Short stature	1	1.67	0	0.00
	Twin pregnancy	2	3.33	4	6.67
	Elderly primi	0	0.00	1	1.67
	Total	60	100.00	60.00	100.00

	ONDANESETRON		FENTANYL	
	MEAN	S.D.	MEAN	S.D.
AGE	24.48	3.91	24.93	3.75
HEIGHT	149.38	3.69	148.73	2.66
WEIGHT	59.45	5.67	59.50	5.62
DURATION OF SURGERY	81.17	15.63	81.25	16.76

p VALUES	INFERENCE
0.648	NS
1.000	NS
0.666	NS
0.154	NS
1.000	NS
0.273	NS
0.559	NS
0.309	NS
0.315	NS
0.402	NS
0.315	NS

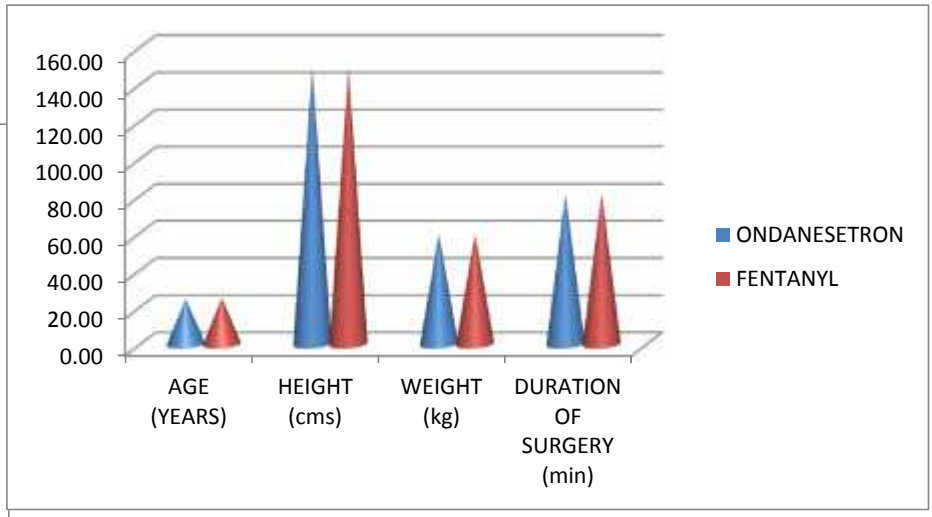
	ONDANESETRON	FENTANYL
Bad obstretric history	3	2
Breech presentation	5	5
CPD	15	13
Failed induction	2	0
Precious pregnancy	1	1
previous LSCS	26	32
Primi with HIV	2	1
Primi with non progres	3	1
Short stature	1	0
Twin pregnancy	2	4
Elderly primi	0	1

p VALUE	INFERENCE
0.5216	NS
0.2704	NS
0.9614	NS
0.9776	NS



	ONDANESETR	FENTANYL
AGE (YEA	24.48	24.93
HEIGHT (c	149.38	148.73
WEIGHT (k	59.45	59.50
DURATION	81.17	81.25

AGE	24.48	24.93
HEIGHT	149.38	148.73
WEIGHT	59.45	59.50
DURATION	81.17	81.25



	ONDANESETR	FENTANYL
Nausea	16	7
Retching	12	3
Vomiting	11	2

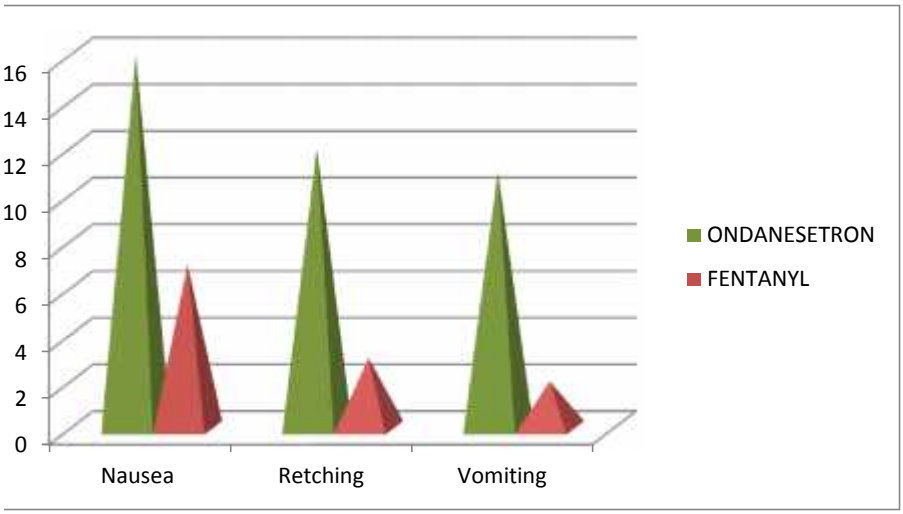


TABLE FO

11

R PERCENTAGE

18.33