COMPARATIVE TRIAL OF DICLOFENAC SUPPOSITORY, PARACETAMOL INFUSION AND THEIR COMBINATION FOR POST CAESAREAN DELIVERY ANALGESIA

By

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Dr. MANDEM SADANA REDDY

ABSTRACT

TITLE: COMPARATIVE TRIAL OF DICLOFENAC SUPPOSITORY, PARACETAMOL INFUSION AND THEIR COMBINATION FOR POST CAESAREAN DELIVERY ANALGESIA

INTRODUCTION

Pain is unpleasant, emotional and sensory experience. One of the most important aspect of post operative care is pain management. Non-steroidal anti-inflammatory drugs (NSAIDS) have recently gained more popularity in postoperative pain management.Though post-operative pain is better achieved with higher modalities like epidural analgesia but lack of availability of high skilled personnel in peripheral areas of developing countries like India and moreover as they are expensive.

Diclofenac suppository and paracetamol infusion are more economical and easily available so these drugs are used to conduct this study. There are very few studies available in literature comparing the postoperative analgesic effect of i.v paracetamol, diclofenac suppository or in combination. Therefore, the aim of present study is to compare the effects of diclofenac suppository, paracetamol infusion and their combination in post caesarean delivery analgesia.

By doing this comparative study which helps in finding out efficient analgesic drug and better mode of administration of drugs individually or in combination we can implement for achieving better post operative analgesia.

AIMS AND OBJECTIVES

- To determine the analgesic efficacy by visual analogue scale pain scores and safety of i.v paracetamol.

- To determine analgesic efficacy and safety of diclofenac suppository.
- To compare analgesic efficacy and safety of individual use of i.v paracetamol and diclofenac suppository and in combination.

MATERIALS AND METHODS:

This prospective and comparative study conducted from Oct 2018 to June 2020 at Department of Obstetrics and gynecology on the patients admitted in R.L.Jalappa Hospital attached to Sri Devraj Urs Academy of Higher Education and Research,Tamaka, Kolar. A proforma containing detailed information of each patient was designed according to the study protocol. Ethical clearance obtained from the Institutional Ethics Committee. Written and informed consent obtained from patients . A total of 90 women underwent caesarean section have been recruited for the study and were randomly allocated using lottery method into three groups. Three groups, each group comprises of 30 participants. The patients underwent lower segment caesarean section under spinal anaesthesia with the same technique and medicine, (Bupivacaine % 0.5) without receiving any sedation, using No. 27 spinal needle in sitting position at L3-L4 and L3-L2 space by an anaesthesiologist. Post operatively for analgesia patients in Group A received diclofenac suppository 50mg every 8th hrly,Group B received paracetamol infusion 1000mg every 8 th hrly and Group C received 50mg diclofenac suppository and 500 mg intravenous paracetamol every 8th hrly.Pain severity(VAS score) and duration of analgesia ,frequency of additional analgesia required and any side effects were evaluated at 2,4,6,8,12,24hrs post operatively.Patient satisfaction score was evaluated at 24hrs after caesarean section.

RESULTS-

Patients who underwent caeserean section included in the study were in the mean age group of 24 to 25 years. Mean duration of surgery in each of three groups was 60 minutes. Patients received either intravenous paracetamol or diclofenac suppository or the combination of both the drugs. VAS score indicated mild pain during first 24 hours of post-operative period which was comparable between the groups.

There was statistically significant difference in median VAS score for a pair of

1) Group A and Group B at 2hrs, 8hrs and 24hrs with P value < 0.05.

2) Group B and Group C at 2hrs, 4hrs, 6hrs, 8hrs, 12hrs, 24hrs with P value < 0.05.

3) Group A and Group C at 2hrs, 4hrs, 6hrs, 8hrs, 12hrs, 24hrs with P value < 0.05.

The major findings of the study are VAS score indicated mild pain during first 24 hours of post-operative period which was comparable between the groups. In the present study, there was reduction of pain indicated by VAS score however this reduction was significant in patients receiving paracetamol and diclofenac suppository combination group.

Present study reported that combination group was superior to both individual paracetamol infusion group and diclofenac suppository group in post caesarean analgesia. We have observed that pain relief by individual use of paracetamol infusion and diclofenac suppository was similar.

The satisfaction score was categorized as excellent by 80% patients in combination group. In Diclofenac group 30% and in Paracetamol group 16.6% categorised as excellent patient satisfaction score. This study indicates a significant effect of concomitant use of intravenous acetaminophen and diclofenac suppository on pain severity reduction and prolonging the postoperative analgesia.

In present study the adverse effects such as nausea and epigastric discomfort was higher with diclofenac suppository group 10% followed by Paracetamol group (6.6% side effects) and minimal with combination group(3.3%)

CONCLUSION:

Paracetamol infusion is as effective as diclofenac suppository in reducing post-operative pain following caesarean section. Diclofenac suppository and i.v paracetamol combination provides more effective postoperative analgesia compared with individual usage of i.v paracetamol or Diclofenac suppository in patients following caesarean section.The combined use of paracetmol and diclofenac suppository has less side effects compared with individual use of either i.v paracetamol or diclofenac suppository

Key Words : Caesarean section, Diclofenac ,Paracetamol,Postoperative analgesia , Caesarean Delivery

LIST OF ABBREVIATIONS

NSAIDs	Non Steroidal Anti-inflammatory Drugs
COX	Cyclooxygenase
VAS	Visual Analogue Scale
WHO	World Health Organisation
PCA	Patient Controlled Analgesia
NMDA	N-Methyl D-Aspartate
TRPV1	Transient Receptor Potential Vanilloid 1
PG	Prostaglandin
LSCS	Lower segment caesarean section
IQR	Inter Quartile range
ANOVA	Analysis Of Variance

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INTRODUCTION

INTRODUCTION

Pain is unpleasant, emotional and sensory experience . One of the most important aspect of post operative care is pain management. Adverse side effects and addiction of the opioids have made physicians to focus on Non steroidal anti inflammatory drugs (NSAID) for pain control[2,3].Non-steroidal anti-inflammatory drugs (NSAIDS) have recently gained more popularity in postoperative pain management.Though post-operative pain is better achieved with higher modalities like epidural analgesia but lack of availability of high skilled personnel in peripheral areas of developing countries like India and moreover as they are expensive.

Diclofenac suppository and paracetamol infusion are more economical and easily available so these drugs are used to conduct this study. There are very few studies available in literature comparing the postoperative analgesic effect of i.v paracetamol, diclofenac suppository or in combination. Therefore, the aim of present study is to compare the effects of diclofenac suppository, paracetamol infusion and their combination in post caesarean delivery analgesia.

All types of NSAIDS can be used for alleviating postoperative pain including non-selective cyclo-oxygenase (COX) inhibitors. Their peripheral and central analgesic effect, anti-inflammatory properties are relatively more tolerable than opioids, which have made them as treatment of choice in postoperative pain.

On alleviating post operative pain in caesarean delivery mothers

-Early bonding can be established with baby resulting in early commencement of breast feeding and good perinatal outcomes [1].

-Early ambulation is possible through which complications like Deep vein thrombosis, embolism can be avoided.

-It also reduces the hospital stay and prevents nosocomial infections.

AIMS & OBJECTIVES

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1. To determine the analgesic efficacy by visual analogue scale(VAS) pain scores and safety of i.v paracetamol.
2. To determine analgesic efficacy and safety of diclofenac suppository.
3. To compare analgesic efficacy and safety of individual use of i.v paracetamol and diclofenac suppository and in combination.

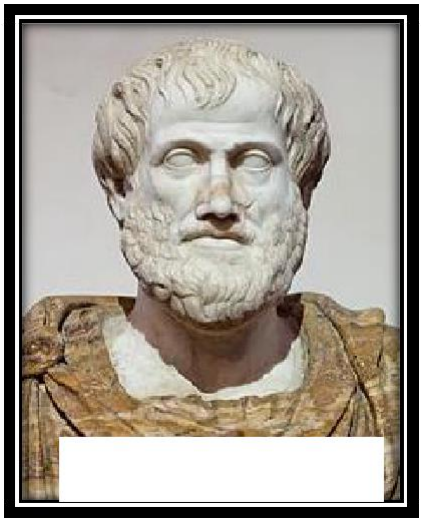
REVIEW OF LITERATURE

REVIEW OF LITERATURE

Historical background of pain

Ever since humans have experienced painful sensations, they have given justification for its existence and tried to find soothing agents to reduce the agonising pain. Primitive man considered illness and pain as the work of evil spirits. Treatment consisted of extracting the intruding object or frightening away the spirits. Archaeologists have uncovered clay tablets dating back to 5,000 BC which mentions the cultivation of the opium poppy and used it for pleasure and cease pain.[2]

Acupuncture, a method prevailing in China since 2700 B.C. involves inserting metal needles on skin at certain points to varying depths, to counteract pain and other symptoms. E.H.Hume described that Hunt O, a renowned surgeon in Chinese history of medicine, born in 190A.D used acupuncture for carrying out surgeries on various organs.[3]



Aristotle (Figure 1) did not embrace sense of pain when he enumerated the five senses. He saw pain and pleasure not as sensations but as emotions. Alternatively, Hippocrates believed that pain was caused by an disproportion in the vital fluids of a human.

In Greece – Alcamaeon gave the idea that the brain and not the heart was the center for pain.[4] Benjamin Bell (1749–1806), surgeon of the Royal Infirmary, Edinburgh, described the use of a nerve compressor to decrease pain during amputations in his textbook dated 1796.

In 1804, Descartes (Figure 2) described in his book called "L Homme (Man)" that the transmission of sensation including pain was via delicate threads confined in the nerves which linked the tissue to the brain.[5] The new era of analgesia was started with Joseph

Priestley‟s discovery of nitrous oxide. Charles Beu explained that the functions of dorsal root are distinct from the ventral root and after 15 years, Johannes Muller developed this idea. The era of systemic analgesia began in 1806 when morphine was isolated by Sertuner and was frequently used intramuscularly as preoperative medication and for postoperative analgesic.[4]

In 1874 the cannabis plant from which marijuana was obtained became a well-regarded remedy for headache prescribed by treating physicians. In 1898, heroin the newest opium derivative was produced commercially by Germany Bayer Company. Significant advances were made in pain management during the 19th century.[5] Injection of dilute

solutions of cocaine into the epidural space through the sacral hiatus was first described by Sicard in 1901, to treat patients suffering from severe sciatic pain. In 1912, Kappis described paravertebral somatic blocks pain relief during surgeries. In 1953 John J. Bonica developed an interest in pain management and published a seminal book - The Management of Pain, where therapy of pain was focused on nerve blocks. In 1970 neurostimulators, based on a theory that electric current can produce magnetic field was used for pain relief.[4]

In 1988, Brian Ready used Patient Controlled Analgesia (PCA) mode to provide safe and effective management of severe post-operative pain. In 1997 Intra Discal Electrothermic Therapy (IDET) was introduced to investigate chronic low backache. In 2004-05, the first rechargeable spinal cord stimulation systems became available in United States which represent the new advancement in neuromodulation devices for the treatment of pain. In 2008 St. Jude introduced smallest long lasting neurostimulator to treat failed back surgeries and chronic pain of trunk and limbs.[4, 5]

Definition and classification of pain

Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Pain is always subjective. The term "nociception" is obtained from “noci” (Latin word for harm or injury) and is used to define the neural response only to noxious or traumatic stimuli.[6]

Pain is categorized as follows[7]

I) **Acute pain** - Typically appears suddenly and has a limited duration. It is frequently caused by damage to bone, muscle or organs and the onset is often accompanied by anxiety or emotional distress. It is considered as good pain as it serves an important protective mechanism. Acute pain stimulates sympathetic nervous system resulting in increased heart rate, respiratory rate, sweating, dilated pupils, restlessness and apprehension.

A) Somatic pain: Further classified as, superficial or deep

(a) Superficial type of somatic pain is due to nociceptive feedback arising from skin, tissues and mucous membrane. It is well localized and sharp, pricking, throbbing or burning in character.

(b) Deep somatic pain arises from muscles, tendons, bones or joints. It is a dull, aching quality and is not well-localized.

B) Visceral Pain

The visceral acute pain is due to abnormal function of an internal organ or its covering or due to disease process. It is dull and diffuse in character and is associated with atypical sympathetic or parasympathetic activity. Ischemia, chemical stimuli, spasm or over distension of hollow viscus are some of the causes for visceral pain.

C) Referred pain

The site of stimulus and the area of the referred pain is supplied by the same spinal segment . Hence the patients feel the pain in the area distant from site of stimulus .

II) **Chronic pain-** Lasts longer than acute pain and generally does not respond to medical treatment. Prolongs and persist beyond expected normal time. This period can vary from 1 to 6 months or longer. Chronic pain can be the result of damaged tissue, but very often is attributable to nerve damage.

Post operative pain

Post-operative pain is one of the most common adverse consequence following surgery and is a type of acute nociceptive pain. The pain, a patient experiences after surgery, is related to the extent of tissue damage and the site of surgery. Unrelieved pain after surgery can interfere with patients physical functioning and wellbeing which will in turn extend the duration of hospital stay. Effective pain control is important in order to prevent complications such as hypertension, myocardial ischemia, arrhythmias, respiratory impairment and poor wound healing.[8]

Pain receptors

The receptors of pain are present in the skin and other tissues, are all free nerve endings. They are widely present in superficial layers of skin, periosteum , the arterial walls, falx and the tentorium in the cranial vault and the joint surfaces . Most other tissues are only supplied with pain endings.

Three type of stimuli which excite pain receptors in response to tissue injury are mechanical, thermal and chemical pain. Fast pain (Aδ fibres) which is felt within 0.1s is elicited by mechanical and thermal stimuli. Bradykinin, serotonin, histamine, acetylcholine, prostaglandins are some of the compounds involved in exciting pain (Figure 3). Slow pain (C fibres) which begins over seconds or even minutes is elicited by all three stimuli.[9]

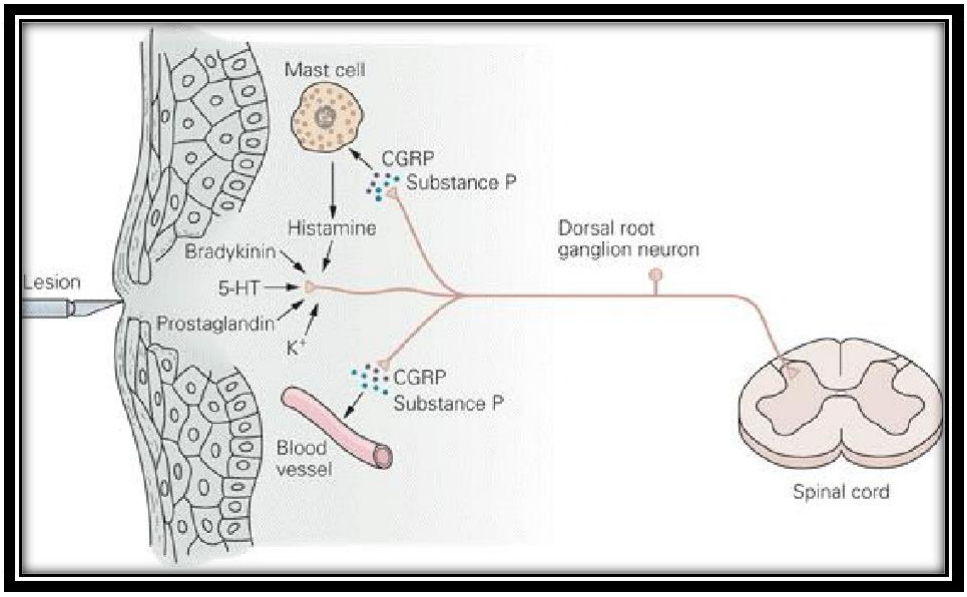


Figure 3.Chemical mediators of pain

Primary afferent fibres **:**

- Aβ fibres are highly myelinated and of large diameter, therefore allowing rapid signal conduction. They have a low activation threshold and usually respond to touch and transmit non noxious stimuli.
- Aδ fibres are lightly myelinated and smaller in diameter, hence conduct more slowly than Aβ fibres. They carry fast pain and are responsible for the initial reflex response to acute pain .
- C fibres are the smallest type of primary afferent fibre which are unmyelinated, hence they demonstrate the slowest conduction.

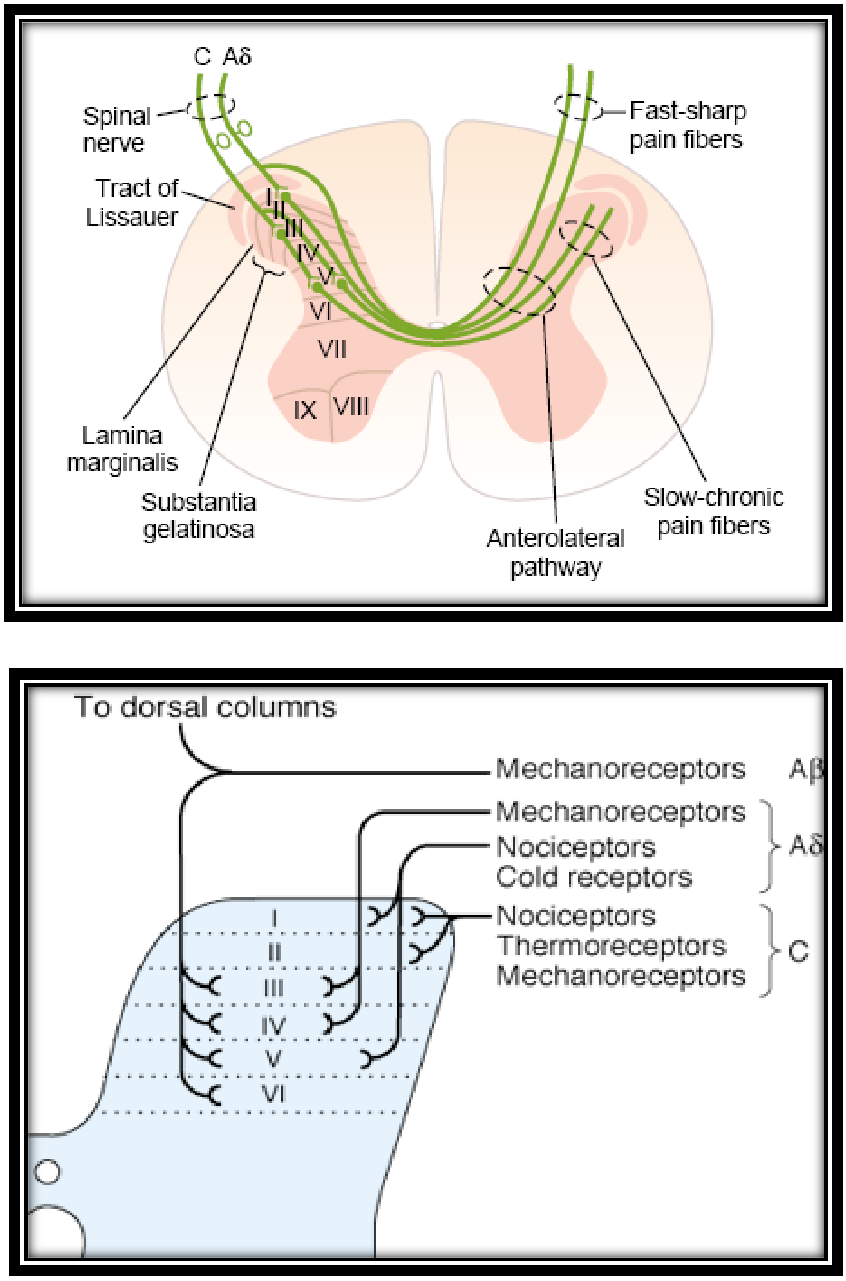


Figure 4 . Transmission of the fast and slow pain signals to spinal cord

The fast (Aδ) and slow fibers (C), on arriving at the spinal cord terminate on relay neurons in the dorsal horns. Substance P and glutamate released in the dorsal horn, is a regulator of pain and channels pain impulses from the peripheral receptors to the central nervous system. Spinal cord grey matter is divided into 10 laminae called as Rexed laminae.

The first six laminae which make up the dorsal horn receive all afferent neural activity and represent principal site of pain modulation (Figure 4).[10]

Dual pathways for transmission of pain signals into the CNS

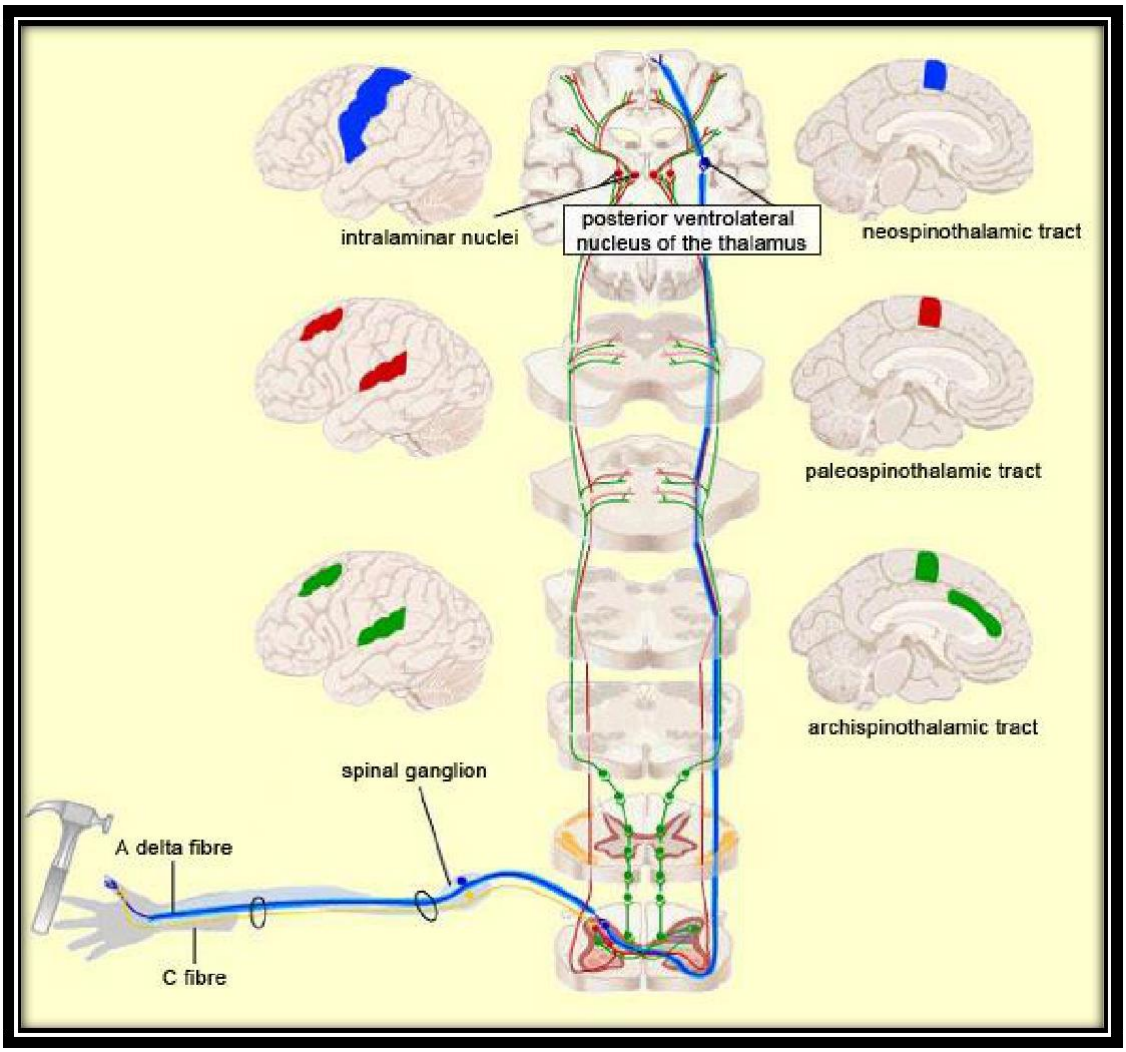


Figure 5. Neospinothalamic and paleospinothalamic tract

Pain signals take two pathways on entering the spinal cord to the brain via,

1. Neospinothalamic tract[8]

This transmits fast pain (Aδ fibres) which mainly terminate in lamina 1(lamina marginalis) of the dorsal horn (Figure 4). They excite second order neurons of the tract.

These give rise to long fibers that cross immediately to the opposite side of the cord over the anterior commissure and pass to the brain in the anterolateral column.

A few fibers of the tract terminate in the reticular areas of the brain stem but most pass to thalamus without interruption terminating in the venterobasal complex along with dorsal column medial leminiscal tract for tactile sensations. Some fibres also terminate in the posterior nuclear group of the thalamus. From these areas, signals are transmitted to the cortex (Figure 5).

2. Paleospinothalamic tract [8]

Slow chronic pain is carried by the type C fibres in paleospinothalamic tract which terminate in lamina II, III of dorsal horn (substantia gelatinosa) (Figure 4). Signals then pass through the second order nerve fibres within dorsal horns before entering lamina V. The last neurons in the series give rise to long axons that join the fibers from fast pain pathway, passing through anterior commissure first to the opposite side of the cord, then upward manner to brain in anterolateral pathway. (Figure 5)

They then terminate widely in the brain, only one tenth to one fourth of fibers pass all the way to thalamus. Most terminate in one of the following three areas.

a) The reticular nuclei of medulla, pons and mesencephalon

b) The tectal area of mesencephalon

c) The periaqueductal gray region surrounding the aqueduct of sylvius

Theories of pain[11-13]

A) Specificity Theory

It is one of first modern theories for the pain**.** It states that specific pain receptors convey signals to "pain center" in brain that produces perception of the pain. This theory also says that separate fibers do carry pain signals to the brain eventually.

However, this theory did not explain the psychological factors that influence perception of pain.

B) Pattern Theory

Specificity theory explains that pain signals are conveyed to brain only when stimuli combine together to produce a specific combination or pattern. The theory neither postulates specialized receptors for the pain nor does it see brain as having control over the amount of pain experienced. Here, the brain is only observed as a recipient for the messages.

C) Gate Control Theory

It was proposed in 1965 by Ronald Melzack and Patrick Wall. They suggested that there is a gate or control system in the substantia gelatinosa of dorsal horn of spinal cord, which modulates the sensory information from primary afferent fibres before reaching the brain. The substantia gelatinosa controls whether the gate is open or closed. An open gate means that the small fibres (C) can carry signals to the brain where pain is perceived whereas stimulating large diameter fibres inhibits the transmission of pain and closing gate and no pain signal is sent to brain (Figure 6).

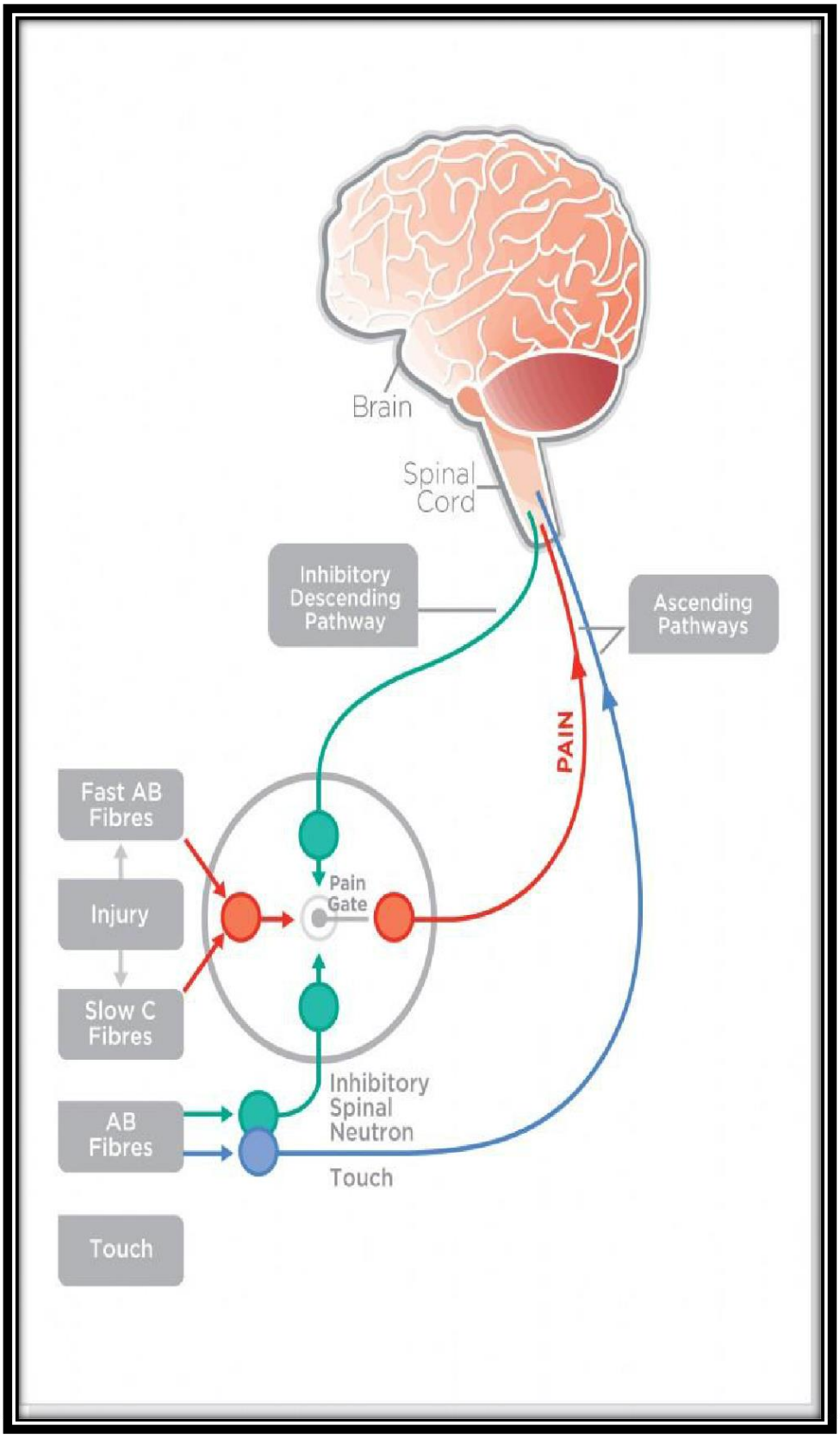


Figure 6. Gate control theory

Assessment of pain

Ideal pain management is carried out by assessing the pain experienced by the patient. It aims at assessing the intensity, duration and quality of pain. Pain assessments are done in the form of a scale which will help in deciding the choice and effectiveness of therapy.[14]

Pain assessment scale[15, 16]

1. Visual analogue scale

   VAS is the most universally used method of pain assessment at present. First described

by Aitken is 1966. The patient makes a mark on a 10cm line, one end of which is marked as „No pain" which is indicated by 0 and the other as „The worst(excruciating) possible pain one can perceive" which is indicated by 10. Here patients are asked to indicate pain intensity on a scale of 0 to 10 (Figure 7).

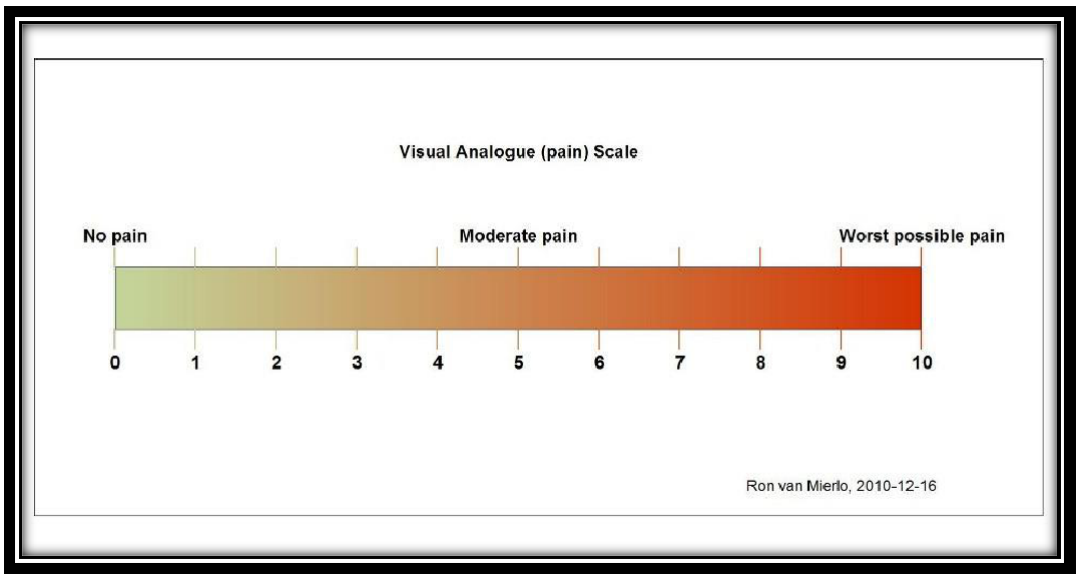


Figure 7. Visual Analogue Scale Score

2. Faces rating scale

Recommended for children above 3 years of age. Ask the child to choose the face that best describes his or her pain and note the appropriate number(Figure 8).

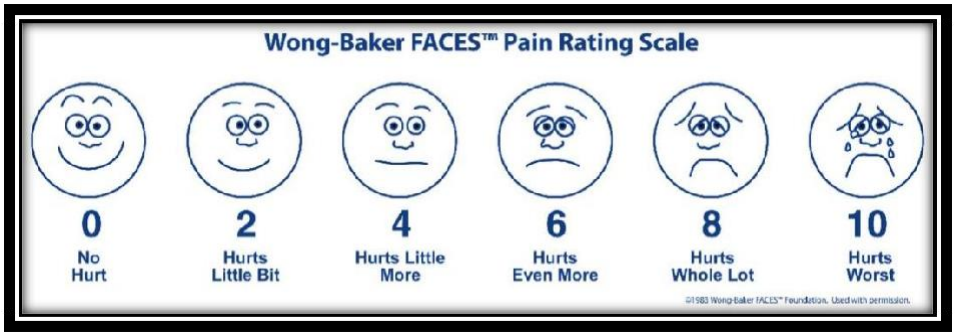


Figure 8. Faces Rating Scale

3. McGill pain questionnaire(MPQ)

In 1971, Melzack and Torgerson developed a scale of rating pain at McGill University in Canada. It is a self-reported questionnaire that guides the doctor with a good description of the quality and intensity of pain that patients are experiencing. It consists primarily of 3 major classes of word descriptors: sensory, affective and evaluative. It contains an intensity scale to determine the properties of pain experienced and are used by patients to specify subjective pain experience.

4. Behavioral rating scale

It is designed for use in critically sick patients who are unable to provide self-reports of pain. Observe the patient for 10 minutes. Assess the patient on the four behaviors (restlessness, tense muscles, frowning/grimacing, patient sounds from none-severe). A pain score is obtained based on the highest behavior observed.

5. Functional activity scale

This is an activity related score. Ask your patient to perform an activity related to their painful area (eg: deep breathe and cough for thoracic injury or move affected leg for lower limb pain).

Observe your patient during the chosen activity and score A, B or C A – No limitation means the patient‟s activity is unrestricted by pain

B – Mild limitation means the patient‟s activity is mild to moderately restricted by pain

C - Severe limitation means the patient ability to perform the activity is severely limited by pain

6. CHEOPS scoring

The CHEOPS (Children's Hospital of Eastern Ontario Pain Scale) is a behavioral scale for evaluating postoperative pain in young children. It can be used to monitor the effectiveness of interventions for reducing the pain and discomfort. According to Mitchell (1999) it is intended for ages 0-4. It involves 6 parameters such as facial, torso, cry, legs, child verbal and touch. Minimum score is 4 and maximum score is 13.

7. FLACC (Face, Legs, Activity, Crying and Consolability) scale score[17]

The FLACC pain scale was developed to help doctors to assess the level of pain in children who are not able to self report the pain intensity. Also it can be used in adults who are unable to communicate. It is based on observations made regarding the patient’s face, the position of their legs, their actions, and whether they are calm or consolable. Zero to two points were assigned for each of these 5 areas of observation. The score is graded as follows:

0 = Relaxed and comfortable

1-3 = Mild discomfort

4-6 = Moderate pain

7-10 = Severe discomfort/pain

Modes of analgesia

A) Preemptive analgesia[18, 19]

It is initiated before the surgical procedure in order to reduce pain intensity. It has potential to be more effective than any similar treatment initiated post surgery. Acute post-operative pain can be reduced and the development of chronic pain may be prevented. The only way for the prevention of the sensitization of the nociceptive system is to block completely any pain signal arising from the surgical wound from the time of incision until final wound healing. Interventions with flupirtine and gabapentin, may interfere with the induction and maintenance of sensitization.

B) Multimodal analgesia

This involves the use of the specific drugs in combination. The concept relies on using several analgesic drugs with different modes of action (eg: non-opioid combined with opioid) or via different routes of administration (eg: local anaesthetic block combined with a systemic analgesic). This approach improves analgesia due to additive or synergistic effects. The dosage of the individual drugs can be reduced, thereby reducing severity and incidence of adverse effects.

C) Patient controlled analgesia[19]

Patient Controlled Analgesia (PCA) is a method of pain control, where in it allow the patient to administer preset doses of an analgesic, on demand. PCA pump is an electronic micro processing machine which

Figure 9.PCA pump

is programmed to deliver a required amount of medication on demand, at specified intervals, by pressing of a button (Figure 9). Supplemental clinician loading doses of medication can also be delivered. Morphine is one of the most common medicine used to administer via PCA pump.

Post-operative pain management[19, 20]

1. Opioid analgesics

Opioids act as agonists on stereospecific opioids receptors (mu, delta and kappa) at presynaptic and postsynaptic sites at spinal and supra spinal levels and in the peripheral

tissues. Opioids imitate actions of the endogenous ligands by binding to opioids receptors, resulting in the activation of pain – modulating system.

2. NSAIDs

NSAIDs are the frequently used drugs because of their anti-inflammatory, both antipyretic and analgesic properties. Their action is mediated through inhibition of cyclooxygenase enzymes 1 and 2, which convert arachidonic acid to prostaglandins, responsible for both central and peripheral sensitization of neurons to pain.

3. Non opioids – non NSAIDs[21]

Flupirtine exerts its analgesic action through blockade of N – methyl – D – aspartate (NMDA) receptor. It also has muscle relaxant, neuroprotective and antiparkinsonian property. It is devoid of adverse effects of opioids and NSAIDs because of its unique mechanism of action. It is used in musculoskeletal pain, post-operative pain, neurogenic pain, cancer pain and fibromyalgia.

3. Adjuvants

Drugs which by themselves have undesirable side effects or low potency but in combination with opioids, allows reduction of opioid dosing for postoperative pain management. Examples- Ketamine, gabapetin, pregabalin, dexmedetomidine and clonidine.

4. Local anaesthetics

A local anaesthetic is a drug that causes reversible local anaesthesia and loss of nociception by interfering with pain transmission in the spinal cord by blocking sodium channels leading to analgesia. When used on specific nerve pathways (nerve block), effects such as analgesia and loss of muscle power can be achieved. It allows patients to undergo

surgical and dental procedures with reduced pain and distress. Lignocaine, bupivacaine, ropivacaine, tetracaine, prilocaine are some of the local anaesthetics in use.

5. Transient Receptor Potential Vanilloid 1(TRPV1) antagonists[22]

TRPV1 is expressed on small myelinated and unmyelinated sensory neurons in dorsal root and trigeminal ganglia, where sensory neurons cluster. It is also found in muscles, joints, the urinary bladder and kidneys. Activation of TRPV1 causes influx of calcium and sodium ions which in turn initiates a cascade of events that result in membrane depolarization, neuronal firing and transduction of neural impulses. Orally active TRPV1 antagonist substances have evolved into clinical development and several more are in preclinical development. Capsazepine blocks the painful sensation caused by capsaicin which activates TRPV1 ion channel and is therefore considered to be a capsaicin antagonist.

Adverse effects and addiction of opioids have made physicians to focus on Non-steroidal anti-inflammatory drugs (NSAID) for control of pain[23,24] . Though post operative pain is better achieved with higher modalities like epidural analgesia but lack of availability of high skilled personnel in peripheral areas of developing countries like india and moreover they are expensive .

Only because of poverty they should not suffer from pain. Diclofenac suppository and paracetamol infusion are more economical and easily available to conduct this study. Very few studies are available in literature comparing the postoperative analgesic effect of i.v paracetamol , diclofenac suppository or in combination Therefore, the aim of present study is to compare effects of diclofenac

suppository , paracetamol infusion and their combination in alleviating the post operative pain for post caesarean delivery mothers.

By doing this comparative study which helps in finding out efficient analgesic drug and better mode of administration of drugs individually or in combination we can implement for achieving better post-operative analgesia.

Patients given the combination of diclofenac and paracetamol required less morphine than patients given paracetamol alone. Morphine use in patients given diclofenac alone was not significantly different from morphine use in the other two groups. Eight out of 26 patients receiving paracetamol alone were not satisfied with pain management; two required intravenous morphine injections. [25]

In Acetaminophen, indomethacin, diclofenac, and placebo suppositories were used in groups, respectively, after operation and the dosage was repeated every 6 hrs, opioid usage and pain score were compared 24 h after the surgery and results showed are Significantly higher pain score is noted in control group than other groups, and also pain score in acetaminophen group was higher than indomethacin and diclofenac. The intervention groups, which are three in number received the first dose of pethidine far more than control group and the distance for diclofenac and indomethacin were significantly longer ($P < 0.001$). The use of indomethacin, diclofenac, and acetaminophen significantly reduces the amount of pethidine usage in 24 h after the surgery relation to control group.[1]

A study was conducted to compare efficacy of analgesia and safety of three most frequently used analgesic drugs-intramuscular diclofenac sodium, diclofenac

suppository and intravenous tramadol hydrochloride in patients undergoing gynaecological surgery. Postoperative pain intensity was assessed by visual analogue scale. In this study diclofenac suppository provides effective postoperative analgesia when compared with Inj. Diclofenac I.M. and Inj. tramadol I.V. in patients undergoing infraumbilical gynaecological surgeries with stable vitals and no side effects.[26]

In another prospective,double-blind randomized study of comparison of analgesic efficacy of parenteral paracetamol and diclofenac for postoperative pain relief. The quality and duaration of analgesia in both the groups were similar in postoperative period. i.v paracetamol provides effective non sedating pain relief in postoperative period. i.v paracetamol and i.v diclofenac can be a part of multimodal analgesia.[27]

A randomised control trail compared the analgesic efficacy of rectal diclofenac and intramuscular diclofenac for pain relief following caesarean section.Total number of sixty six (66) patients undergoing elective caesarean(lower section) delivery under spinal anaesthesia were randomized into two groups. Thirty-three (33) patients in each group received either 100mg of rectal diclofenac sodium or 75mg of intramuscular diclofenac sodium for duration of 24 hours, following caesarean section. Both routes of administration demonstrate good pain control, however rectal route appears more tolerable among the patients.[28]

INTRODUCTION TO NON STEROIDAL ANTI INFLAMMATORY DRUGS

The NSAIDs, are the most widely used of all drugs because of their analgesic, anti-inflammatory and anti-pyretic effects. [29]

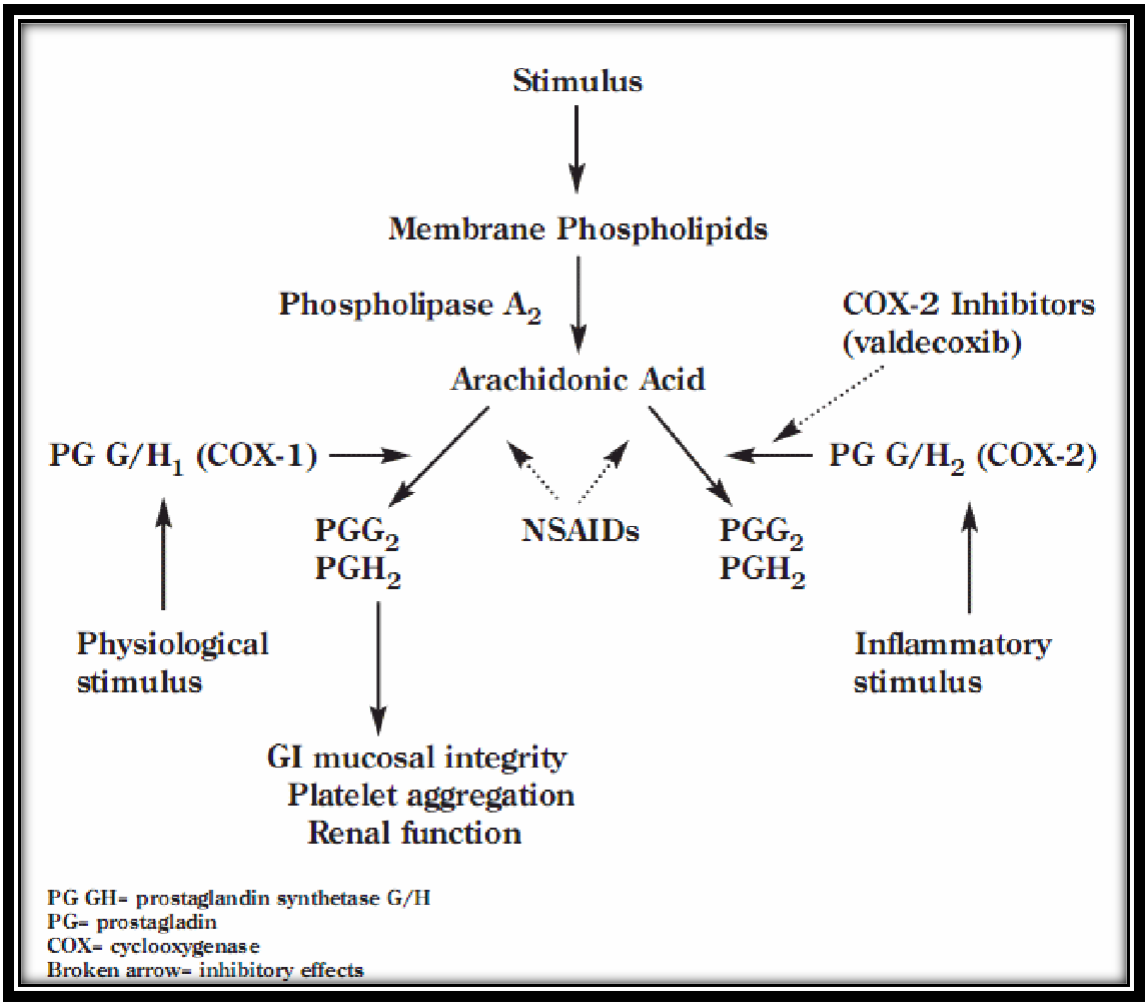


Figure 10. Mechanism of action of NSAIDs

NSAIDs have the ability to inhibit prostaglandin (PG) production by inhibiting cyclooxygenase (COX) enzyme also known as PG G/H synthase. COX enzymes are of two forms: COX-1 and COX-2. COX-1, expressed in most cells, is the dominant source of prostaglandins for housekeeping functions, such as gastric epithelial cytoprotection and hemostasis whereas COX-2, induced by cytokines, stress, and tumor promoters, is the more

important source of prostaglandin formation in pain, inflammation, fever and carcinogenesis.[30]

This enzyme converts arachidonic acid to the unstable intermediates such as PGG_2 and PGH_2 and leads to the production of the PGE_2, PGI_2 (Key mediators of central and peripheral pain sensitization) and Thromboxane A_2 (Figure 8). PGE2 contribute to hyperalgesia by sensitizing nociceptors via its receptors EP_1 and EP_4 which causes phosphorylation of transient receptor potential vanilloid 1 and other ion channels on nociceptors and increase their membrane excitability

Centrally PGs enhance pain transmission at the level of dorsal horn increasing the release of substance P and glutamate from first order neurons, increasing the sensitivity of second order neurons and inhibiting neurotransmitter release from pain modulating pathways.

Advantages of NSAIDs in management of post-operative pain:

NSAIDs are effective in the treatment of post-operative pain. They lack unwanted effects of opiates like nausea, vomiting, sedation, respiratory depression, absence of cognitive impairment and potential for the development of physical dependence. [31, 32]

Commonly used NSAIDs for the management for post-operative pain are diclofenac, lornoxicam, piroxicam, aceclofenac, etorcoxib and parecoxib.

Pharmacology of Diclofenac

Introduction

Diclofenac derives from its chemical name: 2-(2, 6-dichloranilino) phenylacetic acid which was first introduced in the UK in 1979. It was originally developed by Novartis in 1973.

History

The purpose of developing diclofenac sodium was to synthesize a NSAIDs with high activity and exceptional tolerability. Factors considered were drug transport through biologic membranes, the spatial and atomic structure of the molecule and the electronic structure. Based on analysis of other NSAIDs, it was hypothesized that an effective antirheumatic agent should have the following characteristics, an acidity constant between 4 and 5, a partition coefficient of approximately 10, and two aromatic rings twisted in relation to each other. The result was diclofenac sodium, which has an acidity constant of 4.0 and a partition coefficient of 13.4 with a maximum twisting in its ring structure.

Structure and chemistry of diclofenac

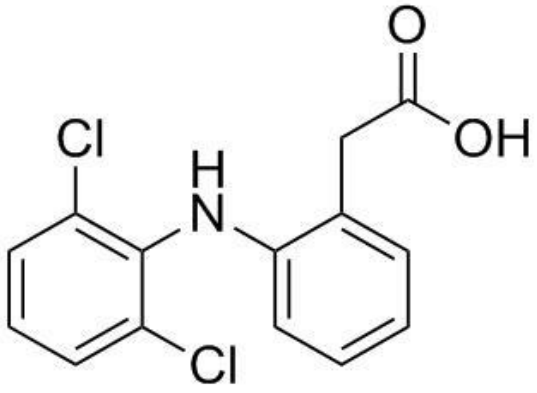


Figure 11. Chemical structure of diclofenac[30]

Mechanism of action

A non selective inhibitor of cyclooxygenase enzyme, inhibits prostaglandin production which are important mediators of pain. Hence decreases the post-operative pain by decreasing the nociceptive transmission to brain.[35]

Pharmacokinetics

Diclofenac is rapidly absorbed when given as a sugar coated tablet, rectal suppository or intramuscular injection. Absorbed more slowly when given as an enteric coated tablets and when given with food. Only 50% of drug reaches systemic circulation in an unchanged form following first pass metabolism and 99% bound to plasma proteins.

Diclofenac is predominantly eliminated through hepatic biotransformation with less than 1% of the dose being excreted unchanged through the kidneys. The major primary metabolites of diclofenac are 3‟ hydroxyl diclofenac, 4‟ hydroxyl diclofenac, 5‟ hydroxy

diclofenac, and 4‟, 5‟ dihydroxydiclofenac. Its hydroxylated metabolites undergo glucuronidation and sulphation and are excreted in urine.[30, 35]

Uses

- Rheumatoid arthritis
- Osteoarthritis
- Ankylosing spondylitis
- Bursitis, tendinitis, sprains and strains
- Acute gout
- Renal colic

- Dysmenorrhea
- Migraine
- Post-operative pain in hernioplasty[36], lower limb fractures, tonsillectomy

Dosage and route

Diclofenac is administered either through oral or rectal route in a dose of 75-150mg. A dosage of 50mg is used for migraine. Diclofenac can be given intra-muscular in a dose of 75 mg once or twice daily for post-operative pain management. It can an also be given as continuous or intermittent intravenous infusion with glucose or sodium chloride. Diclofenac sodium is used as 0.1 % ophthalmic solution.[30]

Table 1. Adverse effects of diclofenac[30]

Systems	Manifestations
Eyes	Blurring of vision
Ear	Hearing loss, tinnitus
RS	Pneumonitis, alveolitis, pulmonary fibrosis
CVS	Increase blood pressure, heart failure, MI, stroke (COX 2) Inhibitors
GIT	Peptic ulcer, bleeding , perforation
CNS	Dizziness
Blood	Agranulocytosis, neutropenia
Bone	Delayed bone healing process
Liver	Acute non-infectious liver injury
Renal	Interstitial nephritis- Acute and chronic
Pancreas	Pancreatitis
Skin	Maculopapular rash, systemic lupus erythromatosus, tissue necrosis[37]
Hypersensitivity	Rash, urticaria, bronchoconstriction, angioedema, anaphylactic
Reaction	Shock

The most frequently reported side effects were gastrointestinal which was reported in 7.6 % of patients followed by CNS related adverse effects which was reported in 0.7% and allergy in 0.4%.

Drug Interactions

- Corticosteroids, selective serotonin reuptake inhibitors, bisphosphonates, antiplatelets such as clopidogrel, ticlopidine may increase the frequency or severity of GI complications when combined with diclofenac

- Since diclofenac is highly plasma protein bound, doses of drugs such as sulfonylurea, methotrexate should be reduced as it displaces other drugs from protein binding sites
- Diclofenac inhibits natriuretic and vasodilatory PGs such as PGE_2 and PGI_2, thereby attenuating the efficacy of diuretics

- Diclofenac should be avoided in patients taking anticoagulants as they interfere with normal platelet function.

- Diclofenac and cyclosporine results in deterioration of renal function and also when given along with triamterene

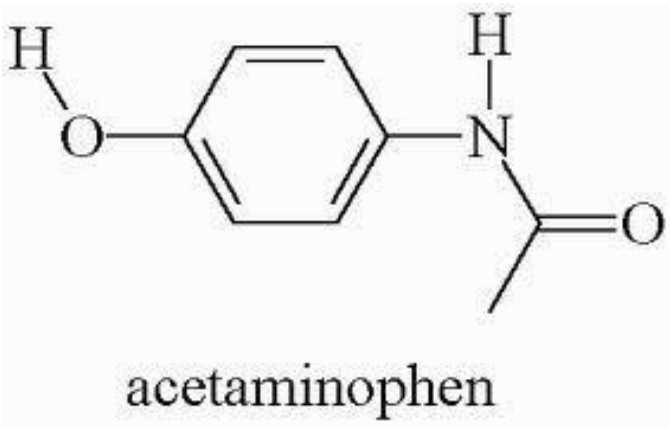
- Sucralfate reduces the plasma concentration of diclofenac

- Bile acid sequestrants reduces the bioavailability of diclofenac

ACETAMINOPHEN

Acetaminophen or paracetamol is a para-amino phenol derivative, widely used as both antipyretic and analgesic for relief of headaches and minor aches and fever.

STRUCTURE OF ACETAMINOPHEN



Mechanism of action

The main mechanism of action of acetaminophen is by inhibition of cyclooxygenase (COX). While it has both antipyretic and analgesic properties comparable to that of aspirin and other NSAIDs, its peripheral anti inflammatory activity is usually limited by several factors one of which is high level of peroxides present in inflammatory lesions.

Antipyretic effects

Endogenous pyrogens produced by leukocytes cause an elevation of prostaglandin E in the cerebrospinal fluid.[38] Acetaminophen reduces fever by blocking the formation and release of prostaglandins in central nervous system and by

inhibiting the endogenous pyrogenic action at the hypothalamic thermoregulatory centers.[39-42]

Analgesic action

Acetaminophen is believed to act primarily in the central nervous system, even though there are many proposed theories as to the precise mechanism of action. Acetaminophen is thought to produce analgesia by inhibiting prostaglandin synthesis centrally and elevating the pain threshold.[43-45] Modern research suggests that clinical pharmacologic characteristics of acetaminophen may be the result of its ability to inhibit a specific site on the prostaglandin H2 synthase (PGHS) molecule, the 2 isoforms of which, PGHS1 and PGHS2, are also referred to as COX-1 and COX-2.[43] In vitro assays and studies in human volunteers have demonstrated that acetaminophen inhibits COX-2 activity.[46,47] PGHS has 2 active sites: the COX site and the peroxidase (POX) site.[43] Acetaminophen acts as a reducing cosubstrate at the POX site, while NSAIDs noncovalently bind at the COX site, obstructing the entry of arachidonic acid. Acetaminophen has a highly variable capacity to inhibit prostaglandin synthesis by different cell and tissue types.[43,46,47] The cellular selectivity of acetaminophen is thought to derive from sensitivity to the ambient peroxide levels of various cell types. The central both antipyretic and analgesic effects of acetaminophen may be exerted through PGHS inhibition within vascular endothelial cells and neurons, where peroxide concentrations are low. In activated leukocytes and platelets, however, where peroxide concentrations are high, acetaminophen is prevented from affecting inflammation and platelet thrombosis.[43]

Another recently proposed hypothesis suggests that actions of acetaminophen is mediated by indirect activation of cannabinoid CB1 receptors,[48-50] as evidenced by complete inhibition of the analgesic effects of acetaminophen in the presence of CB1-receptor antagonists. Other suggested mechanisms of action include modulation of the serotoninergic and opioid systems,[51] inhibition of nitric oxide generation,[52] and hyperalgesia induced by substance P.[53]

Pharmacokinetics

Absorption

Food Effects: Even though maximum dosage of acetaminophen are delayed when administered with food, the degree of absorption is not affected. Acetaminophen can be taken independently of meal times.

Immediate Release: Oral acetaminophen is completely and almost rapidly absorbed from gastrointestinal tract predominantly in small intestine, with minimal absorption occurring in the stomach.[54] This absorption process occurs by passive non ionic diffusion. The bioavailability ranges from 85% to 98% relatively.[55]

Extended Release: Each bilayered acetaminophen extended release 650 mg caplet or gel cap contains 325 mg of immediate-release acetaminophen in one layer and 325 mg of acetaminophen in a matrix formulation designed to release slowly in the other layer. The average maximum plasma concentrations occur within 0.5 to 3 hours following ingestion, ranges from 6.9 to 14.1 mg/mL among individuals.[56]

Distribution

Acetaminophen is extensively distributed throughout the most body fluids except fat. The apparent volume distribution of acetaminophen approximately is 0.7 to 1.0 L/kg in children and adults.[57,58] A small proportion (10% to 25%) of acetaminophen is relatively bound to plasma proteins.[59,60] The sulfate and glucuronide metabolites does not bind to plasma proteins even at relatively high concentrations.[61]

Placental Barrier*:* When given in therapeutic doses to mother, acetaminophen crosses the placenta and reaches fetal circulation as early as 30 minutes after ingestion, with similar serum concentrations in the mother (5.9 μg/mL) and fetus (7.9 μg/mL).[62]

Breast Milk*:* When acetaminophen in recommended analgesic doses are given to the mother, it does not present a risk to the nursing infant. The secreted level in milk range from 0.1% to 1.85% of the ingested maternal dose.[63-65]

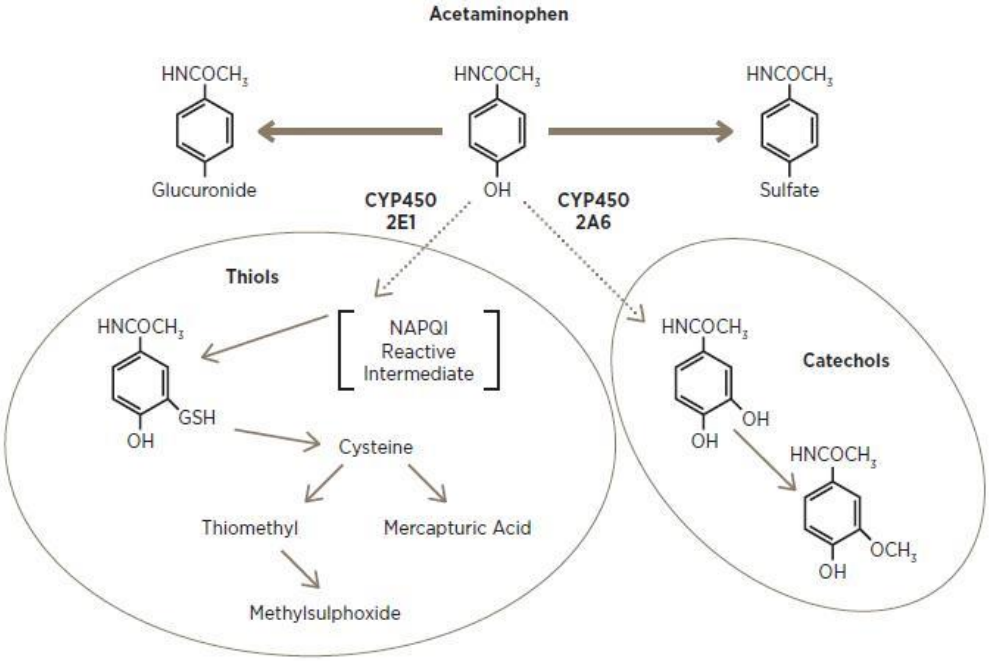
Elimination

Acetaminophen is mainly metabolized in the liver and it involves 3 main pathways: Glucuronide conjugation; Sulfate conjugation; and oxidation via cytochrome P450 (CYP450) enzyme pathway. The oxidative pathway results in a reactive intermediate that is *N*-acetyl-*p*-benzoquinone imine (NAPQI), which is further detoxified by glutathione conjugation to form inert mercapturic acid and cysteine metabolites.[66] The principal CYP450 iso-enzyme involved in vivo is CYP2E1. Two minor additional pathways are involved in acetaminophen metabolism:

hydroxylation to form 3-hydroxy-acetaminophen and the methoxylation to form 3-methoxy-acetaminophen. The catechol metabolites are conjugated further with glucuronide or sulfate.[67,68] The metabolism of acetaminophen changes with age.[57] In adults, the majority of acetaminophen is conjugated with glucuronic acid and, to a lesser extent, with sulfate. These glucuronide, sulfate, and glutathione derived metabolites lack biologic activity. Hepatic glucuronidation is relatively immature at birth. The sulfate conjugate predominates in premature infants, newborns, and young infants.[69-71]

Acetaminophen has a short t1/2 such that steady state is reached within 8 to 24 hours for almost all population groups, and accumulation is relatively low. The elimination t1/2 of acetaminophen in healthy individuals is 2 to 3 hours approximately in the usual dosage range.[72,73] The elimination t1/2 is around 1.5 to 3 hours in children, and approximately 1 hour longer in neonates,in cirrhotic patients,[74,75] in ethnic groups like Nigerians and Chinese.[60]

FIGURE – 11: METABOLISM OF ACETAMINOPHEN



Uses and Administration

Acetaminophen is given orally or as a rectal suppository for mild to moderate pain and for fever. It may also be given by intravenous infusion for the short-term treatment of moderate pain, particularly after surgery and of fever. It is often the analgesic or antipyretic of choice, especially in the elderly and in patients in whom salicylates or other NSAIDs are contra-indicated. Such patients include asthmatics, those with a history of peptic ulcer and children. Acetaminophen can be used in pregnancy.

The usual oral dose is 0.5 to 1 g every 4 to 6 hours up to a maximum of 4 g daily. It can be given as rectal suppositories in a dose of 0.5 to 1 g every 4 to 6 hours, up to 4 times daily.

Acetaminophen is also given by intravenous infusion over 15 minutes; dosage may be calculated based on weight - patients weighing over 50 kg, given single doses of 1g every four or more hours, to a maximum of 4 g daily.[76]

Administration in children.

- 3 months to 1 year: 60 to 120 mg
- 1 to 5 years: 120 to 250 mg
- 6 to 12 years: 250 to 500 mg

These doses may be given every 4 to 6 hours when necessary up to a maximum of 4 doses in 24 hours.

Administration in renal impairment**:** In patients with a creatinine clearance of 30 mL/minute or less the interval recommended between each intravenous paracetamol dose is increased to 6 hours.

Headache: Non-opioid analgesics such as acetaminophen, aspirin, and other NSAIDs are often tried first for the symptomatic treatment of various types of headache including migraine. These drugs given at the onset of symptoms can successfully treat an acute attack of migraine. However, absorption may be poor due to gastric stasis which is commonly present in migraine and so it is generally combined with a prokinetic agent like metoclopramide.[76]

Pain: Acetaminophen is used in the controlling mild to moderate pain. It is of similar potency to aspirin, but with weak anti-inflammatory activity. Acetaminophen may

also be used as an adjunct to opioids in the treatment of severe pain such as cancer pain. It is also the preferred choice for pain in children because of the association of aspirin with Reye's syndrome in this age group. In the treatment of rheumatic disorders, a weak anti-inflammatory effect limits the role of acetaminophen. However, it may be of benefit for simple pain control in rheumatoid arthritis and ankylosing spondylitis, although these patients usually require the additional anti-inflammatory effects provided by NSAIDs.

Synovial inflammation is usually only a minor component of osteoarthritis, and paracetamol is generally recommended as first choice of treatment before NSAIDs are tried. ACR Guidelines for the Medical Management of Osteoarthritis, published in 1995 and updated in 2000, recommend acetaminophen in doses up to 4000 mg/day as a firstline therapy in patients with osteoarthritis of knee joint or hip. Based on the overall cost, efficacy, and toxicity profile of acetaminophen, the ACR Guidelines state that acetaminophen merits a trial as initial therapy .[77]

Guidelines published by EULAR recommend acetaminophen as the oral analgesic to try first for knee, hip, and hand osteoarthritis and if successful, acetaminophen maybe used as the preferred long-term oral analgesic because of its safety and efficacy profile.[78]

Clinical trials proved acetaminophen to be superior to placebo in relieving the pain of osteoarthritis. Two studies conducted by Pincus and colleagues found acetaminophen 4000mg/day to provide superior pain relief when compared with placebo.[79]

In a 3-month, randomized, double-blind study comparing acetaminophen extended-release 3900 mg/ day and 1950 mg/day with placebo, the higher-dose regimen was found to be superior to placebo on measures of pain, physical function, and patient global assessment.[80] It is useful for the relief of acute low back pain.

ADVERSE EFFECTS

Adverse effects of paracetamol are rare and usually mild, although haematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia and agranulocytosis are reported. Skin rashes and other hypersensitivity reactions occur occasionally. Hypotension has been reported rarely with parenteral use. Overdosage with paracetamol can result in severe liver damage and sometimes acute renal tubular necrosis.[76]

Prompt treatment with acetylcysteine or methionine is essential. Angioedema has also been reported. Fixed drug eruptions and toxic epidermal necrolysis were also occurred.[76]

Table – 2: DRUG INTERACTIONS

Metoclopramide	Accelerates gastric emptying and decreases peak concentration of Acetaminophen
Anticholinergics(Propantheline,glycopyrolate)	Decrease gastric emptying and decrease rate of absorption
Alcohol	Increased hepatotoxicity
Ascorbic acid	Inhibits sulfate conjugation of Acetaminophen
Isoniazid	Decreases the formation of toxic metabolite NAPQI
Oral contraceptives	Increase the clearance of Acetaminophen
Anticonvulsants (Phenytoin, carbamazepine)	Chronic use increases risk of Hepatotoxicity
Probenecid	Decreased clearance of Acetaminophen

MATERIALS AND METHODS

MATERIALS AND METHODS

The study was conducted from October 2018 to June 2020, in patients who underwent caesaerean section in RLJH hospital,Kolar .

This was a prospective and comparative study conducted at Department of Obstetrics and gynecology on the patients admitted to the Department of Obstetrics and Gynecology in R.L. Jalappa Hospital & Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

Data collection:

A proforma containing detailed information of each patient was designed according to the study protocol. Ethical clearance obtained from the Institutional Ethics Committee. Written and informed consent obtained from patients. A total of 90 women underwent caesarean section have been recruited for the study and were randomly allocated using lottery method into three groups i.e Group A,B and C.

Inclusion Criteria

- Age between 19 to 40 years
- Pregnancy with gestational age of 37 completed weeks to 42 weeks
- women undergone Lower segment caesarean section (elective and emergency) under spinal anaesthesia

Exclusion Criteria

- Having an allergic history to a medicine like acetaminophen ,diclofenac or local anaesthetics
- Cardiovascular,liver ,renal disease and diabetes
- History of drug addiction

- Usage of analgesic drugs (opioid, NSAID, corticosteroid) within 8-12 hours.

4.1) Sample size:

Sample size is calculated based on difference in VAS scores at rest between Diclofenac suppository group and combination of i.v paracetamol ,diclofenac suppository group in munishankar et al study covariance $(250)^2$,with power 80% and alpha error of 5%.The estimated sample size per group was 30. Total sample size of the study is 90. n MASTER 2.0" software used for calculation.

$$n = \frac{2s_p^2 [z_{1-\alpha/2} + z_{1-\beta}]^2}{\mu^2_d}$$

$$s_p^2 = \frac{s_1^2 + s_2^2}{2}$$

where

s_1^2 :Standard deviation in first group

s_2^2 :Standard deviation in second group

α :Significance level

1- β :Power

4.2) Methodology:

This prospective comparative study was conducted at the Department of obstetrics and gynecology at RL.Jalappa Hospital attached to Sri Devaraj Urs Academy of

Higher Education & Research between october 2018 – june 2020 after obtaining the approval from Institutional Ethics Committee .

- Written and Informed Consent from the participants of the study obtained.
- A total of 90 women underwent caesarean section have been recruited for the study and were randomly allocated using lottery method into three groups.
- Three groups A,B and C. Each group comprises of 30 participants.
- The patients who underwent lower segment caesarean section under spinal anaesthesia with the standard technique and medicine, (Bupivacaine % 0.5) without receiving any sedation, using No. 27 spinal needle in sitting position at L3-L4 and L3-L2 space by an anaesthesiologist.
- Post operatively for analgesia patients in

  Group A receives diclofenac suppository 50mg every 8th hrly

  Group B receives paracetamol infusion 1000mg every 8 th hrly

  Group C receives 50mg diclofenac suppository and 500 mg intravenous paracetamol every 8th hrly
- Pain severity(VAS score) and duration of analgesia ,frequency of additional analgesia required and any side effects are evaluated and recorded at 2,4,6,8,12,24 hrs post operatively.
- Patient satisfaction score will be evaluated and recorded at 24hrs post operatively.

.

STATISTICAL METHODS:

Heart Rate, SBP, DBP, VAS Score etc., Were considered as primary outcome variables. Age, Duration of surgery Were considered as explanatory variables. Study group (Group A vs Group B vs Group C) was considered as Primary explanatory variable.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non normally distributed quantitative variables were summarized by median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.

All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro- wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.

For non-normally distributed Quantitative parameters, Medians and Interquartile range (IQR) were compared between study groups using Kruskal Wallis test (> 2 groups).

Categorical outcomes were compared between study groups using Chi square test /Fisher's Exact test (If the overall sample size was < 20 or if the expected number in any one of the cells is < 5, Fisher's exact test was used.)

P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.(1)

1. IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.

RESULTS

RESULTS:

A total of 90 subjects were included in the final analysis.

Table 1: Comparison of median age between study groups (N=90)

Parameter	Study group Median (IQR)			P value
	Group A (N=30)	Group B (N=30)	Group C (N=30)	
Age	25 (22,28)	24 (21,28)	25 (22,28)	0.609
Age groups				
19-20 (N=13)	19 (19.5,20)	19 (19,19)	19 (20,20)	0.0491
21-25 (N=41)	24 (22,25)	24 (22,24.5)	23 (22,25)	0.200
>25 (N=36)	25 (27,28)	28.5 (27,31.75)	29 (25,36)	0.660

There was no statically significant difference in Median Age (years) between study groups with P value 0.609. (Table 1)

There was no statically significant difference in Median Age group (18-20 years) between study groups with P value 0.0491. (Table 1)

There was no statically significant difference in Median Age group (21-25 years) between study groups with P value 0.200. (Table 1)

There was no statically significant difference in Median Age group (>25 years) between study groups with P value 0.660. (Table 1)

Table 2: Comparison of median Duration of surgery between study groups (N=90)

Parameter	Study group Median (IQR)			P value
	Group A (N=30) minutes	Group B (N=30) minutes	Group C (N=30) minutes	
Duration of surgery	60 (50,60)	60 (53.6,62.75)	60 (54.75,60)	0.626

There was no statically significant difference in Median Duration of surgery between study groups with P value 0.626. (Table 2 & Figure 2)

Figure 2: Line graph comparison of median Duration of surgery between study groups(N=90)

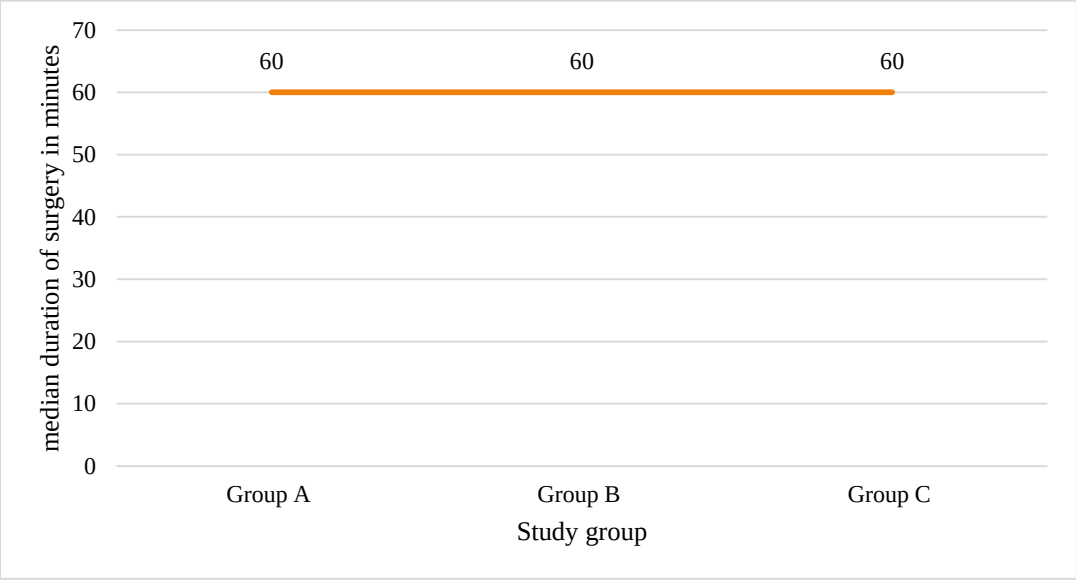


Table 3: Comparison of median Heart rate (HR) follow-ups after surgery between study groups (N=90)

HOURS(HRS)	Study group Median (IQR)			P value
	Group A (N=30) HR	Group B (N=30) HR	Group C (N=30) HR	
@ 2HRS	80 (73,82)	82 (76,84)	82 (76,84)	**0.112**
@ 4HRS	80 (73.50,84)	82 (79,84)	82 (76,84)	**0.261**
@ 6HRS	80 (72,82)	82 (77,84)	82 (77.50,84)	**0.067**
@ 8HRS	80 (74,84)	82 (77.50,84)	82 (77.5,84.50)	**0.120**
@ 12HRS	80 (74,82.50)	82 (79.50,84)	82 (77.75,84)	**0.256**
@ 24HRS	80 (72,82)	82 (77,84)	82 (77.50,84)	**0.67**

There was no statically significant difference in Median Heart rate (HR) at 2hrs (P value 0.112), 4hrs (P value 0.261), 6hrs (P value 0.067), 8hrs (P value 0.120), 12hrs (P value 0.256) and 24hrs (P value 0.67) between study groups. (Table 3 & Figure 3)

Figure 3: Line graph comparison of median Heart rate (HR) follow-ups after surgery between study groups(N=90)

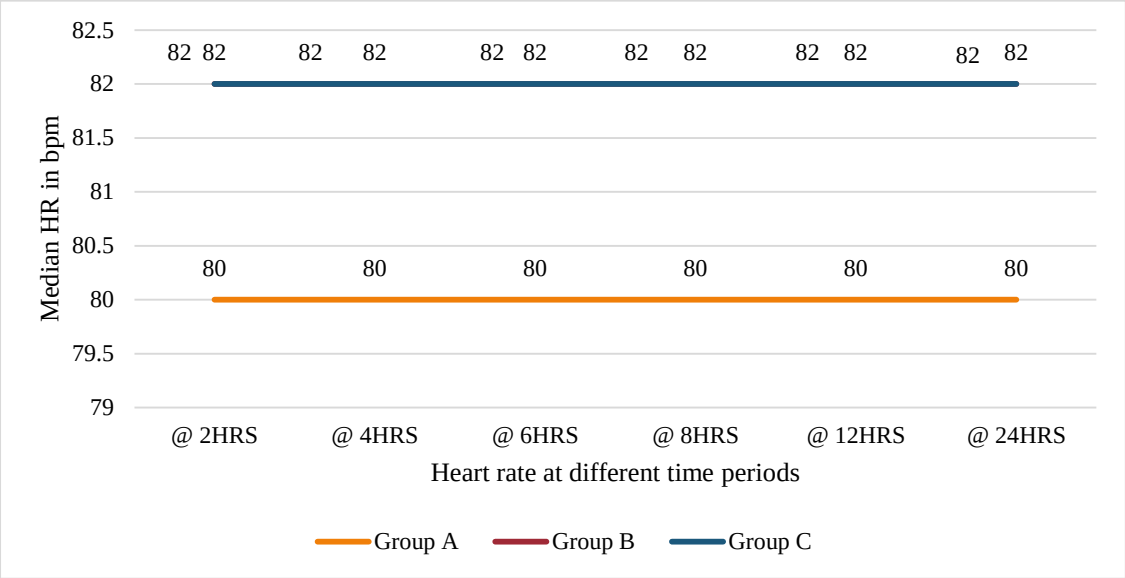


Table 4: Comparison of median Systolic blood pressure (SBP) follow-ups after surgery between study groups (N=90)

HOURS(HRS)	Study group Median (IQR)			P value
	Group A (N=30) SBP	Group B (N=30) SBP	Group C (N=30) SBP	
@ 2HRS	110 (110,120)	120 (112,120)	112 (110,120.5)	**0.159**
@ 4HRS	112 (110,120)	118 (110,120)	116 (110,120)	**0.690**
@ 6HRS	112 (110,120)	116 (110,120)	113 (110,120)	**0.747**
@ 8HRS	112 (110,122)	118 (112,120)	119 (110,120)	**0.870**
@ 12HRS	113 (110,120)	117 (112,120)	113 (110,120)	**0.553**
@ 24HRS	113 (110,120)	119 (112,120)	112 (110,120)	**0.66**

There was no statically significant difference in Median Systolic blood pressure (SBP) at 2hrs (P value 0.159), 4hrs (P value 0.690), 6hrs (P value 0.747), 8hrs (P value 0.870), 12hrs (P value 0.553) and 24hrs (P value 0.66) between study groups. (Table 4 & Figure 4)

Figure 4: Line graph comparison of median Systolic blood pressure (SBP) after surgery follow-ups between study groups(N=90)

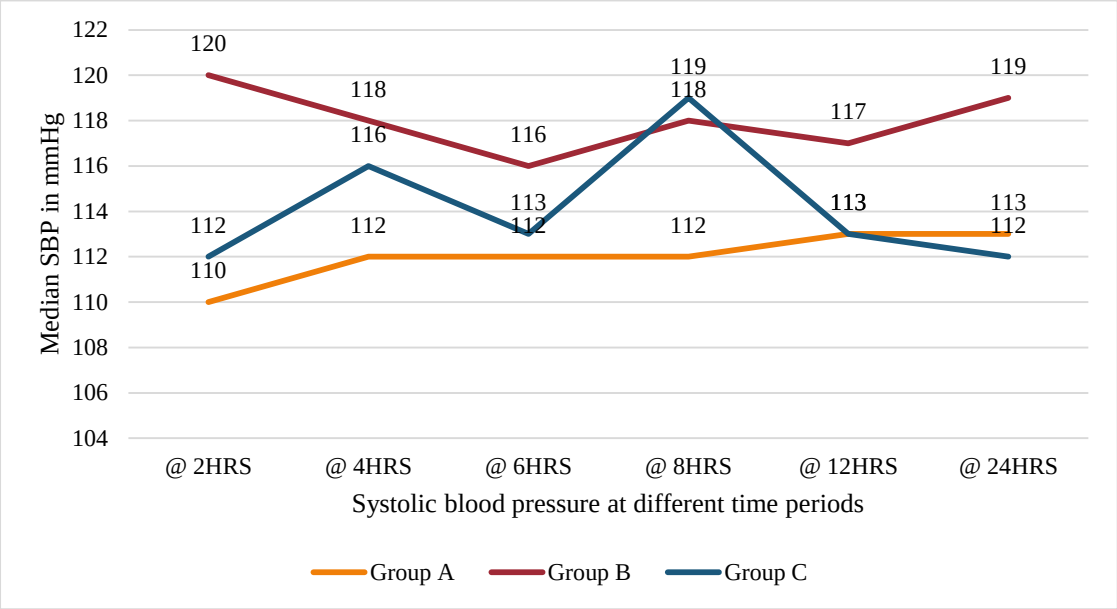


Table 5: Comparison of median Diastolic blood pressure (DBP) follow-ups after surgery between study groups (N=90)

HOURS(HRS)	Study group Median (IQR)			P value
	Group A (N=30) DBP	Group B (N=30) DBP	Group C (N=30) DBP	
@ 2HRS	80 (70,80)	80 (72,80)	80 (71.5,80)	**0.747**
@ 4HRS	80 (70,80)	80 (76,80)	80 (70,80)	**0.519**
@ 6HRS	80 (70,80)	80 (78.5,80)	80 (70,80)	**0.697**
@ 8HRS	80 (70,80)	80 (73.5,80)	80 (70,80)	**0.997**
@ 12HRS	80 (70,80)	80 (73.5,80)	80 (70,80)	**0.681**
@ 24HRS	80 (70,80)	80 (72,80)	80 (70,80)	**0.590**

There was no statically significant difference in Median Diastolic blood pressure (DBP) at 2hrs (P value 0.747), 4hrs (P value 0.519), 6hrs (P value 0.697), 8hrs (P value 0.997), 12hrs (P value 0.681) and 24hrs (P value 0.590) between study groups. (Table 5 & Figure 5)

Figure 5: Line graph comparison of median Diastolic blood pressure (DBP) follow-ups after surgery between study groups(N=90)

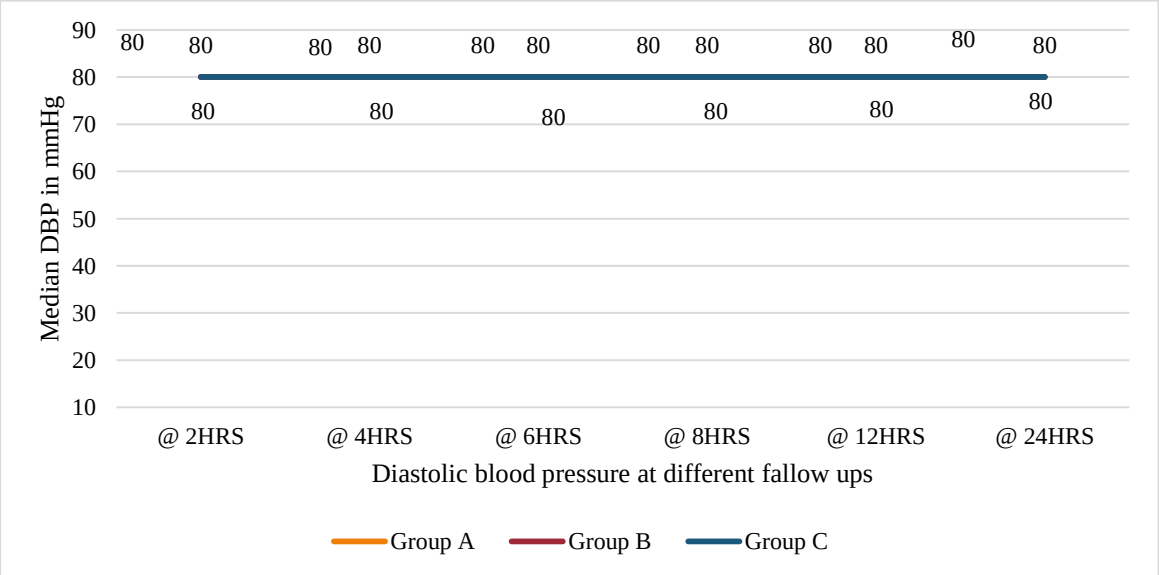


Table 6: Comparison of median Respiratory rate (RR) follow-ups after surgery between study groups (N=90)

HOURS(HRS)	Study group Median (IQR)			P value
	Group A (N=30) RR	Group B (N=30) RR	Group C (N=30) RR	
@ 2HRS	16 (16,18)	16.5 (16,18)	17 (16,18)	**0.544**
@ 6HRS	16.5 (16,18)	17.5 (16,18)	17 (16,18)	**0.370**
@ 12HRS	16 (16.75,18)	17 (16,18)	17 (16,18)	**0.212**
@ 24HRS	17 (16,18)	17.5 (16,18)	16 (16,18)	**0.535**

There was no statically significant difference in Median Respiratory rate (RT) at 2hrs (P value 0.544), 6hrs (P value 0.370), 12hrs (P value 0.212) and 24hrs (P value 0.535) between study groups. (Table 6 & Figure 6)

Figure 6: Line graph comparison of median RR follow-ups after surgery between study groups(N=90)

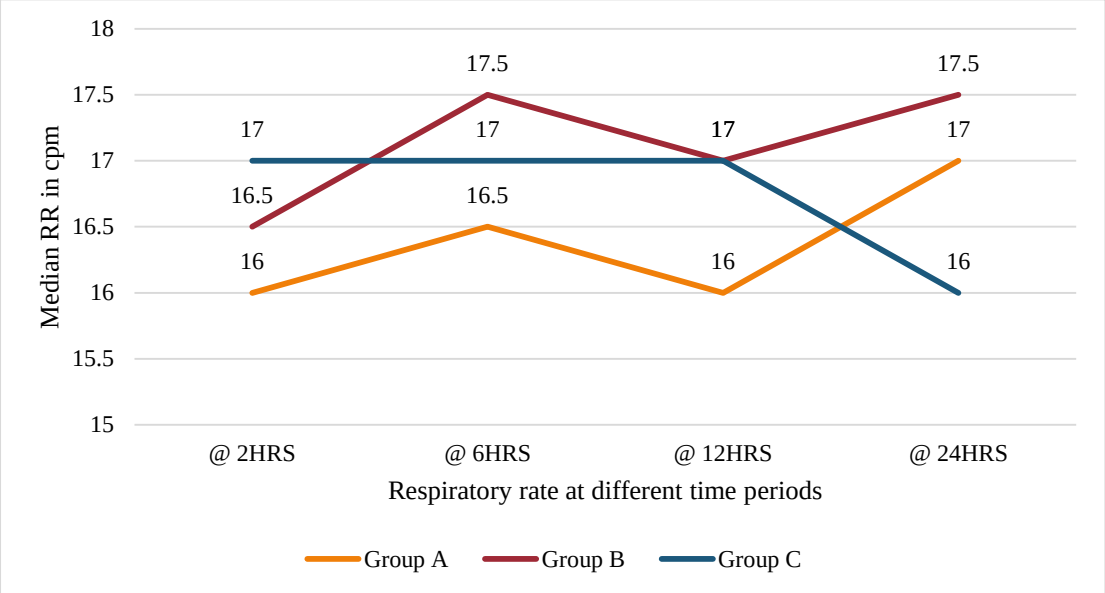


Table 7(a): Comparison of VAS Score at different follow ups across study group (N=90)

HOURS(HRS)	Study group Median (IQR)			P value
	Group A (N=30) VAS score	Group B (N=30) VAS score	Group C (N=30) VAS score	
@ 2HRS	2 (2,2)	2.5 (2,3)	1 (1,2)	**<0.001**
@ 4HRS	3 (2.75,4)	3 (2,4)	2 (1,2)	**<0.001**
@ 6HRS	3(3,4)	3(3,4)	2 (1,2)	**<0.001**
@ 8HRS	2 (2,3)	3 (2.75,4)	2 (1,2)	**<0.001**
@ 12HRS	3 (3,3)	3 (2.75,3)	2 (1,2)	**<0.001**
@ 24HRS	2 (2,2)	3 (2,2)	2 (1.5,2)	**<0.001**

There was statically significant difference in Median Vas Score at different time follow ups with P value < 0.05. (Table 7(a) & Figure 7(a))

Figure 7(a): Line graph comparison of median VAS Score follow-ups between study groups(N=90)

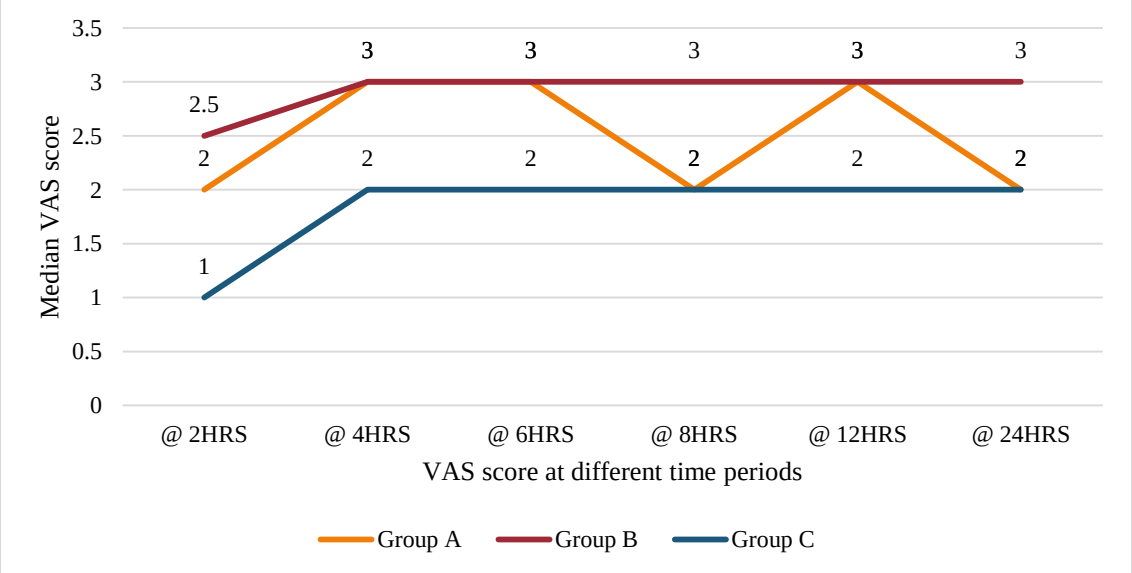


Table 7(b): Multiple Comparison of VAS Score at different follow ups across study group (N=90)

Parameter	Study group (Median IQR)		
	A vs B	**B vs C**	**A vs C**
VAS score at 2Hrs **P value**	0.001	<0.001	<0.001
VAS score at 4Hrs **P value**	0.906	<0.001	<0.001
VAS score at 6Hrs **P value**	0.214	<0.001	<0.001
VAS score at 8Hrs **P value**	0.002	<0.001	<0.001
VAS score at 12Hrs **P value**	0.950	<0.001	<0.001
VAS score at 24Hrs **P value**	<0.001	<0.001	<0.001

There was statistically significant difference in median VAS score for a pair of

1)Group A and Group B at 2hrs,8hrs and 24hrs with P value < 0.05.

2)Group B and Group C at 2hrs,4hrs,6hrs,8hrs,12hrs,24hrs with P value < 0.05.

3)Group A and Group C at 2hrs,4hrs,6hrs,8hrs,12hrs,24hrs with P value < 0.05.

Table 8: Comparison of adverse effects between study group (N=90)

Adverse Effects	Study Group		
	Group A (N=30)	Group B (N=30)	Group C (N=30)
@2 hrs			
Nausea	3 (10%)	0 (0%)	0 (0%)
Vomiting	0 (0%)	0 (0%)	0 (0%)
Epigastric discomfort	0 (0%)	0 (0%)	0 (0%)
No	27 (90%)	30 (100%)	30 (100%)
@4 hrs			
Nausea	1 (3.33%)	1 (3.33%)	0 (0%)
Vomiting	1 (3.33%)	0 (0%)	0 (0%)
Epigastric discomfort	1 (3.33%)	0 (0%)	0 (0%)
No	27 (90%)	29 (96.67%)	30 (100%)
@6 hrs			
Nausea	2 (6.67%)	1 (3.33%)	1 (3.33%)
Vomiting	1 (3.33%)	2 (6.67%)	0 (0%)
Epigastric Discomfort	1 (3.33%)	0 (0%)	0 (0%)
No	26 (86.67%)	27 (90%)	29 (96.67%)
@ 8 hrs			
Nausea	3 (10%)	0 (0%)	1 (3.33%)
Vomiting	0 (0%)	0 (0%)	0 (0%)
Epigastric discomfort	0 (0%)	0 (0%)	0 (0%)
No	27 (90%)	30 (100%)	29 (96.67%)
@12 hrs			
Nausea	0 (0%)	0 (0%)	0 (0%)
Vomiting	0 (0%)	0 (0%)	0 (0%)
Epigastric Discomfort	1 (3.33%)	0 (0%)	0 (0%)
No	29 (96.67%)	30 (100%)	30 (100%)
@24 hrs			
Nausea	0 (0%)	0 (0%)	0 (0%)
Vomiting	0 (0%)	0 (0%)	0 (0%)
Epigastric Discomfort	0 (0%)	0 (0%)	0 (0%)
No	30 (100%)	30 (100%)	30 (100%)

*No statistical test was applied- due to 0 subjects in the cells

Figure 8: Staked bar chart of comparison of Adverse Effect at 2hrs across study group (N=90)

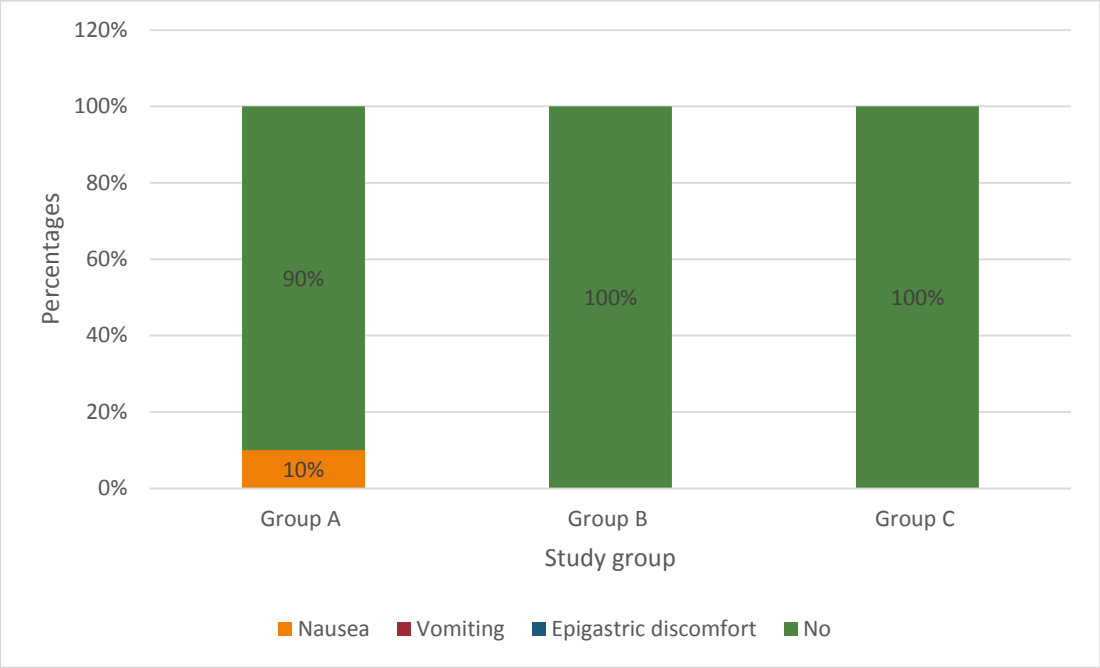


Figure 9: Staked bar chart of comparison of Adverse Effect at 4hrs across study group (N=90)

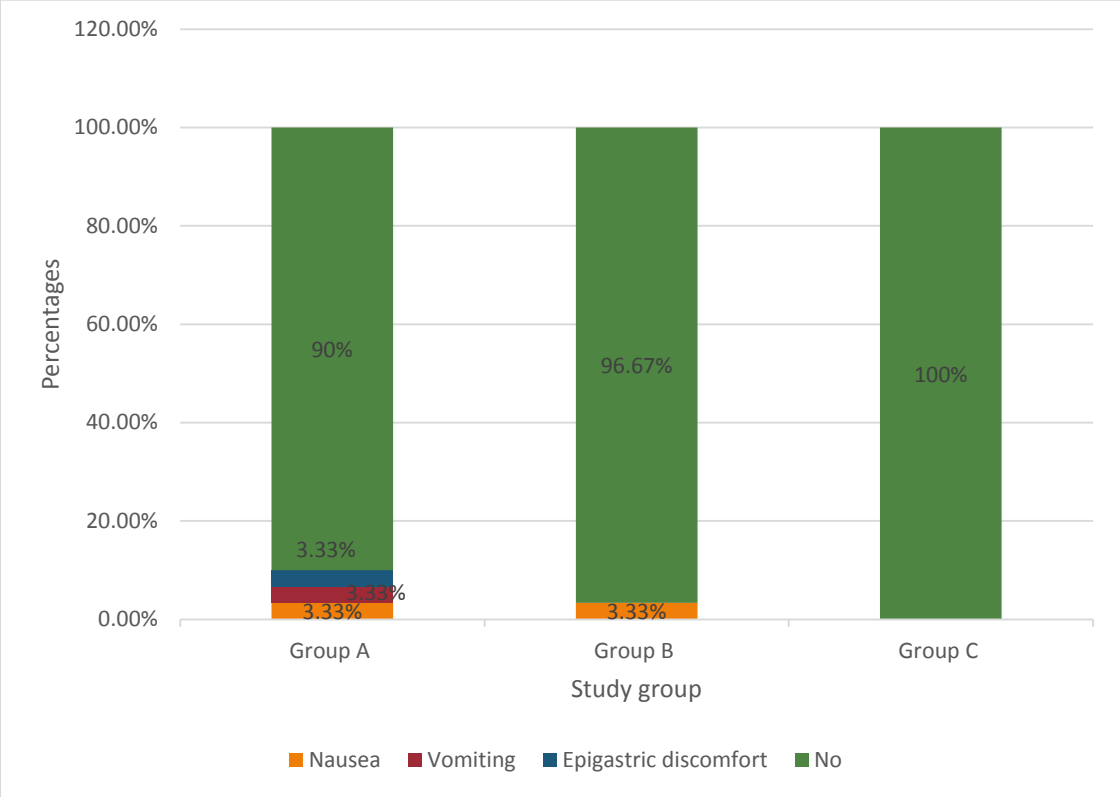


Figure 10: Staked bar chart of comparison of Adverse Effect at 6hrs across study group (N=90)

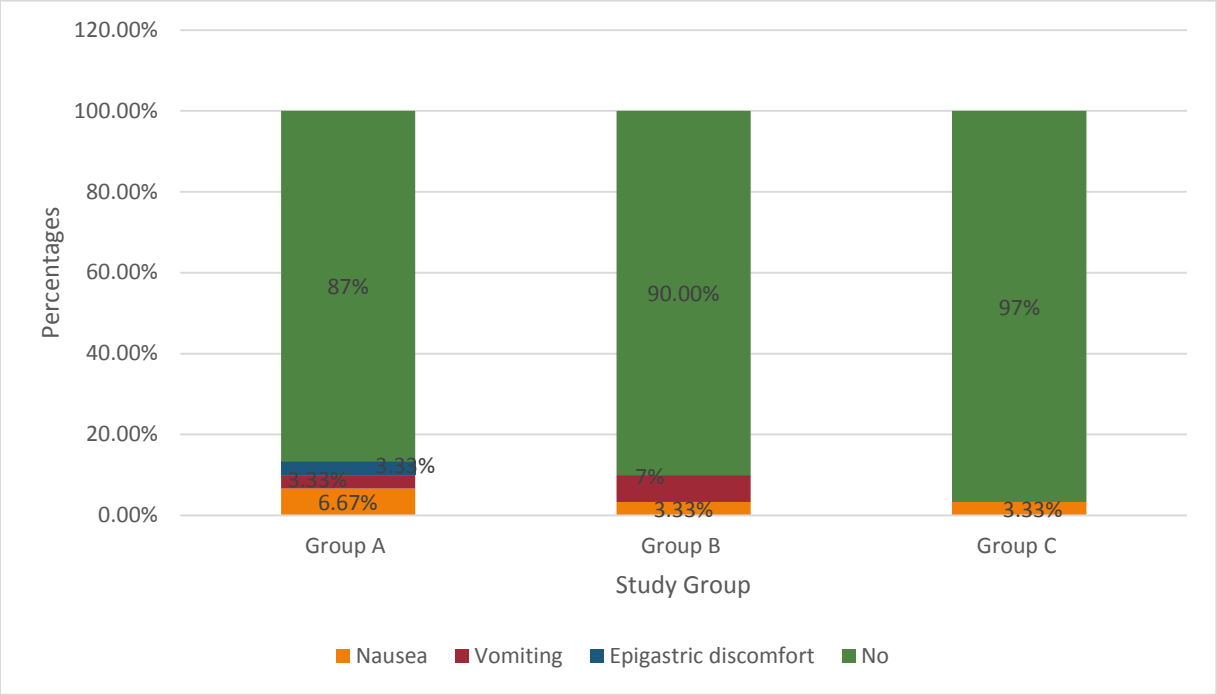


Figure 11: Staked bar chart of comparison of Adverse Effect at 8hrs across study group (N=90)

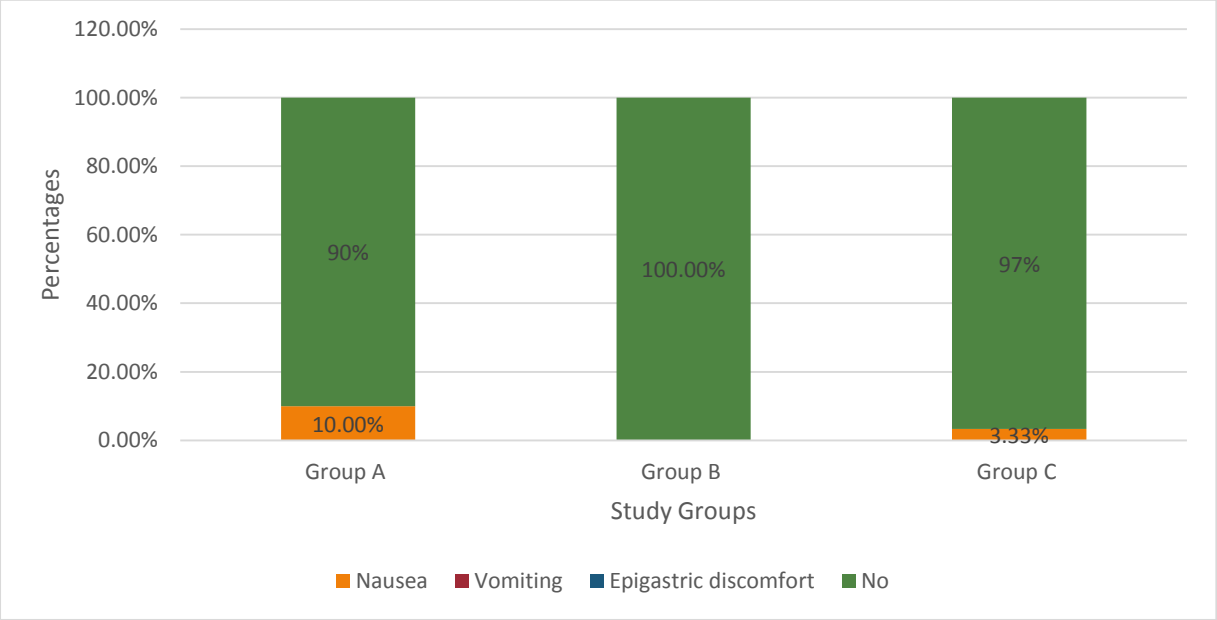


Figure 12: Staked bar chart of comparison of Adverse Effect at 12hrs across study group (N=90)

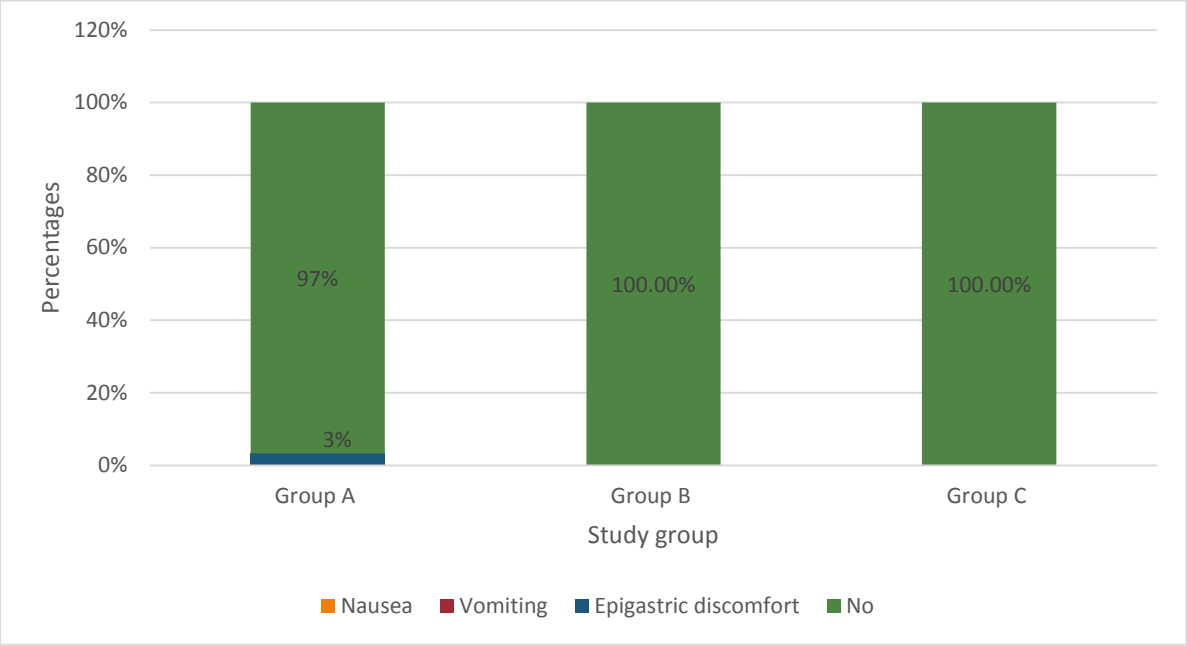


Figure 13: Staked bar chart of comparison of Adverse Effect at 24hrs across study group (N=90)

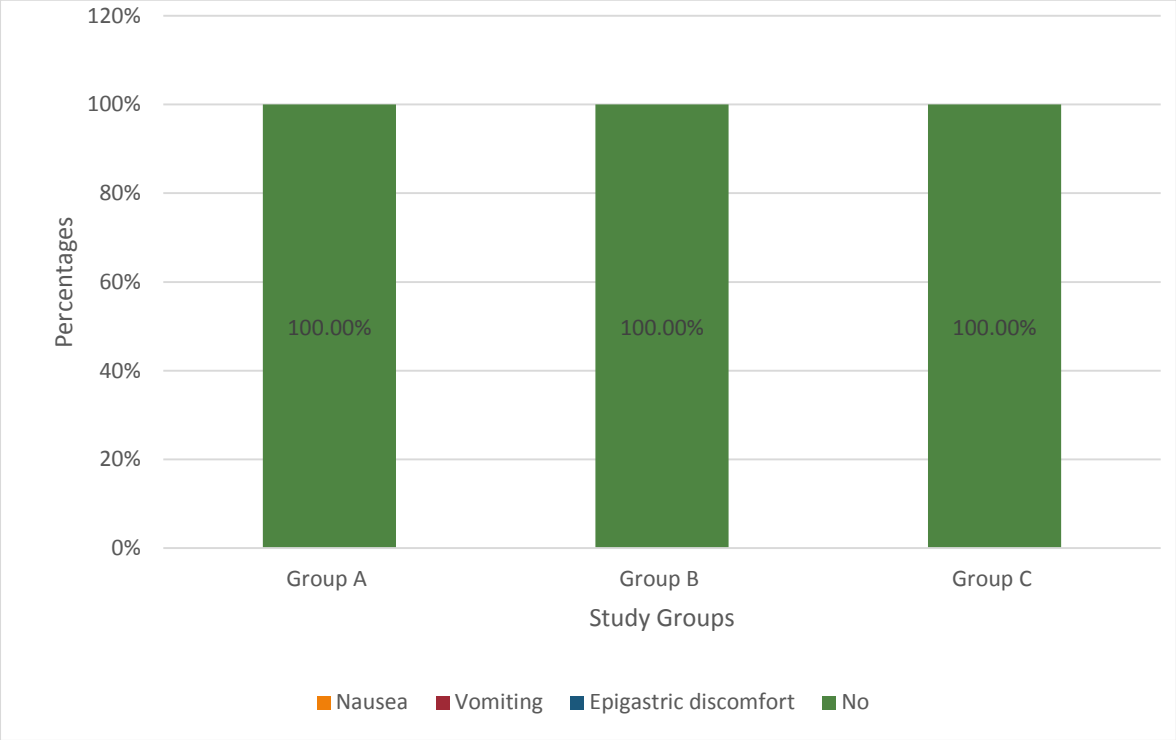
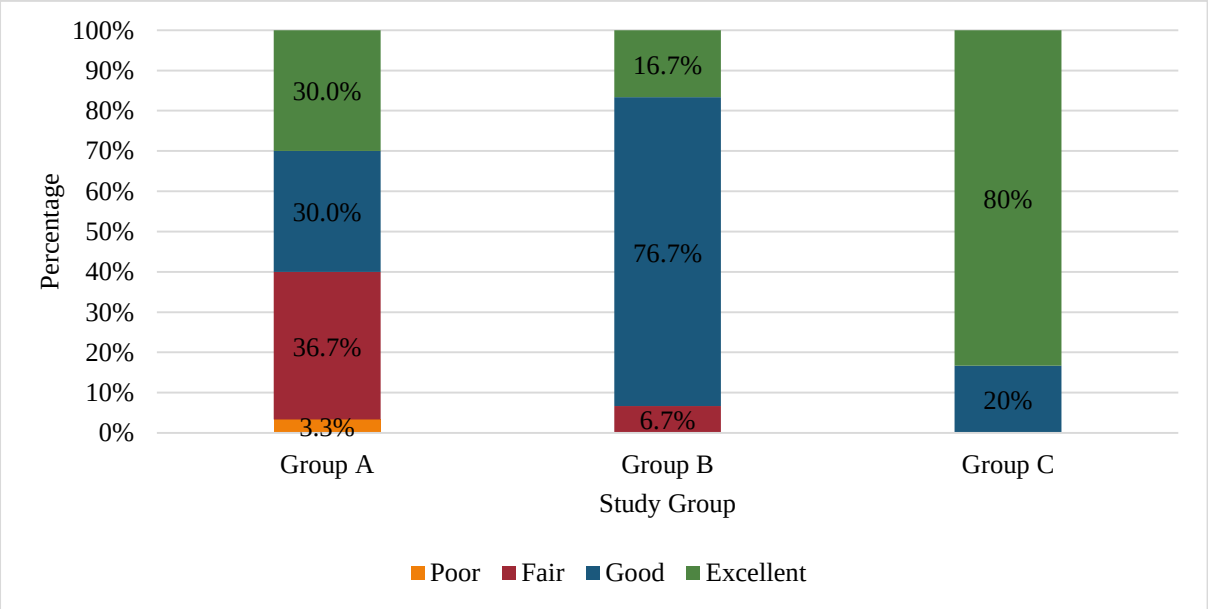


Table 9: Comparison of patient satisfaction score across study group (N=90)

Patient Satisfaction Score	Study Group		
	Group A (N=30)	Group B (N=30)	Group C (N=30)
Poor	1 (3.33%)	0 (0%)	0 (0%)
Fair	11 (36.67%)	2 (6.67%)	0 (0%)
Good	9 (30%)	23 (76.67%)	6 (20%)
Excellent	9 (30%)	5 (16.67%)	24 (80%)

*No statistical test was applied- due to 0 subjects in the cells

Figure 14: Staked bar chart of comparison of Patient Satisfaction Score across study group (N=90)



DISCUSSION

DISCUSSION

In India, prevalence of caesarean section is on rise as per District level household survey 3 (DLHS) caesarean section rate is 28.1% in private sector and 12% in public sector health facilities. As per recently published WHO report "At population level, Caesarean section rates higher than 10% are not associated with reductions in maternal and newborn mortality rates".

Since pain has both sensory and emotional components, adequate relief of pain is essential for the patient well-being.[46-48]

Opioids and NSAIDs are the mainstay for the treatment of moderate to severe postoperative pain.[49] Since NSAIDs are devoid of opioid related adverse effects, we compared acetaminophen and diclofenac suppository in post-operative pain management following caesarean section.

Out of 90 patients recruited, divided into three groups with 30 patients in each group.In present study, the patients were in the mean age group of 24 to 25 years in all three groups which is in concordance to another study conducted in a tertiary care hospital in Gorgon, where the average age of presentation was 26.4years.[44]

Mean duration of surgery in each of three groups was 60 minutes. Patients received either intravenous paracetamol or diclofenac suppository or the combination of both the drugs. VAS score indicated mild pain during first 24 hours of post-operative period which was comparable between the groups.

There was statistically significant difference in median VAS score for a pair of

1)Group A and Group B at 2hrs,8hrs and 24hrs with P value < 0.05.

2)Group B and Group C at 2hrs,4hrs,6hrs,8hrs,12hrs,24hrs with P value < 0.05.

3)Group A and Group C at 2hrs,4hrs,6hrs,8hrs,12hrs,24hrs with P value < 0.05.

In the present study, there was reduction of pain indicated by VAS score however this reduction was significant in patients receiving paracetamol and diclofenac suppository combination group.

We have observed that pain relief by individual use of paracetamol infusion and diclofenac suppository was similar. Present study reported that combination group was superior to both individual paracetamol infusion group and diclofenac suppository group in post caesarean analgesia similar to Munishankar *et al* study pain relief is better in patients received combination of diclofenac and paracetamol after caesarean section when compared with patients received paracetamol alone.[25]

The study findings showed that among all the three studied groups, those who received the combination of acetaminophen and diclofenac resulted in longer analgesia and better pain control compared with the other two study groups.Similarly Romsing *et al* study showed that the combination of acetaminophen and an NSAID has better analgesia than acetaminophen alone and the effect of NSAIDs combination is not better than a single type of NSAID.[18] Ong et al., also showed that using a combination of acetaminophen with an NSAID analgesic compared to the separate use of each drug is more effective.[19]

Results of other similar studies also demonstrated the effectiveness of acetaminophen-diclofenac combination for reducing postoperative pain in patients after surgery compared to

sole administration of acetaminophen[20-22] which is in accordance to our results.In Munishankar study patients receiving the combination of paracetamol and diclofenac required less morphine for pain control compared to the group that was administered paracetamol or diclofenac alone.[25]

Results of Sidik et al., done on 80 patients undergoing scheduled caesarean section in 4 groups, placebo, rectal diclofenac, intravenous paracetamol and paracetamol–diclofenac combination, showed less pain severity score and need for narcotics in patients receiving diclofenac while acetaminophen was less effective than the combination of diclofenac-acetaminophen[16] .

In present study the adverse effects such as nausea and epigastric discomfort was higher with diclofenac suppository group 10% followed by Paracetamol group (6.6% side effects) and minimal with combination group(3.3%) . Similarly to our study in OtutoajaUzoma *et al* study , it was observed that in patients undergoing major abdominal surgeries, 10% of patients receiving diclofenac suppository for postoperative pain management experienced adverse effects such as nausea,vomiting and epigastric discomfort .[28] In contrast to Khobragade SM *et al* study conducted in maharastra diclofenac suppository provides effective postoperative analgesia when compared with Inj. Diclofenac I.M. and Inj. tramadol I.V. in patients undergoing infraumbilical gynaecological surgeries with stable vitals and no side effects.[81]

Few studies have shown that intravenous paracetamol activates the endogenous opioids pathway and thus has less adverse effects on the gastrointestinal tract, inhibition of platelet function and reaches to an effective concentration in a shorter time. [24] Paracetamol is

well-tolerated compared to other NSAIDs.[25] Due to its minimal side effects, NSAIDs are suitable for the treatment of moderate pain.[26]

Diclofenac is one of the most potent cyclooxygenase enzyme inhibitors and by inhibiting the synthesis of prostaglandins it reduces inflammation and promotes peripheral analgesic effect .[27-29]It seems that the combination of these two together will cause better analgesic effects than using them separately and will have longer and more effective analgesia.[16]

In our study patients receiving combination of paracetamol and diclofenac suppository had marginally better pain control when compared to other two individual drugs . The findings of our study imply that early pain relief in postoperative period was better with combination group, but the efficacy of both drugs individually was similar. In individuals with history or risk of gastritis or peptic ulcer, paracetamol can be an alternative to diclofenac.

Both paracetamol and diclofenac drugs are safe to provide analgesia in postoperative period without any major significant side effects similar to Shah et al study the duration and quality of analgesia in paracetamol and diclofenac groups were similar in postoperative period. i.v paracetamol provides effective non sedating pain relief in postoperative period. i.v paracetamol and/or IV diclofenac can be a part of multimodal analgesia.[82]

In contrast to our Toes MJ et al study has shown that, diclofenac was equally effective when compared to combination of diclofenac and paracetamol in terms of rescue analgesic requirement which indicates the combination had no added advantage.[54]

We recorded the patient satisfaction score at the end of 24 hours . The pain satisfaction score was better with combination group at 24 hours, but the patient satisfaction score was similar in individual paracetamol group and diclofenac group. This was in contrast to a study conducted by Sharma et al where 60% of patients who received acetaminophen expressed their patient satisfaction score as excellent following lower limb surgeries when compared to diclofenac.[37]

CONCLUSION

CONCLUSION

Paracetamol infusion is as effective as diclofenac suppository in reducing post-operative pain following caesarean section. Diclofenac suppository and i.v paracetamol combination provides more effective postoperative analgesia compared with individual usage of i.v paracetamol or Diclofenac suppository in patients following caesarean section.The combined use of paracetmol and diclofenac suppository has less side effects compared with individual use of either i.v paracetamol or diclofenac suppository

SUMMARY

SUMMARY

This is a hospital based prospective and comparative study conducted from Oct 2018 to June 2020 at Department of Obstetrics and gynecology on the patients admitted in R.L. Jalappa Hospital & Research Centre attached to Sri Devaraj Urs Higher Education and Research, Tamaka, Kolar. The aim of present study is to compare analgesic efficacy and safety of individual use of i.v paracetamol and Diclofenac suppository and in combination. A total of 90 women underwent aesarean section have been recruited for the study and were randomly allocated using lottery method into three groups, each group comprises of 30 participants.

The major findings of the study are VAS score indicated mild pain during first 24 hours of post-operative period which was comparable between the groups. In the present study, there was reduction of pain indicated by VAS score however this reduction was significant in patients receiving paracetamol and diclofenac suppository combination group. Present study reported that combination group was superior to both individual paracetamol infusion group and diclofenac suppository group in post caesarean analgesia. We have observed that pain relief by individual use of either paracetamol infusion or diclofenac suppository was similar.

The satisfaction score was categorized as excellent by 80% patients in combination group. In Diclofenac group 30% and in Paracetamol group 16.6% categorised as excellent patient satisfaction score.

In present study the adverse effects such as nausea and epigastric discomfort was higher with diclofenac suppository group 10% followed by Paracetamol group (6.6% side effects) and minimal with combination group(3.3%)

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ANNEXURES

ANNEXURE-I

STUDY PROFORMA

Case Proforma

OP No: Date:

Serial No:

1. Name –

2. Age –

3. Occupation –

4. Educational status –

5. Address with phone no. –

6. Date of admission –

7. Time of start of surgery

8. Time of end of surgery

9. Duration of surgery

10. Family history –

11. Personal history – Smoking/ alcohol/ drug abuse/ diabetes mellitus/ hypertension/ bronchial asthma

12. General physical examination

Per abdomen –

Cardiovascular system –

Respiratory system –

Central nervous system -

Post – operative parameters

	Heart rate	Blood pressure	Respiratory rate
Baseline			
2hours			
4hours			
8hours			
12hours			
24hours			

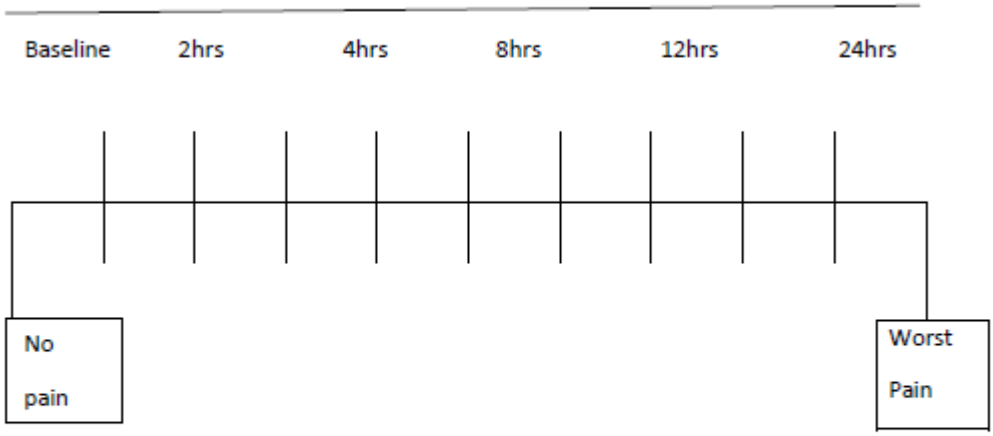
Side effects

	Baseline	2hrs	4hrs	8hrs	12hrs	24hrs
Nausea						
Vomiting						
Epigastric discomfort						
Any other						

ROUTINE LABORATORY ANALYSIS REPORT

Complete hemogram:		
Bleeding time:	Clotting time:	
Random blood sugar		
HIV-	HbsAG	VDRL-

VISUAL ANALOG SCALE FOR ASSESMENT OF PAIN [0 – 10]



Directions – Ask the patients to indicate on the line where the pain is in relation to the two extremes. Measure from left side to mark.

VAS Score

2hrs	4hrs	8hrs	12hrs	24hrs

Painless = 0

Mild = 1 – 4

Moderate = 5 – 8

Severe = 9 – 10

Patient's assessment of the analgesic used (patient satisfaction score)

How would you rate the medication you have received for pain after the operation?

1 = Poor 2 = Fair 3 = Good 4 = Excellent

ANNEXURE-II

Patient consent form

COMPARATIVE TRIAL OF DICLOFENAC SUPPOSITORY , PARACETAMOL INFUSION AND THEIR COMBINATION FOR POST CAESAREAN DELIVERY ANALGESIA

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I have understood that I have the right to refuse consent or withdraw it at any time during the study and this will not affect my treatment in any way. I consent voluntarily to participate in this study

Name of Participant_____

Signature/ thumb print of Participant _____

Date _____

Statement by the researcher/person taking consent:

I have accurately read out the information sheet to the potential participant and to the best of my ability made sure that the participant understands that the following will be done:

I confirm that the participant was given an opportunity to ask questions about the study and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Post operative pain scores of mother who underwent caesarean delivery will be assessed by visual analogue scale.

Name of Researcher/person taking the consent: Dr.Sadana Reddy

Signature of Researcher /person taking the consent_____

Date _____

Name and Address of Principal Investigator:

Dr.SADANA REDDY

R.L Jalappa Hospital

Tamaka, Kolar.

ರೋಗಿಯ ತಿಳುವಳಿಕೆ ಸಮ್ಮತಿ ನಮೂನೆ

ಸಂಶೋಧಕರ ಹೆಸರು: Dr.Sadana reddy.M

ಸಂಸ್ಥೆಯ ಹೆಸರು: ಆರ್.ಎಲ್ ಜಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ - ಶ್ರೀ ದೇವರಾಜ್ ಅರಸ್ ಮೆಡಿಕಲ್ ಕಾಲೇಜ್ಗೆಜೋಡಿಸಲಾಗಿದೆ.

ಪಾಲ್ಗೊಳ್ಳುವವರ ಹೆಸರು: ಕ್ರಮ ಸಂಖ್ಯೆ :

ನಾನು ಶ್ರೀ /ಶ್ರೀಮತಿ

ನನಗೆ ಆರ್. ಎಲ್. ಜಲಪ್ಪ ಆಸ್ಪತ್ರೆಯಲ್ಲಿ ನಡೆಸಲಾಗುತ್ತಿರುವ **COMPARATIVE TRIAL OF DICLOFENAC SUPPOSITORY, PARACETAMOL INFUSION AND THEIR COMBINATION FOR POST CAESAREAN DELIVERY ANALGESIA**

ದಲ್ಲಿ ನನ್ನನ್ನು ಸೇರಿಸಲ್ಪಡಲಾಗುವುದು ಎಂದು ನನಗೆ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ.

ಈ ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನನ್ನನ್ನು ಆಹ್ವಾನಿಸಲಾಗಿದೆ. ಈ ದಾಖಲೆಯಲ್ಲಿರುವ ಮಾಹಿತಿಯು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಬೇಕೇ ಅಥವಾ ಬೇಡವೇ ಎಂಬುದನ್ನು ನಿರ್ಧರಿಸಲು ನನಗೆ ನೆರವಾಗುವುದು.

ಪ್ರಧಾನಸಂಶೋಧಕನೊಂದಿಗೆ ನಾನು ಈ ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನನ್ನ ಅನುಮಾನಗಳನ್ನು ಸ್ಪಷ್ಟಪಡಿಸಿಕೂಂಡಿದ್ದೆನೆ.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಂತೆ ನನಗೆ ಸೂಚಿಸಲಾಗಿದೆ ಏಕೆಂದರೆ ನಾನು ಅರ್ಹತಾ ಮಾನದಂಡಗಳನ್ನು ಪೂರೈಸುತ್ತೇನೆ.

ನನ್ನ ರಕ್ತದ ಮಾದರಿಯನ್ನು ಗೊತ್ತುಪಡಿಸಿದ ಪರೀಕ್ಷೆಗಳಿಗೆ ನಿರ್ವಹಿಸಲು ನಾನು ಡಾ.Sadana reddy ಅವರನ್ನು ವಿನಂತಿಸುತ್ತೇನೆ ಮತ್ತು ಅಧಿಕಾರವನ್ನು ನೀಡುತ್ತೇನೆ.ಕೆಳಗಿನ ನನ್ನ ಸಹಿಯು ಅರ್ಹ ಆರೋಗ್ಯ ವೃತ್ತಿಪರರಿಂದ ಪರೀಕ್ಷೆಯ ಅನುಕೂಲಗಳು,ಅಪಾಯಗಳು ಮತ್ತು ಮಿತಿಗಳನ್ನು ನನ್ನ ತೃಪ್ತಿಗೆ ವಿವರಿಸಲಾಗಿದೆ ಎಂದು ನನ್ನ ಅಂಗೀಕಾರವನ್ನು ರೂಪಿಸುತ್ತದೆ.

ಭಾಗವಹಿಸುವಿಕೆ ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿರುತ್ತದೆ ಮತ್ತು ಮಾದರಿ

ಸಂಗ್ರಹಣೆಗೆ ಯಾವುದೇ ಹಣಕಾಸಿನ ಪಾವತಿಯಿಲ್ಲ. ಎಲ್ಲಾ ಪರೀಕ್ಷಾ ಫಲಿತಾಂಶಗಳನ್ನು

ವೈದ್ಯಕೀಯ ಗೌಪ್ಯತೆಯೊಂದಿಗೆ ಪರಿಗಣಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಕಾನೂನಿನ ಅಗತ್ಯವಿದ್ದರೆ ಹೊರತುಪಡಿಸಿ

ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸುವುದಿಲ್ಲ.

ನನ್ನ ಗೌಪ್ಯತೆ ನಿರ್ವಹಿಸಲ್ಪಡುವವರೆಗೆ ವೈದ್ಯಕೀಯ ಪರೀಕ್ಷೆ, ಪರೀಕ್ಷೆಯ

ಮೌಲ್ಯಮಾಪನ ಅಥವಾ ಶಿಕ್ಷಣಕ್ಕಾಗಿ ನನ್ನ ಮಾದರಿಯನ್ನು ಬಳಸಲು ನನ್ನ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡುತ್ತೇನೆ.

ನಾನು ಈ ಅಧ್ಯಯನದಿಂದ ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಹಿಂತೆಗೆದುಕೊಳ್ಳಲು ಮುಕ್ತವಾಗಿರುತ್ತೇನೆ ಮತ್ತು ಇದು ನನ್ನ

ಮುಂದಿನ ಕಾಳಜಿಯನ್ನು ಬದಲಿಸುವುದಿಲ್ಲ ಎಂದು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ರೋಗಿಯ ಮಾಹಿತಿ ಪತ್ರವನ್ನು ನಾನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಪ್ರತಿಯನ್ನು ಸ್ವೀಕರಿಸಿದ್ದೇನೆ.ಈ ದಾಖಲೆಯಲ್ಲಿ

ಒದಗಿಸಿದ ಮಾಹಿತಿಯನ್ನು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ ಮತ್ತು ಪರೀಕ್ಷೆ,

ಪ್ರಕ್ರಿಯೆ, ಸಂಬಂಧಿಸಿದ ಅಪಾಯ ಮತ್ತು ಪರ್ಯಾಯಗಳ ಬಗ್ಗೆ ನಾನು ಹೊಂದಿರುವ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು

ನನಗೆ ಅವಕಾಶ ಕಲ್ಪಿಸಲಾಗಿದೆ .

ಹೆಸರು ಮತ್ತು ಸಹಿ / ಹೆಬ್ಬೆರಳುಗುರುತು ದಿನಾಂಕ:

ಪೋಷಕರ / ಪಾಲಕರ ಹೆಸರು /ಹೆಬ್ಬೆರಳು ಗುರುತು ದಿನಾಂಕ:

ಒಪ್ಪಿಗೆ ತೆಗೆದುಕೊಳ್ಳುವ ವ್ಯಕ್ತಿಯ ಸಹಿ ದಿನಾಂಕ

PATIENT INFORMATION SHEET

Study title: COMPARATIVE TRIAL OF DICLOFENAC SUPPOSITORY, PARACETAMOL INFUSION AND THEIR COMBINATION FOR POST CAESAREAN DELIVERY ANALGESIA

Study location: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

Patients who visit to OBG department of R L Jalappa hospital attached to Sri Devaraj Urs medical college are recruited in the study after obtaining patient information consent.

Details-

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or from a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact

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Key words for master chart

Sl No-Serial Number; hr-hour;mins-minutes;

VAS Score

Painless = 0

Mild = 1 – 4

Moderate = 5 – 8

Severe = 9 – 10

Patient satisfaction score

1 = Poor 2 = Fair 3 = Good 4 = Excellent

Adverse effects: 1-Nausea, 2-Vomiting, 3-Epigastric discomfort, 4-Headache

sl no	OP NO DICLOFENAC SUPPOSITORY	AGE IN YRS	wt Kg	DIAGNOSIS	Duration of Surgery in mins	Heart rate						blood pressure (systolic/diastolic)						RESPIRATORY RATE				VAS SCORE						patient Satisfaction score				ADVERSE EFFECTS					
						2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	2HRS	6HRS	12HRS	24HRS	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	POOR	FAIR	GOOD	EXCELL	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS
1	725614	22	63	PRIMI 39WEEKS	40	64	68	68	66	70	64	130/80	130/86	130/84	130/84	130/86	130/80	18	16	18	16	1	2	3	0	2	0		2			1	3				
2	727624	20	62	PRIMI 39WEEKS	45	66	68	64	66	66	66	120/80	124/80	122/80	124/82	120/80	120/80	18	18	18	16	2	4	4	0	3	0			3		1					
3	736659	23	64	PRIMI 39WEEKS	60	90	90	88	86	88	84	140/90	126/84	130/80	128/80	126/80	130/84	16	18	18	16	2	4	4	2	3	2			3			1				
4	671606	24	65	G3PILID1 37WEEKS	50	80	84	88	84	88	86	110/80	110/70	110/76	112/74	110/76	110/80	18	16	17	18	2	4	4	2	3	2			3							
5	736864	20	61	PRIMI 37WEEKS	60	82	84	82	90	82	84	118/70	118/72	118/70	120/76	118/76	118/70	19	19	20	20	2	4	4	2	3	2			3					1		
6	737158	29	60	G2P1L1 40WEEKS	60	68	64	66	68	64	68	110/80	110/80	112/84	110/80	110/80	112/86	16	16	17	17	1	3	3	2	3	2				4						
7	737440	37	64	G3P2L139WEEKS	60	82	80	76	78	76	78	120/74	120/70	120/70	120/70	120/70	120/72	19	18	18	18	2	4	4	2	3	2			3		1					
8	737536	22	62	PRIMI41WEEKS	50	70	70	64	68	68	68	100/80	100/80	106/80	100/80	108/80	108/80	16	17	17	18	2	4	3	2	3	2			3							
9	737119	22	64	PRIMI40WEEKS	60	80	82	80	82	82	80	110/70	110/72	110/80	110/74	110/70	110/72	17	17	17	17	1	3	3	2	3	2				4						
10	725985	25	65	PRIMI39WEEKS	60	72	70	72	74	72	74	120/80	120/80	120/80	122/84	120/84	120/80	16	16	17	16	2	4	4	2	3	2			3							
11	728221	23	60	G2P1L138WEEKS	60	76	76	74	78	76	78	110/80	110/82	110/80	110/82	110/80	112/80	20	18	20	18	1	3	3	2	3	2				4						
12	732164	29	62	G2P1L139WEEKS	60	82	80	82	80	88	82	120/70	122/70	120/70	122/74	120/70	120/70	16	16	17	18	2	4	4	5	3	2		2						3		
13	738398	31	61.5	G4P3L341WEEKS	60	82	80	82	80	80	82	110/70	110/70	110/70	112/70	110/70	110/70	16	18	18	17	2	4	4	3	2	3			3							
14	730175	22	64	G2P1L137WEEKS	55	80	82	82	80	82	80	112/80	114/80	112/80	114/80	116/80	114/80	16	14	16	14	2	3	3	2	3	2				4						
15	738740	19	64	PRIMI34WEEKS	60	72	74	72	74	76	74	112/80	110/80	110/80	110/80	110/80	110/80	16	16	17	18	2	3	3	2	3	2				4						
16	737937	24	63	PRIMI40WEEKS	50	68	66	68	64	68	64	120/80	120/80	122/80	122/80	120/80	122/80	18	18	18	17	2	3	3	2	3	2				4						
17	738049	25	64.5	G2A138WEEKS	45	84	84	82	84	82	84	110/80	120/80	110/80	120/80	120/80	122/80	18	16	18	18	2	3	3	2	3	2				4						
18	740414	25	65	G2P1L138WEEKS	60	80	80	82	80	82	82	110/70	110/70	110/74	110/70	110/72	110/70	14	14	16	16	1	3	3	2	3	2				4						
19	733655	28	60	G3P2L2TERM	60	80	78	76	78	76	78	110/60	110/60	110/60	112/62	110/64	110/64	16	16	16	16	2	3	3	2	3	2										
20	754527	20	61	PRIMI40WEEKS	50	84	86	84	86	84	86	130/88	130/92	130/80	140/90	140/90	130/80	16	18	16	18	1	4	3	2	3	2				4						
21	753688	26	64.3	PRIMI40WEEKS	55	82	83	82	84	80	82	120/80	120/82	122/84	120/80	122/80	120/80	17	16	18	18	3	3	2	4	3	2		2					1			
22	754328	20	62	PRIMI40WEEKS	40	80	82	80	80	81	82	110/70	112/70	112/70	112/70	110/70	112/70	15	16	16	17	3	2	4	2	4	4		2								
23	754064	27	64	PRIMI39WEEKS	50	80	82	80	82	80	82	112/80	112/80	114/80	114/80	114/80	118/80	16	16	17	18	2	3	5	2	2	4		2					3			
24	754019	28	62	G4P3A1L2TERM	60	82	80	80	81	80	82	120/80	120/80	120/80	122/82	120/80	120/80	18	18	16	18	2	3	4	5	2	4		2								
25	755839	25	60	G2P1L137WEEKS	55	74	76	72	74	76	74	110/70	110/70	112/70	110/70	110/70	112/70	17	16	18	17	2	2	3	2	2	2		2								
26	774949	25	61	G4P2L1A135WEEKS	60	82	84	82	84	86	82	110/70	100/70	110/72	100/70	110/70	100/70	16	18	18	18	2	3	3	4	3	2		2						1		
27	774203	28	62.5	G2P1L138WEEKS	58	82	84	82	82	84	82	110/80	110/80	112/80	110/80	112/80	110/80	16	18	18	16	3	2	2	3	3	2		2				2				
28	827561	25	64.3	PRIMI38WEEKS	60	74	72	74	72	74	72	110/80	110/80	110/80	112/80	110/80	112/80	16	16	17	16	2	1	5	4	5	2		2					1			
29	832020	26	65	G7P1L1A539WEEKS	60	74	76	72	74	74	74	110/80	120/80	110/80	110/80	120/80	118/80	18	17	18	17	3	2	3	3	4	3		2								
30	829388	28	64.4	G3P2L2 40WEEKS	52	84	84	82	86	86	84	110/70	112/72	110/70	112/70	110/70	112/70	18	18	16	18	3	2	2	3	2	2			3							

sl no	OP NO PARACETMOL INFUSION	AGE IN YRS	WEIGHT IN KG	DIAGNOSIS	Duration of Surgery in mins	Heart rate						blood pressure (systolic/diastolic)						RESPIRATORY RATE				VAS SCORE						patient Satisfaction score				ADVERSE EFFECTS					
						2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	2HRS	6HRS	12HRS	24HRS	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	POOR	FAIR	GOOD	EXCELLENT	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS
1	711344	24	64	G3P1L1A1 39WEEKS	50	84	86	90	86	84	82	126/80	118/80	118/80	120/80	116/80	120/80	14	18	18	16	0	2	2	0	1	0			3			1					
2	697134	19	62	PRIMI 36WEEKS	40	84	86	82	82	84	82	112/70	114/76	110/70	110/70	110/70	112/70	18	16	18	18	0	3	3	0	2	0			3								
3	736159	24	63	PRIMI 38WEEKS	50	82	84	86	82	84	82	120/80	118/80	112/80	120/80	120/80	120/80	16	18	16	18	2	4	3	3	3	3			3								
4	731941	27	61	PRIMI 39WEEKS	50	80	80	80	80	82	80	110/80	110/80	110/80	112/80	112/80	110/80	16	18	16	18	2	3	3	3	2	2				4							
5	734940	24	63	G3A2 40WEEKS	60	74	74	72	74	72	74	110/72	110/72	110/70	112/70	110/72	112/70	17	16	16	17	2	4	3	3	3	3			3				1				
6	736662	23	65	G2A1 39WEEKS	55	82	84	98	80	82	80	120/80	120/80	130/86	120/80	124/80	120/80	18	22	18	16	3	4	5	6	2	3		2					2				
7	731677	21	60	G2A1 40WEEKS	55	74	72	72	74	72	74	112/70	112/70	110/70	112/70	112/70	110/70	18	16	17	16	2	4	3	3	3	2			3								
8	666003	21	61	PRIMI38WEEKS	50	62	62	64	62	64	62	122/80	120/80	120/80	118/80	120/80	120/80	16	14	16	16	3	4	4	3	3	2			3								
9	736627	19	62.5	PRIMI32WEEKS	60	82	84	82	84	82	80	110/70	112/70	110/70	110/72	112/72	112/72	16	18	16	18	3	4	4	3	3	2			3								
10	754359	23	64	G2P1L137WEEKS	55	76	72	74	76	72	74	118/80	118/80	118/82	118/80	118/80	120/80	18	18	17	15	2	2	3	2	3	2			3								
11	739952	26	62	PRIMI37WEEKS	55	82	84	86	82	84	86	110/72	110/76	110/80	110/74	110/74	110/72	16	17	16	17	2	3	3	3	2	2			3								
12	777196	22	61	G3P1L1A1 39WEEKS	60	82	82	80	84	82	80	112/80	110/82	110/80	112/80	110/80	112/80	17	18	16	18	3	4	4	3	3	4			3								
13	777169	19	63	PRIMI 36WEEKS	60	82	84	82	84	82	84	120/80	112/80	114/80	120/80	120/80	118/80	17	18	18	16	2	4	4	3	3	5			3								
14	777387	28	65	PRIMI40WEEKS	55	84	82	86	84	84	84	110/80	112/80	110/80	112/80	110/80	110/80	16	18	18	16	3	3	3	4	3	2			3								
15	778808	24	64.6	G3P1L1A138WEEKS	50	90	88	84	86	82	84	120/70	110/70	100/74	110/70	110/70	110/72	16	16	18	18	3	4	4	3	3	4			3								
16	784525	31	61	G3P2L0 41WEEKS	60	74	76	74	76	74	76	120/80	120/80	118/80	120/80	118/80	120/80	16	18	18	16	3	2	5	4	3	4			3								
17	777196	27	62.5	G3P1L1A139WEEKS	55	74	72	74	76	74	72	122/80	120/80	118/80	120/80	120/80	120/80	18	16	18	18	2	3	3	4	4	3			3								
18	785641	26	64	PRIMI39WEEKS	50	74	76	74	76	78	80	116/80	118/80	118/80	116/80	112/80	120/80	18	16	16	16	2	3	4	4	3	3			3								
19	791349	30	60	G2P1L136WEEKS	60	82	80	82	80	82	80	110/60	110/60	110/60	110/60	112/60	112/60	18	16	18	18	1	2	2	1	2	3				4							
20	792656	25	61	G2P1L138WEEKS	58	84	82	82	84	84	82	120/80	118/80	120/80	120/80	118/80	120/80	18	16	17	19	1	1	2	3	2	1				4							
21	797285	19	60	G2P1L137WEEKS	50	84	82	86	84	82	84	120/80	110/80	112/80	120/80	120/80	122/80	16	18	17	18	3	2	2	4	4	3		2									
22	801302	28	62	G2P1L140WEEKS	60	84	82	84	84	82	84	120/80	120/80	122/80	118/80	120/80	112/80	18	17	16	18	3	4	3	4	3	4		2									
23	801392	19	63.5	G2A138WEEKS	60	84	82	80	82	84	82	122/80	120/80	120/80	118/80	120/80	120/80	16	18	17	18	2	4	3	2	4	3			3								
24	801325	25	64	G2P1L139WEEKS	55	84	82	84	82	84	82	132/82	134/84	130/80	132/80	130/80	130/84	16	17	18	18	1	2	3	2	3	3			3								
25	801228	36	62	G2P1L130WEEKS	60	82	84	82	84	86	84	130/80	130/84	132/84	136/88	140/90	140/90	17	18	16	16	2	4	2	2	3	4			3								
26	802762	32	62	G2A140WEEKS	55	86	84	84	82	84	86	120/80	122/80	124/80	120/80	126/80	120/80	16	18	16	17	2	3	3	4	3	3			3								
27	822594	22	61	G2P1L136WEEKS	40	80	80	78	80	82	80	120/80	120/80	124/80	120/80	118/80	114/80	17	18	16	18	2	2	3	3	2	3			3								
28	830725	29	60	G2P1L138WEEKS	60	80	82	80	78	80	78	120/80	110/80	112/80	114/80	114/80	110/80	18	17	17	18	2	3	3	4	4	3			3								
29	833217	25	60.5	G2A139WEEKS	55	76	84	82	82	84	82	112/70	110/70	112/72	110/72	116/72	114/72	14	16	16	17	2	2	1	2	1	2			3								
30	834156	32	62	G1P1L139WEEKS	50	80	82	80	80	82	80	120/80	120/80	120/80	122/80	116/80	120/80	16	17	16	16	1	2	2	2	3	2				4							

sl no	OP NO COMBINATION GROUP	AGE IN YRS	WEIGHT IN KG	DIAGNOSIS	Duration of Surgery in mins	Heart rate						blood pressure (systolic/ diastolic)						RESPIRATORY RATE				VAS SCORE						patient Satisfaction score				ADVERSE EFFECTS					
						2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	2HRS	6HRS	12HRS	24HRS	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS	POOR	FAIR	GOOD	EXCEL LENT	2HRS	4HRS	6HRS	8HRS	12HRS	24HRS
1	722584	23	62	G3P1L1AI37WEEKS	50	76	72	74	76	74	74	112/72	110/70	112/72	110/70	112/72	110/72	14	16	17	16	2	3	2	2	3	2			3									
2	736815	26	63	G2P1L138WEEKS	60	82	84	82	84	82	84	110/80	110/76	110/80	112/80	112/80	112/70	18	17	16	18	1	2	2	3	2	1				4						
3	737546	26	61	PRIMI 38WEEKS	55	82	84	80	84	82	82	118/80	120/80	118/80	120/80	118/80	120/80	18	16	16	18	2	3	2	2	2	2			3							
4	737572	35	65	G6P2L2A340WEEKS	60	2	80	80	82	80	82	112/70	110/70	112/70	110/70	110/70	112/70	16	18	16	18	2	3	2	2	3	2			3							
5	722247	28	63	G2P1L139WEEKS	60	72	76	84	74	72	74	110/80	112/80	120/84	112/80	112/80	110/80	18	18	18	16	2	2	2	2	3	2			3				1			
6	734680	28	65	G2P1L1WITH37WEEKS	60	82	80	82	82	82	84	112/70	112/70	110/70	110/70	110/70	110/70	20	18	20	19	2	2	2	2	3	1				4						
7	738944	25	64	G2P1L139WEEKS	60	68	68	66	68	68	68	110/70	110/70	110/70	100/70	110/70	110/70	16	16	16	16	1	2	2	2	3	1				4						
8	739259	26	62	G2P1L137WEEKS	60	82	82	84	90	82	84	112/80	110/80	110/80	120/84	110/80	110/80	17	18	16	18	2	3	2	2	3	2			3					1		
9	674805	23	62.5	G3P1L1A138WEEKS	60	80	82	80	82	80	82	102/60	102/60	104/60	104/64	104/62	100/60	16	17	18	16	1	2	2	2	3	1				4						
10	740428	33	61	G2P1L138WEEKS	60	68	68	66	68	66	68	110/70	112/70	110/70	112/70	110/70	110/72	16	18	18	16	2	2	2	2	3	1				4						
11	734535	26	62	G2P1L137WEEKS	55	82	80	82	80	82	80	110/72	112/70	110/70	112/70	110/70	112/70	18	16	18	16	2	2	2	2	2	2			3							
12	753688	23	63.4	G2P1L140WEEKS	60	80	80	82	84	80	82	110/70	110/70	112/70	118/70	112/70	110/70	17	16	17	16	2	1	2	1	2	1				4						
13	753639	25	60.6	G3A240WEEKS	40	83	84	82	84	84	86	120/80	120/80	112/80	120/80	120/80	122/80	18	16	18	16	1	2	2	1	2	1				4						
14	754247	25	62.3	PRIMI40WEEKS	50	76	78	76	78	78	76	120/80	120/80	120/80	120/80	122/80	120/80	18	16	18	18	2	1	1	2	1	1				4						
15	726101	20	64.5	PRIMI39WEEKS	50	82	82	80	81	82	82	110/82	112/80	110/80	110/80	112/80	110/80	16	14	18	16	2	4	3	4	3	3			3							
16	790169	20	62	PRIMI40WEEKS	60	82	86	82	82	84	82	122/80	124/80	120/80	120/80	122/80	126/80	16	18	16	16	1	1	2	2	1	1				4						
17	785888	25	61	G2P1L138WEEKS	60	88	86	88	86	86	86	110/80	112/80	114/84	116/82	114/80	110/80	18	16	16	18	1	1	1	0	2	2				4						
18	777242	38	60	G3P2L236WEEKS	45	86	88	86	88	86	88	122/80	120/80	120/80	120/80	122/80	120/80	16	17	17	16	1	2	2	1	1	2				4						
19	791279	19	65	PRIMI38WEEKS	55	88	86	88	86	88	86	112/80	120/80	122/80	122/80	124/80	120/80	18	17	17	18	1	2	2	1	2	2				4						
20	789781	21	63	G4P1L1A236WEEKS	50	84	86	84	86	84	86	112/80	110/80	112/80	112/80	110/80	112/80	18	16	18	16	1	2	2	2	1	3				4						
21	770082	30	64	G4P1L1A238WEEKS	60	84	86	84	86	84	86	120/80	122/80	120/80	120/80	120/80	122/80	17	18	18	18	1	2	2	1	2	3				4						
22	795154	22	62	PRIMI39WEEKS	55	76	76	76	78	76	76	122/80	120/80	122/80	120/80	122/80	120/80	16	17	16	18	2	3	2	2	1	2				4						
23	792701	22	61	PRIMI39WEEKS	55	86	84	86	84	84	86	130/80	130/80	128/80	130/80	120/80	130/90	18	16	18	18	0	1	0	2	1	2				4						
24	795531	22	63	PRIMI39WEEKS	55	86	82	82	84	82	84	120/80	120/70	120/84	120/82	120/60	120/70	18	18	17	18	2	2	1	1	1	2				4						
25	795464	29	65	G4P3L337WEEKS	55	84	82	84	84	84	86	110/70	120/70	110/70	110/70	110/60	110/70	18	17	16	18	1	2	1	1	2	2				4						
26	750018	39	64.7	PRIMI37WEEKS	60	94	92	90	92	94	96	150/100	140/90	150/100	160/100	150/100	150/100	18	16	18	16	2	1	1	2	1	1				4						
27	828156	21	62.4	PRIMI39WEEKS	60	84	82	82	82	84	86	118/80	120/80	118/80	120/80	118/80	118/80	17	18	16	16	1	2	1	1	2	1			3							
28	776411	23	63	G3P1L1A139WEEKS	54	74	74	72	74	72	74	122/80	120/80	118/80	122/80	118/80	120/80	16	17	16	16	0	1	2	2	1	1				4						
29	711248	23	61	PRIMI38WEEKS	45	76	76	78	76	78	77	110/80	112/80	112/80	110/80	110/80	112/80	16	16	17	16	0	1	1	1	1	2				4						
30	817221	37	65	PRIMI35WEEKS	60	74	76	76	76	77	76	120/82	120/80	122/80	120/80	120/80	120/80	16	17	16	16	0	1	1	1	1	2				4						