"THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH FOR POSTOPERATIVE ANALGESIA IN COMPARISON WITH INTRAMUSCULAR DICLOFENAC IN PATIENTS UNDERGOING LOWER ABDOMINAL AND PERINEAL SURGERIES UNDER SUB-ARACHNOID BLOCK- A RANDOMISED COMPARATIVE STUDY"

BY

DR. VARSHA CHUNDURI

Dissertation submitted to the

B.L.D.E. (DEEMED TO BE) UNIVERSITY

SHRI B.M. PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE

VIJAYAPURA, KARNATAKA

In partial fulfilment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

Under the guidance of

DR. VIDYA PATIL

PROFESSOR AND HOD

DEPARTMENT OF ANAESTHESIOLOGY

B.L.D.E. (DEEMED TO BE) UNIVERSITY

SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA, KARNATAKA 2020

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Date: 28-09-2020

Place: Vijayapura

Ch. Varsha

DR. VARSHA CHUNDURI

B.L.D.E. (DEEMED TO BE UNIVERSITY)

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA.

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled "THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH FOR POSTOPERATIVE ANALGESIA IN COMPARISON WITH INTRAMUSCULAR DICLOFENAC IN PATIENTS UNDERGOING LOWER ABDOMINAL AND PERINEAL SURGERIES UNDER SUB-ARACHNOID BLOCK'' is a bonafide research work done by DR. VARSHA CHUNDURI in partial fulfilment of the requirement for the degree of M.D. in ANAESTHESIOLOGY.

Dr. Vidya Patil

Date: 28-09-2020

Place: VIJAYAPURA

DR. VIDYA PATIL
PROFESSOR AND HOD
DEPARTMENT OF ANAESTHESIOLOGY
B.L.D.E. (DEEMED TO BE) UNIVERSITY
SHRI B.M.PATIL MEDICAL COLLEGE
HOSPITAL AND RESEARCH CENTRE,
VIJAYAPURA, KARNATAKA

B.L.D.E. (DEEMED TO BE UNIVERSITY)

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA.

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This is to certify that the dissertation entitled "THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH FOR POSTOPERATIVE ANALGESIA IN COMPARISON WITH INTRAMUSCULAR DICLOFENAC IN PATIENTS UNDERGOING LOWER ABDOMINAL AND PERINEAL SURGERIES UNDER SUB-ARACHNOID BLOCK'' is a bonafide research work done by DR.VARSHA CHUNDURI under the guidance of DR.VIDYA PATIL Professor and HOD, Department of Anaesthesiology, Shri B.M.Patil Medical College, Hospital and Research Centre, Vijayapura.

Dr. Vidya Patil

Date: 28-09-2020

Place: Vijayapura

DR. VIDYA PATIL
PROFESSOR AND HOD
DEPARTMENT OF ANAESTHESIOLOGY
B.L.D.E. (DEEMED TO BE) UNIVERSITY
SHRI B.M.PATIL MEDICAL COLLEGE
HOSPITAL AND RESEARCH CENTRE,
VIJAYAPURA, KARNATAKA

B.L.D.E. (DEEMED TO BE UNIVERSITY)

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL &

RESEARCH CENTRE, VIJAYAPURA.

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Date: 28-09-2020

Place: Vijayapura

DR. ARAVIND V PATIL

PRINCIPAL

B. L. D. E. (DEEMED TO BE UNIVERSITY)

SHRI B. M. PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE,

VIJAYAPURA, KARNATAKA

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DR. VARSHA CHUNDURI
B.L.D.E. (DEEMED TO BE UNIVERSITY) VIJAYAPURA, KARNATAKA

ACKNOWLEDGEMENT

On completion of this contribution of scientific document it gives me immense pleasure to acknowledge the guidance provided by my distinguished mentors. With all due privilege and respect I would like to express my gratitude and indebtedness to my guide and HOD Dr.Vidya Patil, Department of Anaesthesiology, BLDE(DU) Shri.B.M.Patil Medical College, hospital and research centre for her constant inspiration, extensive encouragement and support which she rendered in pursuit of my postgraduate studies and in the preparation of this dissertation. I am forever grateful to Dr. D. G. Talikoti, Dr.Vijaykumar T. K, Dr. R. R. Kusugal, Dr. VijayKatti, Dr.Renuka, Dr.Nirmala, Dr.ShivanandLK, Dr.BasavarajPatil, Dr.Pratibha, Dr. Ramesh, Dr.Santosh K, Dr. Mala, Dr.Anusha and Dr.Santosh A for their valuable help and guidance during my study. I am extremely thankful to Principal Dr Aravind Patil, BLDE Deemed to be University's Shri B.M.Patil Medical College, Hospital and Research Centre, for permitting me to utilize the resources in completion of my work.

I am deeply indebted to my Parents, Chunduri Srinivas rao, Chunduri Aparna and my sister Chunduri Neha whose constant encouragement and inspiration led me to the right path. I am thankful to my colleagues Dr.Yashoda, Dr.Sandhya, Dr.Nithya, Dr.Sumedha, Dr.Arpitha, Dr.Puneeth, Dr.Nafasat, Dr.Nikhila and my friends Dr.Harshith, Dr.Samhitha, Dr Onkar, Dr Sindhu, Dr Nandini and my juniors for their support, suggestions and care. I express my gratitude to Statistician, Library Staff and OT Staff for their co-operation in my study. Last but not the least, I convey my heartfelt gratitude to all the patients, without whose co-operation, this study would be incomplete.

Ch. Varsha

DR VARSHA CHUNDURI.

ABBREVIATIONS

IM- Intra muscular

ASA- American society of anaesthesiologists

VAS- Visual analogue score

COX- Cyclooxygenase

Hr- Hour

Mg- milligrams

Mins- minutes

NSAIDS- Nonsteroidal anti- inflammatory drugs

Vs- Versus

Inj- Injection

M/s-meters/second

TENS-Transcutaneous electrical nerve stimulation

5-HT- 5-Hydroxy Tryptamine

IASP-International association for the study of pain

GABA- Gamma amino butyric acid

TDS- Transdermal delivery system

α – Alpha

β – Beta

GI - Gastrointestinal

Etc- et cetera

ABSTRACT

Background: Post operative pain is a unique and common form of acute pain. Although ample evidence indicates that an efficacious post operative pain treatment reduces patient morbidity and improves patient outcome, recent studies demonstrate that about 50-70% of patients experience moderate to severe pain after surgery indicating that post operative pain remains poorly treated. The management of post operative pain is an essential and integral part of care given to the patient that assumes an important role in transition from the recovery unit to the home environment[1].

Aim: This clinical study was undertaken to evaluate the efficacy of Transdermal diclofenac patch vs IM diclofenac in patients undergoing lower abdominal and perineal surgeries under Subarachnoid block during postoperative period.

Objectives:

- To compare the efficacy of transdermal Diclofenac patch (100mg) with intramuscular Diclofenac (75mg) for postoperative analgesia in patients undergoing lower abdominal and perineal surgeries under subarachnoid block.
- The time lapse between the operation and the first demand of analgesia by the patient (the need for rescue analgesia).
- To know the side effects of transdermal and intramuscular diclofenac.

Methodology: This randomised comparative study was conducted on 90 ASA I and II patients of either gender aged between 18 – 60 years posted for elective lower abdominal or perineal surgeries**.** The patients were randomly divided by computer generated tables into two groups of 45 patients in each group. Group A was applied with a Transdermal Diclofenac patch (100mg) at the beginning of surgery after subarachnoid block.

In groupB 75mg of Diclofenac sodium was given intramuscularly half an hour before the end of surgery. Data was analysed using Chi-square test and Mann Whitney U test

Results: The mean difference in the time of administration of rescue analgesia in group A is 8hr 37 mins ± 1 hr 4.2 mins and group B is 6hrs 19 mins ±58.6 mins (P value is < 0.0001)that is highly significant. Side effects in group A were very minimal i.e. only 3 patients complained of local erythematous rash whereas in group B almost 13 patients developed nausea, vomiting, gastritis and pain at the injection site.

Conclusion: Based on the results obtained we conclude that the application of transdermal diclofenac patch (100mg) significantly prolongs the time at which patient requires rescue analgesia compared to IM diclofenac (75mg).

Thus transdermal diclofenac patch is effective, non- invasive and safer way of treating postoperative pain.

KEYWORDS: TRANSDERMAL DICLOFENAC PATCH, IM DICLOFENAC, POSTOPERATIVE ANALGESIA.

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INTRODUCTION

"All sane would agree that the relief of suffering of both human and animals is one of the noblest activity of man and in this field of human endeavour who can rank higher than the anaesthesiologist"-Sir John C Eccles

Post operative pain is a unique and common form of acute pain. Although ample evidence indicates that an efficacious post operative pain treatment reduces patient morbidity and improves patient outcome, recent studies demonstrate that about 50-70% of patients experience moderate to severe pain after surgery indicating that post operative pain remains poorly treated[1].

Effective management of postoperative pain leads to increased patient satisfaction; earlier mobilization and reduced hospital stay.

"Pain signals from damaged tissue are not transmitted to the central nervous system (CNS) through hard-wired pathways. In contrast, nociceptive signals once initiated, will launch a cascade of alterations in the somatosensory system, including an increase in the responsiveness of both peripheral and central neurons. These alterations will increase the response to subsequent stimuli and thus amplify pain"[2].

Peripheral tissue injury, as seen in postoperative patients, provokes two kinds of modification in the responsiveness of the nervous system.

- In peripheral sensitisation, there is a reduction in the threshold of nociceptive afferent peripheral terminals.
- In central sensitisation, an activity-dependent increase in the excitability of spinal neurons occurs. This results in an overall hypersensitivity state in the postoperative period[1].

Prevention of this hypersensitivity state could lead to reduced postoperative pain. This forms the basis of pre-emptive analgesia[1].

Nonsteroidal anti-inflammatory drugs (NSAIDs) exert anti-inflammatory and analgesic effects through the inhibition of prostaglandin synthesis, by blocking the activity of Cyclooxygenase.

Diclofenac is an analgesic-antipyretic-anti-inflammatory drug. It inhibits prostaglandins synthesis by inhibiting Cyclooxygenase enzyme.

Parenteral route (intramuscular) of administration is most commonly employed for pain relief. But it has a lot of short coming and may produce discomfort on injection and undesirable side effects like nausea and vomiting. Other alternative routes includes intravenous, suppository and transdermal route.

The transdermal diclofenac patch is a newly introduced delivery system for postoperative pain management. Transdermal route has advantage of being painless, non irritant and increased bioavailability[3].

Though transdermal route has distinct advantage over parental route, there are very less studies which compared transdermal and parenteral route in patients undergoing surgeries[3]

AIM AND OBJECTIVES

Aim: To compare the efficacy of transdermal diclofenac patch in comparison with intramuscular diclofenac for postoperative analgesia undergoing elective lower abdominal and perineal surgeries under subarachnoid block.

Objectives:

PRIMARY OBJECTIVE:

To compare the efficacy of transdermal Diclofenac patch (100mg) with intramuscular Diclofenac (75mg) for postoperative analgesia in patients undergoing lower abdominal and perineal surgeries under subarachnoid block.

SECONDARY OBJECTIVES:

1. The time lapse between the operation and the first demand of analgesia by the patient (the need for rescue analgesia).

2. To know the side effects of transdermal and intramuscular diclofenac.

REVIEW OF LITERATURE

1. Dinesh Govind rao, RavikumarGV, Akshay in 2016 conducted a study to evaluate transdermal diclofenac patch as pre-emptive analgesic in providing post-operative analgesia in hernioplasty as compared to intramuscular diclofenac injection in 60 healthy subjects of either sex undergoing hernioplasty under spinal anaesthesia. The patients were monitored for pain at 2, 6 and 12 hours post-operatively using Visual Analogue Scale (VAS). This study concluded that preoperative application of single dose of 100 mg transdermal diclofenac patch provides prolonged analgesia compared to single dose of 75 mg intramuscular diclofenac for acute post-operative pain, without any significant side effects[1].

2. Pragati AroraTrivedi, Malini Mehta in 2015 conducted a comparative study to know the analgesic efficacy of a 100mg transdermal diclofenac patch and 75 mg intramuscular diclofenac for post operative pain relief in patients undergoing abdominal hysterectomy and their side effects in 60 patients posted for abdominal hysterectomy of ASA I and II. They were randomly allocated in two groups of 30 each. Pain was assessed postoperatively at 2, 6 and 12-hour intervals using a visual analogue scale (VAS). An injection of Tramadol 2 mg/kg was administered intramuscularly as rescue analgesia. The study ended when the patients asked for rescue analgesia, or when the VAS score was> 5. This study concluded that the intraoperative application of transdermal diclofenac 100 mg is as effective as a single dose of intramuscular diclofenac 75 mg for post operative pain relief after abdominal hysterectomy under spinal anaesthesia, without any significant side effects[26].

3. **US Gupta, UK Bhagat and A M Lakra in 2018** conducted a study to compare the analgesic efficacy of diclofenac sodium via two different routes, IM and transdermal in the management of postoperative pain. 60 patients of ASA grade I-III, scheduled for abdominal hysterectomy under subarachnoid block were randomized into two groups. Transdermal or IM diclofenac were repeated 12 hours later. Postoperative visual analogue scores (VAS), hemodynamic data, requirement of rescue analgesic, patient satisfaction and adverse reaction if any were recorded every 2 hrs over 24 hours period. If VAS score was >4, 2mg/kg Tramadol was given intravenously as rescue analgesia. They concluded that postoperative VAS, hemodynamic data, requirement of rescue analgesia and patients satisfaction were comparable in both the groups ($p>0.05$), IM diclofenac has more side effects and Diclofenac transdermal patch provided postoperative pain relief as effectively as IM diclofenac for abdominal hysterectomy, without any significant side effects[3].

4. **R Krishna, Nataraj MS in 2012** has conducted comparative study to know analgesic efficacy of a transdermal diclofenac patch 100 mg and intramuscular diclofenac sodium 75 mg for postoperative analgesia, and the associated side-effects of the transdermal diclofenac patch. 60 participants in the study were randomly allocated to two groups of 30 each, by a computer-generated randomization table. A transdermal diclofenac patch 100 mg was applied to the participants in the study group at the beginning of the surgery. Pain was assessed postoperatively at 2, 6 and 12-hour intervals using a visual analogue scale (VAS). Inj Tramadol 2 mg/kg was administered intramuscularly as rescue analgesia. The study ended when the patients asked

for rescue analgesia, or when the VAS score was > 5.They observed that the intraoperative application of a single dose of 100 mg transdermal diclofenac patch is as effective as a single dose of intramuscular diclofenac (75 mg) for acute postoperative pain, without any significant side-effects[27].

5. **Soumya Samal, Saubhagya kumar Jena, Basanta kumar behera in 2013** conducted a prospective comparative study in the department of anaesthesiology in a medical college & general hospital on 200 patients of either sex between 18-50 years of age who were scheduled for elective laparoscopic, gynaecological & orthopaedic surgeries. The outcome measures were pain intensity, changes in vital parameters, requirement for rescue analgesia & adverse effects. Concluded that Transdermal diclofenac is more effective in reducing the intensity of postoperative pain following laparoscopic & gynaecological surgeries but the effect is similar to intramuscular diclofenac in orthopaedic surgeries[25].

6. **Franco Alessandri, Davide Lijoi, Emanuela Mistrangelo, Nicoletti a, Crosa M, Ragni N in 2006** conducted a randomized prospective study to compare pain management of standard analgesic and standard analgesic plus diclofenac transdermal patch in patients undergoing laparoscopic gynecologic surgeries. The principal measures of outcome were pain intensity at 6, 12, 24 hours post surgery and analgesic dose requirement. No significant difference was observed between the two groups in mean pain intensity at 6 hrs post surgery. Mean pain intensity at 12, 24 hrs post surgery was significantly lower in the diclofenac group. 21 patients (35%) in the diclofenac group required analgesia in the first 36 hrs after the surgery versus 43 patients (71.7%) in the

control group (p<.001).So, this study concluded that diclofenac transdermal administration is a valid help to standard analgesic treatment in postoperative pain control and could also help in reducing the hospital stay[28].

7. **A Agarwal, S.Dhiraaj,A.Kumar,V.Singhal and U.Singh in 2006** evaluated the efficacy of transdermal diclofenac patch placed over the venipuncture site in decreasing the pain of cannulation .72 patients posted for elective surgery were included in this randomized, prospective, double-blind, placebo-controlled study. Patients were divided into three equal groups. Both the placebo and diclofenac patches were applied 1 hr before cannulation. Pain during cannulation was assessed by VAS .Median pain scores were 3.0 in the diclofenac-hand group, 5.0 in the diclofenac-buttock group and 6.5 in the control group.The numbers required were six and two in the diclofenac–buttock and diclofenac-hand groups, respectively. Hence the application of a diclofenac transdermal patch at the cannulation site was effective in decreasing cannulation pain[29].

8.Hemant Bhaskar, Pranv Kapoor and Ragini in 2010 compared the degree of post operative analgesia , patient compliance, frequency of adverse events with the use of oral diclofenac and transdermal diclofenac patch following multiple premolar extractions in patients undergoing orthodontic treatment .Concluded that the transdermal diclofenac patch is a promising analgesic modality for the management of mild to moderate pain following dental extractions, because of its good analgesic properties along with a lower incidence of systemic adverse effects[30].

9. Dr Rajeev DS, Dr Sanjay Sahadevan in 2018 conducted studies exclusively on transdermal diclofenac patch. Dicofenac patch is a novel approach to a less invasive mode of analgesia. Most of the older versions of analgesia were invasive, which needs the assistance of medical or Para medical staff. In methods like intramuscular or intravenous strict sterile precautions are necessary for proper outcome, sterility of the needle or person who is administering it is needed. Here this method eliminates the need for multiple injections, avoids first pass metabolism, plays definitive role in topical anaesthesia and acute musculoskeletal and neuropathic pain management. Diclofenac patches are available at a dosage of 100mg and 200mg. 50 patients were randomised by computer generated table method. Study group (I) was administered 100 mg transdermal patch and the control Group (II) was not administered anything at all. Quality of analgesia in the two groups was compared by duration of post operative analgesia, VAS score and the mean dose of rescue analgesic needed. Standard deviation was 1 and 0.2 respectively for Group I and II patients. Mean duration of analgesia was 4.5 hrs and 0.7 hrs respectively in group I and II. Mean VAS score and mean dose of the rescue analgesic shows that the transdermal patch is a good analgesic[20].

10. **Grijesh Lakhan Paserkar, Mahavir Singh Griwan, Janardhan Singh in 2017** studied the efficacy and safety of diclofenac patch in comparison with IM diclofenac in patients posted for appendicectomy.60 participants of either sex scheduled for appendicectomy were randomized into two groups of 30. A transdermal diclofenac patch 100 mg was applied to the participants in the study group 3 hours prior to surgery. In the control group, 2 doses of 75 mg diclofenac sodium injections were given intramuscularly, first dose 2 hours after the surgery and second dose repeated after 12 hours. In postoperative ward, assessment of intensity of pain was done by visual analogue scale (VAS) and verbal rating scale (VRS) every six hours for duration of 24 hours. If any patient had VAS score >5 or VRS >2, Inj Tramadol 50mg was given. Results concluded that Diclofenac patch can be considered as an alternative option for pain management in post appendicectomy patients, as it also improves compliance due to its once in 24hrs application. If the dose of diclofenac patch is increased to 200 mg instead of 100 mg it is more efficient to control post-operative pain in appendicectomy patients[31].

11**. Aditi Maruti Abnave, Sunita Sunil Sankalecha** in 2018 compared the analgesic effectiveness and adverse effects of transdermal diclofenac patch and intramuscular diclofenac in patients undergoing laparoscopic cholecystectomy. 60 ASA I and II patients of either sex aged 18-60 years posted for laparoscopic cholecystectomy were selected for this study. Patients were divided equally into 2 groups, A received Transdermal diclofenac patch (100 mg) three hours before surgery and B was given intramuscular diclofenac (75 mg) 45 minutes before surgery. Postoperative pain was

assessed using Visual Analogue Scale (VAS). Side effects were noted over a period of 12 hours. Patients with VAS score greater than 3 received intravenous Tramadol 2mg/ Kg to relieve pain. In each group the VAS scores were higher for 10 hrs post surgery. There was no significant difference neither in the surgical pain nor in the need of rescue analgesia. Erythema was observed in group A patients whereas pain at injection site and rubor was observed in group B who received Inj Diclofenac. **Conclusion:** Diclofenac skin patch and IM injection are unit comparable in terms of effectiveness for pain relief in surgical laparoscopic cholecystectomy patients. Transdermal patch is thought of as an efficient, non-invasive and value effective means of managing surgical pain[32].

12**. Manish Banjare, Kaushal Kishor Kabir, Arpit Agarwal, K K Arora** in 2018 evaluated the efficacy and safety of diclofenac transdermal patch with intramuscular diclofenac as pre-emptive analgesia in post operative patients undergoing inguinal hernioplasty. This study aims to compare the duration and quality of analgesia provided by diclofenac transdermal patch and intramuscular injection and to estimate time at which patients demands rescue analgesia postoperatively. 60 healthy patients divided into two groups of 30 each, scheduled for elective inguinal hernioplasty under subarachnoid block were taken. A transdermal diclofenac patch containing 100 mg of diclofenac diethylamine was applied to the participants in the study group just before the induction of anaesthesia. In the control group, 75 mg of diclofenac sodium Inj. was given intramuscularly half-an-hour before the end of surgery.

Data for postoperative pain was assessed at 2, 4, 6, 8, 12, 16 and 24 hours by using visual analogue scale (VAS) score and verbal rating scale (VRS) score. Statistical

difference in duration, quality of pre-emptive analgesia and need for rescue analgesia was found between the two groups in terms of postoperative pain.

Conclusion: Transdermal diclofenac patch (100 mg) is a better analgesic route of administration than intramuscular diclofenac sodium (75 mg) for pre-emptive analgesia in patients undergoing inguinal hernioplasty[33].

13. **Vandana Chhabra**, **Hemant Batra**, **Vandana Gupta** , **Ajay Chhabra** , **Poonam Sood in 2019** evaluated the efficacy of transdermal diclofenac patch in the management of post surgical pain**.** Postoperative pain is one of the most dreadful experience for patients because millions of cells are damaged intraoperatively. The efficacy of pain relief post surgery is one of the most important factors necessary for minimal hospital stay **.**Diclofenac sodium, a NSAID, has anti-inflammatory, analgesic and anti-pyretic activity. Oral diclofenac was the route of choice in daily practice but because of its first pass metabolism and intolerability in few patients it is now seldomly used. The parenteral route is painful at the site of administration. Intramuscular injections of NSAIDS have many side effects like erythema, pruritus, oedema, abscess and necrosis. The transdermal delivery system has the advantages of therapeutic efficacy and safety of the drugs as the drug is delivered through the skin at a preplanned and controlled rate[34].

PAIN

Pain is described as physical sensation induced by disease or injury that is extremely unpleasant. Pain comes from the Latin term "Poena" which implies penalty. Hippocrates and Aristotle saw pain and pleasure as feelings that originated in the heart rather than the brain. [4, 5]

Pain was theorized to originate outside the body before the renaissance in Europe. Prayer was the most prevalent therapy choice, as it was thought to be God's penalty. [6]René Descartes theorized in 1644 that pain was a disturbance going through the nerve cells until the disturbance reached the brain, a development that changed the perception of pain from a spiritual, mystical experience into a physical, mechanical experience.[7,8]This moved the centre of pain sensation and perception from the heart to the brain.

Pain was described in three dimensions by Melzack R, Casey KL (1968) [9]: "Sensory-discriminative"-sense of the magnitude, location, quality and duration of the pain, "affective-motivational"-unpleasantness and willingness to get away with it and "cognitive-evaluative"-cognitions such as assessment, cultural beliefs, distraction and hypnotic suggestion.

Now pain has been described in terms of danger very aptly by the International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”.[10]

Pain Physiology:

Pain is a defensive mechanism of the body. It occurs whenever tissues are being harmed and cause the individual to act upon to get relieved from the painful stimulus. Thus pain may be defensive, protective and diagnostic. Pain, as a sensation is a function of nerve impulses that ascend from the periphery and are modulated by mechanisms to appreciate and then evoke appropriate reaction.

Classification of Pain:

There are two major types.

Fast Pain:

It is also known as sharp pain, pricking pain, acute pain and electrical Pain. It occurs within 0.1 seconds when a painful stimulus is applied. They are transmitted via peripheral nerves to spinal cord by small myelinated type A delta fibers at a velocity between 6-30 m/sec. [11, 12]

Slow Pain:

It is also known as burning pain, aching pain, and throbbing pain or noxious pain. It is transmitted by unmyelinated type C fibers at a velocity of 0.5-2 m/sec. Their threshold for stimulation is higher than Adelta fiber sand is responsible for more delayed burning pain. It is usually associated with tissue damage and can cause prolonged unbearable distress. [11, 12]

Pain Receptors:

Nociceptors are tissue receptors that are activated by painful stimuli in particular. The receptors transform this noxious data into an electrical signal and transmit it along axons from the periphery to the central nervous system. [13]

Types of nociceptors:

• High-threshold mechanoreceptors (HTM), that reacts to mechanical distortion.

• Polymodalnociceptors (PMN), that reacts to a multitude of tissue-damaging signals such as prostaglandins, 5-hydoxytryptamine (5HT), leukotrienes, bradykinine, hydrogen ions, histamine and cytokines. [13]

Nociceptors are the free nerve endings of primary afferent A delta and C fibers. They are distributed throughout the body (skin, viscera, muscles, joints, meninges) and can be stimulated by mechanical, thermal or chemical stimuli. [13]

Neurotransmitters in Pain Pathway:

These are chemical substances and enzymes are released from the damaged tissues, increasing the transduction of painful stimuli. These include prostanoids (prostaglandins, leukotrienes and hydroxyacids) and kinins, such as bradykinin, kallidin, etc. [11]

Several neuro-peptides and excitatory amino acids function as neurotransmitters for afferent neurons sub serving pain. The most important of these peptides are substance P and calcitonin gene related peptide (CGRP). Glutamate is the most important excitatory amino acid. [11, 12]

The other neurotransmitters that help in sub serving pain are glutamate, aspartate and adenosine triphosphate (ATP) which are excitatory in function. Somatostatin, acetylcholine, enkephalins, β endorphins, nor epinephrine, adenosine, serotonin, GABA and glycine are inhibitory in function. [12, 13]

Inflammatory mediators [e.g. bradykinin, serotonin, prostaglandins, cytokines, and hydrogen ions] are released from tissue damage and may directly activate nociceptors.

They can also act to lower nociceptors activation threshold so the stimulus needed to trigger activation is lower. This process is called as primary sensitisation. (11, 12, 13)

Prostaglandins and bradykinin sensitize nociceptors to be activated by low-intensity stimuli. When applied straight to nerve endings, histamine and 5-HT cause pain. 5-HT and hydrogen ions act directly upon the cell membrane's ion channels, but most others bind to membrane receptors and stimulate second-messenger systems through G proteins. (12, 13)

Pain Pathways:

Impulses from these receptors utilize separate pathways for transmitting acute sharp pain and chronic pain. The impulses are conducted along sensory afferent fibers. They are the A delta (myelinated large fibers) and C (unmyelinated small fibers) in peripheral nerves. A delta conducted pain is felt quickly and well localised. They have conduction velocity of 12-20 meters per second. (14, 15, 16)

They transform in to free nerve endings in the superficial layers of the dermis. They respond particularly well to pinching or pinprick. They conduct sharp pain produced by pinprick and are responsible for withdrawal reflex. C fibers are small, fine and non myelinated and have a conduction velocity of 0.1to 2 meters per second or less. They also form part of the free nerve ending network of the skin. Their threshold for stimulation is higher and they are probably responsible for delayed noxious pain. (14, 15, 16)

Primary afferent neurons are situated at each level of the spinal cord in the dorsal ganglia that exists in the vertebral foramina. Each neuron has one axon that subdivides, sending one end to the peripheral tissue and the other to the spinal cord's dorsal horn. The majority of first-order neurons at each cervical, thoracic, lumbar and

sacral level bring the proximal end of their axons into the spinal cord via the dorsal (sensory) spinal root. It has been shown that some unmyelinated afferent (C) fibers enter the spinal cord via ventral nerve (motor) root.

In the dorsal horn, other than synapsing with neurons of second order, in the grey matter of ipsilateral dorsal horn neurons, the axons of the first order neurons may synapse with interneurons, sympathetic neurons and ventral horn with neurons of second order. Afferent fibers after entering the spinal cord differentiate according to size i.e. large myelinated fibers becoming medial, and small unmyelinated fibers becoming lateral. [14, 15, 16]

Pain fibers can ascend or descend one to three spinal cord segments in the Lissauer's tract before synapsing. The axons of majority second-order neurons cross the midline near to their level of origin (at the anterior commissure) to the contra lateral side of the spinal cord before forming the spinothalamic tract and sending their fibers to the thalamus, the nucleus raphe magnus, the reticular formation, and the periaqueductal grey. Second order neurons synapse in thalamic nuclei with third order neurons, which send projections through the internal capsule and corona radiata to the post-central gyrus of the cerebral cortex.

The spinothalamic tract which is a major pain pathway lies in the white matter of the spinal cordanterolaterally. This very ascending tract is divided as lateral and medial spinothalamic tract. [14, 15, 16]

The lateral spinothalamic tract projects mainly in to the ventral posterolateral nucleus of the thalamus and carries differentiating features of pain such as intensity, location and duration. The medial spinothalamic tract projects to the medial thalamus and is responsible for mediating the autonomic as well as unpleasant perception of pain. Some spinothalamic fibers also project to the periaqueductal grey and they may

be an important link between the ascending and descending pathways. Collateral fibers project to the reticular activating system and the hypothalamus; these are likely to be responsible for the arousal response to pain. (14, 15, 16)

The spinoreticular tract, spinomesencephalic tract, spinohypothalamic tract and spinotelencephalic tract are also other pathways, which help in pain perception. Spinocervical tract ascends uncrossed to the lateral cervical nucleus, which relays the fibers to the contra lateral thalamus; this tract is a major alternative pathway. (14, 15, 16)

Neurophysiology of Pain:

Nociception is the encoding and processing of harmful stimuli in the nervous system, and therefore, ability of the body to sense potential harm. The nociceptive mechanism (prior to the perceptive event) consists of a multitude of events as follows:

Transduction:

Transduction is the conversion of one form of energy to another. It starts when the free nerve endings (nociceptors) of A-delta fibers, C fibers and the primary afferent neurons react to noxious stimuli. Nociceptors are susceptible to noxious stimuli when tissue deformation and inflammation happens as a result of trauma, infection, inflammation, ischemia and surgery. This stimulation causes release of chemical mediators from the damaged cells including bradykinin, histamine, substance P, prostaglandin, potassium, serotonin etc.

These chemical mediators stimulate and/or sensitise the nociceptors to the noxious stimuli. This causes an exchange of potassium and sodium ions

(Re-polarisation and depolarisation) at the cell membranes which results in generation of an action potential. (16, 17, 18)

Stages of transduction:

• Events of stimulation to tissue chemical events.

• Tissue chemical and synaptic cleft events to Electrical events in neurons.

• Electrical events in neurons to tissue chemical events at synapses.

Transmission:

Electrical signals are transmitted along neuronal systems, while molecules are transferred from one cell surface to another in the synaptic cleft. The method of transmission takes place in three phases. The pain impulses are transmitted:

1. from the transduction site along the fibers of the nociceptor to the spinal cord's dorsal horn.

2. from the spinal cord to the brain stem.

3. through the connections between the thalamus, cortex and higher levels of the brain.

These are chemicals, which are formed in the nerve endings and act on specific receptors. Example: Serotonin, Acetylcholine, Bradykinin, Potassium ions, Acids, Histamine and proteolytic enzymes. Prostaglandins enhance the sensitivity of pain in the nerve endings. [16, 17, 18]

Modulation:

Pain modulation takes place at the nociceptor level peripherally, in the spinal cord, or in supraspinal structures. This modulation can either inhibit or activate pain.

Peripheral Modulation: Inflammatory mediators as well as prolonged, intense or repeated noxious stimulation, or both can sensitize the nociceptors. These nociceptors exhibit a low threshold for stimulation.

Peripheral (nociceptor) sensitization plays a vital role in central sensitization and pain states like allodynia and hyperalgesia. [16, 17, 18]

Central Modulation: This can either activate or inhibit pain.

The mechanisms for activation are:

• Sensitization of second order neurons.

• Receptive field expansion.

• Flexion responses' hyper excitability. [16, 17, 18]

Inhibitory mechanisms can be either Supraspinal or Spinal.

Spinal:

Segmental inhibition involves stimulation of large afferent fibers that sub serve wide dynamic range (WDR) neuron and spinothalamic activity that inhibits epicritic sensation. Glycine and gamma amino butyric acid (GABA) are amino acids that act as inhibitory neurotransmitters. GABA 'b' receptor activity, which increases potassium conductance across the cell membrane, appears to mediate segmental inhibition. [16, 17, 18]

Supraspinal:

There is a supraspinal inhibition where several supraspinal structures send fibers down the spinal cord to prevent dorsal horn-level pain. These include periaqueductal grey, reticular formation, and nucleus raphe magnus (NRM). Axons from these structures operate on the main afferent neurons presynaptically and on cells or interneurons of the second order neurons post-synaptically. [16, 17, 18]

These inhibitory pathways use monoamines as neurotransmitters, such as nor adrenaline and serotonin, and end with nociceptive neurons in the spinal cord as well as spinal inhibitory interneurons that store and release opioids.

Using α2 receptors, nor adrenaline facilitates this action. The opiate endogenous mechanism acts through enkephalins and β-endorphins. These operate predominantly presynaptically, while exogenous opiates act post-synaptically. [16, 17, 18]

Brainstem neurons may control nociceptive transmission by:

• Direct action on dorsal horn cells

• Inhibition of excitatory dorsal horn neurons

• Excitation of inhibitory neurons

Perception:

The experience of pain is complex and subjective, and is affected by factors such as cognition, mood, beliefs and genetics. Pain perception is an uncomfortable recognition of some portion of the body, characterized by a strikingly unpleasant feeling and adverse emotion that is best defined as a threat. There is involvement of both cortical and limbic system structures. Nociceptive input from some projection neurons flows through the thalamus to the somatosensory contra lateral cortex, where the input is somatotopically mapped to maintain data about the place, severity, and quality of pain. [16, 17, 18]

Types of Pain:

Nociceptive Pain: Includes visceral and somatic pain and refers to pain due to peripheral stimulation of nociceptors in the visceral or somatic structures. [17, 18]

Neuropathic Pain: Pain involves peripheral or central afferent neural pathway and is commonly described as burning type of pain. It is caused by impulse generation within the pathway proximal to nociceptor. [17, 18]

Visceral Pain: Pain receptors in viscera are comparable to those in the skin, but in somatic structures they are more widely dispersed and are not linked with intense pain. If any incident that triggers nerve stimulation occurring throughout the

viscera, it creates intense pain that is diffuse, poorly localized and often related with nausea and signs of autonomic activation of the nervous system such as either pulse or blood pressure surge or fall. Visceral pain is frequently correlated with muscular rigidity and hyperesthesia. Typically, visceral pain radiates and can be referred to the body's surface area with the same dermatome as the affected viscera. [17, 18]

Somatic Pain: It is described as sharp, stabbing, well localized pain that typically arises from skin, skeletal muscle and peritoneum. Superficial pain in general is well localized showing dermatomal pattern. Deep pain has a dull aching character and it may be accompanied by an unpleasant sickening sensation due to autonomic response. It is poorly localized. [17, 18]

Referred Pain: Deep pain whether visceral or somatic in origin, may be felt in some part of the body other than the site of stimulation. Visceral pain tends to have characteristic localization for each organ and commonly referred to the dermatome of spinal segments through which the afferent fibers enter. The diaphragmatic pain referred to the shoulder is well known example. The neurophysiologic basis of referred pain depends upon convergence of several cutaneous and visceral afferent fibers on the same secondary neuron at some point in pain pathway. [17, 18]

Neuropathic Pain: It can be of three types such as:

- Neural injury pain
- Nerve compression pain
- Complex regional pain syndrome

Neural injury pain involves anatomic abnormality in peripheral nerves, in pain receptors or central pain pathway. It has dermatomal distribution. Nerve compression

pain occurs when there is extrinsic pain on the neural structures. It can be central or peripheral depending on site of origin of pain impulse. [17, 18]

Theories of Pain:

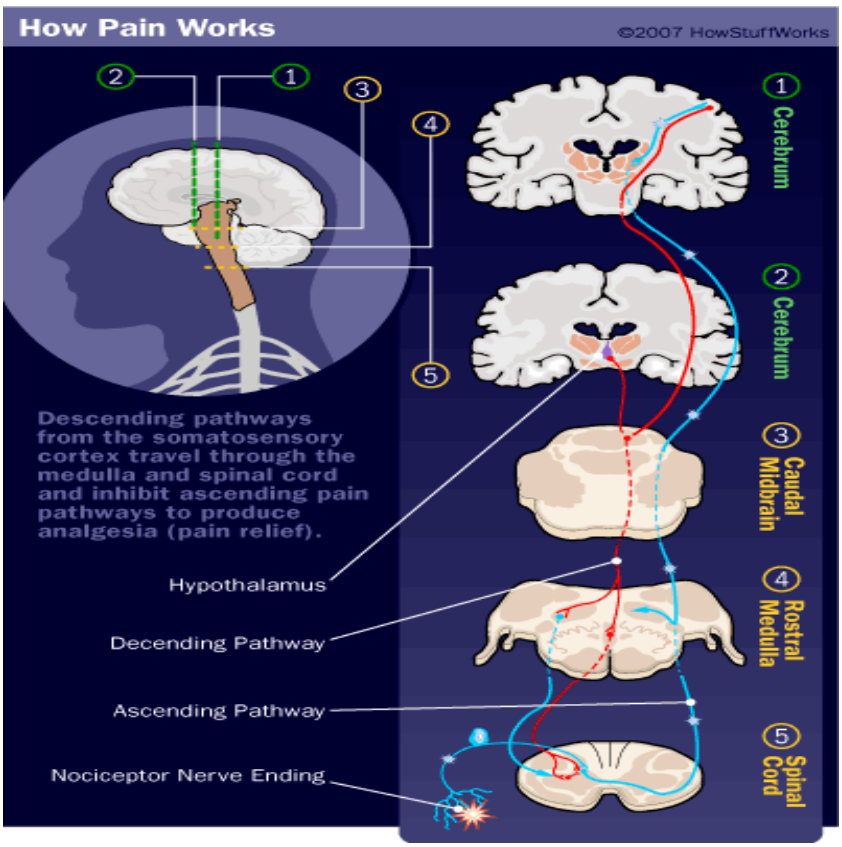
Specificity Theory: Specificity theory proposes that all sensation including pain is receptor specific and that pain receptors respond only to noxious stimuli. [17, 18]

Intensity Theory: Intensity theory holds that stimulation of any sensory receptor will cause pain if stimulus is excessive. [17, 18]

Pattern Theory: Pattern theory proposes that sensory impulses are coded according to the number of receptors stimulated and the rate of their discharge. [17, 18]

Gate theory for control of pain: Melzackand wall (1965) proposed this theory, which states that dorsal horn at the spinal cord mainly the substansia gelatinosa function as gates for controlling entry of pain signals into the pain pathway.[17,18]

Figure 1: Pain pathways



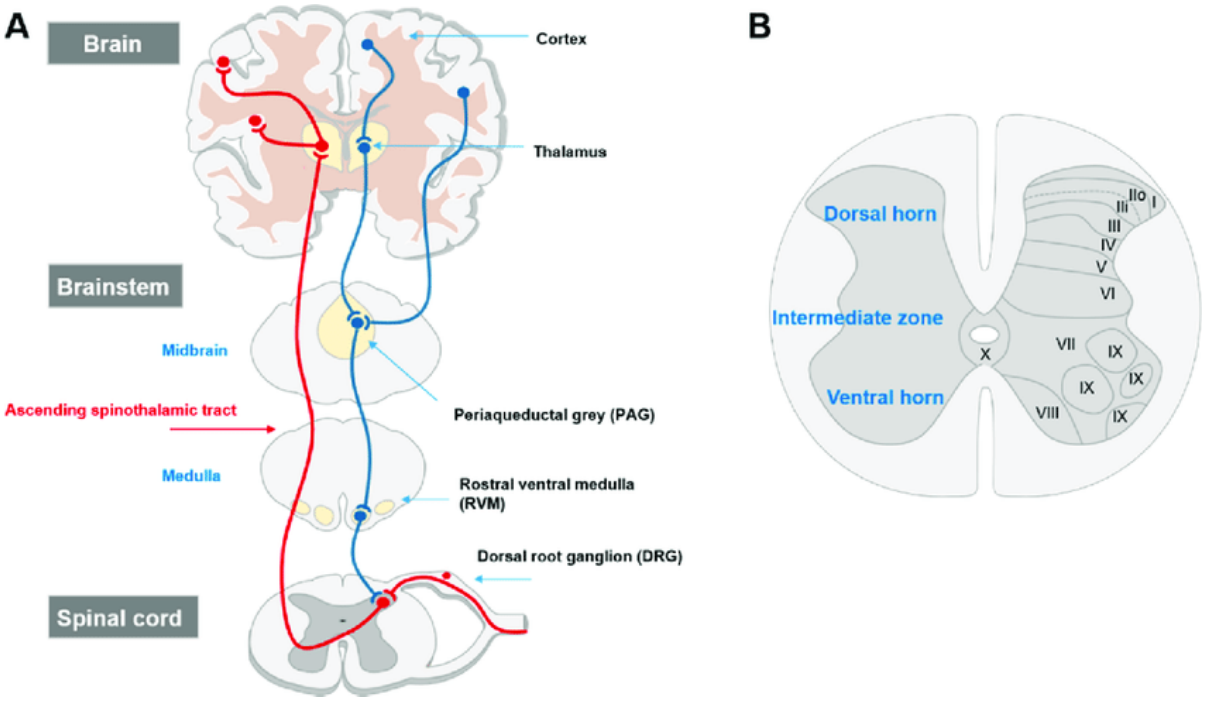


Figure 2: Pain pathways

Pain Assessment Scales:

Pain is a complex and subjective experience. The evaluation of pain is the vital precondition for effective pain management. Deciding the initial medication plan is helpful, but also revaluating the degree of accomplishment. This treatment and reassessment cycle will continue until a good result has been achieved. (19)

In the immediate postoperative period, physiological responses such as pulse rate, blood pressure, respiratory rate are important indicators of pain.

Visual analogue scale: It is 10 cm scale with end points labelled 0 for NO PAIN and 10 for WORST POSSIBLE PAIN. The person was asked to compare the severity of current pain with worst pain he ever faced in his life. (19)

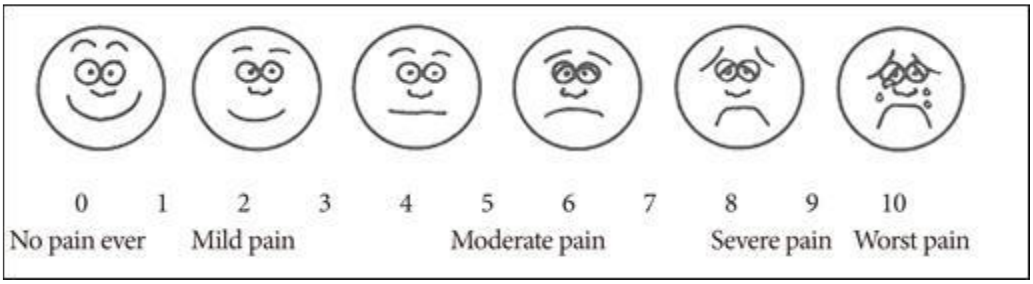


Figure 3: Visual Analogue Scale

Visual Rating Scale (Prince Henry Scale):

Scores	Severity of Pain
1	No pain on coughing
2	Pain on coughing or movements but not on deep
3	Pain on deep breathing but not on rest
4	Slight pain at rest
5	Severe pain at rest

Table 1: Point Scale of Prince Henry for Postoperative Pain Assessment

Numerical rating: With the two anchors of NO PAIN and AGONISING PAIN, it is comparable to the visual analogue scale, but it has numbers across the scale from 0-10. This scale needs the patient to realize how their severity of pain can be translated into number. It is less sensitive in calculating the intensity of small changes. [19]

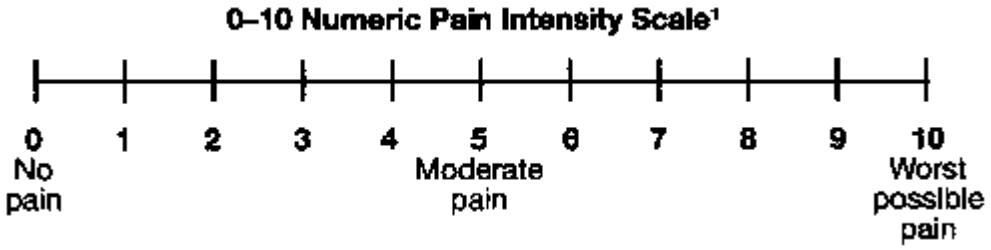


Figure 4: Numerical Rating Scale

ACUTE POSTOPERATIVE PAIN

Management of acute postoperative pain by anaesthesiologists is improving as the knowledge regarding dose ranges; duration of action is being widely studied across the globe.

Factors that modify postoperative pain-

1. The site, nature and duration of surgery.
2. The type and extent of the incision.
3. The physiological and psychological makeup of the patient.
4. Preoperative preparation of patient
5. Anaesthetic management before, during and after surgery
6. Postoperative care

Methods adopted for postoperative pain relief:

1. By increasing the pain threshold

Pharmacologic- centrally and peripherally acting analgesics

Non-pharmacologic-counselling

2. By modulating the pain pathways

a. TENS

b. Acupuncture

c. Cryotherapy

d. Heat therapy

By interrupting the nociceptive pathway

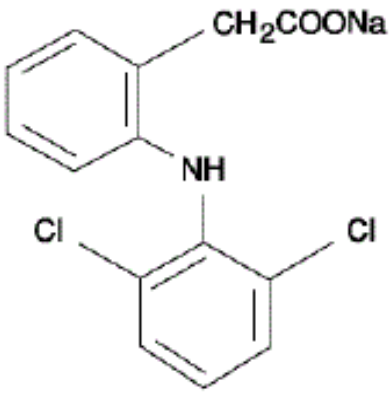
a. Nerve blocks and neurolysis

b. Surgical ablation

DICLOFENAC SODIUM

Diclofenac sodium is a phenyl acetic acid derivative which is relatively nonselective COX inhibitor. It is one of the most potent NSAIDS. Diclofenac is supplied either as sodium or potassium salt. It bears the formula C14H11Cl2NO2. Molecular mass is 296.148 g/mole, 99% protein bound, metabolised hepatically with no active metabolite. It is excreted mainly by biliary route and 1% excreted in urine[20.]

Figure5-The chemical structure of diclofenac sodium

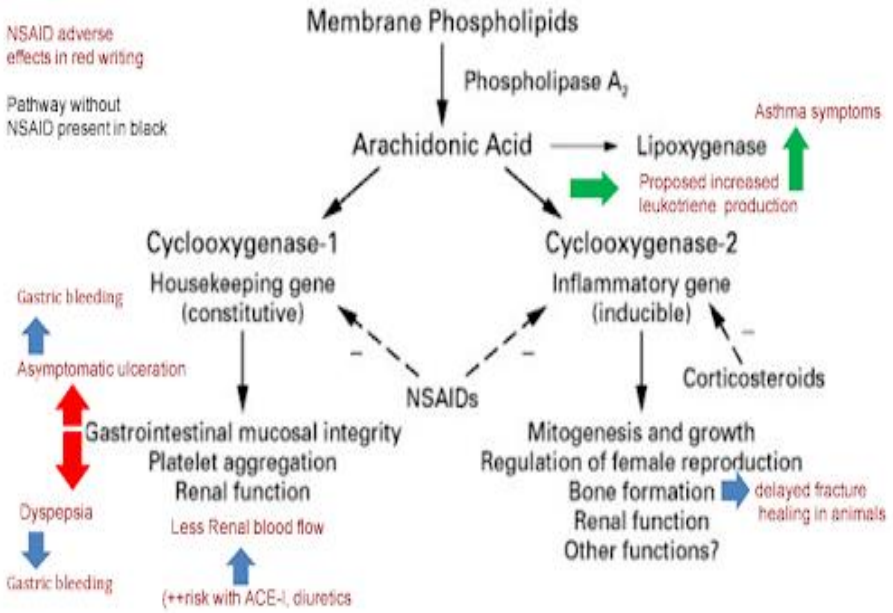


NSAIDS have anti – inflammatory and analgesic effects through the inhibition of prostaglandin synthesis, by blocking the activity of COX.

Available in parenteral preparations, oral tablets, ointments, rectal suppositories and transdermal patches. Transdermal diclofenac patch is the most advanced delivery system.

Diclofenac [sodium-0-(2, 6-dichlorophenyl)-aminophenylacetate] is a non steroidal compound with anti-inflammatory, analgesic, anti rheumatic and anti-pyretic properties. When given in high doses diclofenac temporarily inhibits platelet aggregation. Post operatively, diclofenac rapidly relieves pain, inflammation and edema.

Figure 6: COX pathways



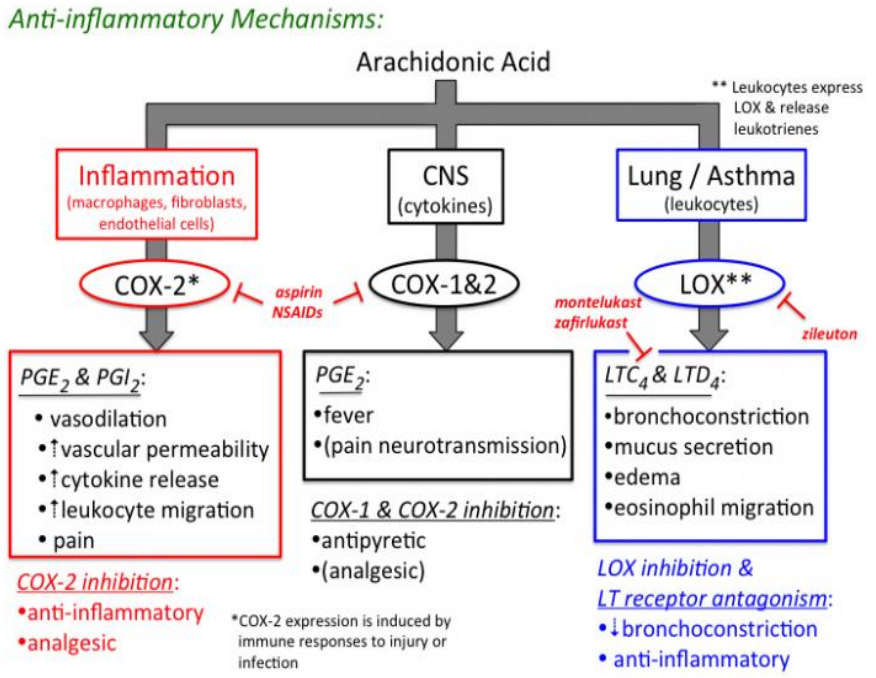


Figure 7: Anti-inflammatory mechanisms

PHARMACOKINETICS

When administered orally, due to first pass metabolism only 50% of the absorbed dose is systemically available. Peak plasma concentration is achieved in 1 hr when taken orally. Whereas in transdermal patch, peak plasma levels are less compared to oral administration but more stable throughout the time. Median plasma levels of diclofenac are 20-50 ng/ml. Plasma protein binding is extensive (99.7%). It is rapidly metabolized in the liver by hydroxylation to phenolic derivatives with subsequent conjugation or by direct glucuronidation of the unchanged drug.60% is excreted in urine unchanged as either glucuronide conjugates or the metabolites. Can cross the placenta and small amounts can be present in breast milk also.

SAFETY MEASURES

1. Mandatory supervision when given to patients with gastro-intestinal ulceration.
2. Use with caution in asthmatics since brochospasm has been reported
3. In patients with impaired cardiac or renal function, prostaglandins are necessary in maintaining renal blood flow.
4. Cautious use in patients with heart failure or conditions predisposing to fluid retention since diclofenac can cause retention of salt and water [21, 22].
5. Patients with impaired haemostasis should be carefully monitored since platelet aggregation may be inhibited temporarily.

6. Cautious use in impaired liver function. Usually any elevations in liver enzymes are temporary but chronic therapy can lead to permanent changes.

7. Should be avoided in pregnancy unless the benefits outweigh the potential risk to the fetus especially in the last three months of pregnancy when like other prostaglandin inhibitors, Diclofenac may cause closure of fetal ductal arteriosus, fetal renal impairment, inhibition of platelet aggregation and delayed labour.
8. Can be detected in breast milk following 50mg every 8 hours, but the amounts are so small that no undesirable effects on the baby are seen.

TRANSDERMAL DICLOFENAC PATCH-

It is a transdermal delivery system (TDS) designed for continuous release of diclofenac. It has diclofenac diethylamine as its active ingredient. Each 50 square cm patch contains 100 mg of diclofenac diethylamine and a 75 square cm patch contains 200 mg .Delivers a slow release of drug into the body over time providing long term effectiveness. Drug contained on the transdermal patch enters the body through the skin in contact with the patch.

The dermis contains an extensive network of capillaries that transport blood into the system. If the drug is able to penetrate the stratum corneum, it can enter the blood stream by passive diffusion typically by a pathway around the cells.

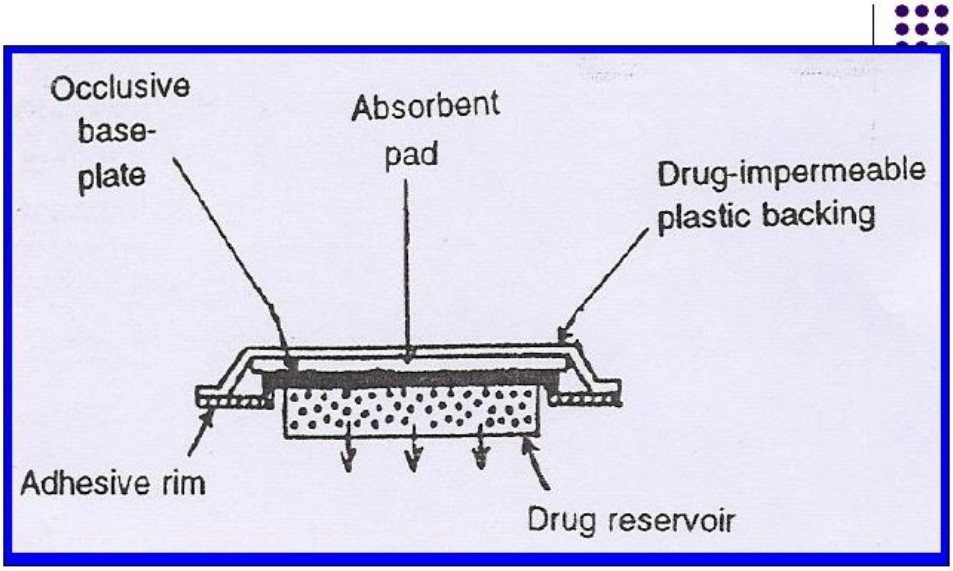


Fig. Matrix diffusion controlled Transdermal drug delivery system

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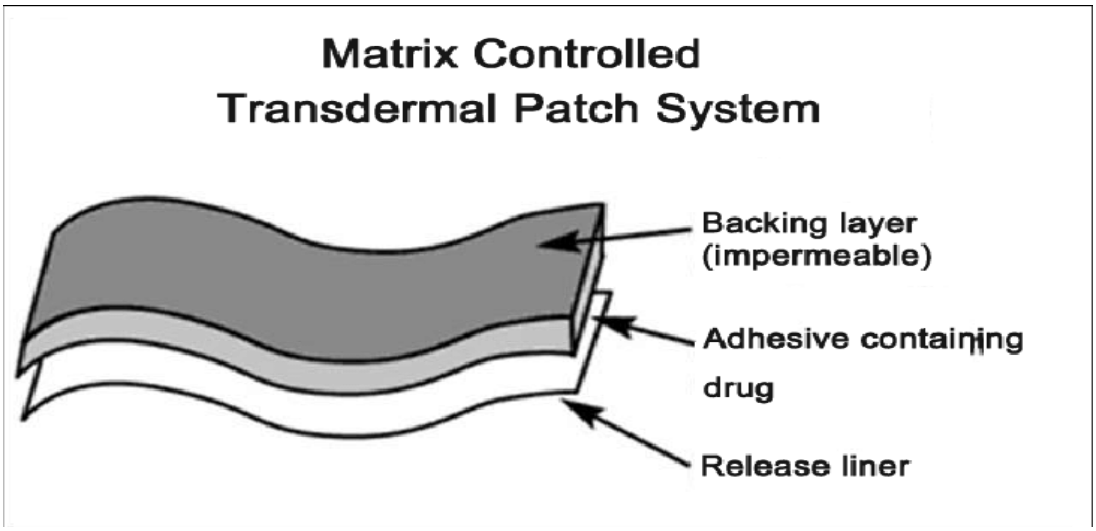


Figure 8, 9: Matrix controlled Transdermal patch system

COMPONENTS-

1. Polymer matrix or matrices - Controls the release of the drug from the device.

2. Drug

3. Permeation enhancers - Promote skin permeability by altering the skin as a barrier to the flux of a desired penetrant.

4. Adhesives that bind the patch to the skin.

5. Backing membrane is flexible and provides a good bond to the drug reservoir and prevents drug from leaving the dosage form through the top. It is impermeable substance that protects the product during use on the skin [23, 24].

ADVANTAGES-

1. The steady permeation of drug across the skin allows for more consistent serum drug levels, which is often the goal and the lack of peaks in the plasma concentration reduce the risk of side effects.
2. If toxicity develops, can be eliminated by removing the patch.
3. Long duration of action. Simple dosing regimen can help in increasing patient compliance to the drug.
4. Steer clear of first pass metabolism.
5. Better mode of delivery in a nauseated or unconscious patient.

DISADVANTAGES-

1. Plasma levels are much lower than that of oral or parenteral route.
2. Local skin irritation
3. Relatively costlier.

METHODOLOGY

SOURCE OF DATA:

This study was carried out in the Department of Anaesthesiology, B.L.D.E's (Deemed to be university) Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura. The study was conducted from December 2018 to August 2020.

METHOD OF COLLECTION OF DATA:

STUDY DESIGN: A randomised comparative study

STUDY PERIOD: One and half year from December 2018 to August 2020.

SAMPLE SIZE: With the anticipated average Mean and SD of duration of surgery in study group and control group 12 and 25.8 (118±24.6 and 130.0±27 resp.)[1] The minimum sample size is 45 per group with 95% level of significance and 90%power.

Formula used is

$$N = 2\left[\frac{\left(Z_{1-\alpha/2} + z_{\beta}\right) * S}{d}\right]^2$$

$Z_{1-\alpha/2}$ Level of significance=95%

$Z_{1-\beta}$ Power of study =90%

d=clinically significant difference between two parameters

SD= Common standard deviation

STATISTICAL ANALYSIS:

1) Data was represented using Mean±SD, percentages and diagrams.
2) Significant difference between quantitative data was found using Mann Whitney U test to compare two groups.
3) Significant difference between Qualitative data was found using Chi square and Fisher's Exact test.

STUDY GROUP: Study was conducted on 90 ASA grade I or II adult patients of either sex, aged between 18-60 years scheduled for elective lower abdominal and perineal surgeries.

Inclusion criteria:

- ASA Class I and II.
- Age 18 – 60 years.
- Either sex
- Scheduled for elective lower abdominal and perineal surgeries
- Consent for study procedure.

Exclusion criteria:

- Body mass index >30
- Pregnancy and lactation
- History of bronchial asthma, urticaria or any other allergic reactions induced by aspirin or any other NSAIDs

Investigations Required:

- Complete Blood count , Bleeding Time, Clotting Time
- HIV, HBsAg.
- Random Blood sugars
- Blood urea and serum creatinine
- Electrocardiogram and chest X-ray (whenever required)

Preliminaries:

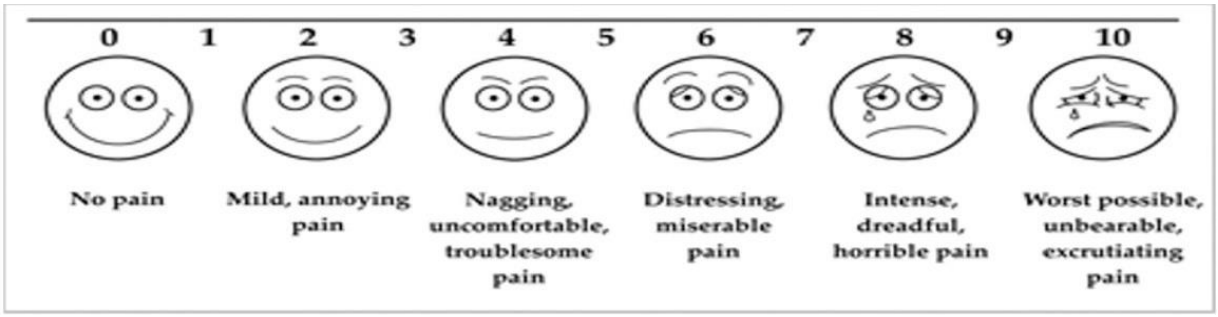
- Written informed consent.
- Intravenous access with a 20 gauge I.V cannula under aseptic techniques.

Procedure: A randomized comparative study was undertaken, 90 patients posted for elective lower abdominal and perineal surgeries were assigned randomly into 2 groups, each containing 45 patients. After approval from the institute and ethical clearance from college Ethical Committee, informed consent was taken from the patients.

- All patients were examined on the day before surgery and thoroughly investigated according to institution protocol and were counselled with regards to spinal anaesthesia
- Patient meeting above criteria were asked to participate in the study after informed consent and overnight fasting. Visual Analogue Scale (VAS) was explained to the patient during preoperative visit.
- On the day of surgery, patient was taken to operation theatre. Standard monitoring devices including ECG, Sphygmomanometer cuff, and pulse oximeter were connected and baseline values were recorded
- All participants were administered subarachnoid block in lateral position using 0.5% hyperbaric Bupivacaine with a 25or26 gauge Quincke's needle to obtain a sensory level block of T6-T8.
- Both groups did not receive any intravenous analgesics or sedatives during the surgery.
- Participants in Group A were applied with a Transdermal Diclofenac patch containing 100mg of Diclofenac diethylamine directly on the chest or the back at the beginning of surgery after subarachnoid block.
- In Group B 75mg of Diclofenac sodium was given intramuscularly half an hour before the end of surgery.

- Pain was assessed postoperatively at 2,4,6,8 hrs using a visual analogue scale (VAS).If the VAS during any time during study is more or equal to five then injection Tramadol 2mg/kg was administered intramuscularly as rescue analgesia.
- Time duration between the administration of transdermal patch or intramuscular diclofenac and the demand for rescue analgesia was noted
- Side effects of transdermal diclofenac patch such as erythema, irritation at the site of application were noted.
- Side effects of intramuscular diclofenac such as nausea, vomiting were also noted.

Figure10: Transdermal diclofenac patch **Figure11: IM Diclofenac**



OBSERVATION AND RESULTS

90 patients posted for lower abdominal and perineal surgeries with ASA grade I and II of either sex aged 18-60 years were randomly allocated into Group A and Group B.

Table 2: Distribution of patients according to Age (Years)

Age (Years)	Group A		Group B	
	No. of patients	Percentage	No. of patients	Percentage
< 20	1	2.2	2	4.4
20 – 29	8	17.8	9	20.0
30 – 39	14	31.1	4	8.9
40 – 49	2	4.4	9	20.0
50+	20	44.4	21	46.7
Total	45	100.0	45	100.0

Graph 1: Distribution of patients according to age

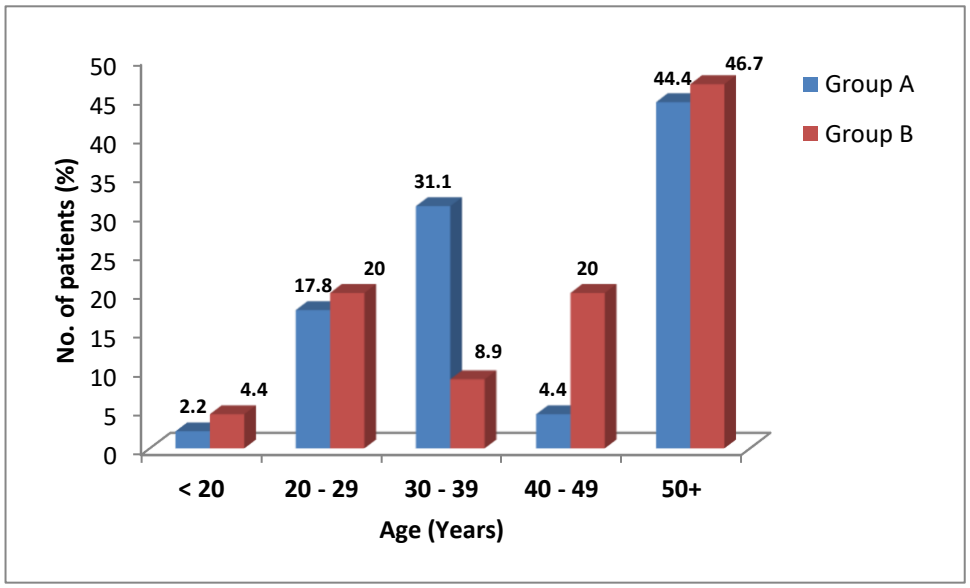


Table 3: Comparison of patients according to Gender between two groups

Gender	Group A		Group B		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
Female	14	31.1	9	20	X^2=1.460	P=0.2269
Male	31	68.8	36	80		
Total	45	100.0	45	100.0		
Insignificant						

Graph 2: Comparison of patients according to gender

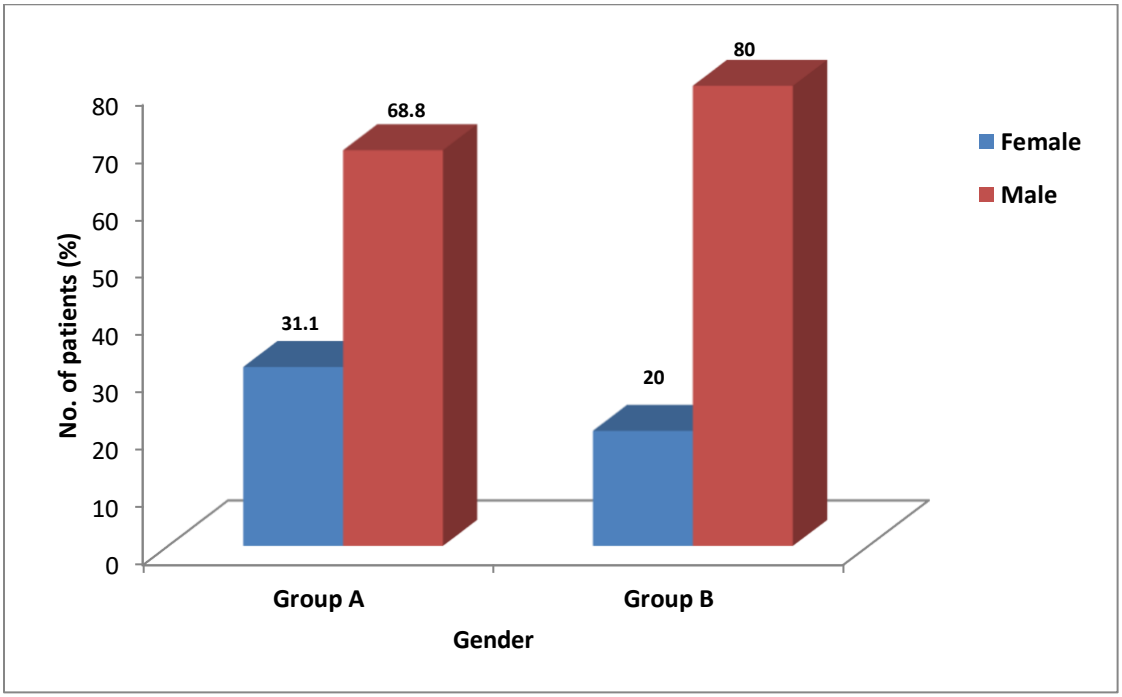


Table 4: Comparison of patients according to ASA Grades between two groups

ASA Grades	Group I		Group II		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
I	22	48.9	20	44.4	X^2=0.1786	P=0.6726
II	23	51.1	25	55.6		
Total	45	100.0	45	100.0		
Insignificant						

Graph 3: Comparison of patients according to ASA grades

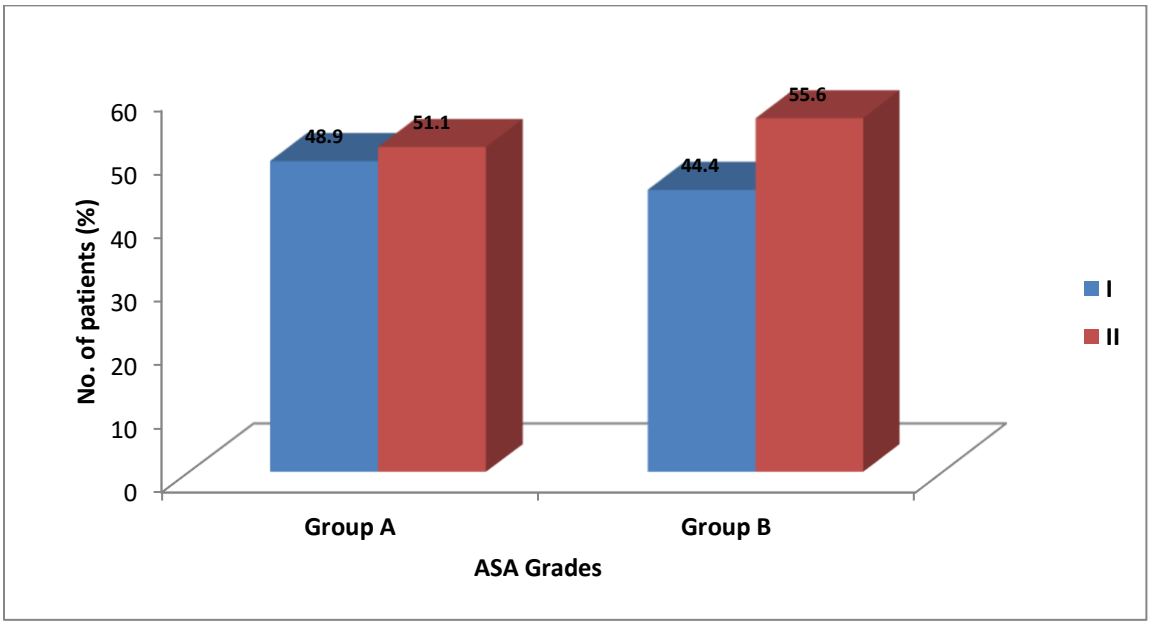


Table 5: Comparison of Visual Analogue Score between Group A and Group B

Visual Analogue Score	Group A		Group B		Mann Whitney U test	P value
	Mean	±SD	Mean	±SD		
2Hours	0.02	0.149	0.76	0.609	U=358.000	P=0.001*
4 Hours	1.02	.723	2.58	0.753	U=171.000	P=0.001*
6 Hours	2.58	.723	4.21	0.630	U=74.000	P=0.001*
*: Highly Significant						

Graph 4: Comparison of VAS scores.

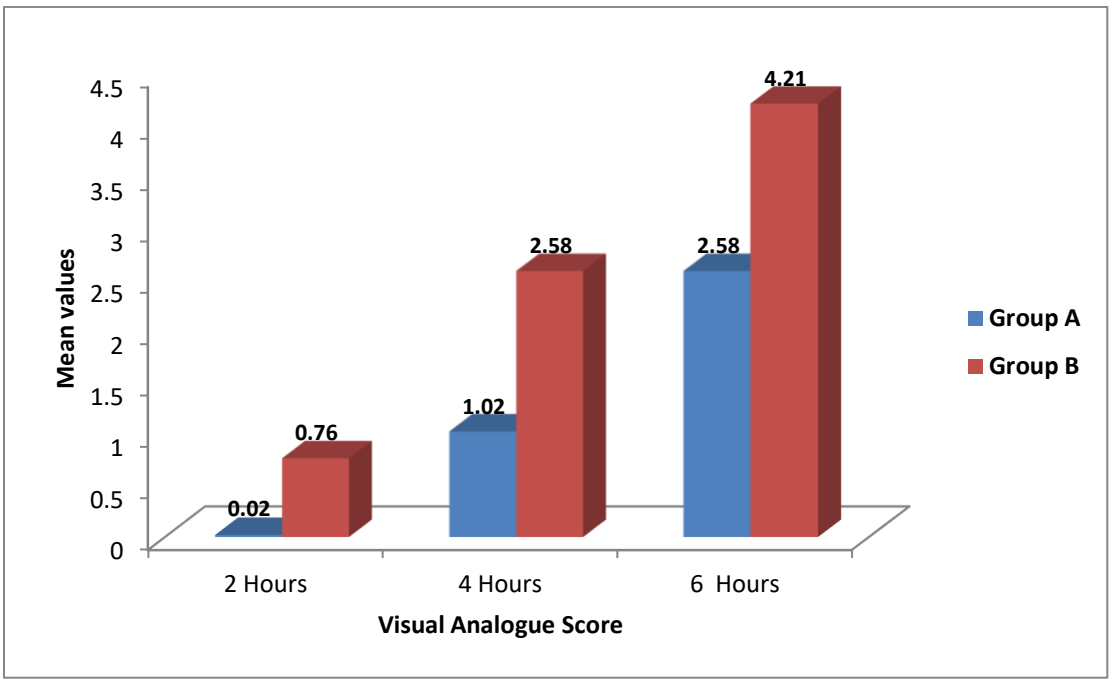


Table 6: Comparison of Visual Analogue Score between two groups

Visual Analogue Score	Group A		Group B		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
2 hours						
0	44	97.8	15	33.3	X^2=41.402	P<0.0001*
1	1	2.2	26	57.8		
2	0	00	4	8.9		
4 hours						
0	11	24.4	0	0	X^2=51.302	P<0.0001*
1	22	48.9	3	6.7		
2	12	26.7	17	37.8		
3	0	0	21	46.7		
4	0	0	4	8.9		
6 hours						
1	2	4.4	0	0	X^2=48.433	P<0.0001*
2	19	42.2	0	0		
3	20	44.4	3	6.7		
4	4	8.9	16	35.6		
5	0	0	9	20.0		
8 hours						
3	6	13.3			NA	
4	23	51.1				
5	10	22.2				
Total	45	100.0	45	100.0		

***:Highly significant , NA: Not applicable**

Graph 5: Comparison of each individual VAS score in between two groups

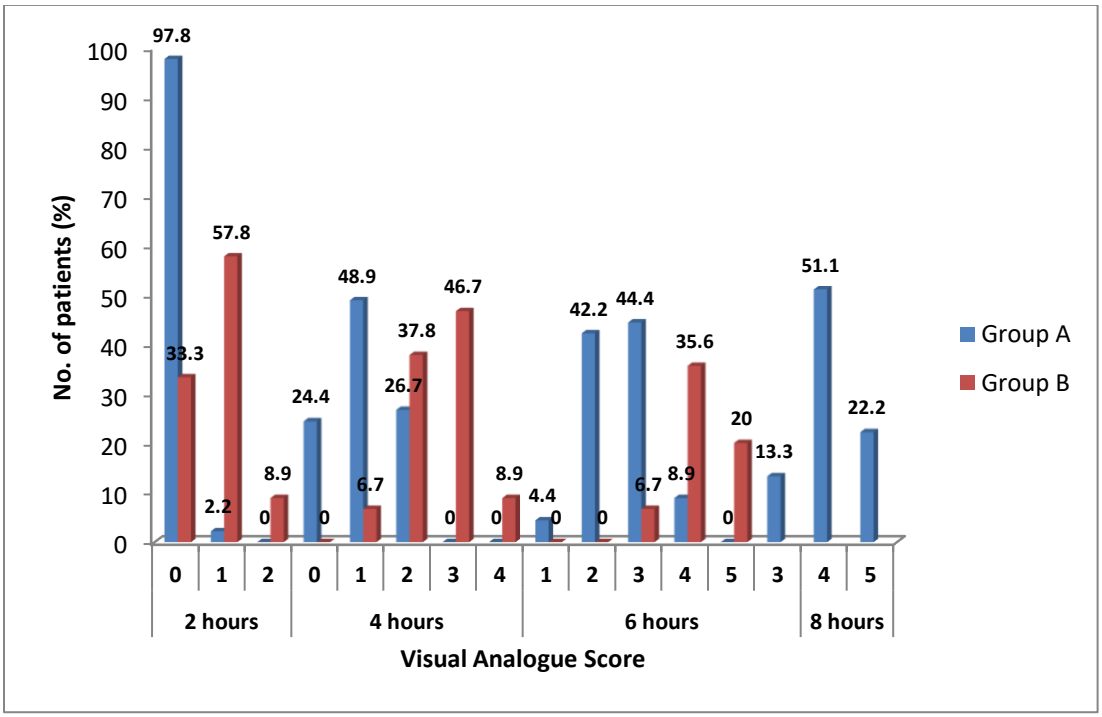


Table 7: Comparison of Basic variables between group A and Group B

Comparison of	Group A		Group B		Mann Whitney U test	P value
	Mean	±SD	Mean	±SD		
Age (Years)	41.91	14.111	43.71	14.770	U=957.000	P=0.652
Duration of surgery (Hours)	1.59	0.549	1.41	0.378	U=807.000	P=0.154
Insignificant						

Pain was assessed postoperatively using VAS score at 2,4,6,8 hrs. If the patient's VAS score is 5 or > 5 rescue analgesia of Inj Tramadol 2mg/kg was given and assessment was stopped.

In group A – At

- 2 hrs postoperatively, 44 patients out of 45 had no pain, 1 patient had VAS score 1.
- 4 hrs postoperatively, 11 patients had VAS score 0, 22 patients had VAS score 1, 12 patients of score 2.
- 6hr postoperatively, 2 patients had VAS score 1.19 patients score 2, 20 patients score 3 and 4 patients of score 4.
- 8hrs postoperatively, 6 patients had VAS score 3, 23 patients score 4 and 10 patients 5.

In Group B – At

- 2hrs postoperatively, 15 patients had VAS score 0, 26 patients had score 1, 4 patients scored 2.
- 4hrs postoperatively, 3 patients scored 1, 17 patients VAS score 2, 21 patients had score of 3, 4 patients of score 4.
- 6hrs postoperatively, 0 patients scored VAS score 0and 1, 3 patients scored 3, 16 patients of VAS score 4 and 9 patients of score 5.
- 8 hrs postoperatively all patients had VAS score above 5 and rescue analgesia was supplemented hence VAS score was not calculated.

Table 8: Comparison of Visual Analogue Score at different period of times in group A

Comparison of Visual Analogue Score **Within group**	**Group A**		**Friedman's test**	**P value**
	Mean(Median)	**±SD**		
2 hours	0.02(0)	0.149	Fr=85.574	P<0.001*
4 hours	1.02(1)	0.723		
6hour	2.58(3)	0.723		
8hour	4.10(4)	0.64	Not included in the test. Because of missing values at 8th hour	
*Highly significant				

Graph 6: Comparison of VAS scores within group A

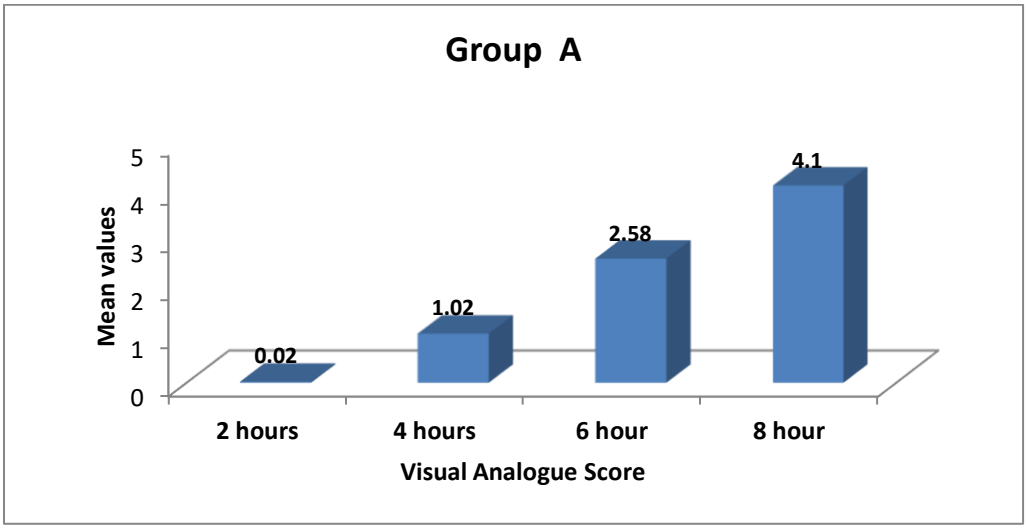


Table 9: Dun's multiple Post hoc test in group A

Visual Analogue Score	**Comparison between**	**Post hoc test**	**Remark**
2nd hours vs	4th hours	P<0.01	Highly significant difference
	6th hours	P<0.001	Highly significant difference
4th hours	6th hour	P<0.001	Highly significant difference

Table 10: Comparison of Visual Analogue Score at different period of times in group B

Comparison of Visual Analogue Score **Within group**	**Group B**		**Wilcoxon signed paired rank test**	**P value**
	Mean(Median)	**±SD**		
2 hours	0.76(1)	0.609	Z=6.150	P<0.001*
4 hours	2.58(3)	0.753		
6hours	4.21(4)	0.630	Not included in the test. Because missing values at 8th hour	
8 hours			Not included in the test. Because missing values at 8th hour	
*Highly significant				

Graph 7: Comparison of VAS scores within group B

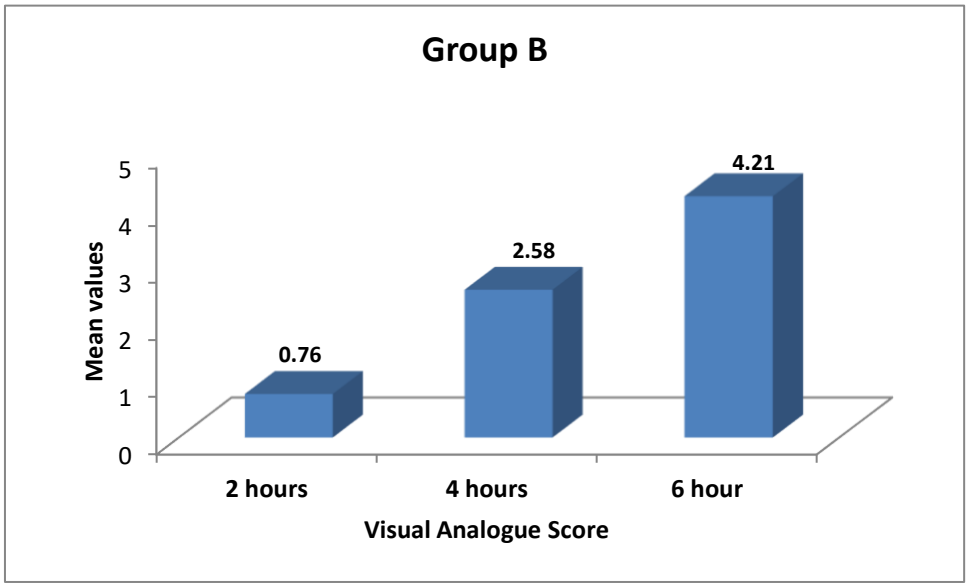
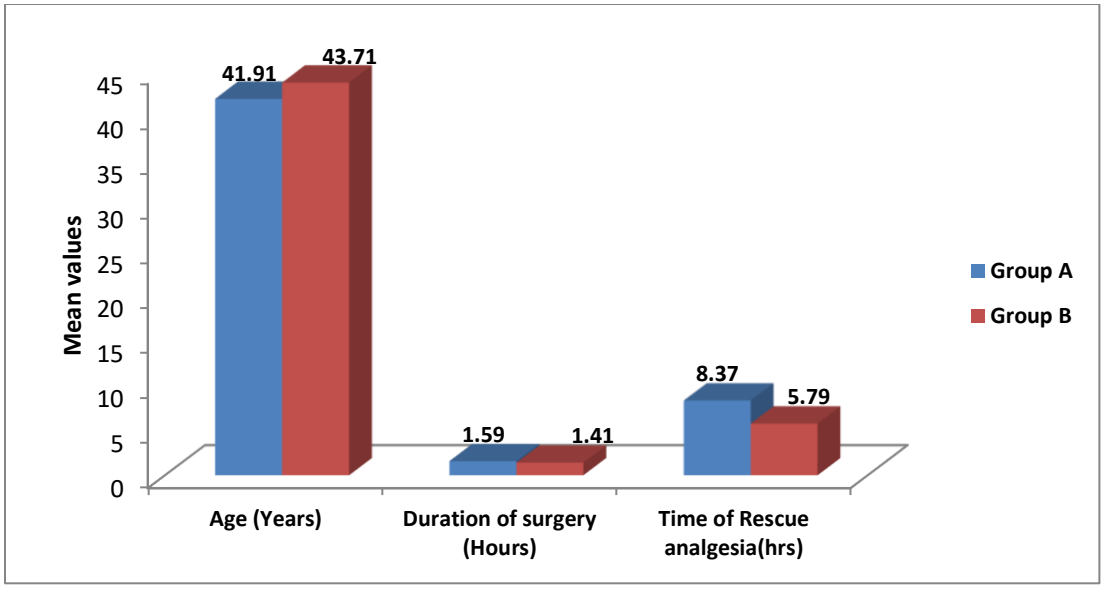


Table 11: Comparison of Time of Rescue analgesia (hrs) between Group A and Group B

Comparison between	Group A		Group B		Mann Whitney U test	P value
	Mean	±SD	Mean	±SD		
Time of Rescue analgesia(hrs)	8.37	0.642	5.79	0.586	U=00.0	P=0.001*
*: Highly Significant						



Graph 8: Comparison of age, duration of surgery, time of rescue analgesia (hrs) between two groups

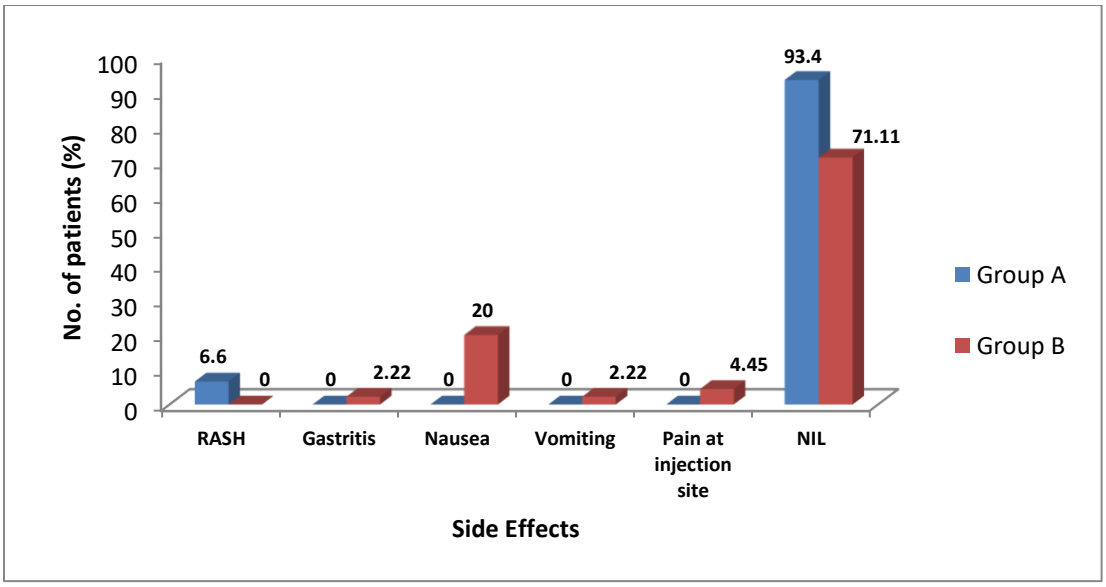
The amount of rescue analgesia is 2mg/kg according to the weight of the individual patient. The time at which rescue analgesia was given in Group A is 8 hr 37 minutes ± 1 hr 4.2 minutes and Group B was 6 hrs 19 minutes ± 58.6 minutes. The need for rescue analgesia between two groups is highly significant ($p < 0.001$).

SIDE EFFECTS-

Table 12: Distribution of patients according to side effects

Side Effects	Group A		Group B		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
RASH	3	6.6	0	0	X^2=17.351	P=0.0039*
Gastritis	0	0	1	2.22		
Nausea	0	0	9	20		
Vomiting	0	0	1	2.22		
Pain at injection site	0	0	2	4.45		
NIL	42	93.4	32	71.11		
Total	45	100.0	45	100.0		
*: Highly significant						

Graph 9: Distribution of patients according to side effects



SIDE EFFECTS-

Group A (transdermal diclofenac patch) – 3 Patients had erythematous rash at the local site whereas the other 42 patients showed no symptoms.

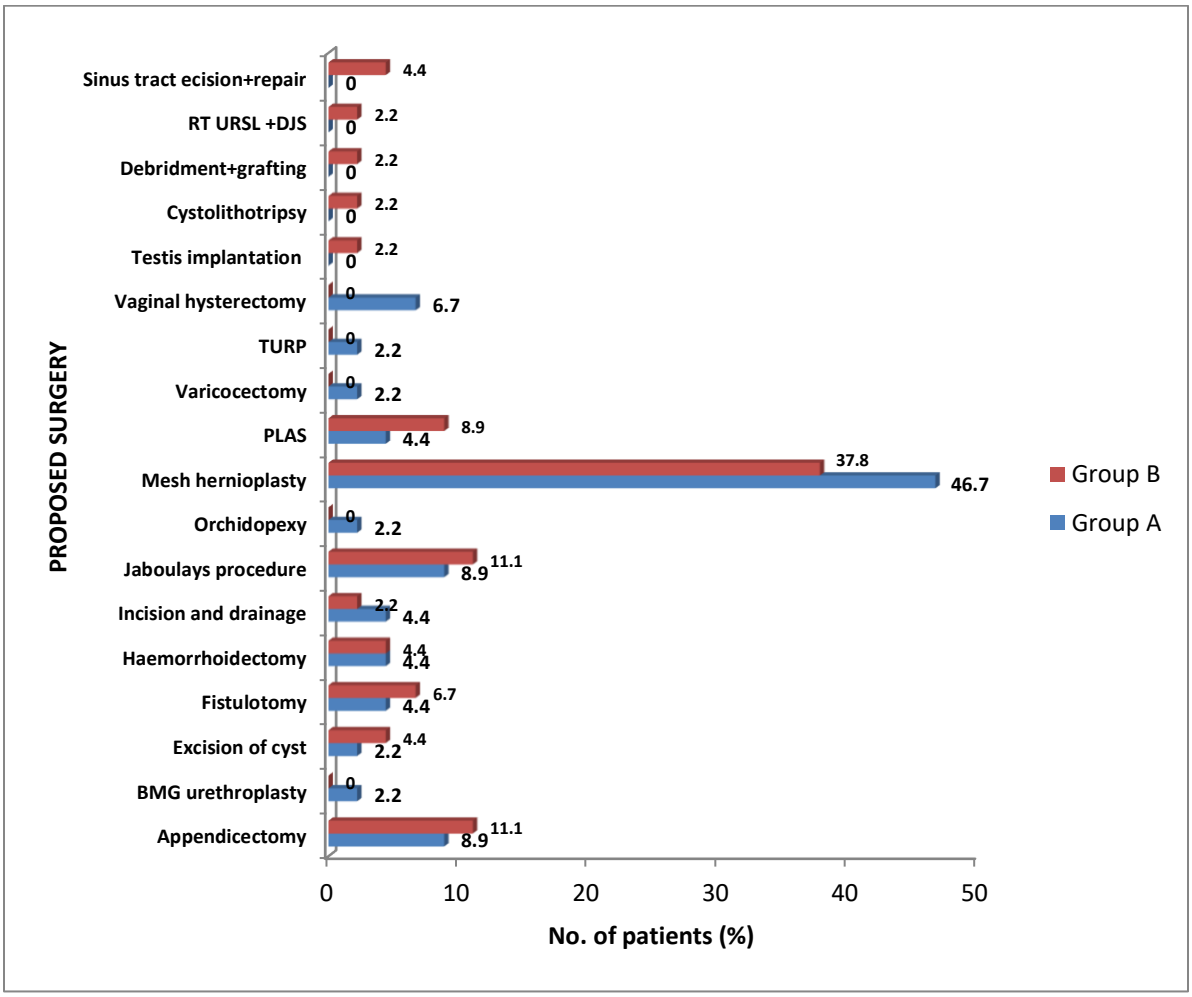
Group B (IM Diclofenac) - 9 patients developed nausea, 2 patients had pain and swelling at the injection site, 1 had one episode of vomiting, 1 patient had gastritis and rest of 32 patients had no symptoms.

Trandermal patch is highly effective is reducing the gastric symptoms of IM Diclofenac (P value of 0.0039 is highly significant).

Table 13: Distribution of patients according to PROPOSED SURGERY

PROPOSED SURGERY	Group A		Group B		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
Appendicectomy	4	8.9	5	11.1	X^2=15.177	
BMG urethroplasty	1	2.2	0	0	P=0.5828	
Excision of cyst	1	2.2	2	4.4		
Fistulotomy	2	4.4	3	6.7		
Haemorrhoidectomy	2	4.4	2	4.4		
Incision and drainage	2	4.4	1	2.2		
Jaboulays procedure	4	8.9	5	11.1		
Orchidopexy	1	2.2	0	0		
Mesh hernioplasty	21	46.7	17	37.8		
PLAS	2	4.4	4	8.9		
Varicocelectomy	1	2.2	0	0		
TURP	1	2.2	0	0		
Vaginal hysterectomy	3	6.7	0	0		
Testis implantation	0	0	1	2.2		
Cystolithotripsy	0	0	1	2.2		
Debridment + grafting	0	0	1	2.2		
RT URSL +DJS	0	0	1	2.2		
Sinus tract excision + repair	0	0	2	4.4		
Total	45	100.0	45	100.0		
Insignificant						

Graph10: Distribution of patients according to proposed surgery



STATISTICAL ANALYSIS-

With the anticipated average Mean and SD of duration of surgery in study group and control group 12 and 25.8(118±24.6 and 130.0±27 resp.)[1] The minimum sample size is 45 per group with 95% level of significance and 90%power.
We used the following formula for sample size calculation.

$$N = 2\left[\frac{\left(Z_{1-\alpha/2} + z_{\beta}\right) * S}{d}\right]^2$$

$Z_{1-\alpha/2}$ Level of significance=95%
$Z_{1-\beta}$ Power of study =90%
d=clinically significant difference between two parameters
SD= Common standard deviation

- Data is represented using Mean±SD, percentages and diagrams.
- Significant difference between quantitative data was found using Mann Whitney U test to compare two groups and Friedman's test was used to find the significant difference of paired data within groups.
- Similarly, Dun's multiple Post hoc test was used to compare two group variables of paired data. Wilcoxon signed paired rank test was used.
- Significant difference between Qualitative data was found using Chi square and Fisher's Exact test.
- If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.21 and Microsoft office 2007.

DISCUSSION

Postoperative pain may result in psychological, physiological, neuroendocrine, respiratory and cardiovascular problems ultimately increasing the risk of postoperative morbidity and mortality. Effective control of postoperative pain remains one of the most important & pressing issues in the field of anaesthesia[25]. Intra operative pain management has to be extended to the post operative period immediately to provide pre-emptive analgesia.

Narcotics and NSAIDS are the drugs easily available in the post operative period. Narcotic analgesia is associated with drowsiness, constipation, urinary retention, circulatory and respiratory disturbances and hence NSAIDS are preferred. In NSAIDS, routine oral administration is impractical in post operative period. First pass metabolism, decreased patient compliance, painful parenteral administration are few issues that make them inadvisable; there comes the importance of transdermal patch[20].

The efficacy of NSAIDs in reducing pain is largely a result of their capacity to inhibit cyclo-oxygenases 1 and 2 (COX-1 and COX-2), key enzymes in prostaglandin (PG) biosynthesis. Diclofenac is an NSAID, which exhibits anti-inflammatory, analgesic, and anti-pyretic activity and has been routinely used as an analgesic following surgical procedures.

Oral administration of NSAIDs, however, carries a risk of first pass metabolism with significant amount of the drug being lost before it is systemically absorbed.

Oral NSAIDs are also known to cause several adverse effects, particularly gastro intestinal effects, which are dose dependant[26].

Topical formulations of NSAIDs have been developed as alternate routes of drug administration, offering the advantage of local, enhanced drug delivery to the affected tissues with a lower incidence of systemic adverse effects. Topical NSAIDs have thus carved out a niche for themselves as therapeutic analgesic modalities with established benefits and lower incidence of adverse events.

Transdermal systems for NSAIDs are an innovative delivery mechanism replacing oral and IM forms of drug administration. Its bioavailability is 50%. It addresses the two significant problems posed by the traditional oral dosage form, gastric symptoms and the need for repeated doses. The transdermal delivery route also scores over the gel as it is not cream based, non greasy and most importantly it need not be applied at the local site of pain. The drug contained in the transdermal patch enters the body through skin and ultimately diffuses into capillaries for systemic delivery. The steady permeation of drug across the skin allows for more consistent serum drug levels is often the goal of therapy[26].

In this study, diclofenac was used as analgesic, both in its intramuscular and transdermal form, in patients undergoing lower abdominal and perineal surgeries under spinal anaesthesia.

The two formulations of diclofenac used in this study were 100 mg Transdermal Diclofenac patch (NU-patch) applied immediately after spinal anaesthesia in Group A, which is designed to remain at the site of application for 24 hours. The 50-sq. cm patch used in the study contains 100 mg of DiclofenacDiethylamine as its active agent and allows for sustained release of the drug. Injection Diclofenac 75 mg intramuscular was given half an hour before the end of surgery in Group B.

In this study patients in both groups were compared regarding age, gender and mean duration of surgery. Mean duration of surgery was 1hr 59 mins and 1hr 41 mins in group A and B respectively which was insignificant. The Duration of surgery is important as prolonged duration of tissue handling increases the local inflammation and edema which in turn increases the analgesic requirement.

In this study, pain was assessed with the help of VAS score at 2,4,6,8 hrs postoperatively.

In **Group A at**

- 2 hrs - 44 patients out of 45 had no pain, 1 patient had VAS score 1.
- 4 hrs-11 patients had VAS score 0, 22 patients had VAS score 1, 12 patients of score 2.
- 6hrs- 2 patients had VAS score 1.19 patients score 2, 20 patients score 3 and 4 patients of score 4.
- 8hrs -6 patients had VAS score 3, 23 patients score 4 and 10 patients 5.

In Group B at

- 2hrs -15 patients had VAS score 0, 26 patients has score 1, 4 patients scored 2.
- 4hrs-3 patients scored 1, 17 patients VAS score 2, 21 patients had score of 3, 4 patients of score 4.
- 6hrs - 0 patients scored VAS score 0and 1, 3 patients scored 3, 16 patients of VAS score 4 and 9 patients of score 5.
- 8 hrs -all patients had VAS score above 5 and rescue analgesia was supplemented hence VAS score was not calculated

VAS scores of both the groups were statistically analysed using Chi-square test, the P Value is < 0.0001 at 2hrs, 4hrs, 6hrs and 8hrs which was highly significant. The time of rescue analgesia was compared using Mann Whitney U test which showed the need of rescue analgesia in Group A was significantly prolonged (8 hrs 37 mins ±1 hr 4.2 mins) as compared to Group B i.e. 6hrs 19 mins± 58.6 mins. P value = 0.001 which was highly significant.

Rao DG et al also applied transdermal diclofenac patch at the beginning of surgery in their studies, similar to our study. In their study post operative analgesia was assessed by using VAS (Visual Analogue Scale) at 2, 6 and 12 hours post operatively. The mean duration of post-operative analgesia in their study was 8.9±2.16 hours for IM diclofenac and 10.28±2.54 hours for transdermal diclofenac patch[1]which were very consistent with Krishna et al studies[27].

In Banjare M et al studies, mean time for the requirement of rescue analgesia in the transdermal diclofenac patch group is 8.28 ± 0.86 hours while in IM diclofenac injection group mean time of the first analgesia is 6.63 ± 0.81 hours and was statistically significant (p=0.000)[33].

These findings correlate with Pragati et al[26] and Krishna et al[27] where transdermal patch group had duration of analgesia for 8 hours 6 minutes ± 1 hour 4 minutes.

The difference in mean of the number of times rescue analgesia required was found to be statistically significant in laparoscopic & gynaecologic surgeries & highly significant in orthopaedic surgeries (P = 0.003) in Soumya Samal et al studies[25].

Other studies in this aspect reported similar findings. F. Alessandri[28]&Colleagues found that 35% of patients required rescue analgesia in transdermal diclofenac group where as 71.7% of patients required rescue analgesia in placebo group ($p<0.001$) in patients undergoing laparoscopic surgery for benign gynaecologic conditions.

The transdermal drug delivery offers several advantages as it avoids the need for intravenous or intramuscular drug administration, and is an option in patients who are unable to swallow oral medications.

Transdermal drug administration also bypasses first-pass metabolism in the liver, and overcomes concerns regarding drugs that are poorly absorbed in the gastrointestinal tract[26].

An important concern with regard to transdermal drugs is the prolonged duration of onset and offset and that is why use of a transdermal agent requires planning and careful timing. In the postoperative setting, these agents are applied in anticipation of pain, and not after the patient experiences pain.

It has been found that if Diclofenac sodium is contained in a pressure sensitive adhesive material layer in combination with an organic acid, Diclofenac sodium can be converted to free based Diclofenac in the pressure sensitive adhesive material layer.

As a result the solubility of Diclofenac sodium is increased and transfer of the drug to the skin surface is facilitated, whereby Diclofenac sodium can easily penetrate through the stratum corneum as a barrier layer[20].

Because of its low systemic concentrations, topical NSAIDs have a reduced risk of upper gastrointestinal complications, such as gastric and peptic ulcers, and gastrointestinal nuisance symptoms, such as dyspepsia[26].

Parenteral drug delivery with intravenous, subcutaneous, or intramuscular injection, can gain easy access to systemic circulation with rapid drug absorption. Unfortunately, this rapid drug absorption is also accompanied by a rapid decline in the drug levels in the systemic circulation

Development of skin, subcutaneous and injection site muscle tissue necrosis leading to abscess formation named " NICOLAU" syndrome is rare but serious complication following IM diclofenac injection. Other side-effects to note include GI bleeding, renal dysfunction, and platelet dysfunction[20].

Topical and transdermal preparations are associated with a lower incidence of systemic side-effects because of the lower plasma concentration achieved by these modes. The most often side effects were local tissue reactions, such as pruritus and minor rash.

In our study, out of 45 patients in group A only 3 patients developed local erythematous rash at the site of application of patch. Out of the 45 in Group B, 9 of them were nauseous, 2 of them had pain and swelling at injection site, 1 developed gastritis and 1 patient had an episode of vomiting.

Similarly, in Banjare M et al[33] study, In IM diclofenac injection group 12 patients (40%) had pain at local site while in the transdermal diclofenac patch group, none of the patients had any side effects. These findings show that safety and compliance of the transdermal diclofenac patch is better. Safety profile was documented in MASON et al[42] in which topical NSAIDs were used for chronic musculoskeletal pain and he found only 6% local adverse event and 3% systemic adverse event.

Safety profile was also documented in PREDEL et al[41] in which the diclofenac patch used in blunt impact injuries was well tolerated.

CONCLUSION

90 patients of ASA grade I and II posted for elective lower abdominal and perineal surgeries were randomly allocated into two groups A and B. All patients were given spinal anaesthesia with 3 ml of Bupivacaine heavy with no adjuvant. Patients in Group A were applied transdermal diclofenac patch (NU patch) immediately after spinal anaesthesia on the either side of the chest wall or on the back. Patients in group B were given IM diclofenac half an hour before the end of surgery.

All patients were assessed post operatively by using VAS score at 2, 4, 6 and 8 hrs. At VAS score 5 or above Inj Tramadol 2mg/kg was given as rescue analgesia and the assessment was stopped. Side effects were also noted.

Based on the results obtained we conclude that the application of transdermal diclofenac patch (100mg) significantly prolong the time at which patient requires rescue analgesia i.e. 8hr 37 mins ± 1 hr 4.2 mins compared to 75 mg of intra muscular diclofenac i.e. 6hrs 19 mins ± 58.6 mins with minimal side effects.

Thus transdermal diclofenac patch is effective, non- invasive and safer way of treating postoperative pain.

SUMMARY

This study was undertaken on 90 ASA grades I and II patients of age 18-60 years of either sex posted for elective lower abdominal and perineal surgeries under subarachnoid block.

The aim and objective of our study was to evaluate the efficacy of transdermal diclofenac patch (100mg) vs IM diclofenac (75mg) for postoperative analgesia and the associated side effects. After approval from the ethical committee and written informed consent 90 patients were randomly allocated into Group A and Group B, each containing 45 patients.

Thorough pre anaesthetic check up was done and all patients were administered subarachnoid block in lateral position using 0.5% hyperbaric bupivacaine with a 25 G Quincke's needle .Both groups did not receive any intravenous analgesics or sedatives during the surgery.

Patients in group A will be applied with a Transdermal Diclofenac patch containing 100mg of Diclofenac diethylamine directly on the chest or the back at the beginning of surgery after subarachnoid block.

In group B 75mg of Diclofenac sodium will be given intramuscularly half an hour before the end of surgery.

Pain will be assessed postoperatively at 2,4,6,8 hrs using a visual analogue scale (VAS).If the VAS during any time during study is more or equal to 5 then injection Tramadol 2mg/kg will be administered intramuscularly as rescue analgesia.

Time duration between the administration of transdermal patch or intramuscular diclofenac and the demand for rescue analgesia will be noted. Side effects of transdermal diclofenac patch and IM diclofenac were noted.

Using Chi-square test and Mann Whitney U test the two groups were compared keeping the differences in mean age, sex, duration of surgery insignificant so that the results are consistent.

We observed that mean time at which rescue analgesia was administered was significantly prolonged in Group A i.e. 8hr 37 mins ± 1 hr 4.2 mins as compared to Group B i.e. 6hrs 19 mins ± 58.6 mins (P value is < 0.0001) which is highly significant.

The VAS scores at 2,4,6,8 hrs postoperatively were significantly low in patients with transdermal diclofenac patch.

Incidence of side effects were very low in group A i.e. only 3 patients complained of local skin irritation and rash whereas in group B almost 13 patients had different variety of complaints including nausea, vomiting, pain at the site of injection and gastritis.

So, based on the results of our study we conclude that transdermal diclofenac patch (100mg) is effective as well as safer mode of administration than IM Diclofenac 75mg for providing postoperative analgesia in lower abdominal and perineal surgeries with minimal side effects.

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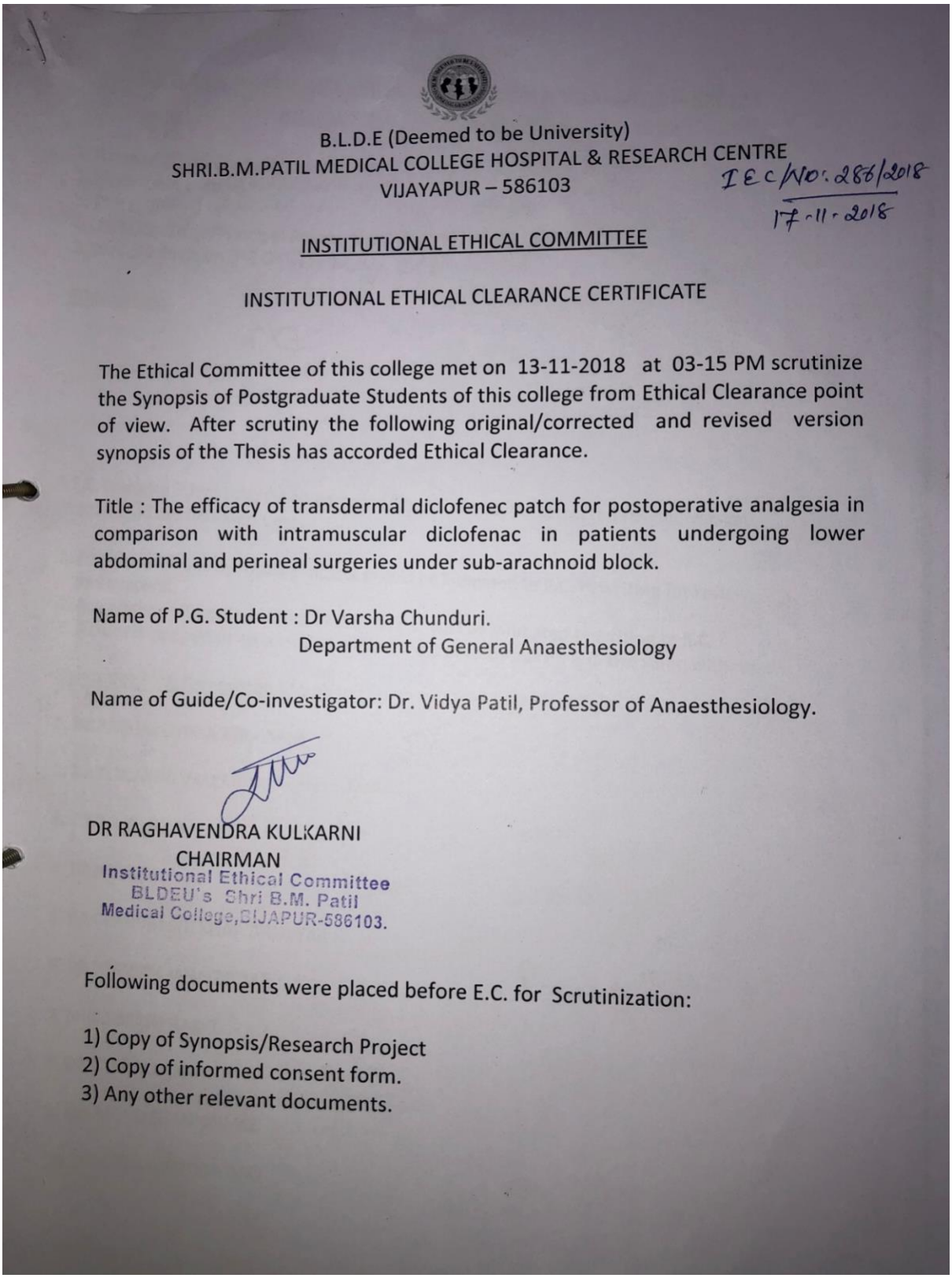
ANNEXURE I

ETHICAL COMITTEE CLEARANCE CERTIFICATE



B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC/NO: 286/2018
17-11-2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : The efficacy of transdermal diclofenec patch for postoperative analgesia in comparison with intramuscular diclofenac in patients undergoing lower abdominal and perineal surgeries under sub-arachnoid block.

Name of P.G. Student : Dr Varsha Chunduri.
Department of General Anaesthesiology

Name of Guide/Co-investigator: Dr. Vidya Patil, Professor of Anaesthesiology.

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

B.L.D.E.Us, SHRI.B.M.PATIL MEDICAL COLLEGE, VIJAYAPUR – 586103

INSTITUTIONAL ETHICAL COMMITTEE, Date : 13-11-18

1. Name of UG/PG Student/Researcher : Dr. Varsha Chunduri
2. Department : Anaesthesiology
3. Title : The efficacy of - - - - - - Block
4. Guide/Co-Guide/Principal Researcher : Dr Vidya Patil
5. Date of Admission (PG Only) : May 2018

Observation:

OC

I.E.C. Remarks: Ethical clearance accorded/be chairman after corrected revised version Is submitted by stipulated time.

1. Any alternation in Synopsis protocol should be intimated to E.C. in writing for review and approval.
2. Any adverse effects to subject of the study should be intimated in writing to E.C.
3. If study is stopped or an included patient is out of study inform E.C. the same with reason.

Signature of the Committee Members:

1. DR RAGHAVENDRA KULKARNI
2. DR TEJASWINI VALLABHA
3. DR.B.R.YELIKAR
4. DR P.BJAJU — P.Bjaju
5. DR CHANDRASHEKHAR BHUYYAR
6. DR PRANESH JAHAGIRDAR — Pranesh
7. SHRI.SURESH HAKKI
8. DR G V KUKARNI
9. DR.MOHD SHANNAWAZ
10. DR RAGHAVENDRA RAO

ANNEXURE II

INFORMED CONSENT FORM

B.L.D.E.U.'s SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYPURA – 586103, KARNATAKA

TITLE OF THE PROJECT :" THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH FOR POSTOPERATIVE ANALGESIA IN COMPARISON WITH INTRAMUSCULAR DICLOFENAC IN PATIENTS UNDERGOING LOWER ABDOMINAL AND PERINEAL SURGERIES UNDER SUB-ARACHNOID BLOCK

PRINCIPAL INVESTIGATOR : DR VARSHA CHUNDURI

Department of Anaesthesiology

Email: chundurivarsha@gmail.com

PG GUIDE : Dr. VIDYA PATIL

Professor and HOD

Department of Anaesthesiology

B.L.D.E. University's Shri B. M. Patil Medical College Hospital Centre & Research, Sholapur Road, Vijayapura

PURPOSE OF RESEARCH:

I have been informed about the above mentioned study and have been explained about the reason for doing this study (to compare the efficacy of transdermal diclofenac patch in comparison with intramuscular diclofenac for postoperative analgesia) and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

RISKS AND DISCOMFORTS:

I understand that I/my ward may experience some postoperative pain due to inadequate analgesia and I understand that necessary measures will be taken to reduce these complications as and when they arise.

BENEFITS:

I understand that my/my wards participation in this study will help in finding out appropriate medication for analgesia following the surgery.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time **Dr.VARSHA CHUNDURI** are available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me to keep for careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that **Dr. VARSHA CHUNDURI** will terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to _____ the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Date: DR.VIDYA PATIL (guide)

DR. VARSHA CHUNDURI (Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that **Dr. VARSHA CHUNDURI** has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

_____ (PARTICIPANT) DATE:

_____ (Witness to above signature) DATE:

ANNEXURE – III

(PROFORMA)

STUDY: "THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH FOR POSTOPERATIVE ANALGESIA IN COMPARISON WITH INTRAMUSCULAR DICLOFENAC IN PATIENTS UNDERGOING LOWER ABDOMINAL AND PERINEAL SURGERIES UNDER SUB-ARACHNOID BLOCK"

Serial No: Group [A] Group [B]

Name: I.P. No. : Age:

Sex: DOA: DOS:

Preoperative diagnosis:

Proposed surgery:

PRE- ANESTHETIC EXAMINATION

BRIEF SIGNIFICANT HISTORY:

Past History:

Presence of any co-morbid conditions – DM/ HTN/ IHD/ CVD/Asthma/ Bleeding disorders/ Drug allergy/ any other:

Previous anaesthetic exposure:

Present medication/Previous drug therapy:

General Physical Examination:

Pallor/ Icterus/ Cyanosis/ Clubbing/ Lymphadenopathy/ Pedal edema

Vitals

Pulse rate: Blood Pressure: Respiratory rate:

Weight: Teeth: TMJ movement:

Mallampatti grade: **SPINE**

Systemic Examination:

Cardiovascular system: Central Nervous system: Respiratory system: P/A:

INVESTIGATIONS:

HEMOGLOBIN: TLC: PLATELET COUNT:

BLOOD UREA: SERUM CREATININE:

BT/CT

RBS: CHEST X-RAY: ECG:

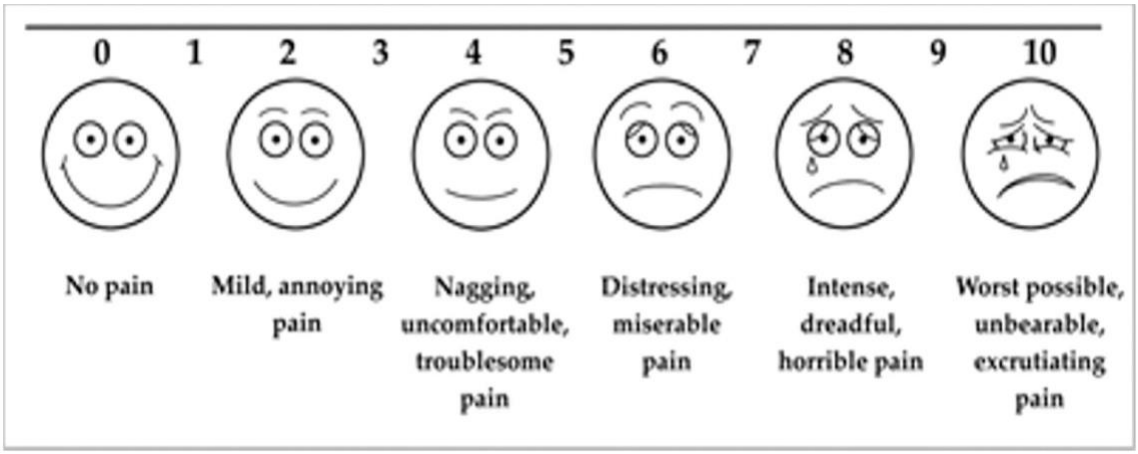
ASA Grade:

Anaesthetic Technique: Spinal anaesthesia

Drug and Dose used:

Duration of surgery:

POSTOPERATIVE FOLLOW UP



TIME: 2HRS 4HRS 6HRS 8HRS

ANY SIDE EFFECTS:

SIGNATURE OF THE ANAESTHESIOLOGIST:

Table- 1:

The time duration between administration of drug and rescue analgesia	GROUP-A	GROUP-B

TABLE-2:

VAS SCORE	TIME (IN HRS) {POST OPERATIVELY}							
	GROUP-A				GROUP-B			
	2HRS	4HRS	6HRS	8HRS	2HRS	4HRS	6HRS	8HRS
0								
1								
2								
3								
4								
5								

KEY TO MASTER CHART

M- Male

F-Female

RT- Right

LT-Left

YRS-Years

HRS-Hours

VUJ- Vesicoureteric junction

URSL+DJS- Ureteroscopic lithotripsy with DJ stenting

PLAS- Posterior lateral anal sphincterotomy

BPH- Benign prostatic hyperplasia

AUR- Acute urinary retention

TURP- Transurethral resection of the prostate

UV prolapse- Uterovaginal prolapse

SI .NO.	INPATIENT NUMBER	AGE(YRS	SEX	PREOPERATIVE DIAGNOS	PROPOSED SURGERY	ASA GRADE	DURATION OF SURGERY (HOURS	VISUAL ANALOUGE SCORES 2HRS	4HRS	6HRS	IME OF RESCU HR	ALGESIA(HRS)	SIDE EFFECTS
1	44089	21	M	Fistula in ano	open fistulectomy	I	1	1	3			4.45	NIL
2	44079	45	M	LT indirect inguinal hernia	m esh hernioplasty	I	2	1	3			5	NIL
3	44159	22	M	RT inguinal hernia	m esh hernioplasty	I	1.5	0	2	4		6.2	NIL
4	43867	30	F	Umbilical hernia	m esh hernioplasty	I	1.5	2	4			5.2	NIL
5	43935	20	M	Fistula in ano	fistulectomy	I	1	1	3			5.3	NAUSEA
6	42930	58	M	LT inguinal hernia	mesh hernioplasty	I	1.5	2	4			4.3	NIL
7	41808	41	F	acute appendicitis	ppen appendicectomy	II	2	1	3	5		6	nil
8	41807	59	M	rt hydrocele	rt jaboulays	II	1	1	3			5.45	NIL
9	322	42	M	Perianal sinus + rectal pro	nus tract ecision+repa	I	2.5	2	4			5	NIL
10	431	30	M	LT inguinal hernia	mesh hernioplasty	I	1.5	1	2	4		6.15	NAUSEA
11	607	27	M	RT VUJ calculus	RT URSL +DJS	I	1.5	1	3	5		6	NIL
12	605	45	M	Vesical calculus	cystolithotripsy	II	1	1	2	4		6.2	NIL
13	649	17	M	Epigastric hernia	mesh hernioplasty	I	I	1	3			5.15	NIL
14	43875	33	M	Peri anal discharge sinus	sinus tract excision	II	2	0	3			5.3	NAUSEA
15	567	25	F	Chronic fissure in ano	PLAS	I	1	0	2	4		6.1	NIL
16	292	50	M	LT bakers cyst	excision	II	1.5	1	3			5	NIL
17	11	60	M	RT direct inguinal hernia	mesh hernioplasty	II	1.5	0	2	5		6	NIL
18	1115	60	M	RT inguinal hernia	mesh hernioplasty	II	1.5	1	2	4		6.3	Vomiting
19	43826	48	M	fistula in ano with fissure i	fistulectomy+PLAS	II	1.5	2	4			5	NAUSEA
20	640	50	M	Ulcer over rt inguinal regio	debridment+grafting	II	2	1	3	5		6	NIL
21	43449	60	M	LT inguinal hernia	mesh hernioplasty	II	1.5	1	3			5.4	NIL
22	44103	60	M	rt hydrocele	rt jaboulays	II	1	1	2			5.45	NAUSEA
23	43045	60	M	Healing ulcer over scrotun	B/L testis implantation	II	2	0	2	4		6.45	NIL
					into thigh+ suturing								
24	1795	35	M	acute appendicitis	ppen appendicectomy	I	1	1	2	4		6.3	NIL
25	431	26	M	LT hydrocele	lt jaboulays	II	1.5	0	3			5.4	NIL
26	2116	40	F	Grade III haemorrhoids	haemorrhoidectomy	I	1	1	3	5		6	NAUSEA
27	2040	50	M	fissure in ano	PLAS	II	1.5	0	2	4		6.25	NIL
28	1136	23	M	RT bubonocele	rt mesh hernioplasty	I	1.5	0	1	3		6.15	NIL
29	2078	53	M	RT bubonocele	rt mesh hernioplasty	II	1.5	1	2	4		6.45	NIL
30	1941	60	M	Grade IV Harmorrhoids	haemorrhoidectomy	II	1	0	2	4		6.25	NIL
31	1991	60	M	RT inguinal hernia	mesh hernioplasty	II	1.5	1	3	5		6	NIL
32	2394	28	F	acute appendicitis	ppen appendicectomy	I	1.5	1	2	4		6.45	NAUSEA
33	2424	18	M	acute appendicitis	ppen appendicectomy	I	1	1	3	4		6.3	NAUSEA
34	2327	60	F	LT bakers cyst	excision	II	1	1	3	5		6	NIL
35	2207	60	M	rt hydrocele	rt jaboulays	II	1	1	3	4		6.2	NIL
36	2450	60	M	LT hydrocele	lt jaboulays	II	1	0	1	3		6.5	NIL
37	41678	45	M	RT inguinal hernia	mesh hernioplasty	II	1.5	0	2	4		6.3	Pain at injection site
38	2940	25	F	Chronic appendicitis	ppen appendicectomy	I	1.5	1	3			5	NIL
39	3339	54	M	Umbilical hernia	mesh hernioplasty	I	2	0	2	4		6.4	Gastritis
40	3313	60	M	RT direct inguinal hernia	mesh hernioplasty	II	1.5	0	2	5		6	NIL
41	3377	40	F	LT canal of neck hernia	mesh hernioplasty	I	1.5	1	3			5.35	NIL
42	3444	43	M	Chronic fissure in ano	PLAS	I	1	0	1	3		6.55	NIL
43	13286	60	M	Fissure in ano	PLAS	II	1	1	3	5		6	NAUSEA
44	13379	54	F	Peri anal abscess	Incision and drainage	II	1	1	3			5.3	Pain at injection site
45	13560	50	M	RT inguinal hernia	mesh hernioplasty	II	1.5	0	2	4		6.15	NIL

SI .N	INPATIENT	AGE(YI	SEX	PREOPERATIVE DIAGNOS	PROPOSED SURGERY	ASA GRA	DURATION OF	VISUAL ANALOGUI			E SCO	TIME OF	SIDE EFFE
	NUMBER						(HOURS)	2HRS	4HRS	6HRS	8HRS	ANALGESIA(HRS)	
1	13910	25	M	Fistula in ano	fistula tract excision	I	1	0	0	1	3	8.45	NIL
2	13518	30	m	bilateral inguinal hernia	bilateral hernioplastyI	I	2 .30	0	1	2	4	9	NIL
3	14125	31	M	fissure in ano	PLAS	I	1	0	1	2	4	8.3	NIL
4	14086	30	M	Left inguinal testis	left orchidopexy	I	1.5	0	0	2	4	8.3	NIL
5	13908	23	F	Rectovaginal fistula	fistulotomy	I	2.5	0	1	2	3	10	NIL
6	14283	55	M	RT Direct Hernia	Hernioplasty	II	1	0	0	2	4	8.15	nil
7	14535	22	m	Rt. gradeII varicocele	rt. Varicocectomy	II	2	0	1	2	4	9.15	NIL
8	15153	55	M	RT inguinal hernia	Hernioplasty	II	1.5	0	1	3	5	8	NIL
9	15158	30	M	fissure in ano	PLAS	I	1	0	0	2	4	8.45	NIL
10	15855	32	M	Epididymal cyst	excision of cyst	I	1.5	0	0	2	3	9.45	NIL
11	15874	28	M	RT inguinal hernia	Hernioplasty	I	2	0	1	3	5	8	NIL
12	16368	31	M	RT inguinal hernia	mesh hernioplasty	I	2	0	1	2	4	8.4	NIL
13	459	24	M	distal penis urethral strictu	BMG urethroplasty	I	3	1	2	3	5	8.05	RASH
14	818	60	F	Acute appendicitis	open appendicectomy	II	2	0	1	3	5	8	NIL
15	40481	60	M	RT inguinal hernia	mesh hernioplasty	II	1.5	0	2	3	4	8.3	NIL
16	1321	50	M	Umbilical hernia	mesh hernioplasty	II	1	0	2	4		7.45	NIL
17	961	60	M	BPH with AUR	TURP	II	2.5	0	2	3	4	8.2	NIL
18	1923	60	F	Incisional hernia	mesh hernioplasty	II	2.5	0	1	3	4	8.15	NIL
19	2882	23	F	RT inguinal hernia	mesh hernioplasty	I	1.5	0	0	2	3	9.3	NIL
20	3518	35	M	LT indirect inguinal hernia	mesh hernioplasty	I	1.5	0	1	2	4	9	nil
21	13393	40	M	appendicitis + RT VUJ calc	Appendicectomy +URSL	I	2.5	0	2	4		7.3	NIL
22	3617	30	F	Umbilical hernia	hernioplasty	I	1.5	0	0	2	4	8.3	NIL
23	1438	60	F	LT parietal wall abscess	incision and drainage	II	1	0	0	2	4	9	nil
24	12601	60	M	RT inguinal hernia + LT hyc	Hernioplasty + Jaboulay	II	2	0	1	3	5	8	RASH
25	12801	36	M	Bilateral hydrocele	bilateral jaboulays	I	1.5	0	0	2	4	8.4	NIL
26	12923	35	F	Umbilical hernia	mesh hernioplasty	I	1.5	0	1	3		7.5	NIL
27	12909	25	F	Recurrent appendicectom	appendicectomy+tubec	I	1.5	0	1	2	4	9	NIL
28	12904	51	M	LT hydrocele	lt jaboulays	II	1	0	0	2	4	8.35	NIL
29	12995	60	M	RT inguinal hernia	mesh hernioplasty	II	1	0	1	2	4	8.15	nil
30	12974	55	M	LT inguinal hernia	mesh hernioplasty	II	2.5	0	1	2	3	9.05	nil
31	13412	60	F	Grade 4 haemorroids	Haemorrhoidectomy	II	1	0	2	3		7.45	NIL
32	13607	54	M	LT inguinal hernia	mesh hernioplasty	II	1.5	0	1	3	4	8.3	NIL
33	13625	38	M	RT inguinal hernia	mesh hernioplasty	I	1	0	1	3	5	8	NIL
34	13783	60	M	LT indirect inguinal hernia	mesh hernioplasty	II	1.5	0	2	3	4	8.2	NIL
35	13771	37	F	Infra umbilical hernia	mesh hernioplasty	I	1.5	0	2	3	5	8	nil
36	16154	52	F	second degree UV prolaps	vaginal hystrectomy	II	2	0	1	3	5	8.15	NIL
37	16279	50	F	UV prolapse	vaginal hystrectomy	II	2.5	0	2	4		7.4	NIL
38	16006	36	F	UV prolapse	vaginal hystrectomy	I	2	0	1	3	5	8	NIL
39	20598	54	F	LT inguinal hernia	mesh hernioplasty	II	1.5	0	2	3	4	8.25	rash
40	20639	42	M	Acute appendicitis	open appendicectomy	II	1.5	0	1	3	5	8.05	nil
41	20903	52	M	RT inguinal hernia	mesh hernioplasty	II	1.5	0	1	2	4	8.45	NIL
42	20894	32	M	RT hydrocele	RT jaboulays	I	1	0	0	1	3	10	nil
43	20987	18	M	LT hydrocele	lt jaboulays	I	1	0	2	3	4	9	NIL
44	13652	60	M	Fourniers gangrene +glute	incision and drainage	II	1.15	0	2	4		7.3	NIL
45	17850	25	M	Grade 3 haemorrhoids	Haemorrhoidectomy	II	1	0	1	3	4	9.15	NIL