"A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH WITH INTRAMUSCULAR DICLOFENAC AS PRE-EMPTIVE ANALGESIA IN PATIENTS UNDERGOING LICHTENSTEIN'S INGUINAL HERNIOPLASTY"

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ENDORSEMENT

This is to certify that the dissertation entitled **"A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH WITH INTRAMUSCULAR DICLOFENAC AS PRE-EMPTIVE ANALGESIA IN PATIENTS UNDERGOING LICHTENSTEIN'S INGUINAL HERNIOPLASTY"** is a bonafide research work done by **CANDIDATE REG NO. BH0113003**.

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LIST OF ABBREVIATIONS USED

BP	-	Blood pressure
cGMP	-	Cyclic guanosine monophosphate
COPD	-	Chronic obstructive pulmonary disease
COX	-	Cyclooxygenase
DNA	-	Deoxyribonucleic acid
e.g.	-	For example
ECG	-	Electrocardiogram
EMLA	-	Eutectic mixture of local anesthetic
ESR	-	Erythrocyte sedimentation rate
FDA	-	Food and Drug Administration
GA	-	General anaesthesia
i.e.	-	That is,
IASP	-	International Association for the Study of Pain
mg	-	Milligrams
Min	-	Minutes
ml/min	-	Milliliters per minute
mm Hg	-	Millimeters of mercury
n	-	Total number
NMDA	-	N-methyl-D-aspartate
NRS	-	Numeric Rating Scale
NSAIDs	-	Non-steroidal anti-inflammatory drugs
NYHA	-	New York Heart Association
OAS	-	Oral Analog Scale
p	-	Probability

PCA	-	Patient controlled analgesia
PPARgamma	-	Peroxisome proliferator activated receptor gamma
PR	-	Pulse rate
PVB	-	Paravertebral blocks
RR	-	Respiratory rate
SD	-	Standard deviation
TDDS	-	Transdermal drug delivery systems
Temp	-	Temperature
TENS	-	Transcutaneous electrical nerve stimulation
TTS	-	Transdermal therapeutic systems
VAS	-	Visual Analog Scale
viz,	-	Namely

ABSTRACT

Background and objectives

Postoperative pain is a common problem in any surgical setup and requires appropriate analgesia. This study was planned to assess the efficacy of transdermal diclofenac patch, a new modality in the surgical pain management, with intramuscular diclofenac sodium (75 mg) as pre-emptive analgesia in patients undergoing Lichtenstein's inguinal hernioplasty.

Methodology

This one year randomized controlled trial was carried out in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2014 to December 2014. A total of 60 patients diagnosed with inguinal hernia and posted for Lichtenstein's inguinal hernioplasty were studied. Patients were divided into two groups of 30 each as Group A (single transdermal diclofenac patch [100mg]) and Group B (Single intramuscular injection of diclofenac sodium [75mg]). Patients were evaluated for requirement of rescue analgesia in first 24 hours and time at which patient first requires rescue analgesia.

Results

All the patients in group A and B were males (100%) and mean age was 36.30 ± 7.75 years in group A compared to 35.33 ± 8.40 years in group B ($p=0.645$). The mean duration of hernia, type and extent of hernia, mean duration of surgery ($p>0.050$) were comparable in group A and B. Pain as measured by VAS immediately post operative and at three, six, twelve and twenty four hours

(p>0.050) was comparable in group A and B. Also, the mean number of doses and time request for first for dose of rescue analgesia did not differ significantly (p>0.050). In group A, erythema was noted in 3.33% of the patients while in group B, 6.67% had pain at injection site and 3.33% had nausea (p=0.612).

Conclusion and interpretation

Transdermal diclofenac patch is as effective as intramuscular diclofenac sodium in the management of post operative pain among patients undergoing Lichtenstein's inguinal hernioplasty.

Keywords

Intramuscular diclofenac sodium; Lichtenstein's inguinal hernioplasty; Post operative pain; Transdermal diclofenac patch;

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INTRODUCTION

The experience of pain is complex, multifaceted and "an unpleasant sensory and emotional experience" as defined by the International Association for the Study of Pain. It is a personal, subjective experience that involves sensory, emotional and behavioral factors associated with actual or potential tissue injury. The differential behavior response to surgical incision can be influenced by many variables including global (i.e. personality, gender, age, cultural background, pre-existing pain syndromes, genetic makeup, type of surgical approach) and specific (i.e. fear, anxiety, depression, anger and coping, psychological factors).[1] Pathophysiology of acute pain, includes changes in neuroendocrine, respiratory and renal function, gastrointestinal activity, circulatory and autonomic nervous system activity.[2]

In postoperative patients, due to peripheral tissue injury, two kinds of modifications are seen in the responsiveness of the nervous system. These are peripheral sensitization, in which the threshold of nociceptive afferent peripheral terminals is reduced; and central sensitization, in which there is an increase in the excitability of spinal neurons. Due to these changes an overall hypersensitivity state results in the postoperative period. Postoperative pain could be reduced by prevention of this hypersensitivity state. This forms the basis of pre-emptive analgesia.[3,4]

Non-steroidal anti-inflammatory drugs (NSAIDs) block the activity of cyclooxygenase and inhibit the synthesis of prostaglandins, leading to anti-inflammatory and analgesic effects. Diclofenac sodium, which is available in various forms, is a commonly used non-selective NSAID.[5-7]

The diclofenac transdermal patch is a recently introduced drug delivery system for the management of postoperative pain. Transdermal patches are innovative topical delivery systems for diclofenac as well as other NSAIDs that have been developed in the recent past. These patches offer the advantage of sustained delivery of the drug[8] with lesser systemic side effects due to lower plasma concentrations.[9,10]

A hernia, as defined by Astley Cooper, is the protrusion of any viscus from its proper cavity. The protruded viscus is usually contained in a sac-like structure, which is formed by the membrane which naturally lines the cavity.[11] Various different types of abdominal wall hernias have been identified and are associated with various eponyms. Hernias are diagnosed either during a routine physical examination for other medical complaints or when the patient develops a complication associated with the hernia.[11]

An inguinal hernia is the protrusion of contents of the abdominal cavity through the inguinal canal. There are two types of inguinal hernia, direct and indirect, based on their relationship to the inferior epigastric vessels. Direct inguinal hernia occurs when abdominal contents herniate through the weakened posterior wall of the inguinal canal and appear medial to the inferior epigastric vessels. An indirect inguinal hernia appears lateral to the inferior epigastric vessels, when the abdominal contents protrude through the deep inguinal ring; this could be caused by failure of obliteration of the processus vaginalis.[11]

Inguinal hernia is one of the most common problems encountered by general surgeons and may be associated with significant complications.[12] Globally, it is the

most common type of hernia, representing approximately 75% of all abdominal wall hernias.[12-14] Inguinal hernia repair is one of the most common general surgical procedures performed worldwide, accounting for 10-15% of all the surgical procedures. It is the second most common surgical procedure after appendicectomy.[13-15] It is estimated that more than 20 million inguinal hernia repairs are carried out worldwide each year, the rates varying between countries from approximately 100 to 300 per 100,000 population per year.[16] Data from developing countries is limited hence the exact prevalence and incidence is not known.

Although numerous surgical approaches have been developed to treat inguinal hernias, the Lichtenstein tension-free mesh repair remains the standard. This technique is widely used since it has a low rate of recurrences and complications.[11] However, immediate postoperative pain is an important issue that can delay ambulation and prolong hospital stay.[17] Besides, the presence of chronic pain after hernia repair, which can affect up to 50% of patients, is a growing concern.[18] This seems to be related to inadequate postoperative pain management, which makes control of postoperative pain fundamental. Opioids, non-steroidal anti-inflammatory drugs and analgesics are commonly used to treat postoperative pain.[18]

This clinical study was undertaken to compare the efficacy of transdermal diclofenac patch (100mg) with intramuscular diclofenac sodium (75mg) as pre-emptive analgesia in patients undergoing Lichtenstein's inguinal hernioplasty by estimating the number of times patients require rescue analgesia in the first 24 hours following surgery and the time at which the patients require rescue analgesia after surgery.

This study was conducted in patients undergoing inguinal hernioplasty as it is a standard and commonly performed procedure and to remove variables in the study.

OBJECTIVES

This study was carried out to compare the efficacy of transdermal diclofenac patch (100mg) with intramuscular diclofenac sodium (75mg) as pre-emptive analgesia in patients undergoing Lichtenstein's inguinal hernioplasty.

The objectives of the present study were;

1. To estimate the number of times the patient requires rescue analgesia in the first 24 hours following surgery.

2. To estimate the time at which the patient requires rescue analgesia after surgery.

REVIEW OF LITERATURE

ACUTE POST OPERATIVE PAIN

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". This definition declares that pain, as well as having a physiological basis has a very real psychological or subjective component.[19]

Pain has always been a major concern of humankind since the beginning and has been the object of ubiquitous efforts to understand and control it. Management of pain remains one of the most important issues of health care professionals.[20]

Immediate postoperative pain is an important issue that can delay ambulation and therefore, delay hospital discharge. Besides, the presence of chronic pain after hernia repair, which can affect up to 50% of patients, is a growing concern. This picture seems to be related to inadequate postoperative pain treatment, which makes control of postoperative pain fundamental.[18]

Postoperative pain is under treated for a number of reasons which include, lack of knowledge regarding the effective dose ranges and duration of action of opioids and unfounded fear of respiratory depression and addiction in hospitalized patients experiencing pain. The concept of postoperative pain management by anaesthesiologists is growing. These, along with the advent of newer opioids with higher safety levels and better techniques of administration, have brought about large improvements in the successful alleviation of postoperative pain.

Postoperative pain is caused due to alterations in the pain pathways as a response to peripheral tissue injury which leads to a state of hypersensitivity. Peripheral sensitization reduces the threshold of nociceptors while central sensitization results in a state of hyperalgesia.

Factors that modify postoperative pain

a. The site, nature and duration of surgery.
b. The type and extent of the incision and other surgical trauma.
c. The physiologic and psychological make up of the patient.
d. Presence of complications related to surgery.
e. Preoperative psychological, physiologic and pharmacologic preparation of the patient.
f. The anesthetic management before, during and after surgery.
g. The quality of post operative care.[21]

Management of pain

The common methods adopted for giving postoperative pain relief are:

By increasing the pain threshold

Pharmacologic

a. Centrally acting analgesics
b. Peripherally acting analgesics

Non-pharmacologic

a. Counseling
b. Hypnosis

By modulating the pain pathways

a. Transcutaneous electrical nerve stimulation (TENS)
b. Acupuncture
c. Cryotherapy
d. Heat therapy

By interrupting the nociceptive pathway

a. Nerve blocks and Neurolysis
b. Surgical ablation – Cryoanalgesia

Adequate analgesia in the postoperative period is a priority in enabling the post-surgical patient to cope with the tissue damage of surgery. Irrespective of whether the hernia is repaired under local, regional or general anaesthesia, the patient will not be deemed fit for discharge until the pain of surgery is controlled with appropriate analgesia. Inguinal hernias have been repaired under general, regional or local anaesthesia. It is well established that open inguinal hernia repair can be conducted under local anaesthesia, regardless of comorbidity and with minimal morbidity.[22]

Paravertebral blocks (PVB) have recently been used as the sole anaesthetic technique and randomized against general anaesthetic (GA) fast tracking for inguinal hernia repair. Patients who had their hernia repaired using PVB were discharged sooner, ambulated earlier, had less postoperative adverse events including acute postoperative pain than those in the GA group.[23]

Acute Postoperative Pain Following Lichtenstein's repair

It is thought that acute post inguinal hernia surgery pain, that is pain in the first few days and weeks following surgery can influence the development of long term chronic pain. Therefore adequate and effective immediate postoperative pain control not only determines timing of discharge but may also contribute to a reduction in chronic pain. It has been suggested that treatment designed to prevent pain in advance of surgical trauma may be more effective than simply instituting analgesic therapy in response to the pain after surgery.

In a simplistic model of pain, the analgesic component of anaesthesia can be considered to block a pathway. Examples are binding to peripheral and central receptors (opiates) or inhibition of cyclo-oxygenase synthesis (NSAID).[24.25] Preferably different classes of analgesics and different sites of analgesic administration are used. The concept of multimodal analgesia is to provide superior pain relief while reducing the analgesic-related side effects.[25,26]

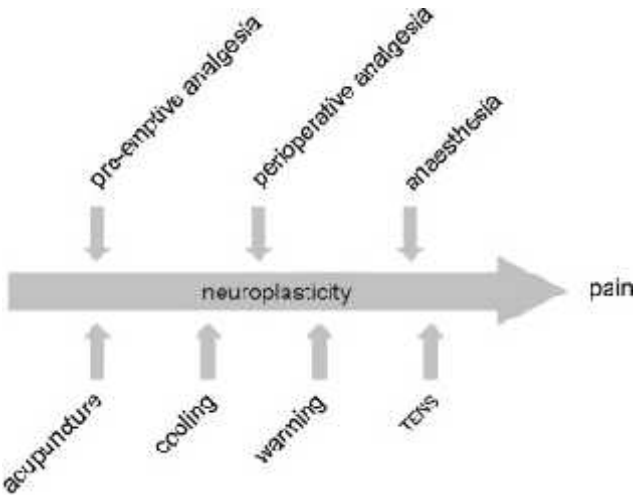


Figure 1. Medical pain reducing interventions. Above the arrow: anaesthesia, below the arrow: adjuvants[25]

The influence of some non-pharmacological interventions on neuronal transmission has been studied. Cooling has been hypothesized to decrease the excitability of free nerve endings and to slow down noxious stimuli transmission whereas warming was suggested to diminish pain by lowering the local inflammatory response. Both cooling and warming were reported to diminish postoperative pain in clinical studies.[25]

Based on the gate-control-theory, non-noxious stimuli of the perioperative field may inhibit passage of noxious stimuli, a principle that is applied in transcutaneous electrical nerve stimulation (TENS) therapy.[24] Based on the same principle, analgesia can be provided with acupuncture.[25,27]

There is increasing recognition that long-term changes occur within the peripheral and central nervous system following noxious input.[24,28] This neuronal plasticity may alter the response to sensory input. Roughly translated for practical use, this is the memory for pain and is the theoretical base for pre-emptive analgesia. Preoperative and direct postoperative pain is associated with chronic pain. It is unclear whether this association is an indication of neuronal plasticity or predisposing constitution of the patient or both. The use of perioperative analgesics is anyhow to diminish direct postoperative pain, preferably established by multimodal analgesia. Treatment with analgesia before noxious stimuli cause excitation of the nociceptors is called pre-emptive analgesia. Its benefit has been shown in basic animal models and in several studies on pre-emptive analgesia in human clinical models, however, these results could not be confirmed.[25]

Preemptive analgesia

The use of an analgesic drug before surgical incision is a promising and innovative strategy for better pain control in the perioperative period. Pre-emptive analgesia deals with pharmacological intervention which is initiated prior to a painful stimulus with the goal of inhibiting nociceptive mechanisms before they are triggered. Pre-emptive analgesia includes three objectives: to reduce pain arising from the activation of inflammatory mechanisms which is triggered by surgical incision; to impede the pain memory response of the central nervous system; and to avoid the development of chronic pain by ensuring a good control of postoperative pain.

Pre-emptive analgesia has been shown to reduce postoperative pain as well as analgesic requirement. When compared to postoperative analgesia, it has been associated with lesser side-effects like nausea and vomiting, contributing to a smooth and rapid recovery and reduced hospital stay. It has also been associated with a reduced incidence of chronic pain. However, preemptive analgesia has certain drawbacks such as a longer time taken for onset of action and to reach effective serum levels before surgery, while postoperative analgesia acts immediately without a latency period.

ANATOMICAL AND PHYSIOLOGICAL ASPECTS OF PAIN PERCEPTION

Definition of pain[28,29]

Pain is an extraordinarily complex sensation which is difficult to define and equally difficult to measure in an accurate objective manner. It has been variously defined as:

An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damages. Pain is a complex constellation of unpleasant sensory, perceptual, and emotional experiences with associated autonomic psychological and behavioral responses.[28,29] Pain can be represented as a Venn diagram.

Figure 2. Pain represented as Venn diagram

This shows that the sensation of pain differs among individual patients

Emotional – varies according to patient's psychological composition.

Rational – varies with patient's previous experience, insight and motivation.

Physical – varies with type and site of surgery.

Postoperative pain is usually transitory, which shows progressive improvement over a relatively short time course.

All pain perception depends upon the transmission of impulses through pathways within the nervous system from the site of the stimulus to the higher centers of the brain; they may impinge upon our consciousness and be interpreted. The principal parts of the nervous system involved in this process are:

- Receptors in the skin and other organ.
- Peripheral nerves.
- Neuronal aggregates in the spinal cord and associated fiber tracts.
- The brainstem and thalamus.
- The limbic system.
- The cerebral cortex.
- Other parts of the brain indirectly involved.

PAIN THEORIES IN THE TWENTIETH CENTURY[28,29]

Peripheral Pattern Theory by Sinclair and Weddell in 1950's stated that all fiber endings (apart from those that innervate hair cells) are alike, so that the pattern of pain is produced by intense stimulation of nonspecific receptors.

Central Summation Theory by Livingston in 1943 suggested that the intense stimulation resulting from tissue and nerve damage stimulates fibers which project to internuncial neuron pools in the spinal cord which in turn project to brain mechanisms that underline pain perception.

Strong proposed the *Fourth Theory of Pain* and believed that pain can be separated into two parts: pain perception and the reaction to pain.

In 1959 *Sensory Interaction Theory* was proposed by Noordenbos who believed that large fibers inhibit and small fibers excite central transmission neurons, which project to a multisynaptic system that leads to the brain.

Gate Control Theory The term "Gate Control" is now applied to the rapidly acting mechanisms which accept and control the passage of impulses from the afferent fiber input to cells which may then trigger the various effector systems and evoke sensation.

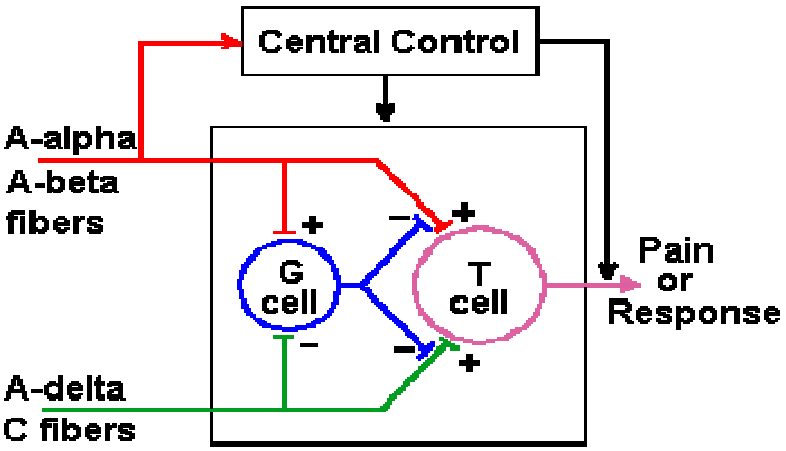


Figure 3. Gate control theory

Melzack and Wall (1965) observed in decerebrated and spinal cats, that peripheral stimulation of large myelinated fibers produced a negative dorsal root potential and that stimulation of C fibers caused a positive dorsal root potential. They postulated that these potentials, which were a reflection of presynaptic inhibition or excitation, modulated the activity of secondary transmitting neurons (T cells) in the dorsal horn, and that this modulation was mediated through an

inhibitory interneuron (I cell) placed the T cell in lamina V of the dorsal horn and the still unidentified inhibitory cells, in laminae II and III. The essence of this theory is the large diameter fibers excite the I cells, which is turn cause a presynaptic inhibition of T cells. Conversely, the small pain afferent fibers inhibit the I cells leaving the T cells in an excitatory state.

Melzack and Wall emphasized that the transmission of pain impulses from the dorsal horn must also be under the control of a descending system of fibers from the brain stem, thalamus and limbic lobes. In their view, the descending control mechanism was sensitive to environmental factors and also utilized information from large primary afferents.

Pain receptors and peripheral afferent pathways

The skin and subcutaneous tissues contain a variety of receptors of varying degree of complexity. These are the terminations of the unmyelinated and finely myelinated afferent nerves having their cell bodies in the posterior (dorsal) root ganglia of the spinal cord. The nerve endings which respond to painful stimulation are known as nociceptors. Some nociceptors respond mainly to mechanical injury whereas others, polymodal nociceptors are responsive to noxious heat and chemical irritation as well as mechanical injury. Receptors similar to those innervating the skin are found in muscle and viscera. However, their response differs and they produce pain of a dull, vague nature following distension, stretch or traction and do not respond to burning, crush or incision. Central representation of somatic and visceral nociception may be different thus accounting for some of the paradoxical difference between these two types of pain.

Afferent conduction

The nerve fibers of which the nociceptors are the terminal portion are relatively small in cross section and comprise of finely myelinated delta fibers 1-5 micrometer in diameter with conduction rate at 5-45 m/sec, the unmyelinated C fiber diameter 0.4–1.1 micrometers conducting at 0.5 – 2.0 m/sec, while other modalities of sensation are transmitted in the rapid myelinated A–beta fibers of 5-15 micrometer diameter with conduction at 30-100 m/sec. A-delta generated pain is well localized whereas C fiber pain is poorly localized.

Organization of pain pathways

The cell bodies of the primary pain afferents (the first order neurons) are located in the dorsal root ganglia. Central extensions from the primary neurons project to the dorsal horn of the spinal cord via the dorsal root and to the nucleus of the trigeminal nerve in the case of cranial pain afferents. These A-delta and C fibers occupy the lateral part of the root entry zone and within the spinal cord form a discrete bundle, the ‘tract of lissauer’ (Neospinothalamic tract). After traversing the lissauer’s tract, they terminate in the dorsal horn of the spinal cord. In the dorsal horn, cell bodies are arranged in series of laminae some of which have classical names, but which are most simply given roman numerical by Rexed i.e. laminae I-IX.

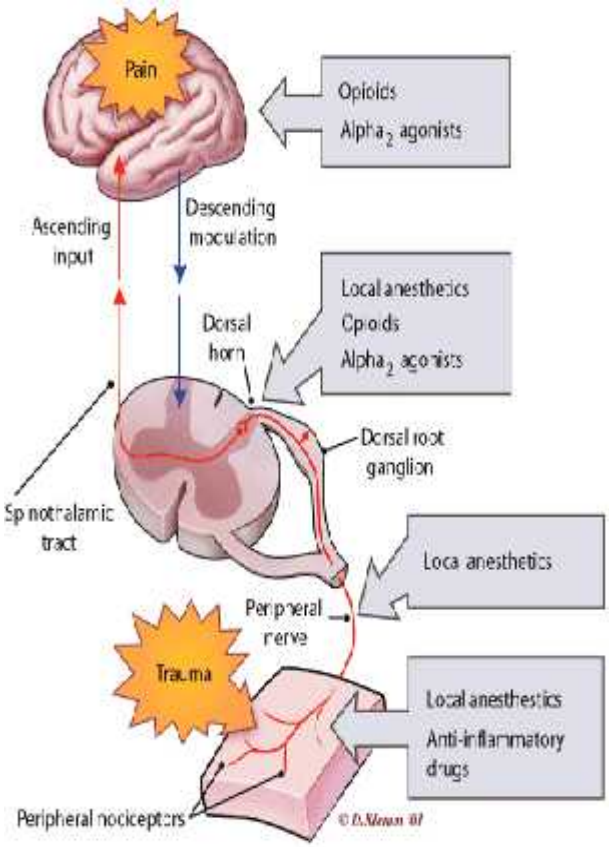


Figure 4. Level of action of drugs along the pain pathway[30]

The A-delta fibers terminate in lamina I, also known as the marginal cell layer of Waldeyer, whereas C fibers terminate in the lamina II also known as 'substantia gelationosa'. Many of the afferents ending in these marginal layers contain neuropeptides, including substance P, cholecystokinin and somatostatin. There is increasing evidence that these peptides play an important role in the normal transmission of pain. Chemical destruction of fibers containing substance P in animals produces analgesia. Most of the fibers terminate in the segment of their entry into the cord, but some extend rostrally and caudally to one or two adjacent segments ipsilaterally and some to the contralateral dorsal horn via the anterior commissure. Some pain fibers penetrate the dorsal gray matter and terminate in lamina V.

The secondary neurons connect with ventral and lateral horn cells in the same and adjacent spinal segments and subserve somatic and autonomic reflexes. In addition to this the secondary neurons decussate in the anterior spinal commissure to the opposite side and ascend in the anterolateral fasciculus (of which the lateral spinothalamic tract forms a major part) to the brain stem and thalamic structure.

The axon from each dermatome enters the spinal cord one to the three segments higher than the level of root entry. Crossing fibers are added to the inner side of the spinothalamic tract, so that the longest fibers from successively rostral segments occupy a progressively deeper position. Thus at the cervical level the fibers in the spinothalamic tract from without inwards are sacral, lumbar, thoracic and cervical.

In addition to the lateral spinothalamic tract, which is a fast conduction pathway that projects directly to the thalamus, the anterolateral fasiculus of the spinal cord contains a slowly conducting, medially placed system of fibers, which reaches the thalamus via one or more relays in the reticular core of the brain stem. This latter group of fibers is referred to as spinoreticulothalamic tract or paleospinothalamic tract. The conduction of diffuse, poorly localized pain arising from the deep structures (gut or periosteum) has been ascribed to this tract.

Thalamic terminus

Most of the fibers of the lateral spinothalamic tract terminate in the nucleus ventralis posterolateralis. A lesser number of them terminate in the nucleus ventralis posteromedialis, the intralaminar nuclei and the venterobasal complex, which also

receive extensive projections from the brain stem reticular nuclei. Some afferent connections are also made with the hypothalamic nuclei.

Thalamo cortical projections

The nuclei of the posterior thalamic complex send their projections to two main cortical areas, the post central cortex and the upper bank of the sylvian fissure.

Physiology and Psychology of pain

Stimuli that produce pain vary for different tissues. An adequate stimulus for skin is one that produces tissue damage or injury, such as pricking, cutting, crushing, burning or freezing. However these stimuli are inadequate when applied to stomach and intestines where the local effects of an engorged or inflamed mucosa, spasm or distension of smooth muscle and any traction on the mesenteric attachment causes pain.

In skeletal muscle, pain is produced by ischemia (intermittent claudication), necrosis, hemorrhage, injury to connective tissue sheaths and injection of irritating solutions. Prolonged contraction of the skeletal muscle produces an aching variety of pain. Ischemia is the most important cause of pain in cardiac muscle. Though joints are insensitive to cutting, pricking and cautery, pain can be produced by inflammation of the synovial membrane and by exposure to hypertonic saline. Arteries, when involved in an inflammatory process or pierced by a needle, are a source of pain. Distension and excessive pulsation of meningeal arteries resulting in stretching of the dura, produces headache.

Perception of pain

The threshold for the perception of pain i.e. the lower intensity of stimulus recognized as pain is approximately the same in all persons. However, the emotional reaction and verbalization varies between individuals based on their personality and character. The threshold for pain is lowered by inflammation and raised by centrally acting analgesic drugs and lesions of the nervous system. Neurotic patients in general have the same pain threshold as normal subjects, but their reaction may be excessive or abnormal.

The conscious awareness of pain occurs only when the pain impulses reach the thalamocortical levels. The precise roles of the thalamus and cortical sensory areas in this mental process are not fully understood. However, it is traditional teaching that the recognition of a noxious stimulus as such is the function of the thalamus, and that the parietal cortex is essential for the appreciation of the intensity, localization and other discriminating aspects of sensation.

This seems to be an over simplification. Probably a close and harmonious relationship between the thalamus and cortex must exist in order for a sensory experience to be complete, that the cerebral cortex governs the patients reaction to pain cannot be doubted as frontal lobotomized subject react briefly, if at all to pain.

Methods of Pain Measurement[31-33]

One cannot determine for the individual patient how much nociception occurs in response to tissue damage for which we have to rely on the expression of the patient to accurately measure the subjective nature of pain.

University of Washington put forward a multifaceted model. The core of the model is the immeasurable nociception resulting from tissue damage. The next layer is the human experience of emotional and sensory components integrated pain which is not available for direct inspection. Pain leads to suffering and suffering leads to painful behaviors which are available for observation in the form of:

a. Withdrawing
b. Grimacing
c. Crying
d. Asking for analgesics.

Thus if one relies on the patient's report of pain it is possible to measure pain intensity and the response to analgesic medications.

Introspective Method

Patient or trained attender attempts to assess pain.

Behaviourise Method

Some physical parameters which get altered in the presence of pain are objectively measured and correlated with the severity of pain e.g. like tachycardia, tachypnoea and increased blood pressure.

Pain as self-report on a single dimension

Verbal Descriptor Scales – Melzack and Torgerson introduced the following scale for pain intensity: "Mild, Discomforting, Distressing, Horrible, Excruciating."[31]

Numeric Rating Scale (NRS) – here patients are asked to indicate how strong their pain is on a scale form 0 to 10 on which 0 represents "no pain at all" and 10 "the worst pain imaginable".[31]

Visual Analog Scale (VAS) - Currently, the most commonly used method; first described by AITKEN is 1966. The subject makes a mark on a 10cms line – horizontal or vertical, one end of which is marked as "No pain" and the other as "The worst pain one can imagine". The position of the mark on the line measures how much pain the subject experiences.[32]

Oral Analog Scale (OAS) - First put forward by AUSTIN et. al. It is a simple and clinically relevant rating scheme. Absence of pain, presence of pain, and if the patient desired more analgesics are rated 0, 1 and 2 respectively. This rating is simple, yet addresses the essence of problem for the patient whether pain present and if it is, does the patient desire more pain relief with more analgesic medications.[33]

Pain as self-reports on multiple dimensions

McGill Pain Questionnaire – It scales pain in three dimensions: Sensory, Affective, and Evaluative.[34]

West Haven-Yale Multidimensional Pain Inventory – This has been designed to be briefer and more classical in its psychometric approach.

Brief Pain Inventory – is a quick, multidimensional pain measurement that has demonstrated reliability and validity.

Memorial Pain Assessment Card – It scales pain, pain relief and mood on VAS and adds a set of adjectives reflecting pain intensity.

Pain Perception Profile is based on cross-modality matching.

Non steroidal anti-inflammatory drugs

NSAIDs are widely used analgesics in various scenarios such as perioperative pain management, chronic musculoskeletal conditions, soft tissue injuries, etc. Non-steroidal anti-inflammatory drugs (NSAIDs) block the activity of cyclooxygenase and inhibit the synthesis of prostaglandins, leading to anti-inflammatory and analgesic effects.

Diclofenac

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) taken to reduce inflammation and as an analgesic to reduce pain in conditions such as arthritis or acute injury. It can also be used to reduce menstrual pain, dysmenorrhea. The name is derived from its chemical name: 2-(2,6-dichloranilino) phenylacetic acid.

Diclofenac is an effective analgesic and anti-inflammatory compound with good uricosuric and antipyretic properties. It is amongst the most potent inhibitors of prostaglandin synthetase. Considering its efficacy it shows an encouraging therapeutic ratio, and has been proved to be superior to the reference drugs when comparing gastrointestinal tolerability. All metabolites are less potent compared to the parent compound.[35]

Diclofenac sodium is the active ingredient. Its pharmacologic activity, especially its effects in acute and chronic inflammation, and its analgesic activity have been studied in animal models. The tolerability of the compound is favorable compared to other nonsteroidal anti-inflammatory drugs, as judged by several parameters (i.e., ratio between the acute lethal dose or the dose inducing gastrointestinal blood loss and the desired pharmacologic activity). Diclofenac sodium acts by inhibiting cyclo-oxygenase, reducing arachidonic acid release, and enhancing uptake of arachidonic acid. In this way it causes a dual inhibitory effect on both the cyclo-oxygenase and lipoxygenase pathways.[36]

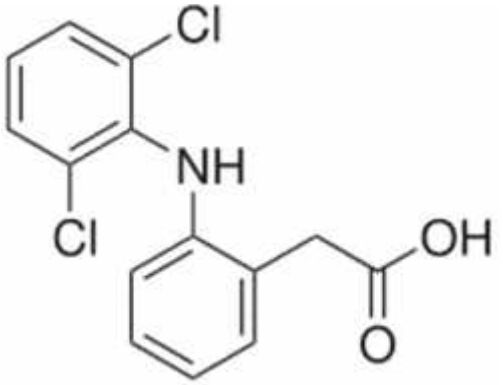


Figure 5. Chemical structure of diclofenac

Mechanism of action[36]

The exact mechanism of action is not completely understood, but it is presumed that the primary mechanism responsible for its anti-inflammatory, antipyretic, and analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). It also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis.

Inhibition of COX also decreases prostaglandins in the epithelium of the stomach, rendering it more sensitive to the corrosive action of gastric acid. This is the main adverse effect of diclofenac. Diclofenac has a low to moderate preference to block the COX2-isoenzyme (approximately 10-fold) and therefore has a slightly lower incidence of gastrointestinal side effects compared to indomethacin and aspirin.

Though the drug has a very short half-life, one single dose has a much longer action (6 to 8 hours). This could be partly because it persists for over 11 hours in synovial fluids.

Diclofenac may also be considered a unique member of the NSAIDs. There is some evidence to suggest that diclofenac inhibits the lipoxygenase pathways, thus reducing formation of the leukotrienes (also pro-inflammatory autacoids). There is also speculation that diclofenac may inhibit phospholipase A_2 as part of its mechanism of action. The high potency of diclofenac may be explained by these additional actions – it is considered the most potent NSAID on a broad basis.

The NSAIDs vary in their selective inhibition of the two subtypes of cyclo-oxygenase, COX-1 and COX-2. An attempt has been made to focus on selective COX-2 inhibition in order to minimize the gastrointestinal side effects of NSAIDs like aspirin. While the use of some COX-2 inhibitors has led to a massive number of lawsuits due to their adverse effects, others such as diclofenac have been well-tolerated by most of the population.

Diclofenac is an established, routinely used nonsteroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic properties, and is

effective in treating acute and chronic pain as well as a variety of inflammatory conditions. Like all NSAIDs, diclofenac acts by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) with relative equipotency leading to inhibition of prostaglandin synthesis. However, research shows that diclofenac's pharmacologic activity extends beyond COX inhibition, and includes multimodal and novel mechanisms of action.

Research suggests that diclofenac can inhibit the thromboxane-prostanoid receptor, alter arachidonic acid release and uptake, inhibit lipoxygenase enzymes and activate the nitric oxide-cGMP anti-nociceptive pathway. Other novel mechanisms of action include the inhibition of substrate P, inhibition of N-methyl-D-aspartate (NMDA) receptor hyperalgesia, blockage of acid-sensing ion channels, inhibition of peroxisome proliferator activated receptor gamma (PPARgamma) and alteration of interleukin-6 production. This diversity in diclofenac's mechanisms of action makes it relatively more favorable compared to other NSAIDs.[37]

Contraindications

- Hypersensitivity against diclofenac
- History of allergic reactions (bronchospasm, shock, rhinitis, urticaria) following the use of Aspirin or another NSAIDs
- Active stomach and/or duodenal ulceration or gastrointestinal bleeding
- Inflammatory intestinal disorders such as Crohn's disease or ulcerative colitis
- Pregnancy
- Severe renal insufficiency (creatinine clearance <30 ml/min)
- Severe insufficiency of the heart (NYHA III/IV)

- Patients recovering from heart surgery
- Severe liver insufficiency (Child-Pugh Class C)
- Caution in patients with preexisting hepatic porphyria, as diclofenac may trigger attacks
- Caution in patients with severe, active bleeding such as cerebral hemorrhage
- NSAIDs in general should be avoided during dengue fever.

Diclofenac transdermal patch

Diclofenac sodium, which is available in various forms, is a commonly used non-selective NSAID to treat pain.[5-7] The diclofenac transdermal patch is a recently introduced drug delivery system for the management of postoperative pain.[7]

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. An important concern with regard to transdermal drugs is the prolonged duration of onset and offset, typically 12-24 hours[7,38] unlike intravenous or intramuscular medications, which can be used as needed for pain control or nausea. Use of a transdermal agent requires planning and careful timing. This is due to the long duration of onset. In the postoperative setting, these agents are applied in anticipation of pain, and not after the patient experiences pain. Topical NSAIDs may have potential advantages when compared with oral NSAIDs. Neadal demonstrated that because of low systemic concentrations, topical NSAIDs have a reduced risk of upper gastrointestinal

complications, such as gastric and peptic ulcers, and gastrointestinal symptoms, such as dyspepsia.[7,39] 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.[7,40]

Although opioids are effective analgesics with no analgesic effect ceiling, their efficacy is often limited by their tolerability profile. Currently, regimens consisting of a combination of analgesics (multimodal analgesia) are recommended for the management of postoperative pain. Adjunctive techniques, such as wound infiltration with local anaesthetics, the use of NSAIDs or corticosteroids, and epidural administration of opioids, have been recommended to treat postoperative pain.[3,4] Of these, the NSAIDs have gained increasing popularity in treating postoperative pain. NSAIDs are excellent analgesics, with no clinically important difference in efficacy among specific drugs. Side-effects to note include gastrointestinal bleeding, renal dysfunction, and platelet dysfunction.

In a study by Alessandri et al.[41] the authors noted that the rate of discharge in patients receiving a transdermal diclofenac patch with a standard analgesic was comparable to a standard analgesic alone in patients undergoing laparoscopic benign gynecologic surgery.

Side-effects encountered in patients receiving intramuscular diclofenac were abdominal pain in three patients, and pain at the injection site in two patients. There were no significant side-effects in patients who received the transdermal diclofenac patch, except for two who had erythema at the application site.[42]

Topical and transdermal preparations are associated with a lower incidence of systemic side-effects because of the lower plasma concentration achieved by these modes.[41,43,44]

A study done to assess the analgesic efficacy of the transdermal diclofenac patch in patients undergoing laparoscopic benign gynecologic surgery found that topical and transdermal preparations are associated with a lower incidence of systemic side-effects because of the lower plasma concentration achieved by these modes.[41]

Pharmacokinetic studies have been done which show that a transdermal diclofenac patch releases the drug in concentrations that are sufficient to exert local therapeutic activity on tissues.[45] Another study was done on the diclofenac patch in acute traumatic blunt soft tissue injuries, and found that it was effective and well tolerated in these cases. The most frequently observed adverse effects were local tissue reactions, such as pruritus and a rash of minor severity.[46]

A review of published literature suggests that the patch is safe to use, well tolerated, clinically efficacious and a good treatment option for managing acute pain associated with strains, sprains, contusions and other localized painful conditions.[47]

A study done in patients undergoing premolar extractions found that the patch is as potent as oral tablets in providing pain relief with the added advantage of better patient compliance owing to the single daily application and the lesser frequency of systemic side effects.[48]

A few studies have been conducted to evaluate the efficacy of the patch in the management of post-operative pain. One such study noted that transdermal

diclofenac is more effective than intramuscular injections in reducing the intensity of postoperative pain and the need for rescue analgesia in laparoscopic and gynaecological surgeries while the effect of both routes was similar in orthopaedic limb surgeries.[49]

A similar study found that the patch was as effective as intramuscular diclofenac in providing pain relief following laparoscopic surgeries.[50]

Another study showed similar results in elective lower limb orthopaedic surgeries. They observed side effects like gastritis and injection pain in the intramuscular group while few patients developed local erythema following patch application.[7]

Pradel et al.[46] used a diclofenac patch for acute traumatic blunt soft tissue injuries, and they found that the diclofenac patch was effective and well tolerated. The most frequently observed adverse events were local tissue reactions, such as pruritus and a rash of minor severity.

The safety profile of diclofenac patches has been documented by Mason et al [43] in a systematic review on the use of topical NSAIDs in the UK and by other studies assessing the use of the transdermal diclofenac patch in osteoarthritis[51] as well as in sports-related injuries.[46]

Inguinal hernia

According to the Astley Cooper (1804) hernia is the protrusion of any viscus from its proper cavity. The protruded viscus is usually contained in a sac-like structure, which is formed by the membrane which naturally lines the cavity.[52]

Various different types of abdominal wall hernias have been identified and are associated with various eponyms.[11] Approximately 96% of all groin hernias are inguinal hernias, with the remaining 4% being femoral. Hernias are bilateral in 20% of cases. The most common abdominal wall hernia is an inguinal hernia with a male to female preponderance of 9:1. Femoral hernias are more common in women.[53]

Surgical anatomy[54-58]

The anterior abdominal wall extends from the costal margins and xiphoid process superiorly to the iliac crests, pubis and pubic symphysis inferiorly. The groin is a portion of the anterior abdominal wall below the level of the anterior superior iliac spines.

Inguinal canal

The inguinal canal is a passage in the anterior abdominal wall which conveys the spermatic cord in men and the round ligament in women. It is around 4 cm long and lies above the medial half of inguinal ligament. Its size varies with age, and although present in both sexes, is well developed in males. It extends from the deep to the superficial inguinal ring. The ilioinguinal nerve passes through the inguinal canal in both the sexes.

The anterior wall of the inguinal canal is formed by the external oblique aponeurosis, and laterally by the internal oblique muscle. The posterior wall is formed by the strong conjoint tendon medially and weak transversalis fascia throughout. Its floor is the reflected part of the inguinal ligament, reinforced medially by the lacunar ligament. Its roof is formed by the lower edges of the internal oblique and transverses muscle, which arch over and in front of the cord

laterally and behind the cord medially, where their conjoined aponeurosis constitutes the conjoint tendon, which is inserted into the pubic crest and the pectineal line of the pubic bone.

Superficial inguinal ring is a triangular opening in the external oblique aponeurosis, which lies above and lateral to the public crest. Deep inguinal ring is an oval opening in the fascia transversalis, located midway between the anterior superior iliac spine and symphysis pubis approximately 1.25 cm above the inguinal ligament.

Relations

The inferior epigastric vessels lie posterior to the inguinal canal medially. They lie on the transversalis fascia, as they ascend obliquely behind the conjoint tendon and pass posterior to the rectus sheath.

The Hesselbach's triangle is bounded inferiorly by medial half of inguinal ligament, medially by lower lateral border of rectus sheath and laterally by inferior epigastric artery. A hernial sac passing lateral to the artery (i.e. through the deep ring) is an indirect hernia, while one passing medial to the artery through the Hesselbach's triangle is a direct hernia.

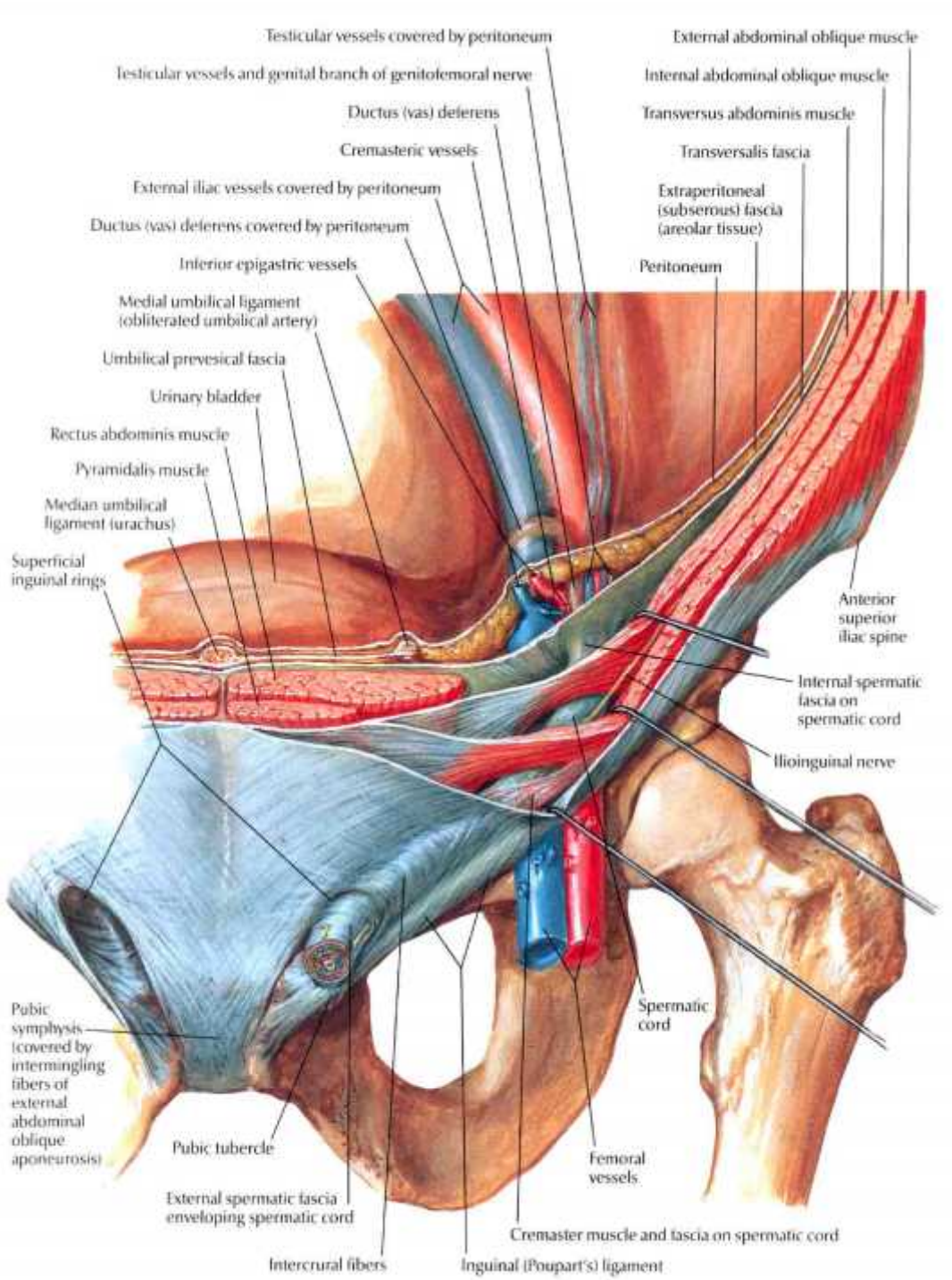


Figure 6. Inguinal canal in the male

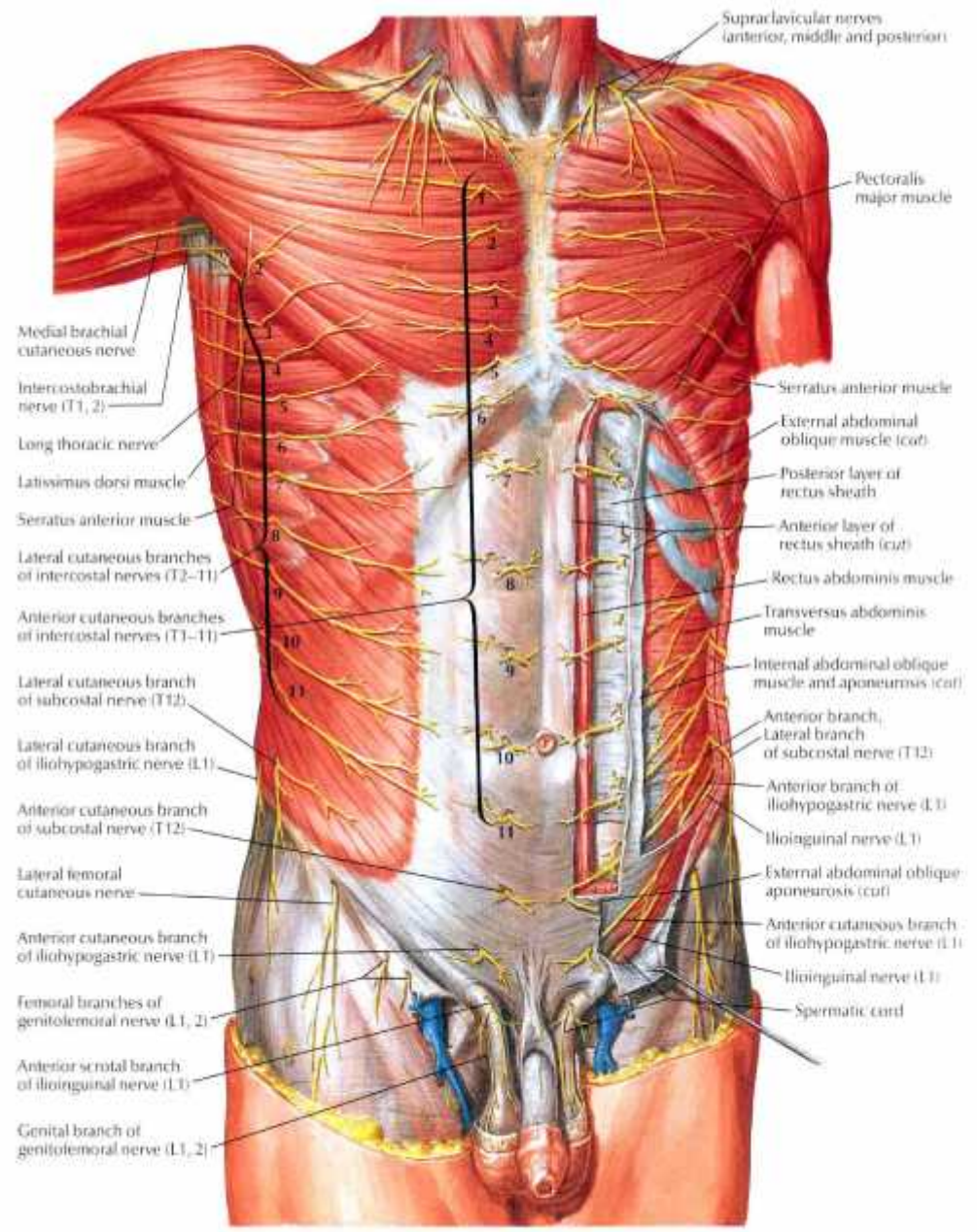


Figure 7. Nerve supply of the anterior abdominal wall in the male

Spermatic cord

It is covered by internal spermatic fascia (fascia transversalis), cremaster muscle and cremasteric fascia (internal oblique and transverse abdominis) and external spermatic fascia (external oblique aponeurosis). It contains the vas deferens, processes vaginalis, arteries (testicular artery, artery to Vas, and the cremasteric artery), veins (pampiniform plexus, cremasteric veins, veins of Vas deferens), lymphatics and nerves (genital branch of genitofemoral nerve).

Innervation

The rectus muscle and external oblique are supplied by lower intercostal and subcostal nerves (T7 – T12), and the internal oblique and transverses by the same with the addition of iliohypogastric and ilioinguinal nerves (L1). The ilioinguinal nerve accompanies the spermatic cord and passes through the superficial inguinal ring. It supplies the medial thigh proximal to the inguinal ligament, the root of the penis and upper anterior scrotum. In the female, it supplies the mons pubis and labia majora. Iliohypogastric nerve has some fibers in common with subcostal and ilioinguinal nerve. The genital branch of genitofemoral nerve supplies the cremaster muscle. The femoral branches (L1, L2) supply the skin overlying the femoral sheath.

Epidemiology

Abdominal wall hernias are common, with a prevalence of 1.7% for all ages and 4% for those aged over 45 years. Inguinal hernias comprise 75% of abdominal wall hernias, with a lifetime risk of 27% in men and 3% in women.[59,60] Inguinal hernia repair is amongst the most common procedures in general surgery, with rates

varying from 10 per 1,00,000 of the population in the United Kingdom to 28 per 1,00,000 in the United States.[59,61]

Ninety five per cent of the patients presenting with an inguinal hernia are male, and in men the incidence rises from 11 per 10,000 person years aged 16-24 years to 200 per 10,000 person years aged 75 years or above.[59,62]

As data from developing countries is limited, an accurate occurrence value is unavailable.

Etiology

Any condition that increases the intra-abdominal pressure may lead to the formation of a hernia, including the following:[11,63]

- Heavy weight lifting
- Straining with defecation or urination
- Coughing
- Chronic obstructive pulmonary disease (COPD)
- Marked obesity
- Ascites
- Family history of hernias

Clinical presentation

Patients with an inguinal hernia present with a lump in the groin which disappears on lying down or with minimal pressure. There may be mild to moderate discomfort which increases with activity. A third of the patients that undergo surgery

have no pain, and severe pain is uncommon (1.5% at rest and 10.2% on movement).[59,64]

Patients with hernias present to the casualty because of a complication associated with the hernia. Hernias may also be detected on routine physical examination. The different presentations of an inguinal hernia are as follows:[11]

- Asymptomatic hernia
- Incarcerated hernia
- Strangulated hernia

Management

Inguinal hernia repairs are of the following three general types viz. Herniotomy (removal of the hernial sac only), Herniorrhaphy (herniotomy with repair of the posterior wall of the inguinal canal) and Hernioplasty (herniotomy with reinforcement of the posterior wall of the inguinal canal with a synthetic mesh).

Various techniques of repair have been described since Eduardo Bassini first published his anatomy-based repair with great success in 1890.[65] A summary of current options of inguinal hernia repair are listed below.

Different methods of repairs[66]

A. Tension-free prosthetic repairs
    a. Anterior repairs
        i. Lichtenstein repair and its modifications
        ii. Plug repairs
        iii. Patch and plug repairs

iv. Double-layer devices

b. Posterior (preperitoneal) repairs

i. Open techniques via inguinal incision

ii. Stoppa repair

iii. Laparoscopic repairs

1. Transabdominal preperitoneal

2. Total extraperitoneal

B. Tissue-Suture repairs

a. Bassini-Shouldice technique and its modifications

b. Marcy repair

A mesh is required in every type of tension free repair. Placement of the mesh is either by open anterior, open posterior approach or by laparoscopic approach.

The Lichtenstein hernioplasty

In 1986, Irving Lichtenstein introduced the term tension-free hernioplasty[56]. It initially included sutured repair of the posterior wall which was later modified to only reinforcing it by bridging the defect with a mesh that was sutured with a continuous monofilament nonabsorbable suture. The method was further improved in the early nineties[67] with recommendations of larger, slightly relaxed mesh, medial mesh overlap, crossing and suturing of the tails of the mesh lateral to the cord and only interrupted absorbable sutures on the upper edge of the mesh. The reported recurrence rate was further decreased.

Advantages of this procedure include low recurrence rate, reduced postoperative pain as a result of the tension-free technique, simple and effective technique, can be performed under local or regional anaesthesia.

At present the Lichtenstein tension-free mesh repair is currently one of the most popular open inguinal hernia repair techniques and includes the following components:

- Incising skin, subcutaneous tissue and external oblique aponeurosis to open up the inguinal canal with mobilization of flaps of the aponeurosis.
- Identification and dissection of the spermatic cord and the hernia sac.
- Inversion, division, resection, or ligation of the sac, as indicated.
- Placement and fixation of mesh to the posterior wall of the inguinal canal and creation of a new artificial internal ring.
- Closure of spermatic cord layers, the external oblique aponeurosis, subcutaneous tissue, and the skin.

Complications[68]

In systematic reviews, the overall risk of complications after inguinal hernia surgery has been in the range of 15-28%. Complications may develop intraoperatively or postoperatively. Early postoperative complications include seroma formation and hematoma (8-22% of cases), urinary retention, and wound infection (1-7% of cases). Late postoperative complications include sensory loss,

hyperesthesia, chronic inguinal pain, mesh-related problems, hydrocele, testicular pain, testicular swelling, atrophy, and recurrence of hernia.

Intraoperative complications

- Vascular injuries
- Injuries to abdominopelvic structures
- Nerve injuries

Postoperative complications

- Urinary retention
- Seroma and hematoma
- Infection
- Pain
- Hydrocele
- Ischemic orchitis and thrombosis
- Recurrence

Since the widespread acceptance of mesh-based repair, the rate of hernia recurrence has fallen substantially, to 1% or less. Consequently, more attention is being paid to other complications, such as post-herniorrhaphy chronic pain.[69]

Large studies examining mortality risk from various groin operations found that elective inguinal herniorrhaphy was safe and had a low mortality risk that was similar to or even lower than the standardized mortality in the studied population.[70]

Another phenomenon that can be experienced after hernia repair is groin numbness. In a large Scottish study that included more than 5,500 patients, this was reported in as many as 9%.[71]

Other complications include seroma formation, bruising, hematoma (7% of cases) and wound infection (1-7% of cases).[72]

Ischemic orchitis leading to testicular atrophy or even necrosis is a catastrophic but well-known complication of inguinal hernia repair. Symptoms include painful testicular swelling and fever commencing 2-3 days after surgery.[73]

Although pain is more common in the acute postoperative period, it remains chronically severe in 3% of patients, having significant effects on their work and social activities.[74]

A large Swedish study found that 30% of post-herniorrhaphy patients reported long-term pain or discomfort, 6% of whom experienced pain intense enough to alter their activities of daily living.[71]

METHODOLOGY

This one year randomized controlled trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2014 to December 2014.

Study design

The study design was a one year randomized controlled trial.

Study period and duration

This study was conducted over a period of one year from January 2014 to December 2014.

Place

This study was carried out in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum attached to KLE University's Jawaharlal Nehru Medical College, Belgaum.

Source of Data

Patients admitted with inguinal hernia undergoing open inguinal hernioplasty under the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum were studied.

Sample size

The present study was comprised of 60 patients undergoing open inguinal hernioplasty divided into two groups of 30 each.

Sampling procedure

The sample size was calculated based on the following formula

$n = 2 (Z\alpha + Z\beta)^2 S^2 / (x_1-x_2)^2$

Where, n = sample size

$Z\alpha$ = 1.96

$Z\beta$ = 0.84

S = Standard deviation

x_1-x_2 = Effect size

Based on this formula the sample size was chosen using the systematic random sampling method.

Total number of cases = 240

Sample size = 60

Every k^{th} case will be chosen in every 4 cases as derived from: 240÷60=4, where 'k' is a randomly chosen number from 1 to 4.

Selection criteria

Inclusion

- All patients with inguinal hernia undergoing mesh repair.

Exclusion

- Patients with peptic ulcer in the last six months
- Pregnant or lactating women
- Patients with cardiac, pulmonary, renal or hepatic pathology
- Patients with history of bronchial asthma, urticaria or other allergic reactions to NSAIDs
- Patients with haemorrhagic diathesis
- Patients undergoing only herniotomies or herniorrhaphies
- Patients requiring general anaesthesia
- Patients presenting with bilateral/complicated inguinal hernia

Ethical clearance

The study was approved by the Ethical and Research Committee, Jawaharlal Nehru Medical College, Belgaum prior to commencement.

Informed Consent

The patients fulfilling selection criteria were informed in detail about the nature of the study and a written informed consent was obtained (Annexure I).

Method of collection of data

Demographic data such as age, sex and history pertaining to inguinal hernia such as duration of symptoms was obtained through an interview. These patients were further subjected to clinical examination and the findings such as type and extent were noted on a predesigned and pretested proforma (Annexure II).

Investigations

The patients were subjected to the following investigations.

- Routine blood counts – Hemoglobin, total leucocyte counts, differential counts, red blood cell counts and ESR.
- Blood urea nitrogen
- Serum creatinine
- Bleeding and clotting time
- Urine Routine and Microscopy
- Chest X-ray and ECG
- Ultrasound abdomen and pelvis

Randomization and intervention

The patients were randomized by asking them to pick an opaque concealed envelop which furnished the information regarding the choice of pain management. Based on the option picked up, the patients were divided into two groups of 30 each as below;

- Group A: Patients in this group received a single transdermal diclofenac patch (100mg) 3 hours before the incision was taken.

- Group B: Patients in this group received a single intramuscular injection of diclofenac sodium (75mg) 20 minutes before the incision was taken.

No other intraoperative or postoperative analgesia was given in both groups till 24 hours following surgery unless the patient required rescue analgesia.

Photograph 1. Transdermal diclofenac patch

Photograph 2. Application of transdermal diclofenac patch

Procedure

All the patients underwent Lichtenstein's inguinal hernioplasty. Anaesthetic procedure was standardized for all patients. Hyperbaric bupivacaine was used to administer spinal anaesthesia in every patient. The surgery was performed using similar instruments and suture materials under accepted general principles of surgery.

Assessment of post operative pain and management

The assessment of pain was based on Visual Analogue Score (VAS) ranging from 0 to 10 considering 0 as no pain and 10 as maximum pain which was explained to the patient during pre operative visit.

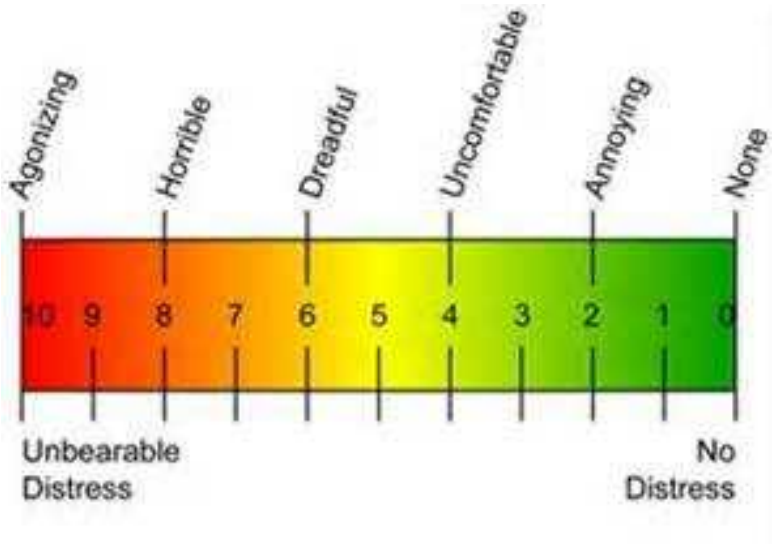


Figure 8. Visual analog scale

The VAS score ≤3 were regarded as satisfactory whereas patients reporting VAS score of >3 were administered injection Diclofenac sodium 75 mg intramuscularly as a rescue analgesia.[75]

Outcome variables

Pain

Post operative pain was monitored based on VAS scores immediately post operative and at 3, 6, 12 and 24 hours.

Requirement of analgesia

Requirement of rescue analgesia that is requirement of 75 mg Diclofenac sodium was recorded immediately post operative and at 3, 6, 12 and 24 hours interval.

The time at which the patient requires rescue analgesia

The time at which the patients requested for rescue analgesia was also noted.

Complications

The patients were monitored for complications including erythema, nausea and pain at injection site.

Statistical analysis

The data obtained was coded and entered in Microsoft Excel Spreadsheet. The categorical data was expressed as rates, ratios and percentages and comparison was done using Fishers exact test and chi-square test. Continuous data was expressed as mean ± standard deviation and data was compared using independent sample ‘t’ test. A ‘p’ value of less than or equal to 0.05 at 95% confidence interval was considered as statistically significant.

RESULTS

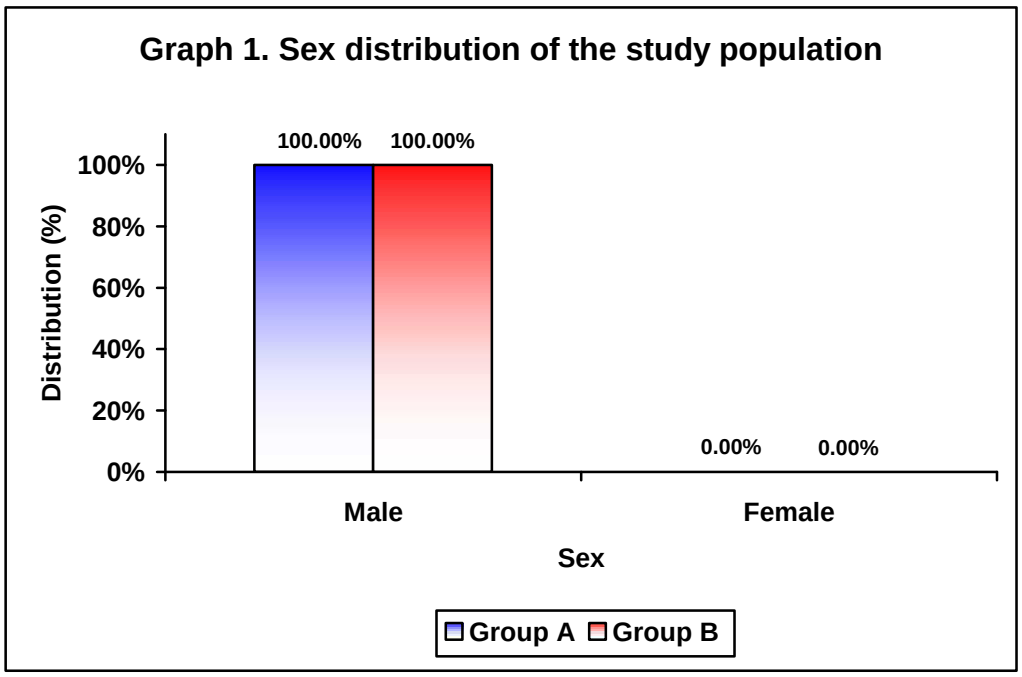
The present one year randomized controlled trial was done in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 60 patients diagnosed with inguinal hernia and posted for Lichtenstein's inguinal hernioplasty during the study period that is, January 2014 to December 2014 were enrolled. Patients were divided into two groups of 30 each as Group A (Patients received a single transdermal diclofenac patch [100mg]) and Group B (Patients received a single intramuscular injection of diclofenac sodium [75mg]).

The data was analysed and the final results were tabulated as below.

Table 1. Sex distribution of the study population

Sex	Group A (n=30)		Group B (n=30)	
	No.	**%**	**No.**	**%**
Male	30	100.00	30	100.00
Female	0	0.00	0	0.00
Total	**30**	**100.00**	**30**	**100.00**

p=1.000

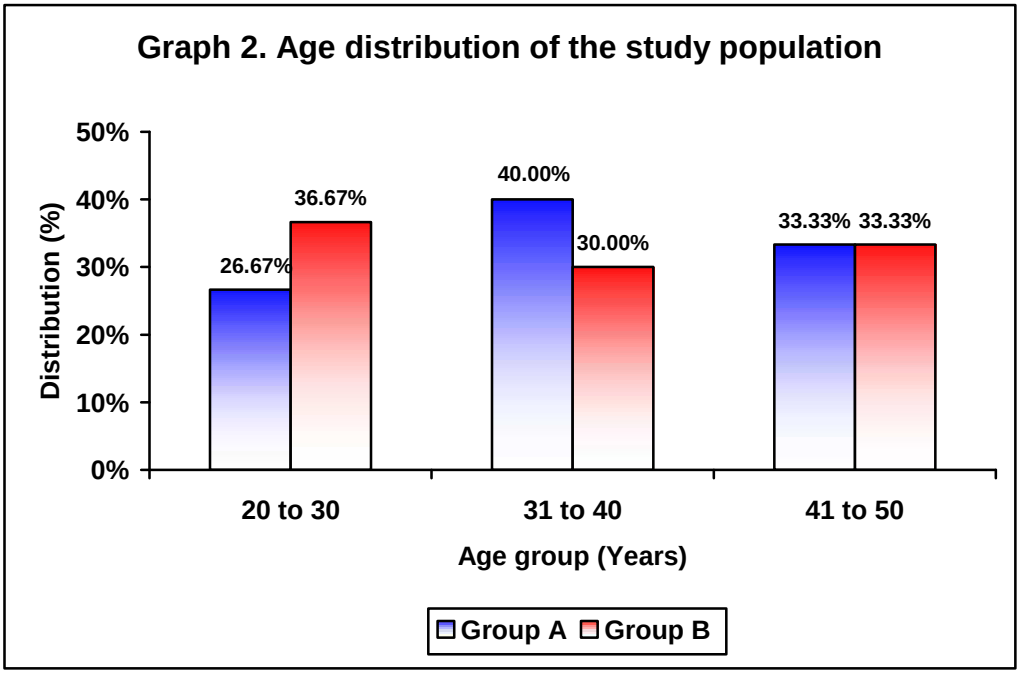


In the present study all the patients in group A and B were males (100%).

Table 2. Age distribution of the study population

Age group (Years)	Group A (n=30)		Group B (n=30)	
	No.	**%**	**No.**	**%**
20 to 30	8	26.67	11	36.67
31 to 40	12	40.00	9	30.00
41 to 50	10	33.33	10	33.33
Total	**30**	**100.00**	**30**	**100.00**

p = 0.653



In this study most of the patients (40%) in group A were aged 31 to 40 years compared to 20 to 30 years in group B (36.67%) but the difference was statistically not significant (p=0.653).

Table 3. Comparison of mean age

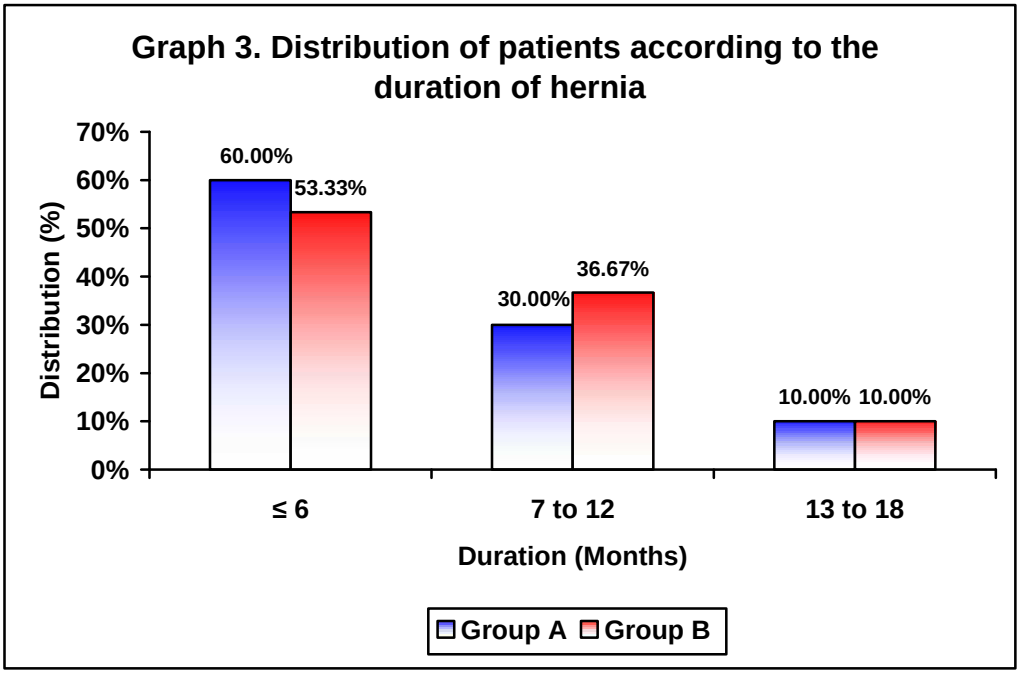
Variables	Group A (n=30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
Age (Years)	36.30	7.75	35.33	8.40	0.645

In the present study the mean age in group A was 36.30 ± 7.75 years comparable to 35.33 ± 8.40 in group B. However the difference was statistically not significant (p=0.645).

Table 4. Distribution of patients according to the duration of hernia

Duration (Months)	Group A (n=30)		Group B (n=30)	
	No.	%	No.	%
≤ 6	18	60.00	16	53.33
7 to 12	9	30.00	11	36.67
13 to 18	3	10.00	3	10.00
Total	**30**	**100.00**	**30**	**100.00**

p = 0.927



In this study the duration of hernia was ≤ 6 months in 60% of the patients in group A compared to 53.33% in group B. But this difference was statistically not significant (p=0.927).

Table 5. Comparison of mean duration of hernia

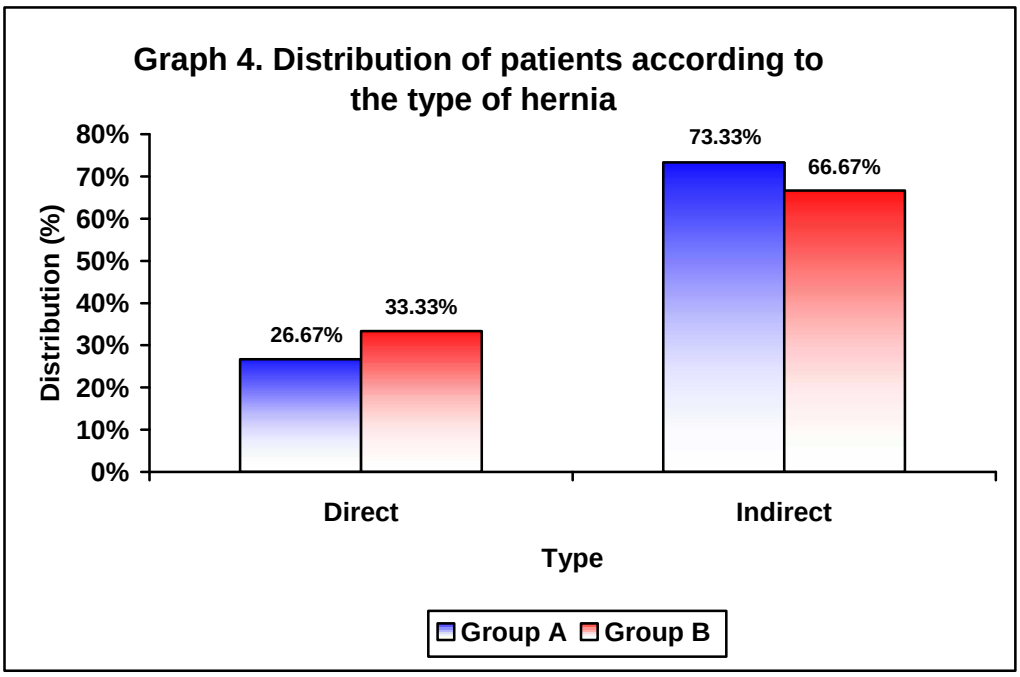
Variables	Group A (n=30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
Duration (Months)	7.07	4.52	7.27	4.44	0.863

In the present study, mean duration of hernia in group A (7.07 ± 4.52 months) and group B (7.27 ± 4.44 months) was comparable (p=0.863).

Table 6. Distribution of patients according to the type of hernia

Type	Group A (n=30)		Group B (n=30)	
	No.	%	No.	%
Direct	8	26.67	10	33.33
Indirect	22	73.33	20	66.67
Total	**30**	**100.00**	**30**	**100.00**

p = 0.573

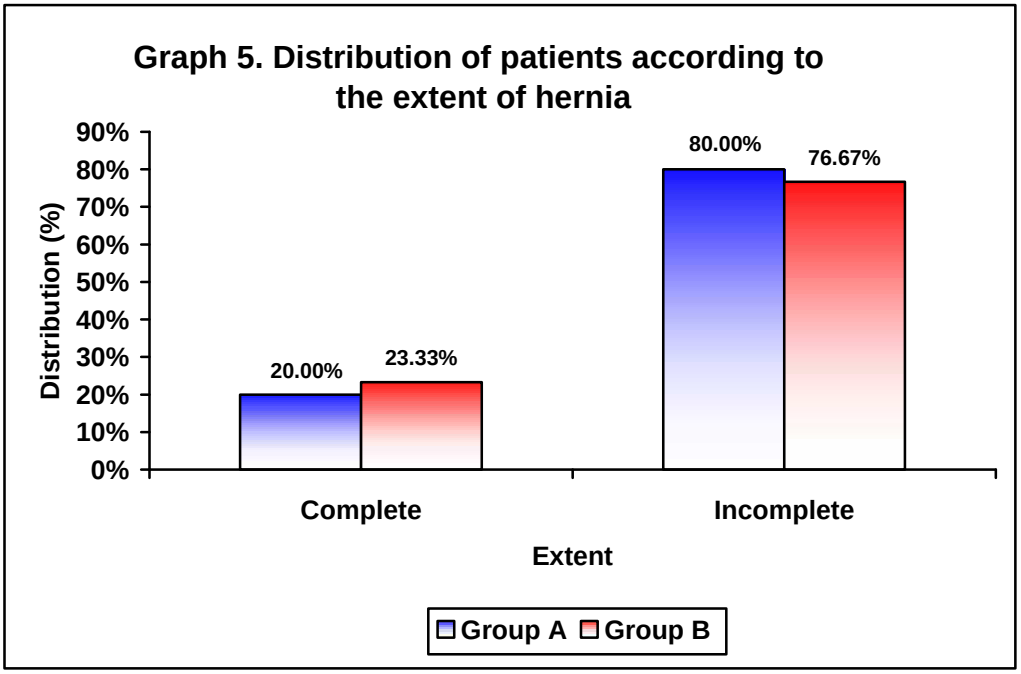


In this study 73.33% of the patients in group A and 66.67% in group B had indirect hernia (p=0.573).

Table 7. Distribution of patients according to the extent of hernia

Extent	Group A (n=30)		Group B (n=30)	
	No.	**%**	**No.**	**%**
Complete	6	20.00	7	23.33
Incomplete	24	80.00	23	76.67
Total	**30**	**100.00**	**30**	**100.00**

p = 0.754

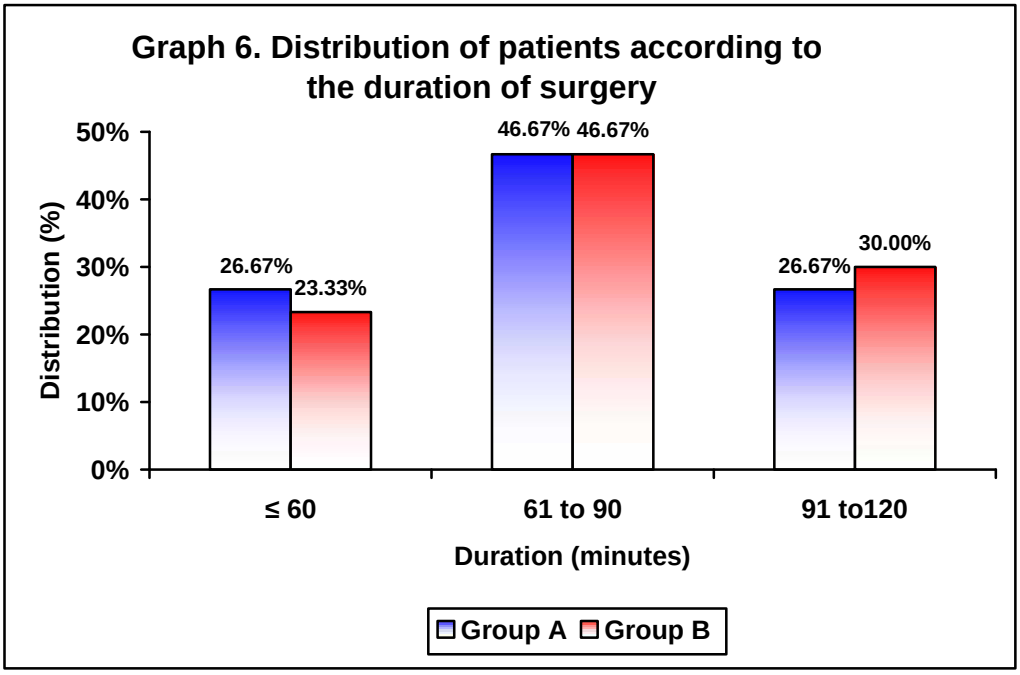


In the present study majority of the patients in group A (80%) and group B (76.67%) had incomplete hernia (p=0.754).

Table 8. Distribution of patients according to the duration of surgery

Duration (minutes)	Group A (n=30)		Group B (n=30)	
	No.	%	No.	%
≤ 60	8	26.67	7	23.33
61 to 90	14	46.67	14	46.67
91 to 120	8	26.67	9	30.00
Total	**30**	**100.00**	**30**	**100.00**

p = 1.000



In this study the duration of surgery was between 61 to 90 minutes in 46.67% of the patients each in group A and group B (p=1.000).

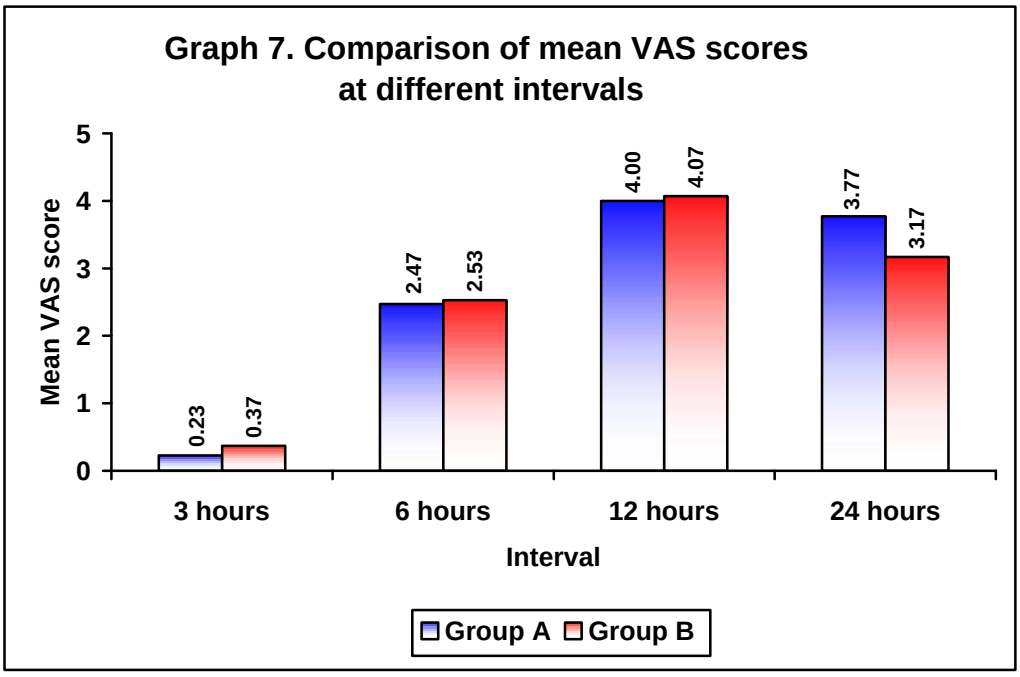
Table 9. Comparison of mean duration of surgery

Duration (Minutes)	Group A (n=30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
Duration (Minutes)	83.00	21.52	83.83	21.56	0.881

In the present study, mean duration of surgery in group A (83.00 ± 21.52 minutes) and group B (83.83 ± 21.56 minutes) was comparable (p=0.881).

Table 10. Comparison of mean VAS scores at different intervals

Interval	Group A (n=30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
3 hours	0.23	0.63	0.37	0.76	0.463
6 hours	2.47	1.59	2.53	1.53	0.869
12 hours	4.00	1.93	4.07	1.84	0.891
24 hours	3.77	1.55	3.17	1.62	0.148

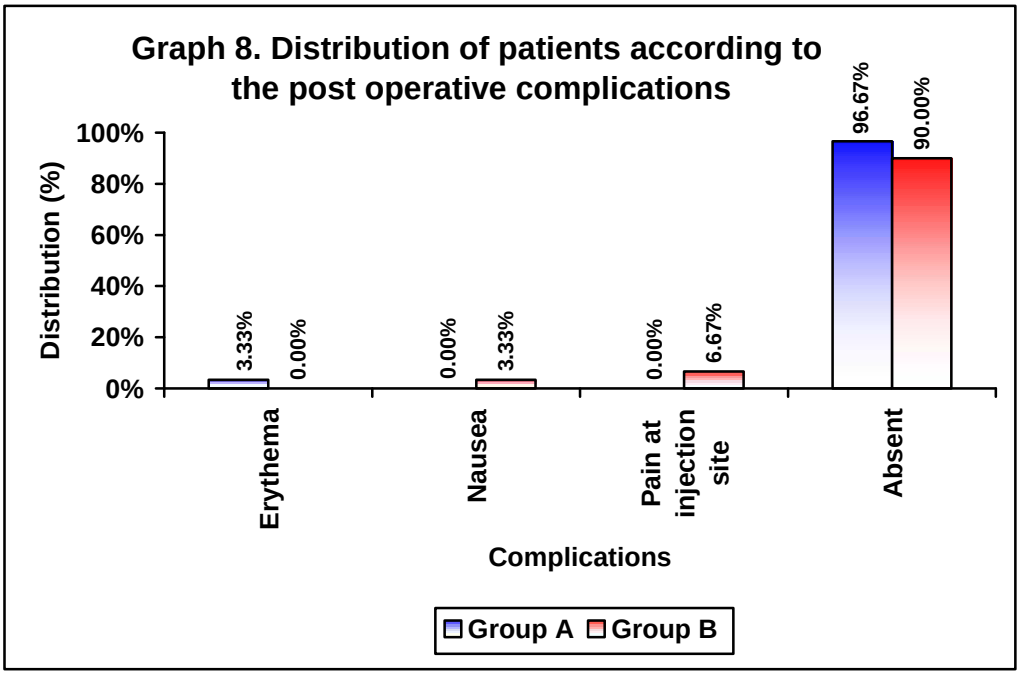


In this study the mean VAS scores in group A and B at three hours (0.23 ± 0.63 vs 0.37 ± 0.76; p=0.463), six hours (2.47 ± 1.59 vs 2.53 ± 1.53; p=0.869), 12 hours (4.00 ± 1.93 vs 4.07 ± 1.84; p=0.891) and at 24 hours (3.77 ± 1.55 vs 3.17 ± 1.62; p=0.148) were comparable.

Table 11. Distribution of patients according to the post operative complications

Complications	Group A (n=30)		Group B (n=30)	
	No.	**%**	**No.**	**%**
Erythema	1	3.33	0	0.00
Nausea	0	0.00	1	3.33
Pain at injection site	0	0.00	2	6.67
Absent	29	96.67	27	90.00
Total	**30**	**100.00**	**30**	**100.00**

p = 0.612

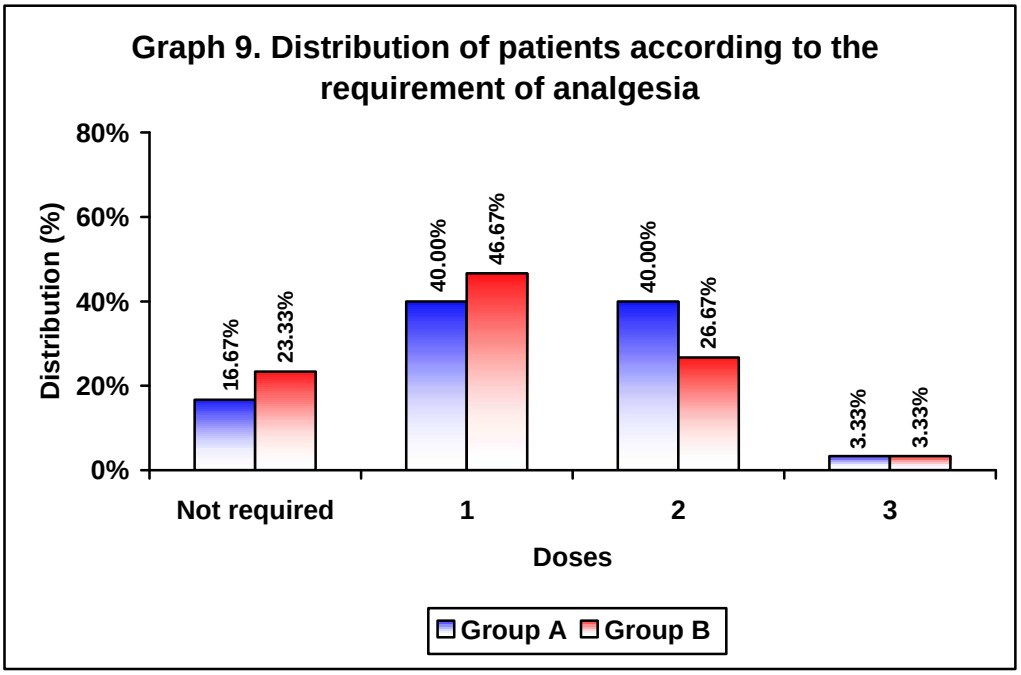


In the present study 3.33% of the patients in group A had erythema compared to nausea in group B. Also in group B, 6.67% of the patients had pain at injection site. However, this difference was statistically not significant (p=0.612).

Table 12. Distribution of patients according to the requirement of analgesia

Doses	Group A (n=30)		Group B (n=30)	
	No.	**%**	**No.**	**%**
Not required	5	16.67	7	23.33
1	12	40.00	14	46.67
2	12	40.00	8	26.67
3	1	3.33	1	3.33
Total	**30**	**100.00**	**30**	**100.00**

p = 0.790

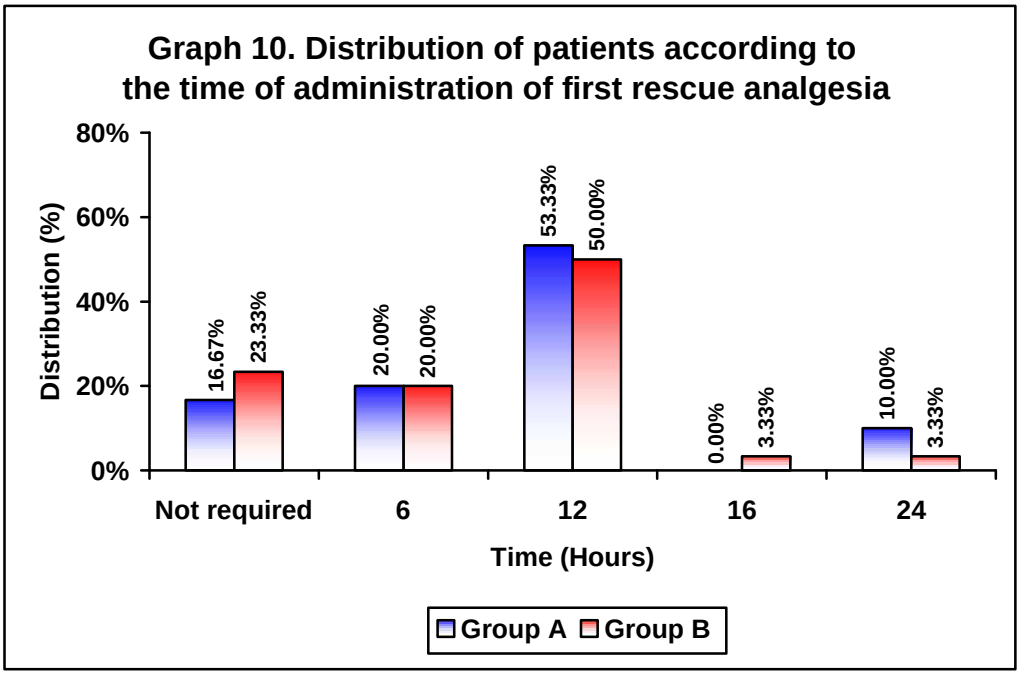


In this study most of the patients that is, 40% in group A and 46.67% in group B required one dose of rescue analgesia. However this difference was statistically not significant (p=0.790).

Table 13. Distribution of patients according to the time of administration of first rescue analgesia

Time (Hours)	Group A (n=30)		Group B (n=30)	
	No.	%	No.	%
Not required	5	16.67	7	23.33
6	6	20.00	6	20.00
12	16	53.33	15	50.00
16	0	0.00	1	3.33
24	3	10.00	1	3.33
Total	**30**	**100.00**	**30**	**100.00**

p = 0.802



In this study most of the patients that is, 53.33% in group A and 50% in group B required rescue analgesia at 12 hours. However this difference was statistically not significant (p=0.802).

Table 14. Comparison of mean doses and time for request of first rescue analgesia

Doses	Group A (n=30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
Mean doses (Doses)	1.30	0.79	1.10	0.80	0.336
Time for request of first rescue analgesia (Hours)	10.00	6.56	8.53	5.94	0.368

In the present study the mean number of doses for rescue analgesia (1.30 ± 0.79 doses) and the mean time request for first post operative rescue analgesia (10.00 ± 6.56 hours) was slightly high in group A compared to group B (1.10 ± 0.80 doses and 8.53 ± 5.94 hours respectively) However, this difference was statistically not significant (p=0.336 and p=0.368 respectively).

DISCUSSION

Inguinal hernia repair is a common surgical procedure performed worldwide, with an annual procedural rate of 2,800 per million people in the U.S.[76] This procedure is often associated with minimal postoperative morbidity. A patient can resume work early and can enjoy a good quality of life following inguinal hernia repair.[77]

Many studies involve postoperative pain as an outcome measure. Minimal pain is always expected in the postoperative period and requires adequate analgesia. Chronic pain following hernia repair can be disabling, with a significant impact on quality of life leading to increased use of health services.[78]

For many decades, inguinal hernia repair has been based on "the radical cure of inguinal hernia" according to Bassini[79] and subsequent other herniorrhaphy techniques based on suture repair developed during the 20th century, such as the McVay and Shouldice techniques. However, these procedures were often associated with severe postoperative pain and high inguinal hernia recurrence rates. The introduction of tension-free repair using prosthetic mesh represented a new era in inguinal hernia repair.[80]

Postoperative pain is a common problem in any surgical setup. It has a significant effect on the rate of recovery of a patient following surgery.[16-18] Non-steroidal anti-inflammatory drugs (NSAIDs) block the activity of cyclooxygenase and inhibit the synthesis of prostaglandins, leading to anti-inflammatory and analgesic effects.

However, it is reported that oral administration of NSAIDs subjects the drug to first pass metabolism with a significant amount being lost before it is absorbed systemically. Oral NSAIDs also cause several dose dependent adverse effects, particularly gastrointestinal effects. Alternate routes of administration of NSAIDs, in the form of topical formulations, have been developed. They are associated with a lower incidence of systemic side effects and enhanced local drug delivery to the affected tissues. Topical NSAIDs have thus established themselves as therapeutic analgesic modalities with recognized benefits and lower incidence of adverse effects.[48]

Transdermal systems are innovative delivery mechanisms for NSAIDs replacing oral and other traditional forms of drug administration. The drug in the transdermal patch permeates the skin and enters the body, ultimately diffusing into capillaries for systemic delivery. The steady permeation across the skin results in more consistent serum levels of the drug, often a goal of therapy.[81,82]

Diclofenac sodium, a non-selective NSAID, is available as oral tablets, intramuscular injections, rectal suppositories and transdermal ointments, gels and patches. Oral and intramuscular routes are routinely used for the management of perioperative pain.

The diclofenac transdermal patch is a recently introduced drug delivery system. It has the advantages of being non-invasive and painless compared to the intramuscular injections and has lesser adverse effects compared to the oral route.

Transdermal therapeutic systems (TTS) are self-contained discrete dosage forms which, when applied to the intact skin, deliver the drugs at a controlled rate to

the systemic circulation. Thus it is anticipated that transdermal drug delivery systems (TDDS) can be designed to input drugs at appropriate rates to maintain suitable plasma drug levels for therapeutic efficacy by using skin as the port. Drug administration in conventional dosage forms like tablets, capsules, injectables or ointments cause fluctuations in drug concentrations in blood stream and tissues and may lead to undesirable toxicity and efficiency. The successful development of TTS depends on a pondered choice of drug, which should be non-irritant and cross the skin in adequate amounts to produce the therapeutic effect. Drugs which produce these effects in small amounts with molecular weight range of 100-800 Da are ideal candidates for TDDS.[83]

Transdermal route offers several advantages over other routes for the delivery of drugs with systemic activity. It provides a continuous mode of administration at rates approaching zero-order similar to that provided by an intravenous infusion and the delivery is non-invasive with no requirement of hospitalization. Additionally, the transdermal route as compared with the oral route reduces drug degradation at the site of administration due to its lower metabolic activity. Once the drug is absorbed, the hepatic circulation is bypassed, thus avoiding another major site of potential drug inactivation.[83]

Transdermal drug delivery systems are adhesive, drug containing devices which are of a defined surface area and deliver a pre-determined amount of drug at a pre-programmed rate to the surface of intact skin. These systems release the drug at a predictable rate and maintain that rate for extended time periods.[83]

However, transdermal diclofenac patch being a new modality in the surgical pain management, its effect on Lichtenstein's inguinal hernioplasty remains unknown. Hence this study was designed to evaluate the efficacy of transdermal diclofenac patch (100 mg) with intramuscular diclofenac sodium (75 mg) as pre-emptive analgesia in patients undergoing Lichtenstein's inguinal hernioplasty.

This one year randomized controlled trial was carried out in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 60 patients undergoing Lichtenstein's inguinal hernioplasty from January 2014 to December 2014 were enrolled. These patients were divided into two groups of 30 each as Group A (single transdermal diclofenac patch [100mg]) and Group B (single intramuscular injection of diclofenac sodium [75mg]). Patients were evaluated for requirement of number of rescue analgesia doses and the time at which patient first required rescue analgesia in the first 24 hours following surgery.

In this study all the patients (100%) in group A and group B were males. The commonest age group was 31 to 40 years in group A (40%) while in group B most of the patients were aged 20 to 30 years (36.67%) (p=0.653). The mean age in group A and B were comparable (36.30 ± 7.75 vs. 35.33 ± 8.40; p=0.645).

In the present study, 60% of the patients in group A had ≤ 6 months duration of hernia compared to 53.33% in group B (p=0.927). The mean duration of hernia in group A (7.07 ± 4.52 months) and group B (7.27 ± 4.44 months) were comparable (p=0.863). Majority of the patients in group A (73.33%) as well as group B (66.67%) had indirect hernia (p=0.573). With regard to extent of hernia, 80% of the

patients in group A and 76.67% of the patients in group B had incomplete hernia (p=0.754).

In this study, 46.67% of the patients in group A and group B had duration of surgery between 61 to 90 minutes (p=1.000). The mean duration of surgery in group A and group B (83.00 ± 21.52 vs. 83.83 ± 21.56 minutes; p=0.881) were comparable.

These findings suggest that, demographic characteristics, features of hernia and surgical parameters in both the groups were comparable ruling out the bias (p>0.050).

In this study no statistically significant difference was noted with respect to mean VAS score. In group A the mean VAS scores at three hours were low that is, 0.23 ± 0.63 which increased to 2.47 ± 1.59 at six hours. There was further increase in mean VAS scores at 12 hours that is 4.00 ± 1.93 and at 24 hours slight reduction was noted that is, 3.77 ± 1.55. In patients with group B similar trend was noted that is, the mean VAS scores at beginning were 0.37 ± 0.76 which increased to 2.53 ± 1.53 at six hours and there was further increase at 12 hours that is, 4.07 ± 1.84 and at 24 hours the scores were 3.17 ± 1.62. VAS score at three hours was slightly lesser in group A, while at 6, 12 and 24 hours VAS score was more in group A compared to group B. However this difference was not statistically significant. At all the intervals that is, three hours (p=0.463), six hours (p=0.869), 12 hours (p=0.891) and 24 hours (p=0.148) the mean pain scores were comparable in patients with group A and group B. These findings suggest that, a single transdermal diclofenac patch [100mg] was as effective as intramuscular diclofenac sodium (75 mg) as pre-emptive analgesia for

post operative management of pain among the patients undergoing Lichtenstein's inguinal hernioplasty

In this study single dose of rescue analgesia was administered in most of the patients in group A and group B (40% of the patients in group A and 46.67% in group B). Whereas 40% of the patients in group A required two doses compared to 26.67% in group B, while 3.33% in each group required three doses. Furthermore rescue analgesia was not requested by 16.67% of the patients in group A as against 23.33% in group B. However the differences observed were statistically not significant (p=0.790). Also the mean doses of rescue analgesia administered in group A was slightly high (1.30 ± 0.79 doses) compared to group B (1.10 ± 0.80 doses). However, the difference between mean number of doses of rescue analgesia was statistically not significant (p>0.050). Hence, a single transdermal diclofenac patch [100mg] for the management of post operative pain had no specific benefit in terms of reduction in post operative rescue analgesia consumption.

In the present study, nearly half of the patients in group A (53.33%) and group B (50%) required rescue analgesia at 12 hours (p=0.802). The mean time of requirement of first post operative rescue analgesia in group A was prolonged (10.00 ± 6.56 hours) compared to group B (8.53 ± 5.94 hours) but statistically the difference was not significant (p=0.368). These findings show that, the pain relief provided by single transdermal diclofenac patch [100mg] is longer compared to intramuscular diclofenac sodium (75 mg) but the difference was not statistically significant (p>0.050).

In this study, 3.33% of the patients in group A had erythema, while in group B nausea was noted in 3.33% of the patients and 6.67% of the patients had pain at injection site (p=0.612). Hence, the safety of single transdermal diclofenac patch [100mg] was comparable to intramuscular diclofenac sodium (75 mg).

Overall these results suggest that, single transdermal diclofenac patch [100mg] for the post operative pain management in patients undergoing Lichtenstein's inguinal hernioplasty is comparable to that of intramuscular diclofenac sodium (75 mg). However, we have inadequate data to support these findings as no studies have reported the effect of single transdermal diclofenac patch [100mg] as pre-emptive analgesia for the post operative pain management in patients undergoing Lichtenstein's inguinal hernioplasty.

These findings are similar to those of Funk et al,[84] who showed that both transdermal and oral diclofenac showed similar analgesic efficacy when used in patients with post operative shoulder pain.

It has been reported that diclofenac patches provide efficient analgesia following laparoscopic surgery.[41]

Agarwal et al.[85] reported pruritis or a localized erythematous rash at the site of application of the transdermal patch when using the transdermal diclofenac patch to attenuate venous cannulation pain.

The safety profile of diclofenac patches has been documented by Mason et al[43] in a systematic review on the use of topical NSAIDs in the UK and by other studies assessing the use of the transdermal diclofenac patch in osteoarthritis[51] as well as in sports-related injuries.[46]

A study was carried out to compare the efficacy of transdermal diclofenac sodium patch (100mg) with oral diclofenac (100mg) for the control of post-operative pain after surgical removal of mandibular third molars. Visual analogue scale was used to assess post-operative pain intensity and pain relief. The study reported that oral diclofenac was slightly more efficient than transdermal patch on first day, while no significant difference was found on second and third day.[7]

Transdermal analgesics are now being used in many areas of pain management and by many different patient groups. In the management of acute pain, the pain relief patch has two roles: prevention and treatment. Non-steroidal anti-inflammatory drugs (NSAIDs) are available in patch form to treat acute pain from musculoskeletal injury. Transdermal delivery of opioids has been used for many years, but has not been recommended for use in acute pain due to delayed onset of action and risks of toxicity. The fentanyl patient controlled transdermal system incorporates advantages of patient controlled analgesia (PCA) with a transdermal delivery system. It uses an iontophoretic mechanism to speed up drug delivery.[86]

Topical NSAIDs are formulated so that they penetrate the subcutaneous tissues and accumulate under the site of application. A recent review[45] supports a topical effect and not simply a systemic effect. A reduction in pain scores was demonstrated after 3 hours in patients with ankle sprains. As diclofenac first appears in the plasma at a mean of 4.5 hours, after topical application, it is thought that the patch must provide analgesia via a local action. After patch removal, due to a local reservoir effect, the plasma diclofenac half-life is 9–12 hours, compared with 1–2 hours after oral intake. Systemic transfer after removal of the patch compared with oral forms of diclofenac is only about 2%, so systemic side-effects are very rare. No

drug-related gastrointestinal bleeding or ulcers have been reported during diclofenac epolamine patch use. Most side effects relate to topical effects: pruritis, erythema, rashes, and rarely allergic dermatitis. A systematic review[87] comparing oral diclofenac with topical applications, including the patch form, suggested that topical diclofenac is either superior or equivalent to oral diclofenac formulations or placebo in reducing the pain in osteoarthritis of the knee and sports-related soft tissue injuries.

A double blind study was carried out to evaluate the safety and clinical efficacy of transdermal diclofenac sodium patch in treating blunt impact sports injuries. Either the diclofenac patch or a placebo patch was applied twice daily for 7 days. Visual analogue scale, tonometer and a global efficacy assessment scale (four point scale) were used to assess pain relief. The study reported that the diclofenac transdermal patch is safe and effective in treating blunt sports injuries and it results in a constant and continuous delivery of the drug to the affected area by means of an occlusive bandage and slow release of drug.[46]

Another study was done in which the efficacy and side effects of the transdermal diclofenac patch was compared with eutectic mixture of local anesthetic (EMLA) in decreasing pain due to venous cannulation. Patients were divided into 3 groups which received placebo patch, EMLA and transdermal diclofenac patch. Visual analogue scale was used to record pain scores. The study reported that topically applied NSAIDs inhibit the synthesis of prostaglandins at the site of application, decrease the inflammatory response to cannulation and are effective in managing both acute and chronic pain. The transdermal patch was favoured as the incidence of skin blanching was lower with the patch compared to EMLA.[88]

The patch is convenient, simple to use and can be self administered. Owing to its longer half life it can be changed less frequently and prolonged constant plasma levels are achieved. It can be used in unconscious patients and in those who cannot tolerate the oral route. Lesser side effects have been noted. It bypasses the first pass metabolism allowing more availability of the drug. It is non-invasive and painless. These advantages improve the patient compliance.

Overall the transdermal diclofenac patch appears to be a better analgesic modality for the management of post operative pain in patients undergoing Lichtenstein's inguinal hernioplasty given the evidence of its established analgesic potency along with the various advantages over the intramuscular route. However, longer clinical trials need to be conducted with a larger sample before defining the real scope of the transdermal diclofenac patch.

CONCLUSION

The transdermal diclofenac patch (100mg) is as effective as intramuscular diclofenac sodium (75mg) for pre-emptive analgesia in patients undergoing Lichtenstein's inguinal hernioplasty as measured by the requirement of rescue analgesia in the first 24 hours and the time at which patient requires rescue analgesia following surgery.

From our study we conclude that, since the transdermal diclofenac patch has many advantages over the intramuscular route, it is a better option for pre-emptive analgesia in the management of postoperative pain in patients undergoing Lichtenstein's inguinal hernioplasty.

SUMMARY

Postoperative pain is a common problem in any surgical setup and requires appropriate analgesia. Transdermal diclofenac patch is a new modality in the surgical pain management but its effect on Lichtenstein's inguinal hernioplasty remains unknown. This study was planned to assess the efficacy of transdermal diclofenac patch (100 mg) with intramuscular diclofenac sodium (75 mg) as pre-emptive analgesia as determined by number of times the patient requires rescue analgesia in first 24 hours and the time at which patient first requires rescue analgesia after surgery in patients undergoing Lichtenstein's inguinal hernioplasty.

This one year randomized controlled trial was carried out in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2014 to December 2014. A total of 60 patients diagnosed with inguinal hernia and posted for Lichtenstein's inguinal hernioplasty were studied. Patients were divided into two groups of 30 each as Group A (single transdermal diclofenac patch [100mg]) and Group B (Single intramuscular injection of diclofenac sodium [75mg]).

In the present study all the patients in group A and B were males (100%). The mean age in group A was 36.30 ± 7.75 years compared to 35.33 ± 8.40 in group B (p=0.645). Other characteristics like duration of hermia (p=0.927), mean duration of hernia (p=0.863), type (p=0.573) and extent of hernia (p=0.754), mean duration of surgery (p=0.881) were comparable in group A and B. The mean VAS scores in group A and B at three hours (p=0.463), six hours (p=0.869), 12 hours (p=0.891) and at 24 hours (p=0.148) were comparable. In group B, 6.67% of the patients had

pain at injection site and 3.33% of the patients had nausea while, in patients with group A, complications of erythema were noted in 3.33% of the patients (p=0.612). Most of the patients in group A (40%) and group B (46.67%) required one dose of rescue analgesia (p=0.790). The mean number of doses for rescue analgesia and the mean time request for first post operative rescue analgesia was slightly high in group A compared to group B but the same was not true statistically (p=0.336 and p=0.368 respectively).

Overall it may be concluded that, transdermal diclofenac patch seems to be a better analgesic modality for the management of post operative pain in patients undergoing Lichtenstein's inguinal hernioplasty given the evidence of its established analgesic potency and various other advantages compared to intramuscular route.

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ANNEXURE I – CONSENT FORM

TITLE OF RESEARCH STUDY: A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH WITH INTRAMUSCULAR DICLOFENAC AS PRE-EMPTIVE ANALGESIA IN PATIENTS UNDERGOING LICHTENSTEIN'S INGUINAL HERNIOPLASTY

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Introduction and purpose

You are requested to participate in a study that is an attempt to find out the effectiveness of preoperative application of a transdermal patch of an analgesic as compared to intramuscular injection of the same analgesic.

Intramuscular analgesics are routinely used to tackle postoperative pain which is a common issue following surgery. However, these intramuscular analgesics have many disadvantages like GI side effects, local pain during administration, reduced compliance, injection abscess formation, renal and platelet dysfunction.

In an effort to avoid the above mentioned problems, this study has been undertaken to evaluate the efficacy of a new, alternate route of administration, i.e. the transdermal patch. In this study, transdermal administration of the analgesic via a patch will be compared to the standard intramuscular route of administering the drug in the deltoid or gluteal region. About 60 patients with unilateral inguinal hernia will be enrolled in this study.

This study will be conducted by Dr. **** ******, Post Graduate in Department of Surgery, under the direct supervision and guidance of Dr. **** ******, Professor, Department of Surgery, Jawaharlal Nehru Medical College, Belgaum.

You need to be eligible, meeting all the selection criteria to participate in this study. You should be willing to provide information about yourself. 60 subjects will be enrolled in this study who will then be randomized in either of 2 groups (details below).

Procedure

If you agree to participate in this study, you will be randomly allotted into a group (A or B) and accordingly receive either the standard treatment (intramuscular injection) or the newer treatment (transdermal patch). In the 24 hours following surgery, you will be assessed at fixed intervals for post-operative pain. You will be given an intramuscular injection of the analgesic if pain scores exceed a certain limit or on request for rescue analgesia.

Benefits

The transdermal patch has the advantage of being painless as opposed to the intramuscular route which causes pain at the injection site. However, the patch is more expensive than the intramuscular drug.

Risk involved

Apart from the side effects caused by diclofenac such as GI discomfort, the intramuscular route may cause injection site pain or abscess in some patients while the transdermal patch may cause a local allergic skin reaction in some (as observed in previous similar studies).

Compensation

Taking part in the study will not affect the cost of treatment i.e. it will be similar to the cost of standard procedure. In the event that you become injured as a result of taking part in this study, treatment will be offered to you or you will be given information about where to receive medical care: but you/your insurance company will be responsible for the costs. However, no reimbursement, compensation or free medical care will be given.

Confidentiality

Every effort will be made to protect the confidentiality of the information you provide. This means that the researchers will not let anyone, not a part of the study, see the information you provide. Only Dr. ***** ****** and Dr. **** ***** will have access to the information collected. Results of this study may be published but your name will not be revealed.

Voluntary participation / withdrawal

Taking part in this study is voluntary; you may choose not to enroll in this study. Your decision will not change the present or future health care services offered to you at KLES Dr. Prabhakar Kore Hospital, Belgaum. The alternative that you have is to undergo the traditional procedure that is carried out in KLES Hospital.

If you have any queries about the study, you may contact Dr. ***** ***** (Mobile No. ***** *****); or Dr. ***** ****** (Mobile No. ***** *****). If you

need any further information regarding your rights as a study participant, you may also contact Dr. **** ***** (Mobile No. ***** *****), Chairman of Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belgaum.

CONSENT TO PARTICIPATE IN THE STUDY

I Mr./Ms._____ have been explained about the research study, the need of the study, the intervention, their risks, benefits and alternatives available in my own vernacular language.

I voluntarily agree to participate in this study by signing up this form below. I understand that I may withdraw at any time from this study. I have been given adequate time to clarify my doubts about the study and my rights as a study participant.

My signature / thumb impression below indicates that I have read or information in the consent been read to me including the risks and benefits and have cleared my doubts.

Name of participant:

Signature/LTI:

Name of legally authorized

Signature/LTI:

Representative (if applicable):

Relationship with participant:

Name of witness: Signature:

Name of investigator: Signature:

Date:

Place:

ANNEXURE II – PROFORMA / QUESTIONNAIRE TO BE USED FOR DATA COLLECTION

"A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH WITH INTRAMUSCULAR DICLOFENAC AS PRE-EMPTIVE ANALGESIA IN PATIENTS UNDERGOING LICHTENSTEIN'S INGUINAL HERNIOPLASTY"

Patient Identification Data

Group:	Ward:
Name:	In Patient Number:
Age / Sex:	Date of Admission:
Address:	Date of Surgery:
Date of Discharge:	Education:
Religion:	Marital Status:
Occupation:	Socio-Economic Status:

Chief Complaints

History of Presenting Complaints

Previous history of allergy to NSAIDs

Past History

Personal History

Family History

General Physical Examination

Built and Nourishment:

Weight:

Pallor

Icterus

Cyanosis

Clubbing

Edema

Lymphadenopathy

Vital Signs:

PR: / min;

BP: mmHg;

RR: / min;

Temp:

Local Examination

Inspection:

Palpation:

Percussion:

Auscultation:

Systemic Examination

Abdomen:

Rectal:

Cardiovascular system:

Respiratory system:

Clinical Impression

Investigations

Operation Details :

Date of Surgery :

Name of surgery : Lichtenstein's inguinal hernioplasty

Anesthesia : Spinal Anesthesia

Duration of surgery :

Duration of spinal anesthesia :

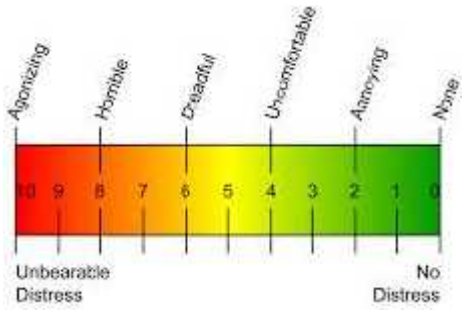
Induction time :

Incision time :

Closure time :

Assessment of post operative pain :

Visual analogue scale :



0 – No Pain; 1-3 – Mild Pain; 4-7–Moderate Pain; 8-10–Severe Pain

Post-operative pain scores at

0 min	3 hours	6 hours	12 hours	24 hours

Rescue Analgesia

Dose:

Time:

Vas Score:

ANNEXURE III – KEY TO MASTER CHART

A	-	Transdermal diclofenac patch group
B	-	Intramuscular diclofenac sodium group
BP	-	Blood Pressure
C	-	Complete
D	-	Direct
i	-	Incomplete
I	-	Indirect
M	-	Male
mg	-	Milligrams
mm Hg	-	Millimeters of mercury
SA	-	Spinal aneathesia
VAS	-	Visual analog scale