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RESEARCH ARTICLE

"TO COMPARE THE POST-OPERATIVE ANALGESIC EFFECT OF PER RECTAL PARACETAMOL AND PER RECTAL DICLOFENAC IN PAEDIATRIC SURGERIES AGE GROUP (5YEARS-12YRS)"

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Abstract

Introduction:-

In ancient civilizations, one can trace the evolution of pain from concepts of demons to concepts of sin in relation to sin and punishment.

The word 'PAIN' is derived from Greek '*Poine*' (penalty) via the Latin 'Poena' (punishment). Pain is a biological phenomenon that is easy to comprehend but difficult to define.

- **Aristotle** defined pain as 'an unpleasantness arising from the body, within the body and within the soul'.
- **Rovenstine** has defined pain as 'the cry (a psychic and efferent response) of nature in distress (imperative afferent stimulus)'.
- In **Samuel Johnson's** words: 'those who do not have pain, seldom think it is great in someone else'.
- **Sherrington** has defined pain as 'the psychical adjunct to an imperative protective reflex'[1].

The International association for the study of pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"[2]. This definition emphasizes that the experience of pain has two inseparable elements processed in parallel by the nervous system, i.e. sensory (nociception) and affective (emotional) and that pain can be experienced without discernable physical cause, i.e. injury or disease.

The term "nociception" which is derived from *noci* (Latin for harm or injury) is used to describe the neuronal response only to traumatic or noxious stimuli. All nociception produces pain, but not all pain results from nociception. Many patients experience pain in the absence of noxious stimuli. Thus pain can be divided into two categories

1. Acute pain, which is primarily due to nociception.
2. Chronic pain, which may be due to nociception but in which psychological and behavioral factors often play a major role.

Most surgical procedures inflict pain during the procedure and this also continues in the post- operative period as post-operative pain. Adequate pain relief should be considered as basic human right. Failure to relieve pain is morally and ethically unacceptable[3]. Providing rapid and effective relief of pain remains a humanitarian issue,

whereas allowing patients to suffer as a result of analgesic under medication may be considered a breach of fundamental human rights [4, 5, 6].

Primary care physicians and pain specialists prescribe opioids to a greater number of their patients and in doses appropriate to needs [5, 6, 7, 8].

Post-operative pain is one of the worst types of pain a patient may suffer. With the birth of effective anaesthesia in the middle of 19th century, it was not long before the post-operative pain was recognized as a discipline worthy of attention in its own right. The goal for the post-operative pain management is to reduce an individual patients pain considerably with minimal or no associated suffering or distress[9]. Noxious stimuli such as surgical trauma and subsequent post-operative pain results in a broad range of endocrinologic, immunologic and inflammatory responses including increased release of catabolic hormones and inhibited secretion of anabolic mediators. Pathophysiologic consequences of undertreated pain may adversely influence peri-operative outcome. Patients subjected to inadequate pain relief are often unable to breathe adequately, cough effectively, move enough even to attend to their own daily needs or participate in their own rehabilitation and hence they experience feelings of helplessness, fear, anxiety, low mood and loss of control[10].
Adverse sequealae of surgical trauma and unrelieved pain include[11]:

- Cardiovascular stress (tachycardia, hypertension etc.).
- Autonomic hyperactivity (sympathetic and parasympathetic stimulation, lacrimation, sweating etc.).
- Pulmonary dysfunction (decreased tidal volume, tachypnoea, miliary atelectesis, cough suppression etc.).
- Tissue breakdown (production of a catabolic state with suppression of anabolic hormones).
- Hypercoagulability and deep vein thrombosis.
- Fluid retention.
- Dysfunction of immune system.
- Delayed return of bowel function.
- Development of chronic pain syndromes.

In the early 1900's **George Crile** suggested, "Control of Post-operative pain could favorably influence the results of surgery"[12]. Study has shown that post-operative pain is maximum during initial 48-72 hours & it declines thereafter[13]. However, post-operative pain still is an overlooked entity that receives little care. Therefore post-operative pain relief is also a major concern for an anaesthesiologist. Intravenous (i.v) or intramuscular (i.m) boluses of opioids with or without non-steroidal anti-inflammatory drugs (NSAIDs) constitute the mainstay of post-operative pain relief.

Recommended approach for postoperative pain management is to initiate treatment with analgesics such as paracetamol, NSAIDS and aspirin followed by adjunctive use of opioids to treat more acute pain symptoms. However the adverse effects associated with opioid use are well established and includes dose dependent respiratory depression, nausea, vomiting, constipation, urinary retention and sedation[14, 15]. NSAIDS are associated with adverse events including dyspepsia, gastric mucosal damage, post operative bleeding and renal effects[16] highlighting a requirement for more tolerable pain relief agents.

Paracetamol acts on both the central and peripheral components of the pain pathway[17, 18]. One mechanism is through the direct inhibition of the N-methyl-D-aspartate receptor, which stimulates the substance P dependent mechanism of the nitric oxide, a primary mediator of noiciception[19]. Paracetamol has also been implicated in the inhibition of the cyclo-oxygenase 2 pathway involved in prostaglandin synthesis. A metabolite of paracetamol also sequesters reduced glutathione, a required cofactor for membrane bound prostaglandin synthetase, another potent mediator of nociception. Therefore paracetamol may also contribute to the alleviation of pain by indirectly attenuating production of prostaglandins. The analgesic effects of paracetamol also involves the serotonergic system[20] agonists of serotonin 5-HT_3 receptors namely tropinesteron and granisetron, completely blocked the analgesic effect of paracetamol, indicating an antinociceptive role for paracetamol[21].

Paracetamol has been recently added to the armamentarium of anaesthesiologists for intra-operative and post-operative analgesia. Moreover this drug has not been used much in clinical anaesthesia, therefore we decided to study this drug and compare it with tramadol hydrochloride when used in providing intra-operative and post-operative analgesia.
NSAIDs are used in infants and children older than 3 months to reduce pain, fever and inflammation, and in

neonates to close the patent ductusarteriosus (PDA). They are commonly used for postoperative pain, because they reduce the need for opioids and increase patient satisfaction (Kokki 2003, Eustace and O'Hare 2007). However, NSAIDs may cause adverse effects, including gastric, renal and central nervous system (CNS) complications. Nevertheless, severe adverse effects are rare in short-term postoperative use in children.

Aims and objectives:-

This Study was undertaken to compare the post operative analgesic effect of two drugs i.e.Group D – Rectal Diclofenac Sodium (1mg/kg) , Group P Rectal Paracetamol (15mg/kg) in paediatric age groups ranges from (5years to 12 years) .

Aim: Sixty paediatric patient between 5-12years of ASA I and ASAII were randomly divided into two equal group of 30 each. Group D-Per Rectal Diclofenac Sodium and Group P Per Rectal Paracetamol were Observed for the following :

Objectives:

- To compare the duration of Analgesia of Per Rectal administered Diclofenac sodium and Paracetamol.
- Observe changes in haemodynamic parameters : Blood pressure, pulse rate and Oxygen saturation.
- To Observe Side effects and complications if any.

Pathophysiology of pain:-

Definition of pain

International association for the study of pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".

CLASSIFICATION OF PAIN

Clinically pain can be either acute or chronic:

1. **Acute pain**

It is defined as pain, which is caused by noxious stimulation due to injury, a disease process or abnormal function of muscles or viscera. It is nearly always nociceptive, severe, well localized and limits tissue damage. It is typically associated with a neuro-endocrine stress, which is proportional to intensity of pain. It includes post-traumatic, post-operative, obstetric pain and pain associated with medical illnesses e.g. acute myocardial infarction, acute pancreatitis etc.

Acute pain can be of two types:

- **Somatic Pain** : Superficial: It is due to nociceptive input from skin, subcutaneous tissue and mucous membrane. It is well localized.
- Deep: It arises from muscles, tendon, joint or bone. It is dull aching and less well localized.

A. **Visceral Pain**: It is due to a disease process or due to abnormal function of an internal organ or it's covering (e.g. parietal pleura, pericardium or peritoneum).

2. **Chronic pain**: It is defined as pain that persists beyond the usual course of an acute disease or after a reasonable time for healing to occur. This period varies between 1 to 6 months. It is commonly associated with musculoskeletal disorders, chronic visceral disorders, lesion of peripheral nerves, nerve roots, or dorsal root ganglia and cancer invading the central nervous system.

Chronic pain may be nociceptive, neuropathic or both. Psychological mechanism or environmental factors frequently plays a major role. Patients often have attenuated or absent stress response with prominent sleep and mood disturbances. Pain has a burning quality and is associated with hyperpathia (hypersensitivity to sensory stimuli, which includes hyperesthesia, allodynia and hyperalgesia).

Pathophysiologically pain is divided into:

1. nociceptive pain: it is due to activation or sensitization of peripheral nociceptors.

2. Neuropathic pain: it is the result of injury or acquired abnormalities of peripheral or central neural structures.

the four processes that make up the nociception are**:**

1. Transduction: translation of noxious stimuli into electrical activity at the sensory nerve endings.

2. Transmission: propagation of impulses via the sensory aspect of nervous system.

3. Modulation: modification of these transmitted impulses through various neuromediatory and chemical factors.

4. Perception: summation of all the three processes takes place and depending upon personal affect and subjective emotional experience, what is percieved as pain is produced, that occurs at the cortical level.

THEORIES OF PAIN

1. Theory of traditional law of specific nerve ending: It was proposed by **Muller in 1842,** it emphasises on the receptor and not on the quality of the stimulus in discerning a particular sensation. He proposed discrete receptors for each individual sensation.

2. Non-specific or Pattern theory: It was proposed by **Weddel in 1950**. This theory primarily opposes Muller's concept and ignores the specialization concept. It states that afferent impulses are carried impartially by nerve fibres of all sizes. Any distinctive feature is entirely due to the merging and confluence of the numerous particles of information into complicated patterns that reflect the quality, intensity and duration of noxious stimuli.

3. Theory of dual system: It was proposed by **Zotterman in 1962,** according to this theory noxious stimulus has two components namely; (i) the fast component or the sting which travels by 'A' group fibers and (ii) slower component; i.e. the burning sensation arrives in 'C' group fibres. The perception by the two routes varies with the length of peripheral nerve.

4. Gate control theory: It was proposed by **Melzack and Wall in 1965**. According to this theory, the stimulation of skin evokes afferent potentials that are conducted through large and small diameter fibres which converge on the substantia gelatinosa. It is the convergence of these fibres that influence the balance created by "gate control" cells located in substantia gelatinosa. The actual perception of pain takes place in brain which is governed by neural mechanism that is collectively known as "action system". The action system in turn is initiated by special cells in "target area" (T) located in dorsal horn of the spinal cord. Afferent impulses in large nerve fibres characteristically occur in burst of impulses[38, 39]. These impulses are mainly inhibitory; they in effect keep the gate partially closed and therefore diminish the intensity of pain. The afferent impulses from smaller fibres travel more steadily and through this continuous discharge on the target area cells the gate is kept open and transmission of pain is enhanced.

It has been known that substantia gelatinosa contains beta-endorphins and enkephalins. Now it is known that it also contains upto 25 more different types of receptors, one of these is cholinergic muscarinic receptor. This is the area, which provides binding site for the opiates, clonidine and anticholinesterases and here nociceptive impulses can be blocked at the spinal level, providing pain relief.

Reynolds in 1969 provided a strong scientific support to the theory suggesting that modulation in the dorsal horn can be affected by input not only from the periphery but also from the supraspinal descending systems. The descending inhibitory tracts originate from cell bodies located in the mesencephalic periaqueductal gray and periventricular gray matter[43]. Axons of these cells descend to the spinal cord in the dorsilateral funiculus and synapse in the dorsal horn, which control, modulate and attenuate the noxious input. The various descending systems; opioid system, alpha – adrenergic system, serotonergic system, cholinergic system, GABAergic system work harmoniously, blocking the nociceptive impulses by inhibiting the synaptic afferent transmission.

Anatomy of nociception fibres and peripheral pathways:

In 1924, Erlanger and Gassa proposed the classification of nerve fibers on the basis of action of Cocaine on these fibers.

Fibers:

Myelinated somatic fibers further sub-divided into:

- A alpha (α): diameter 12-20 μm with conduction velocity of 70-120 m/s; supply muscle spindles and motor to skeletal muscles.
- A beta (β): diameter 5-15 μm with conduction velocity of 30- 70 m/s; supply cutaneous, touch and pressure afferents.
- A gamma (γ): diameter 6-8 μm with conduction velocity 15-30 m/s; supply motor to muscle spindle.

- A delta (δ): diameter 1-4 μm with conduction velocity 12-30 m/s; supply mechano and nociceptors.

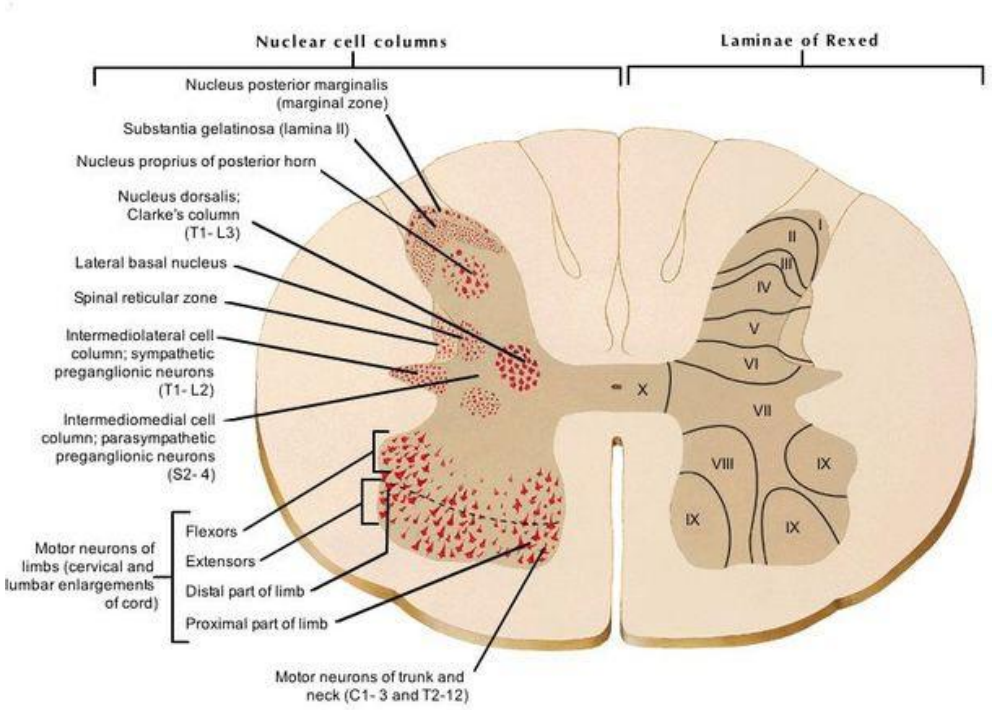
B fibers:
These are myelinated, preganglionic sympathetic white rami having diameter of 1-3 μm and conduction velocity of 3-15 m/s.

C fibers
These are non-myelinated fibers of both somatic and autonomic nervous system. Diameter 0.5-1.5 μm with conduction velocity of 0.5-2 m/s.

Thus Aδ and C fibers sub-serve pain; these fibers have their cell stations in the dorsal root ganglion.

The neuro-anatomical basis of pain was recognized following identification of spinal nerve roots and existence of medullary pathways specialized for pain. There is a multi-synaptic pathway system, which relays in the reticular formation of brainstem. Stimulation of these pathways causes perception of pain at the cortical and sub-cortical levels.

The laminae of rexed in the spinal cord
The grey matter of the spinal cord is organized into laminae, first described by Rexed in cats.



Lamina I
It receives some incoming sensory fibers from the dorsal root and its large neurons contribute to the axons of the contra-lateral spinothalamic tract.

Lamina II: It comprises of substantia gelatinosa cells. It receives collaterals of dorsal root fibers and descending reticulospinal tracts, which modulate transmission of pain sensation to the brain.
Lamina III: Consists of inter-neurons.
Lamina IV: These are tract cells. Their long dendrites receive the largest sensory input from the dorsal horn. Their axons are largely myelinated, cross over to enter the contra-lateral spinothalamic tract.

Laminae V and VI :Consist of inter-neurons which receive some primary afferent fibres and descending fibers such as corticospinal fibres, most of which terminate here. Pool of inter-neurons here is the reticular formation of the spinal cord

Lamina VII :consists of a pool of neurons, which mediate local segmental and inter-segmental reflexes. The axons of nucleus dorsalis is of Clarke form the dorsal spinocerebellar tract. The ventral spinocerebellar tract originates from cell bodies in layers V-VII. The intermediolateral column in segments T_1-L_3 is the site of preganglionic neurons of the sympathetic system, while those located in S_{2-4} are the preganglionic neurons of the parasympathetic system

Lamina VIII:It contains neurons, which receive descending vestibulospinal tracts and reticulospinal tracts and project bilaterally to laminae VII and IX.

Lamina IX:Contain α and γ neurons. The ventro-medial neuron supplies trunk muscles, while the dorso-lateral neuron supplies muscles of the limb. In the cervical region the phrenic nucleus in C_{3-5} supplies the diaphragm.

Lamina X:Surrounds the central canal and receives some dorsal root fibres, and contain some decussating fibres and glial cells.

Pain pathways

Pain is conducted along three-neuron pathways from the periphery to the cerebral cortex.

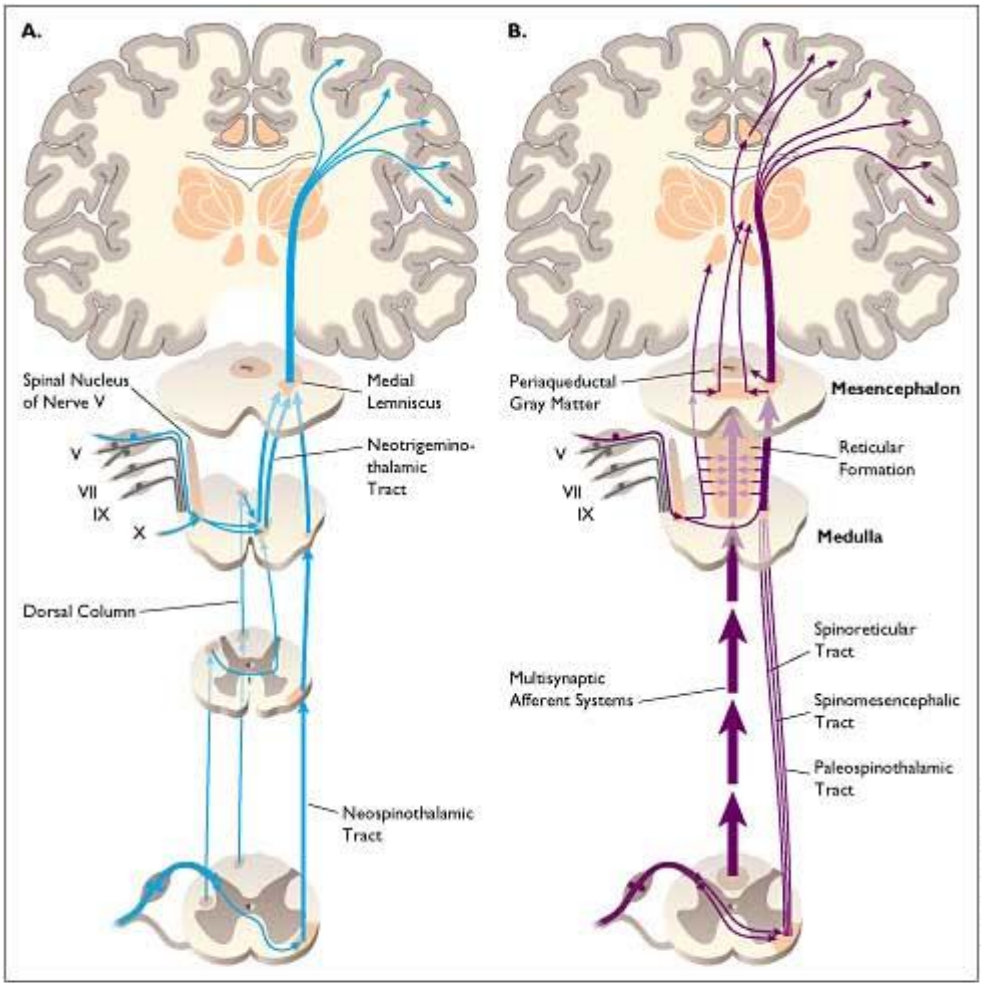


Figure _nals are transmitted to the brain by two main pathways. The lateral system (A) is made up of long thick fibers that transmit information about the onset of injury, and its precise location and intensity. They are designed to carry a rapid flow of pain signals to the thalamus to stimulate an immediate antinociceptive response. The medial system (B) is composed of phylogenetically older fibers that carry slower signals and probably transmit information related to the persistence of injury and level of response induced.

First-order neuron:Majority of first-order neuron send their proximal axons into spinal cord via dorsal (sensory) spinal root at each cervical, thoracic, lumbar and sacral level. Here they synapse with second-order neurons, inter-neurons, sympathetic neurons or motor neurons. Pain fibers originating from head are carried by the trigeminal (V), facial (VII), glossopharyngeal (IX) and vagus (X) nerves. Their first order afferent neuron are located in Gasserian ganglion, geniculate ganglion, superior and petrosal ganglion, jugular ganglion (somatic) and ganglion nodosum (visceral) respectively and proximal axonal processes of these neurons reach the brainstem nuclei, where they synapse with second-order neurons.

Second-order neuron:First-order neuron may ascend or descend 1 to 3 spinal cord segments in Lissauer's tract (a band of fibers that caps the dorsal horn) before synapsing with second-order neuron (either directly or via interneurons) in the gray matter of the ipsilateral dorsal horn.

Second-order neurons are either nociceptive-specific (NS) or wide dynamic range (WDR) neurons. NS neurons are arranged somatotropically in lamina I and have discrete somatic receptive fields. They are normally silent and respond only to high-threshold noxious stimulation, poorly encoding the intensity. WDR neurons are found throughout the dorsal horn but are most abundant in lamina V. During repeated stimulation WDR neurons increase their firing rate exponentially in a graded fashion (wind-up) even with the same stimulus intensity.

The spinothalamic tract (major pain pathway)

Before they form the spinothalamic tract, the axons of most second-order neurons cross to the contra-lateral side close to their level of origin (at the anterior commisure). They send their fibers to thalamus, reticular formation, nucleus raphe Magnus and periaqueductal gray matter. This tract lies antero-laterally in the white matter and is divided as lateral and medial tracts.

The lateral spinothalamic (neospinothalamic) tract projects mainly to the ventral posterolateral nucleus of thalamus and carries discriminative aspects of pain (location, intensity, duration).

The medial spinothalamic (paleospinothalamic) tract projects to the medial thalamus and is responsible for mediating the autonomic and emotional perception of pain. Spinothalamic fibers also project to periaqueductal gray matter and form link between the ascending and descending pathway. Collateral fibers also project to the reticular activating system and hypothalamus and are responsible for arousal response to pain.

The Archispinothalamic tract is phylogenetically oldest and least specific. First order nociceptive neurons synapse in lamina II (substantia gelatinosa) and ascend to laminae IV to VII. From these laminae fibers reach medial reticular formation (MRF) & periaqueductal gray (PAG) by ascending through multisynaptic propriospinal pathways. Diffuse multisynaptic pathways connect MRF, PAG to intralaminar thalamic nuclei, parafascicularis & centromedian complex to the anterior part of cingulated gyrus (emotion) amygdala (memory & emotion) & hypothalamus (visceral & vascular response to emotion).

Alternate pain pathways:

Pain fibers ascend diffusely both ipsilaterally and contralaterally. The spinoreticular tract mediates arousal and autonomic response to pain. The spinomesencephalic tracts may activate anti-nociceptive descending pathways. The spinohypothalamic and spinotelencephalic tract activate the hypothalamus and evoke emotional behaviour. The spinocervical tract ascends uncrossed to the lateral cervical nucleus and relays fibers to contralateral thalamus (a major alternative pain pathway). Some fibres ascending medially and ipsilaterally in dorsal column (carrying light touch and proprioception) are also responsive to pain.

Integration with the sympathetic and motor system

Somatic and visceral afferents are fully integrated with the skeletal motor and sympathetic systems in spinal cord, brainstem and higher centers. Afferent dorsal horn neurons synapse with anterior horn motor neurons and are responsible for reflex muscle activity associated with pain. Synapse between afferent nociceptive neurons and sympathetic neurons (in the intermediolateral column) result in reflex sympathetically mediated vasoconstriction, smooth muscle spasm and release of catecholamines.

Third-order neurons

Third-order neurons are located in the thalamus. As the spinothalamic tract approaches the thalamus, it segregates into medial and lateral divisions.

The medial division of the spinothalamic tract projects to the brain stem reticular formation, the hypothalamus, the periaqueductal gray matter and the medial thalamic nuclei. Subsequent ramifications are to widespread areas of the cortex and limbic system. The medial spinothalamic tract is thought to sub-serve the affective/motivational aspects of pain perception.

The lateral division of the spinothalamic tract terminates in the lateral, ventral basal, and posterior thalamic nuclei. The lateral spinothalamic tract is thought to be involved in the sensory/discriminative aspects of pain perception. Perception and discrete localization of pain take place in these cortical areas. Most neurons from the lateral thalamic nuclei project to the primary somatosensory cortex. Neurons from the intralaminar and medial nuclei project to the anterior cingulate gyrus and likely mediate the suffering and emotional component of pain.

Sensory cortical representation

Mapping of sensory cortical areas involved in sensation has been carried in intact humans by techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). From the specific sensory nuclei of the thalamus, neurons carrying sensory information project in a highly specific way to the two somatic sensory areas of the cortex: somatic sensory area 1 (S1) in the postcentral gyrus and somatic sensory area 2 (S2) in the wall of the sylvian fissure. In addition SI projects to S2. The arrangement of the thalamic fibers in S1 along the postcentral gyrus is represented in order with the legs on top and the head at the foot of the gyrus. The size of the cortical representation from a particular part of the body is proportionate to the number of receptors in that part and the function performed with that part of body.

Physiology of nociception

1. Nociceptors

One of the vital functions of the CNS is to provide information about the occurrence/threat of injury. Nociception is a central response to peripheral noxious stimulation of the nociceptors. Nociceptors is a term applied to specific receptors for pain projecting to pain centers, first postulated by Von Frey in 1894. Anatomically, they are thinly myelinated nerve endings or naked nerve endings.

A Nociceptor has two Characteristics:They have higher threshold than the low threshold mechanoreceptors or thermoreceptors.

a) They respond preferentially to noxious stimuli.

Goldschinder suggested that pain arises from excessive activity of any type of receptors by a central stimulation process.

Nafe proposed that pain is signaled by temporal and spatial patterns or response to nonspecific receptors.

Pert in 1960 worked towards identification of subgroups of nociceptors.

Nociceptors are present in both somatic and visceral tissues. Primary afferent neurons reach tissues by travelling along spinal somatic, sympathetic or parasympathetic nerves.

A. Somatic Nociceptors Include

- Cutaneous nociceptors: These are present in skin. The cornea and tooth pulp are innervated by nociceptive Aδ and C fibers.

A. **Deep nociceptors**: These are located in tissue such as muscles, tendon, fascia and bone. Deep nociceptors are less sensitive to noxious stimuli, but are easily sensitized by inflammation. The pain arising from them is dull and poorly localized. Specific nociceptors may exist in muscles and joint capsules. They respond to mechanical, thermal and chemical stimuli.

B. Visceral nociceptors

Visceral organs are generally insensitive tissues that mainly contain silent nociceptors. Organs such as the intestines are innervated by polymodal nociceptors that respond to smooth muscle spasm, stretching, ischemia and inflammation. These receptors generally do not respond to cutting, burning or crushing that occur during surgery. Some organs appear to have specific nociceptors, such as heart, lung, testes and bile duct. Brain lacks nociceptors but brain's meningeal coverings contain nociceptors.

2. Chemical mediators of pain

3. Several neuropeptides and excitatory amino acids function as neurotransmitters for afferent neurons sub-serving pain. Glutamate is the most important excitatory amino acid. Many neurons contain more than one

neurotransmitters, which are simultaneously released. The most important of these peptides are substance P (SP) and calcitonin gene-related peptide (CGRP).

Major neurotransmitters mediating or modulating pain: neurotransmitter	Receptors	Nociception Effect
Substance P (SP)	NK_1	Excitatory
Calcitonin gene-related peptide (CGRP)	----	Excitatory
Glutamate	NMDA, AMPA, kainite	Excitatory
Aspartate	NMDA, AMPA, kainite	Excitatory
Adenosine triphosphate (ATP)	P_1, P_2	Excitatory
Somatostatin	-----	Inhibitory
Acetylcholine	Muscarinic	Inhibitory
Enkephalins	μ, δ, κ	Inhibitory
β-Endorphin	μ, δ, κ	Inhibitory
Norepinephrine	α_2	Inhibitory
Adenosine	A_1, A_2	Inhibitory
Serotonin	5-HT_1, 5-HT_3	Inhibitory
GABA	$GABA_A$, $GABA_B$	Inhibitory
Glycine	----	Inhibitory

Modulation of pain

Modulation of pain occurs peripherally at nociceptors, in *spinal cord* or in *supraspinal* structures. It can either *inhibit or facilitate* pain.

Peripheral modulation

An important factor responsible for postoperative pain is the development of primary and secondary hyperalgesia. Hyperalgesia is defined as leftward shift of the stimulus response function, which relates magnitude of pain to stimulus intensity[56]. At the site of injury, it is termed as *Primary hyperalgesia* and it is mediated by release of allogens from damaged tissue. Histamine and serotonin are released from mast cells, basophils and platelets. Bradykinin is released from tissue following activation of factor XII. In the uninjured surrounding area it is called *Secondary hyperalgesia* [57]. After cell injury, arachidonic acid (AA) is liberated from cell membrane. The AA metabolised by *cyclooxygenase* pathway and its metabolites are thromboxane, prostacyclin and prostaglandin. The AA metabolites of *lipoxygenase* pathway include 5-HETE (5-Hydroxyeicosatetraenoic acid) and leukotrienes. Prostaglandin enhances transduction by sensitizing nociceptors to the action of other alogenic substances. The leukotrienes produce hyperalgesia.

Nociceptors and their neurons show sensitization after repeated stimulation. Sensitization of nociceptors causes decrease in threshold & response latency, increase in response and spontaneous firing (after-discharges). It commonly occurs after injury or application of heat.

Neurogenic inflammation (secondary hyperalgesia) is manifested by triple response and is due to release of SP from collateral axons of primary afferent neuron. SP degranulates the granulocytes, mast cells and other storehouses to release histamine and 5-HT (serotonin) resulting in vasodilatation, tissue edema and thus induces formation of leukotrienes, which produce hyperalgesia.

Central modulation

Facilitation:

At least three mechanisms are responsible for central sensitization in the spinal cord.

Wind-up sensitization of second-order neuron

WDR neurons increase their frequency of discharge with the same repetitive stimuli and exhibit prolonged discharge even after afferent C fiber input has stopped.

Receptor Field Expansion

Dorsal horn neurons increase their receptive fields such that adjacent neurons become responsive to stimuli (whether noxious or not) to which they were previously unresponsive.

Hyper Excitability of Flexion Reflexes

Enhancement of flexion reflexes is observed both ipsi-laterally and contra-laterally. Neurochemical mediators of central sensitization include substance P; calcitonin G related peptide; vasoactive intestinal polypeptide;

cholecystokinin; angiotensin; Glycine; L-glutamate and L-aspartate. They trigger changes in membrane excitability by interacting with G protein-coupled membrane receptor on neurons. A common pathway is an increase in intracellular calcium concentration. Glutamate and aspartate play an important role in wind-up via activation of N-methyl-D-aspartate (NMDA) and non-NMDA receptor mechanisms. They increase intracellular calcium concentration in spinal neuron and activate phospholipase C. They also induce formation of nitric oxide. Both prostaglandin and nitric oxide facilitates the release of excitatory amino acid in the spinal cord.

Inhibition

Inhibition of pain in the spinal cord occurs either by segmental activity in the cord itself or by descending fibers from supraspinal centers.

Segmental Inhibition

Activation of large afferent fibers subserving epicritic sensation inhibits WDR (wide dynamic range) neuron and spinothalamic tract activity. Activation of nociceptors by noxious stimuli in noncontiguous parts of the body inhibits WDR neurons at other levels, i.e. pain in one part of the body inhibits pain in other parts. Glycine and GABA are inhibitory neurotransmitters responsible for segmental inhibition of pain in the spinal cord. Segmental inhibition appears to be mediated by $GABA_B$ receptor activity. Benzodiazepine potentiates this action. Adenosine also modulates nociceptive activity in the dorsal horn. The A_1 receptor mediates antinociceptive action of adenosine.

Supraspinal Inhibition

Several supraspinal structures send fibers down the spinal cord to inhibit pain in dorsal horn. Important sites of origin for them include the *periaqueductal gray matter, reticular formation and nucleus raphe magnus (NRM).* Their axons act pre-synaptically on primary afferent neurons and post-synaptically on second-order neurons (or inter-neurons). They mediate their antinociceptive action via adrenergic, serotonergic, and opiate (μ, δ, & κ) receptor mechanisms. Activity at these receptors activate secondary intracellular messenger, opens K^+ channel and inhibit the release of SP. They also cause some postsynaptic inhibition. Exogenous opioids preferentially act post-synaptically.

Response to injury

Individual's normal response to injury is, initially to remove HIMSELF from harm's way and then to protect the injured area while healing occurs. This "injury response" manifests clinically as altered organ function and behavior. Surgery causes tissue injury; usually, more the radical surgery, greater the tissue injury. Biological systems are largely unable to distinguish the cause of tissue injury; eliciting broadly similar physiological and psychological responses. Surgery is "controlled" tissue injury that, results in alteration in organ functions and behavior. Hence safe and adequate postoperative pain relief is effective in reducing organ dysfunction and improving postoperative patient outcome by reducing the physiological and psychological responses to tissue injury.

Physiological responses

Physiological responses to injury include following responses, many of which can be eliminated or reduced with currently available analgesic techniques.

Respiratory Effects

Upper abdominal and thoracic surgery produces many pulmonary changes which include reduction in vital capacity, tidal volume, reserve volume, functional residual capacity and forced expiratory volume in one second. Painful surgical incision results in a reflex-mediated increase in abdominal muscle tone & spasm and decrease in diaphragmatic function. Splinting of the diaphragm causes inability to breathe deeply or to cough forcefully and effectively which may leads to hypoxemia, hypercarbia, retention of secretions, atelectasis and pneumonia. Increased muscle tone increases oxygen consumption and lactic acid production. Distended bowel, postoperative ileus or tight binders or dressing may further impair ventilation. Opioids administered to relieve pain can also cause or contribute to respiratory depression.

Cardiovascular Effects

Pain causes stimulation of sympathetic nervous system and release of sympathomimetic amines, namely, epinephrine and nor-epinephrine. As a result there is increase in heart rate, stroke volume, systolic and diastolic blood pressure. Thus there is increase in cardiac work, so myocardial oxygen consumption increases. The adverse effect is increased risk of myocardial ischemia and even frank myocardial infarction. Moderate to severe pain reduces patient's physical activity and keeps the patient confined to bed during early postoperative period. It exposes

the patient to risk of venous stasis in dependent parts of the body, platelet aggregation and deep vein thrombosis which ultimately may lead to pulmonary embolism.

Gastrointestinal and Urinary Effects :Activation of sympathetic nervous system may also delay return of postoperative gastrointestinal motility, which may lead to paralytic ileus or nausea/ vomiting. Although postoperative ileus is the result of combination of inhibitory input from central and local factors, an increase in sympathetic efferent activity, such as from uncontrolled pain, may decrease gastrointestinal activity and delayed return of gastrointestinal motility.
Pain can also cause hypo-motility of urethra and bladder, causing urinary retention.
Stress Response (Neuroendocrine and Metabolic Effects)
Neuroendocrine responses to pain involve interaction between hypothalamus, pituitary gland, adrenal cortex and sympathetic nervous system. Acute pain results in increase sympathetic tone, hypothalamic stimulation, increased catecholamine and catabolic hormone secretion and decreased secretion of anabolic hormones (insulin, testosterone). It results in sodium and water retention, increased levels of blood glucose, free fatty acids, ketone bodies and lactate. Metabolism and oxygen consumption are increased and metabolic substrates are mobilized from storage depots. The overall effect is negative nitrogen balance with catabolic state.

Psychological responses
Acute pain may cause the following responses:
Behavior: Acute severe pain leads to self-absorption and concern, withdrawal from interpersonal contact, increased sensitivity to all external stimuli, grimacing, moaning, abnormal posturing, reduced activity and seeking help & attention.

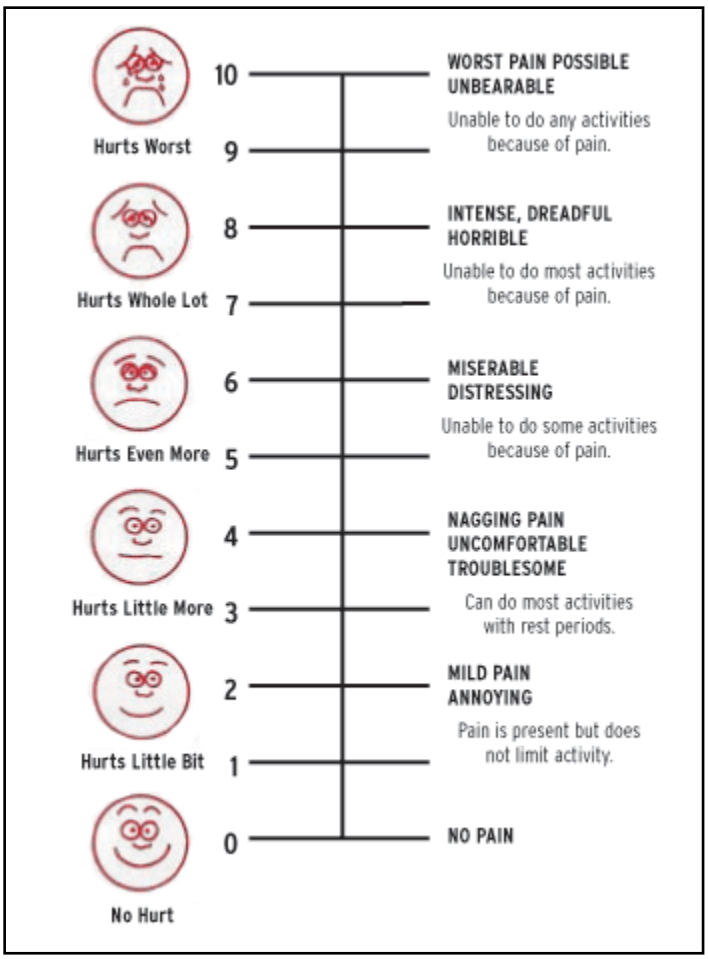
Affect Initially, pain causes fear and anxiety in patient's mind. He feels helpless, loses self-control, and may go into depression if pain remains unrelieved. These effects are exacerbated by sleep deprivation (insomnia) that accompanies unrelieved severe acute pain. It further delays postoperative recovery.

Methods of measuring pain:-

It is difficult to measure pain in studying the subject. Pain is a subjective phenomenon. Only the sufferer perceives it and the observer can only assess its magnitude based on what the sufferer tells him. These techniques of measuring pain are usually referred to as analgesimetry or algesimetry.
The various techniques in common use are

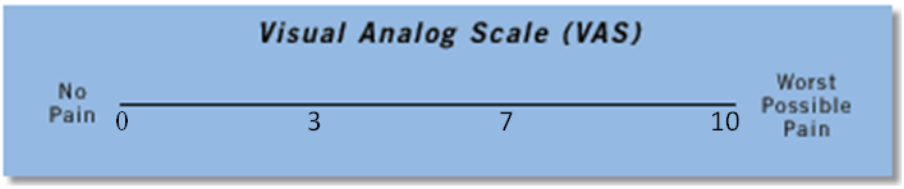
1. Simple descriptive pain scale
   It is described by **Keele**. It is a four point scale, and according to this scale pain is graded as mild, moderate, severe and excruciating. It is a simple method though it lacks sensitivity .

2. Non Verbal method
   This method makes use of visible manifestations of pain such as grimacing, movements and is shown to be unreliable.
   i) Faces pain scale presents pictures of 6 to 8 different facial expressions depicting a range of emotions. This scale may be useful in young children, in patients who have mild to moderate cognitive impairment, or patients with other language barriers.
   ii) Another method is that the subject squeezes a bag in proportion to the severity of pain. As behavioral phenomena cannot be relied on as indicator of pain severity, these methods became unpopular[65].



3. Visual Analogue Scale

This is currently the most commonly used method. The subject informs the observer of the amount of pain, by use of a linear Analogue Scale. The subject makes a mark on a 10 cm line, vertical or horizontal, one end of which is marked "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 is experiencing.



4. Verbal Numerical Rating Scale

In this method patient is asked to estimate his/her pain severity by a number, "0" is no pain and "10" is the worst possible pain.

5. Graphic rating method

It is based on approaches borrowed from psychology in which they have been applied to measure unmeasurable parameters as personality, depression and sleep.

Methods of measuring pain relief

1. Simple descriptive pain relief scale
   This method uses three or more points and grades pain relief as excellent, good, moderate, poor and doubtful. Pain relief can also be described as absent or no pain, slight, moderate and complete relief of pain.

2. Visual Analogue pain relief scale
   It just improves the sensitivity of the above mentioned scale.

3. Numerical Methods
   The patient is asked to assess the severity as a percentage of the initial level of pain or in terms of fraction of pain relief.

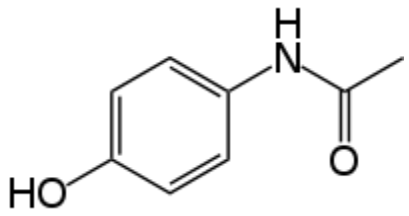
PHARMACOLOGY

PARACETAMOL

Paracetamol is effective for mild to moderate pain and an effective component in multimodal analgesia in combination with morphine, weak opioids and NSAIDs.

CHEMISTRY

The chemical name is *N*-(4-hydroxyphenyl) ethanamide or N-(4-hydroxyphenyl) acetamide The molecular formula is $C_8H_9NO_2$ as shown below.



Chemical structure of paracetamol

Mechanism of action

The main mechanism proposed is the inhibition of cyclooxygenase (COX), and highly selective for COX-2 .The COX family of enzymes are responsible for the metabolism of arachidonic acid to prostaglandin H_2, an unstable molecule that is, in turn, converted to numerous other pro-inflammatory compounds. Classical anti-inflammatories such as the NSAIDs block this step. Only when appropriately oxidized is the COX enzyme highly active.

Paracetamol reduces the oxidized form of the COX enzyme, preventing it from forming pro-inflammatory chemicals. This leads to a reduced amount of Prostaglandin E2 in the CNS, thus lowering the hypothalamic set-point in the thermoregulatory center.

Paracetamol also modulates the endogenous cannabinoid system.

Pharmacokinetics

Paracetamol is available in a tablet, capsule, liquid suspension, suppository, intravenous, and intramuscular form. The paediatric dose is 10-15mg per kg.. Absorption is incomplete; depends upon dosage form. Time to peak plasma levels per rectal is : 10-60 min; . . The plasma half-life ranges from 1.5 to 2.5 hours and the total body clearance from 4.5 to 5.5 ml/kg/min. It distributes rapidly and evenly throughout most tissues and fluids and has a volume of distribution of approximately 0.9L/kg. 10 to 20% of the drug is bound to red blood cells. Protein binding: 8-43%. It can easily cross the blood brain & placental barrier and is also secreted in breast milk to a very small extent which is insignificant.

Metabolism is hepatic via glucuronic and sulphuric acid conjugation. At normal therapeutic levels, glucuronide metabolites are metabolised to reactive intermediate (acetylimidoquinone) which is conjugated with glutathione and

inactivated; at toxic doses, glutathione conjugation is insufficient leading to increased acetylimidoquinone which may cause hepatic cell necrosis.

Pharmacodynamics

Onset and duration of action of paracetamol depends on route of administration. When given rectal administration onset of action is noted within approximately 10-15 min and peak analgesia occurs within one hour. Duration of action with i.m. or i.v. administration is roughly 4-6 hours.
Pharmacological actions

1. *Central nervous system*:

a) Analgesia: has analgesic properties comparable to those of aspirin, while its anti-inflammatory effects are weaker. If given along with opioids, reduces their dose and addictive capacity. It is useful for treatment of moderate to severe pain such as post-operative pain or acute pain due to other causes.

2. Respiratory system

Do not cause respiratory depression.

3. Gastrointestinal system

Paracetamol is metabolised in the liver the major metabolites being the sulphate and glucuronide conjugates. A minor fraction of drug is converted to a highly reactive alkylating metabolite which is inactivated with reduced glutathione and excreted in the urine as cysteine and mercapturic acid conjugates. Over dose of paracetamol cause acute hepatic necrosis as a result of depletion of glutathione and of binding of the excess reactive metabolite to cell constituents.

Indications and dosages

1. *Pre-anaesthetic medication:* given 15 minutes prior to surgery by i.v. Route prior to induction of anaesthesia.

2. *in balanced anaesthesia:* during surgery as analgesic component of balanced anaesthesia .dose is 10-15 mg/kg body weight given over 15 minutes.

3. *Post-operative analgesia:* paracetamol is an excellent and a potent analgesic and therefore useful to provide post-operative pain relief. Dose recommended in paediatric is 15 per kg rectally or intravenously , given 30 min prior to extubation and repeated 4-6 hourly.

   Dose to be reduced in elderly and in those with hepatic disease.

3 adverse reactions

Nausea, allergic reactions, skin rashes, acute renal tubular necrosis.
Potentially fatal: very rare blood dyscrasias (e.g. Thrombocytopenia, leucopenia, neutropenia, agranulocytosis), hepatic damage

Contraindications

1. Allergy or hypersensitivity to this drug.
2. Patients with severe hepatic failure.

Drug interactions

- Reduced absorption of cholestyramine within 1 hr of administration.
- Accelerated absorption with metoclopramide.
- Decreased effect with barbiturates, carbamazepine, hydantoins, rifampicin and sulfinpyrazone.
- Paracetamol increase effect of warfarin.

Precautions

Renal or hepatic impairment; alcohol-dependent patients; g6pd deficiency.

Toxicity

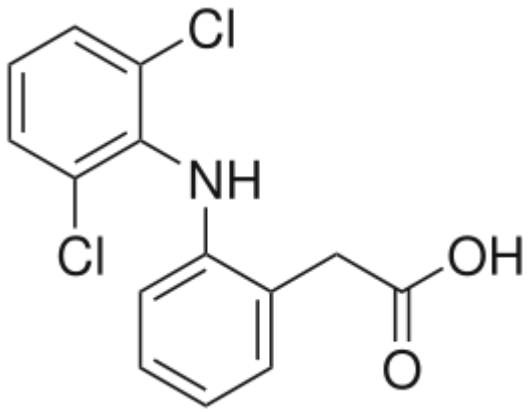
Paracetamol hepatotoxicity is the most common cause of acute liver failure. Signs and symptoms of toxicity are vague.

Early symptoms: nausea and vomiting..In 24 hr symptoms include right subcostal pain and tenderness, indicating development of hepatic necrosis. Liver damage may lead to encephalopathy, hemorrhage, hypoglycemia, cerebral edema and death in following 3 to 4 days. Aim of treatment is replacing glutathione stores . Acetylcysteine protects the liver if administered within 24 hr after ingestion . Dose: 140 mg/kg orally (loading) followed by 70 mg/kg every 4 hr for 20 doses. Parenteral acetylcysteine is given to those unable to tolerate oral dosing.. Activated charcoal is given for inducing Gastric lavage if toxic dose is taken with in one hour.

DICLOFENAC

It is a Non-steroidal anti-inflammatory drugs (NSAIDs) an Aryl Acetic Acid Derivative are used for the management of mild to moderate pain. It is used alone or in combination with opioids.

Chemical Structure of Diclofenac



. Mechanism of action:

Is through the inhibition of cyclooxygenase (COX), the enzyme responsible for metabolizing arachidonic acid, when arachidonic acid is released from traumatized cell membranes, it is metabolized by COX to form prostaglandins and thromboxanes which in turn sensitize peripheral nerve endings and vasodilate vessels, causing pain, erythema, and inflammation.

There are two COX isoenzymes:-

1)The constitutive form of COX (COX-1) is present throughout the body and the prostaglandins and thromboxanes that are produced are essential for functions such as gastric mucosa protection, renal blood flow regulation, and platelet aggregation. Potential complications of COX-1 inhibition include gastric ulceration, bleeding, altered renal function, and bronchoconstriction.

2)COX-2 is called an ‘‘inducible COX’’ and is present only in traumatized cells or inflamed tissue. Most NSAIDs are nonselective COX inhibitors, but the potential attraction of selective COX-2 inhibition in the reduction of side effects is apparent. Presently, the future of COX-2 inhibitors in children is uncertain.

Pharmacokinetics: Oral absorption is good, 99% protein bound , metabolized and excreted in urine and bile. The plasma t half is 2 hours. Tissue permeability is good and synovial fluid concentration is maintained for 3 times longer than in plasma .

Pharmacological actions : a) Analgesia: Effective against inflammation associated pain by blocking pain sensitizing mechanism induced by bradykinin , TNFalpha , interleukins .

b)Antipyresis:Fever during infection is produced by pyrogens . interleukins,TNFalpha, interferons. NSAIDs block

the action of pyrogen.
c)Antiflammatory:inhibiting Pgsynthesis at the site of injury
d)Gastric mucosal damage:inbition of COX 1mediated synthesis of gastroprotective PGs(PGE2, PGI2). Reduces mucus and bicarbonate secretion, enhances acid secretion and proomte mucosal ischemia.
e)Kidneys: renal effect is produced by 3 mechanism
1) COX-1 dependent impairement of renal blood flow and reducution of gfr
2)Juxtaglomerular COX2 dependent Na and water retention.
3)papillary necrosis on habitual intake.
f)Dysmenorrhoea:Intermittant ishemia of myometrium is responsible for menstrual cramps.NSAIDs lower uterine PG levels bring 70percent relief plus ancillary symptoms Headache , muscleache and Nausea are also relieved.
Dose: Diclofenac is a potent and excellent analgesic and thefefore useful to provide post operative pain relief .Dose recommenfed in paediatric is 1-1.5 mg per kg intavenously or Rectally, given 30 min prior to rextubation and repeated 4-6 hourly.

ADVERSE EFFECTS:
Relativecontraindications : Impaired hepatic function, diabetes, bleeding or coagulation disorders, vascular disorders, Operation where an absence of bleeding is important. Non aspirin induced asthma Age>65, pregnancy, lactation, Concurrent use of ACE inhibitors, potassium sparing diuretics, anticoagulant.
Absolute contraindications: High risk of gastro-intestinal bleeding and ulceration Known hypersensitivity to NSAIDs Severe liver dysfunction, Cardiac failure,Dehydration,hypovolaemia, hypotension Hyperkalaemia, Pre existing renal impairment,Uncontrolled hypertension & Aspirin induced asthma.
Side effects of NSAIDs:

1) Gastrointestinal:Nausea, anorexia, abdominal pain, ulcers, anemia, gastrointestinal hemorrhage, perforation &diarrhea.
2) Cardiovascular : Hypertension, decreased effectiveness of anti-hypertensive medications, myocardial infarction, stroke, and thromboembolicevents (last three with selective COX-2 inhibitors); inhibitplatelet activation, propensity for bruising and hemorrhage
3) .Renal: salt and water retention, edema, deterioration of kidney function,decreased effectiveness of diuretic medication, decreased urateexcretion, hyperkalemia, analgesic nephropathy.
4) Central nervous system :Headache, dizziness, vertigo, confusion, depression, lowering of seizure threshold, hyperventilation (salicylates)Hypersensitivity Vasomotor rhinitis, asthma, urticaria.

Review of literature:-

The Word Pain is derived from Greek term ‘ Poine’ meaning punishment .Primitive Pain was religiously associated and was thought as a form of punishment for Sins. Relief from pain was seeked through worships and religious rituals.
It was Aristotle who first thought that pain originated from Heart., but Galen stated that Brain was required for Pain. Many different theories were put forward to understand the origin of pain.
Medieval period Alcohol,Opium and Hypnotism was used to relieve pain. In 77 AD Discorides a Greek physician described the use of wine .Felix Hoffma , a Bier Chemist in 1897 discovered Aspirin in his laboratory.
In 1803 , Morphine was discovered and profoundly used for analgesia however it led to Nausea, Vomiting, Sedation and Respiratory Depression. Arabian traders in 3rd centuary B.C were using Opium for the control of diarrhoea and were well versed with adverse effects.
In 1784 A Glasgow born Surgeon James Moore documented opium use as Post operative Analgesia. Few years later in 1789, Benjamin Bell a scoottish Surgeon also documented the use of opiods as a good post operative analgesia.
1953 Sterling and Winthrop marketed Paracetamol in USA
1986 Diclofenac Sodium was synthesized as NSAID by Salmann AR
In 1984, Saarnivaara : Conducted the study in 91 Adults for tonsillectlomy.they were Randomized and administered Rectally Paracetamol and Pentazocine. They Concluded that both paracetamol and pentazocine suppositories in early post-operative period are weak analgesics for throat pain .
1986 Diclofenac Sodium was synthesized as NSAID by Salmann AR

Peter Sylaidis (1998) et al. They conducted study in Twenty children (6 months to 9 years of age) for repair of the hard or soft palate . Per rectum doses of diclofenac was given at 1 mg/kg after surgery, with additional doses every 12 hour. They concluded that twice daily diclofenac rectal suppositories provided good analgesia in post operative period and also reduce the need of administering opiods , resulting in alert infants who are fed well and discharged early .

Mohamed I. Tawalbeh (1999) et al: They conducted the study between January 1999 and July 2000 in 80 children of 3-14 years age group for tonsillectomy and adenoidectomy for recurrent tonsillitis or adenotonsillar hypertrophy .Post Operatively Forty-one children were administered diclofenac sodium suppositories (1-3mg/kg) and 39 children Paracetamol syrup (10-15 mg/kg) in 4 divided doses. They concluded Diclofenac sodiumwas superior in decreasing the pain associated with swallowing postoperatively which resulted in early oral intake and decreased incidence of nausea and vomiting , which eventually led to earlier hospital discharge. The time to first solid intake was significantly earlier in the diclofenac sodium group ($p < 0.0001$).

Pendeville PE (2000) et al: They conducted study in children for tonsillectomyand Concluded that intravenous proparacetamol 30 mg/kg resulted in higher postoperative pain scores than intravenous tramadol 3.0 mg/kg given before surgical incision.

Van der Marel CD (2001)et al : They conducted study in 40 children for craniofacial correction. The children were administered Rectal loading dose (40 mg/kg)as premedication and (20 mg/kg)acetaminophen either orally or rectally every 6 hours. They concluded that reduced need for opiods in children of per rectal group.

Mane R (2012)et al: Conducted a study in 60 children allocated into 2 groups of 30 each cleft palate repair and were randomized to receive diclofenac 1mg/kg suppository in comparison to the conventional group. They concluded that pre operative rectal diclofenac provides effective analgesia in the immediate post operative period with reduced pain score and reduced opiod requirement. There was no Complication of any increased peri operative bleeding in the diclofenac group.

Riad W (2007) et al:Conducted the Study in one hundred and Eight Children for Inguinal Hernia Surgery . Rectal diclofenac 1 $mg.kg^{-1}$ or paracetamol 40 $mg.kg^{-1}$ or their combination 1 h prior to surgery was administered Randomized .They concluded that children who received the rectal diclofenac-paracetamol combination experienced a lower pain scale(Wang Baker Scale) and a decreased need for morphine compared with children receiving each drug alone. Paracetamol($p<0.01$) , Diclofenac ($p<0.05$)

Gholam Ali Dashti, Shahram Amini(2009) et al : They conducted the study in 104 children for elective adenotonsillectomy . Children were randomizedand were a dminstered either rectal acetaminophen 40 mg/kg or nothing after induction of General anesthesia. They concluded that prophylactic rectal acetaminophen provides good analgesia in post operative period and also reduce the need of administering opiods . Pain scores were significantly lower in acetaminophen group at different times .($p<.001$)

Materials and method:-

Place of the study:

This study was conducted in the Department of Anaesthesiology,

S.B.K.S Medical Institute and Research centre, Dhiraj General Hospital, Piparia, Vadodara: 60 patients of ASA I and II of American Society of Anesthesiologist classification Undergoing paediatric surgery were taken for the study. They were be allocated randomly in two equal groups.The study is retrospective and interventional in nature .All the parents/ Guardian of the concerned patients were explained clearly about the purpose and the nature of study in the language they can understand. They were included in the study only after obtaining a written and informed consent .A random sampling was be done at the time of presentation .The data was collected for one and half year and statistically analized after clearance from the ethical committee.

Methods:

Selection criteria

Inclusion criteria:

- Paediatric in the range 3years – 12years
- ASA I & ASA II paediatric patients undergoing surgery
- No known allergy to the trial drug.

- Normal developmental milestones
- Parents/Guardians willing to sign the informed consent..
- Surgery planned to be performed under general anaesthesia.

Exclusion criteria

- ASA physical status 3 and above
- Patients with congenital anomalies
- Patients with medical complications like anemia, heart disease, renal disease,severe hypovolemia, shock , septicemia .,
- Asthmatics, dehydration, malnourished
- Patients with coagulation disorders or on anti coagulant therapy
- Patients on Nephrotoxic drugs
- Hypersenstivity,Severe eczema, Nasal polyp
- Neutropenic

The patients were visited preoperatively and History will be taken for:

- Asthma, congenital anomaly, Tuberculosis
- Developmental milestone ,Birth history, Weight
- Immunization history
- Bleeding tendency , antiplatelet drug or anticoagulant
- Hepatic or Renal impairement
- Convulsion or any neurological disease
- History or drug intake , History of allergy and sensitivity to any drug and previous anesthetic experience
- Vital data including temperature, pulse,blood pressure,.

Investigations:

- Complete blood count
- Random blood Sugar
- Chest X ray PA view

Method of randomization

All patients were equally divided into two groups .
Group P: (n 30):Received Per Rectal Paracetamol (15mg /kg)
Group D: (n 30): Received Per Rectal Dicolfenac (1mg/kg)

Materials used

Anesthetic procedure
All patients to be kept nil by mouth for 6hrs.
Preparation and drugs:
The patient was wheeled into operation theatre table. All monitors such as NIBP, pulse oximeter, electrocardiogram (ECG) were connected to the patient. The vein preferably on left forearm was secured using age appropriate i.v cannula (20G,22G)and slow i.v infusion of Isolyte P was started. Base line vital parameters namely pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and SPO2 were recorded.
Premedication : inj Ondansetron 0.08mg/kg i.v ,inj Glycopyrrolate 0.004mg/kg , i.v Inj midazolam 0.02mg/kg i.v
Induction : After pre oxygenation with 100%oxygen for 5minutes& All patients were induced with Thiopentone 3-5mg/kg. Succinylcholine 1-1.5mg/kg & than airway was secured via Oral intubation.
Maitenance : All patients were maintained on O2 ,N20,Sevoflurane,Atracurium on appropriate breathing circuit - Jackson Rees Circuit for weight <20kg and Closed Circuit for Weight >20kg

1. Pulse oximetery (SPO2, PR) continuously.
2. ECG continuously.
3. NIBP – SBP, DBP.

Replacement of fluid loss was done with Isolyte P,blood or Colloids as required .Fifteen minutes before reversal Per Rectal Paracetamol or Diclofenac was introduced as per following dose.
After the surgery ***weight based dose*** of the drug will be given

- Group D Rectal Diclofenac Sodium 1mg/kg Group P Rectal Paracetamol 15mg/kg

Reversal: inj Neostigmine 0.05mglkg i.v,inj Glycopyrrolate 0.008mg/kg i.v

Post operative pain assessment was done using Visual Analogue Score (5-12yr). Rescue Analgesia:Fentanyl 1ugm/kg was considered when VAS score >3

(1)The Duration of analgesic effect was considered from the time of introducing the suppository to First Complain of Moderate Pain.
(2)Hemodynamics were monitored post operatively for thirty minutes in first hour than every hourly for next five hours and than two hourly till 12 hours.
(3) Side effects and Complications were also observed and tabulated.
The patient was released from the trial after first complain of moderate pain postoperatively (VAS score >3)

Statistical analysis: analysis was done by SPSS software version 11 by using Z test, proportion test (Z).

Table of Contents

Table 1 : Demographic

Variables	**Group – D**	**Group – P**	**P-value**
Age (yrs)	7.86±2.64	7.73±1.98	0.42
Sex (M/F)	22/8	25/5	0.53
Weight (kg)	22.2±5.36	22.36±4.61	0.43
ASA (I/II)	28/2	30/0	0.12

Table 2: Age groups

Age Group	Group – P		Group – D	
	No	%	No	%
4-6	11	55	9	45
7-9	9	35	17	65
10-12	10	72	4	28
Total	30	50.0	30	50.0

Table 1 and 2 and graph 1shows age (in years) of patients in groups as percentage. The characteristics of both groups were comparable and differences among them were not statistically significant.

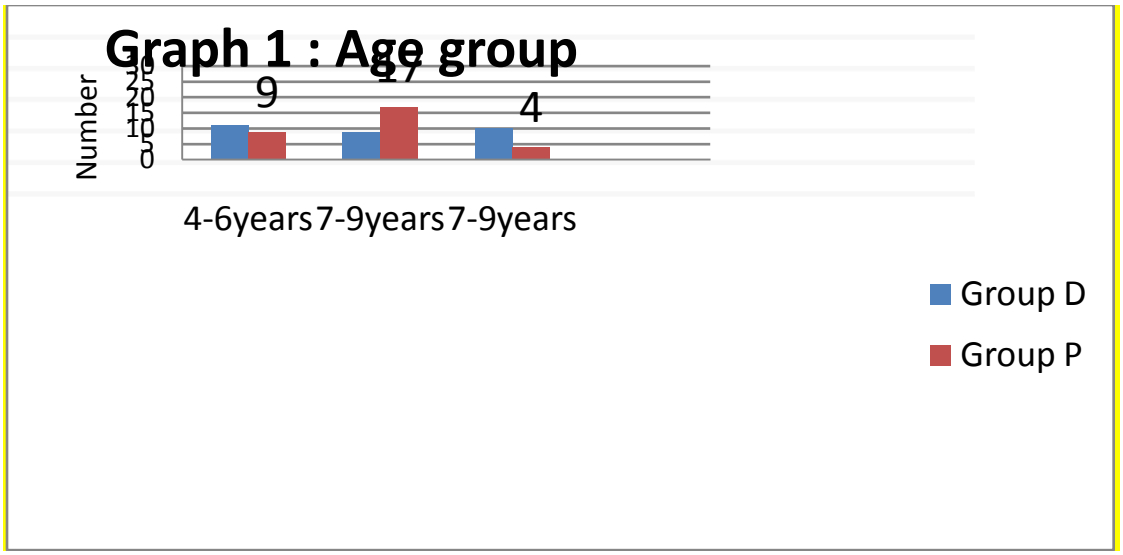
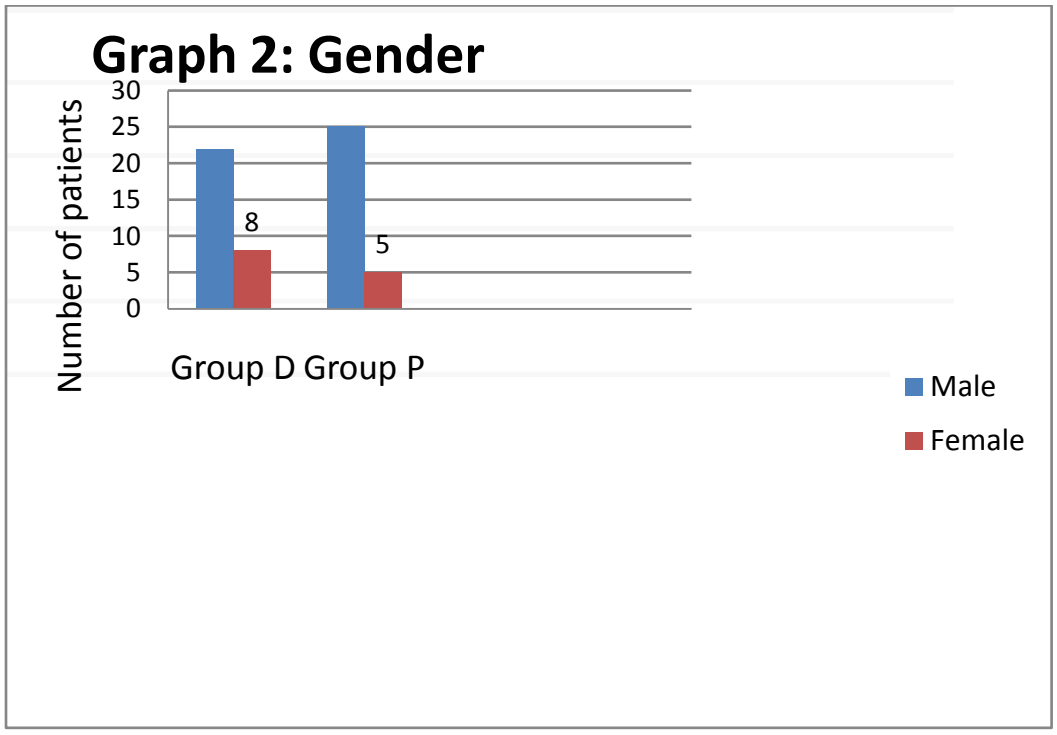


Table 3: Gender

Sex	Group – P	Group – D	p-value
Male	22 (73.33%)	25 (83.33%)	0.532
Female	8 (26.67%)	5 (16.67%)	
Total	30 (100%)	30 (100%)	

Table 1 and 3 and graph 2shows Sex wise distribution of patients in groups as percentage. The characteristics of both groups were comparable and differences among them were not statistically significant.



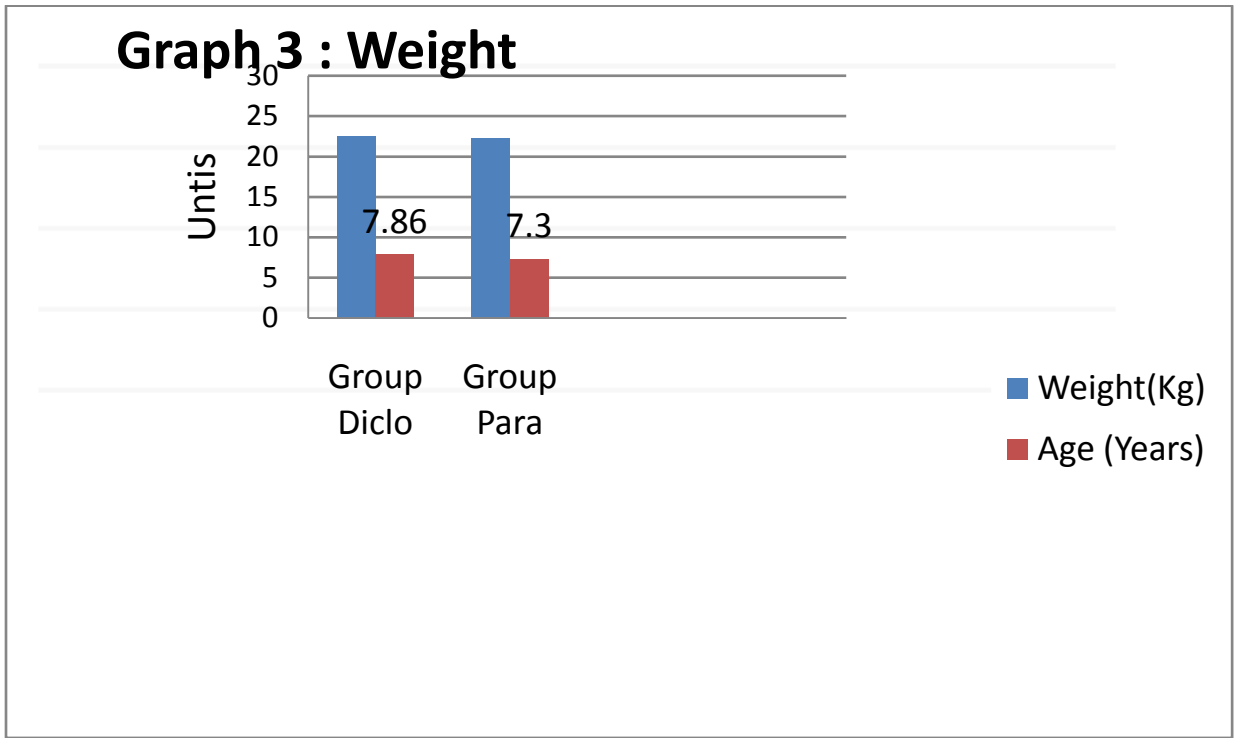


Table 1 and graph 3shows weight (in Kg) in groups as Percentage . The characteristics of both groups were comparable and differences among them were not statistically significant.

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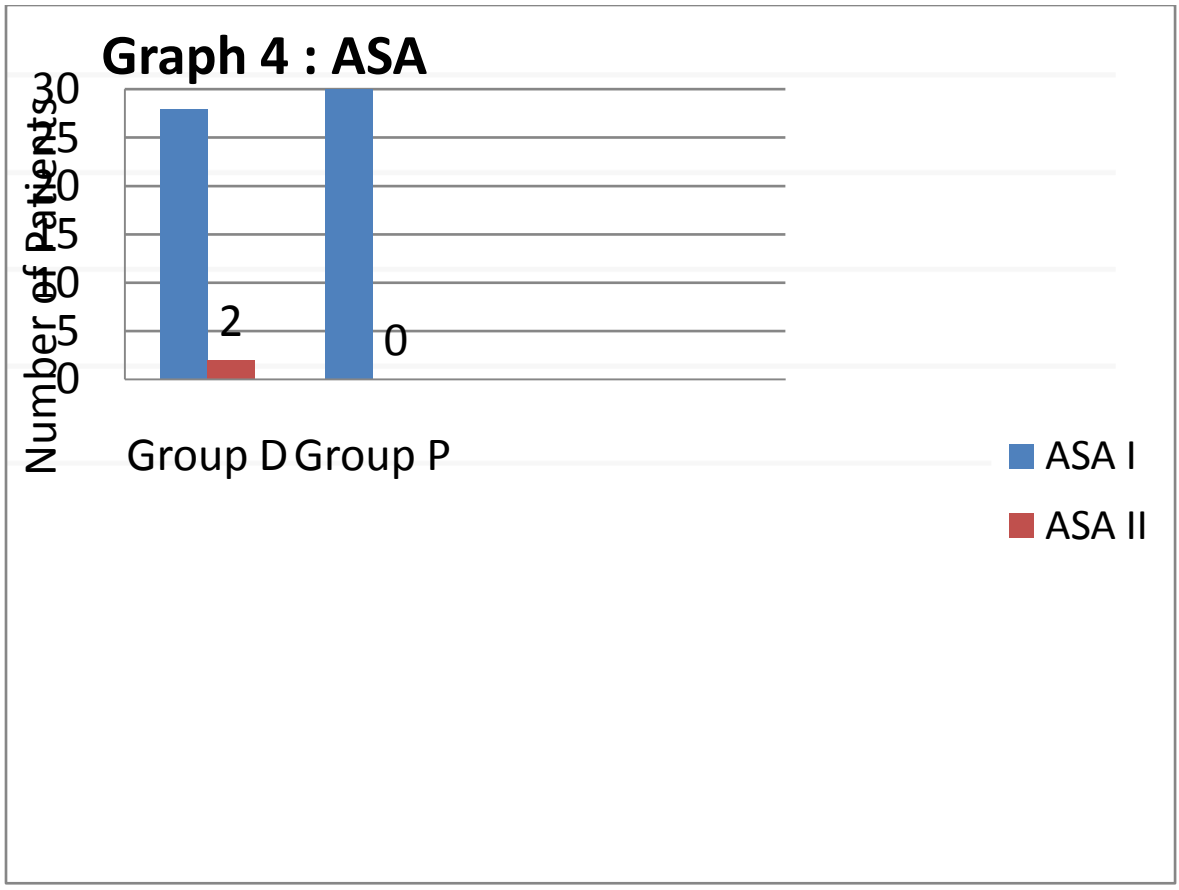


Table 1 and graph 4shows:
In group D there were 28 ASA I patients and 2 ASA II patients.
In group P there were 30 ASA I patients and 0 ASA II patients .

Table 4: Duration of Analgesia

Variable	Group – P	Group – D	P-value
Duration Of Analgesia(min)	180±0.52	246±0.71	<0.001

Table 5 : Mean Pain score

	30 min	60min	120min	180min	240min	300min	360min	480min	600min	720min
D	2.00	0.87	1.00	1.00	2.33	3.17	1.20	3.00	0.00	0.17
P	2.00	2.00	0.80	1.47	3.57	3.57	0.57	1.03	1.00	1.00

Comparison of visual analogue scale in Group D & GroupP

VAS	Group D	Group P	Z Value	P Value
	Mean ± SD (n=30)	Mean ± SD (n=30)		
During Rescue Analgesia	3.17 ± .11	3.57 ± .42	1.57	>0.05

P > 0.05- not significant
P < 0.05- significant

Table 6: PULSE
Independent T-Test

PULSE

Time(min)	Group D		Group P		P-Value
	Mean	Std dev	**Mean**	Std dev	
Initial	90.73	7.38	91.96	2.84	0.433
30	95.80	5.68	92.06	2.74	0.586
60	92.60	6.64	89.91	2.59	0.902
120	94.37	8.21	89.03	2.51	0.868
180	103.13	16.20	104.96	2.76	0.798
240	110.90	6.24	106.21	2.48	0.699
300	100.73	2.57	116.31	2.83	0.807
360	85.20	8.50	96.46	14.83	0.725
480	86.90	12.42	91.93	2.42	0.587
600	83.17	6.15	86.46	10.74	0.065

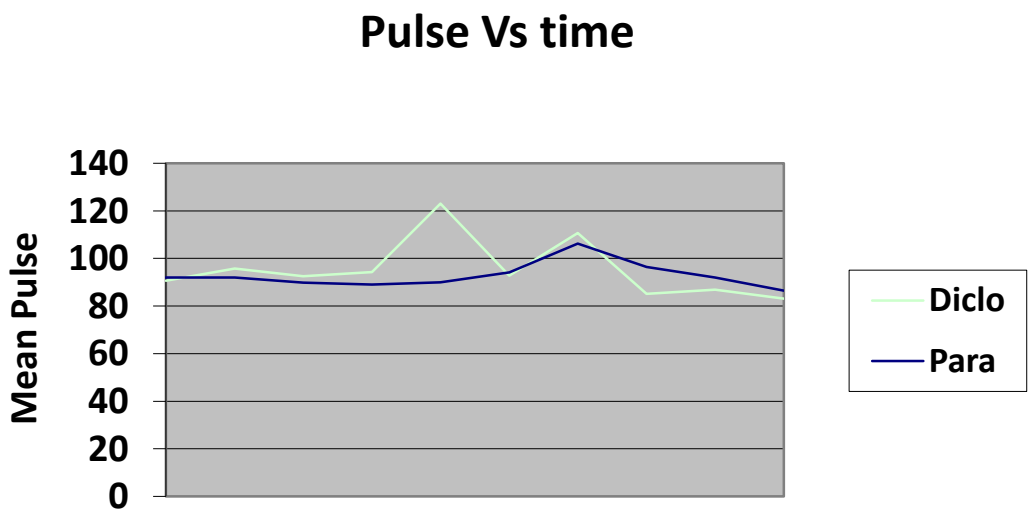


TABLE 7 : SBP

SBP

	Group D		Group P		
	Mean	Std dev	**Mean**	Std dev	
Initial	104.77	10.86	102.66	11.74	0.029
30	122.47	10.02	121.93	12.15	0.041
60	121.13	10.76	111.26	8.96	0.057
120	111.00	9.33	113.93	12.44	0.187
180	124.53	10.43	115.33	13.00	0.092
240	120.27	7.56	118.51	11.20	0.29
300	121.90	7.01	121.96	15.17	0.684
360	121.40	9.84	119.03	7.14	0.343
480	121.93	12.16	122.46	10.02	0.11
600	111.27	8.97	121.13	10.75	0.473

TABLE 8: DBP

DBP

	Group D		Group P		
	Mean	Std dev	**Mean**	Std dev	
Initial	82.57	8.16	76.43	8.63	0.036
030	79.00	7.15	78.33	8.69	0.463
60	80.40	8.41	74	8.51	0.371
120	71.80	8.81	73.2	10.01	0.973
180	84.13	8.52	73.3	11.48	0.308
240	74.97	9.00	76.3	9.95	0.387
300	80.57	9.95	78.66	10.33	0.376
360	80.90	6.81	74.53	9.32	0.582
480	78.33	8.70	78.86	7.17	0.135
600	74.00	8.52	80.4	8.41	0.348

TABLE 9: SpO2

SpO2

	Diclo		Para	
	Mean	Std dev	**Mean**	Std dev
Initial	100.00	0	100	0
30	100.00	0	100	0
60	100.00	0	100	0
120	100.00	0	100	0
180	100.00	0	100	0
240	100.00	0	100	0
300	100.00	0	100	0
360	100.00	0	100	0
480	100.00	0	100	0
12	100.00	0	100	0

Table 10: Post Operative side effects in Group P and D

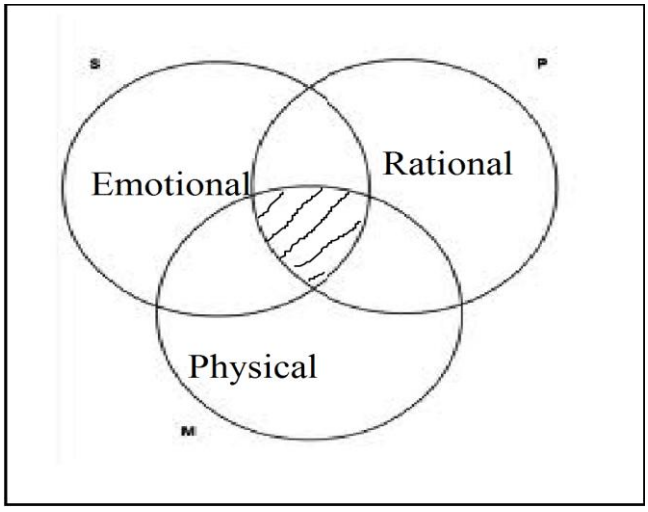
Side Effect	Group – P		Group – D	
	No.	%	No.	%
Vomiting	0	0	0	0

Shows comparison of side effects in the two groups.. No other side effects were noted.

Discussion:-

Pain is a complex sensation which is difficult to define and equally difficult to measure in an accurate objective manner. It has been defined as sensory appreciation of afferent nociceptive stimulation which elicits an affective (or autonomic) component; both are subjected to rational interpretation by the patient.

It may be represented by a venn diagram, shaded area of which represents the quantum of suffering experienced by the patient.



The interrelationship between emotional, rational and physical components of pain. Perceived pain is represented by the area of intersection of all three components

It may be seen instantly from Venn diagram that

i) Sensation of pain differing among individual patients.

ii) Emotional component may vary according to patient's psychological composition.
iii) Rational component varies with patient's previous experience insight and motivation.

Children undergoing surgery have very low pain tolerance thersholds and experience ealier restlessness resulting into negative psychological effects on them and their parents.. It is also very difficult to judge the level of post operatives pain, restlessness or crying due to pain or hunger in the children. An effective pain therapy to block or modify the myriad physiologic responses to stress has become essential component of modern pediatric anaesthesia and surgical practice as it has potential impact on the well being of children.
Historically, children have been under treated for pain and for painful procedures because of the wrong notion that they neither suffer or feel pain, nor respond to or remembered the painful experiences to the same adult did. Pain can be evaluated in terms of self- report, physiological changes or behavioural observation.2 Physiological indicators of pain is often unreliable but may include tachycardia, restlessness, pallor, vomiting, or blood pressure increases. Children older than four years can usually talk about their pain and those older than six to eight years can use visual analogue pain scales in the same manner as adults
In the early 1900's **George Crile** suggested, "Control of Post-operative pain could favorably influence the results of surgery". Study has shown that post-operative pain is maximum during initial 48-72 hours & it declines thereafter[13]. However, post-operative pain still is an overlooked entity that receives little care. Therefore post-operative pain relief is also a major concern for an anaesthesiologist. Intravenous (i.v) or intramuscular (i.m) boluses of opioids with or without non-steroidal anti-inflammatory drugs (NSAIDs) constitute the mainstay of post-operative pain relief.

Postoperative pain is transitory , improves over a relatively short time course. Surgery brings tissue insult leading to sensitization at central and peripheral pain pathways. . Before surgery administration of analgesics reduce sensitization of the central nervous system.Post-operative pain treatment should start before surgery and this treatment should extend into the early post-operative period.
There are many studies put forward comparing NSAID and Acetaminophen for post operative pain management using different routes ,but in our study we are using two different group of drug (diclofenac and paracetamol) in same route(rectally).

Paracetamol acts on both the central and peripheral components of the pain pathway. One mechanism is through the direct inhibition of the N-methyl-D-aspartate receptor, which stimulates the substance P dependent mechanism of the nitric oxide, a primary mediator of nociception. Paracetamol has also been implicated in the inhibition of the cyclooxygenase 2 pathway involved in prostaglandin synthesis. A metabolite of paracetamol also sequesters reduced glutathione, a required cofactor for membrane bound prostaglandin synthetase, another potent mediator of nociception. Therefore paracetamol may also contribute to the alleviation of pain by indirectly attenuating production of prostaglandins. The analgesic effects of paracetamol also involves the serotonergic system agonists of serotonin 5-HT_3 receptors namely tropinesteron and granisetron, completely blocked the analgesic effect of paracetamol, indicating an antinociceptive role for paracetamol.

Diclofenac is a a Non-steroidal anti-inflammatory drugs (NSAIDs) an Aryl Acetic Acid Derivative inhibits cyclooxygenase (COX), the enzyme metabolizes Arachidonic acid. Arachidonic acid is released from injured cell membranes it is than metabolized by COX to prostaglandins and thromboxanes which in turn sensitize peripheral nerve endings and vasodilate vessels : pain, erythema, and inflammation.It has two isoenzymes :-1)COX-1 is present throughout the body and the prostaglandins and thromboxanes thus produced are essential for functions such as stomach mucosa protection, renal blood flow regulation, and platelet aggregation. Complications of COX-1 inhibition include gastric ulceration, bleeding, deranged renal function, and broncho -constriction.
2)COX-2 is called an ''inducible COX'' and is present only in injured cells or inflamed tissue.
With this in mind we conducted a clinical study on 60 paediatric patients of either sex, divided randomly into 2 equal groups to evaluate analgesic efficacy of Per Rectal Paracetamol and Diclofenac Sodium . Both the groups were comparable with respect to their demographic profile, ASA status and surgical procedures carried out and there was no statistical difference between the two groups ($p>0.05$).
In our study we found that Mean Duration of Analgesia at which first dose of Rescue Analgesia was administered in Group D :Diclofenac group 4.1±0.71hrs , (246±42 min) while in Paracetamol was 3±0.525,(180±31min) .
Table 4 depicts the Mean Duration of analgesia of two groups in our study. The differences in duration of analgesia between two groups was very highly significant($p<0.001$).

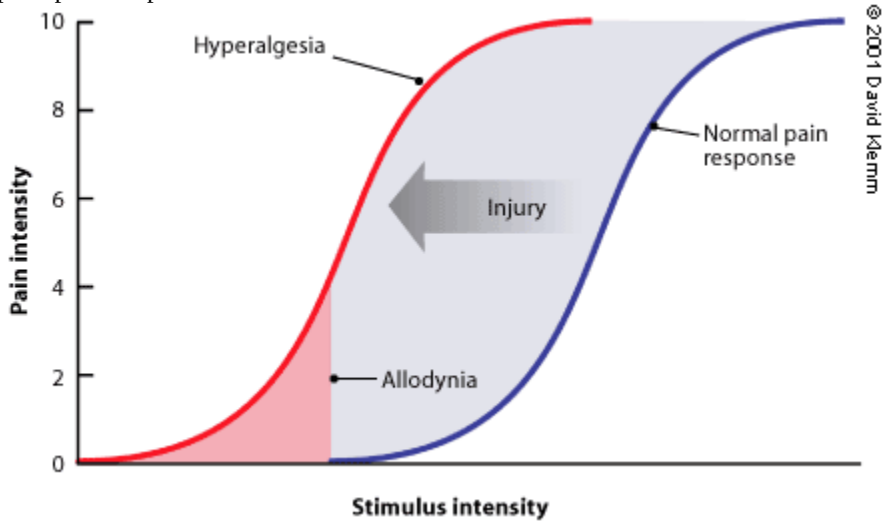
Our Study Coincided with the Study of Gandhi R et al: in which 135 children were operated for elective ophthalmicsurgery were adminstered per rectally acetaminophen 40 mg/kg(groupH), 20mg/kg(groupL) or no rectal drug respectively after randomly allocating into three group. Meantime to requirement of first analgesic was 206±185 min in groupH ,189±203min in groupL , and 196 ±170 min in groupN (*P*=0.985).

Kheskani Divya etal : conducted post operative analgesia study in Paediatric children for Elective Ventriculoperitoneal shunting for Hydrocephalus and observed duration of prolonged analgesia was more in diclofenac sodium(216±89 min) while in paracetamol group is(184±43)min.

Velimatta Kosama etal : conducted the study in 160 peadiatric children from 3months to 12years.After single dose administration (i.v) of Diclofenac sodium (1mg per kg) and paracetamol(15mg per kg) postoperatively CSF concentration was determined . Diclofenac sodium was detected in CSF sample from 5min to 300 minutes . Paracetamol was detected from 6 minute to 330minutes.

In our study significant rise in Pulse rate was seen in In Diclofenac group during (246±42 min)hour mean baseline 90.73 ± 7.38 per min rose to 110 ± 6.24per min . In paracetamol group during (180±31min) similar rise in mean baseline pulse 91.2 ± 2.84min which rose to pulse rate 116± 2.83per min.These values were statistically and clinically significan comparing with other studies.
Table 6.shows Rise in pulse rate was statistically significant.
Rise in pulse rate was clinically significant with duration of analgesia .
Not many studies were done comparing the hemodynamic However in one study by Kheskani Divya etal : conducted post operative analgesia study in Paediatric children for Elective Ventriculoperitoneal shunting for Hydrocephalus and observed Heart rate and SpO2 were stable in after the operation.

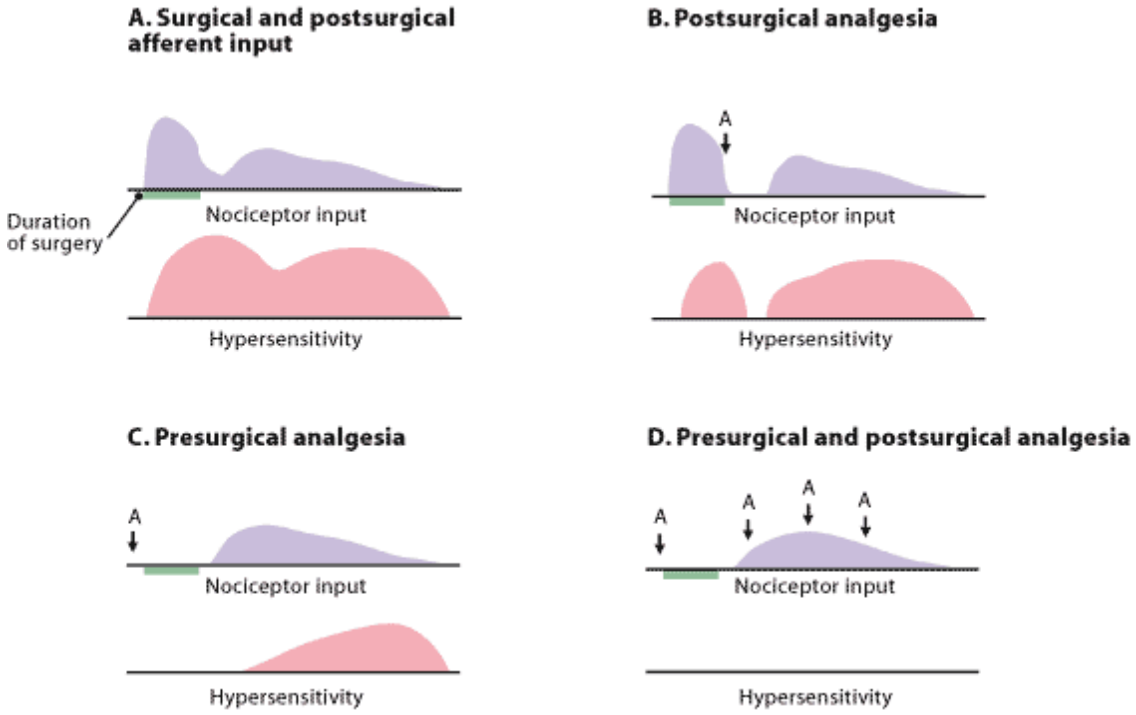
Poor pain control in perioperative period leads to complications in both long term and short term periods. Amongst the complications atelectasis, pneumonia, deep vein thrombosis, pulmonary embolism, psychological trauma, etc. can be severe. With a good analgesic plan, the anxiety, morbidity, cost and the length of the stay in hospital in postoperative period is decreased.



In our study(table 10) no side effects and complications were noted .
However in a study of Velimatta Kosama etal: Gastrointestinal adverse events (vomiting 5%, nausea 4%, abdominal pain 1%)occurred at similar incidences as reported in a previous study in children (Kokki and Hendolin 1996).

Cliff K. S. Ong et al(2010) : conducted a study Combining Paracetamol (Acetaminophen) withNonsteroidal Antiinflammatory Drugs: A Qualitative Systematic Review of Analgesic Efficacy for AcutePostoperative Pain found most common side effect reported were nausea ,vomiting ,headache.Adverse effects were mild ,no serious side effects was noted.

Noxious stimuli can sensitize the nervous system response to subsequent stimuli. The normal pain response as a function of stimulus intensity is depicted by the curve at the right, where even strong stimuli are not experienced as pain. However, a traumatic injury can shift the curve to the left. Then, noxious stimuli become more painful (hyperalgesia) and typically painless stimuli are experienced as pain (allodynia).Tissue damage brings physiological response to prevent futher damage: i) Peripheral sensitization (redness , wheal , flare) this triple response is brought by histamine Bradykinin, serotonin, norepinephrine,and prostaglandins at surgical site ii) central sensitization at dorsal horn of spinal cord is an exaggerated response



Schematic of preemptive analgesia with an emphasis on preventing sensitization of the nervous system throughout the perioperative period. A typical experience without intervention is shown in A, which depicts pain from the initial surgery and the hypersensitivity that subsequently develops. In B, analgesia (A) administered after sensitization may decrease pain somewhat but has little long-term benefit. Analgesia given before surgery limits the pain from that stimulus and decreases subsequent hypersensitivity, as shown in C. The most effective preemptive analgesic regimen is initiated before surgery and continued throughout the postoperative period, as shown in D. Although timing of the intervention is important, it must also be capable of preventing sensitization of the nervous system.Studies Claim if pain is inadequately treated in one half of all the surgical procedures. Immediate unpleasantness and painful experience amplify the response to subsequent noxious stimuli (hyperalgesia) as a result typically painless sensations are experienced as pain (allodynia). A chronic condition sometimes develops that produces continuous pain long after surgery. Prior painful experiences are a known predictor of increased pain and analgesic use in subsequent surgery.

Visual Analogue Scale

In diclofenac group mean pain3.17 ± .11 at the requirement of Rescue Analgesia as 3.57 ± .42compared to in Paracetamol group patients. This difference in two groups was statistically not significant $P<0.05$. Even though the VAS was comparable, pain score was more in the Paracetamol group.

Soudabeh Haddadi et al: 96 children of 4 to 10 years age were operated for elective adenotonsillectomy, The Result analysed indicated a significant relationship between reduction of postoperative pain of rectal acetaminophen ($P = 0.0001$); in group receivingrectal acetaminophen 43.8% of children had mild pain or no pain. Also, on 4 and 6 hour time intervals, pain in rectal acetaminophen receiving groupwas less ($P < 0.05$).

ES Adarsh et al: 60 children were operated for tonsillectomy ,and were administered 1 mg/kg diclofenac suppository after induction.The Results analysed that post operative rectal diclofenac provided effective analgesia in the immediate postoperativeperiod, as evidenced by reduced pain scores and reduced opioid requirement (*P*=0.00002). There was no significant difference in mean pain scores at 0 min and 30 min in the postoperativeperiodbetween both the groups.A significant difference in mean pain scores was observed at 60 min and90 min. Mean pain scores were comparable between the groups at 2, 3, 4, 5 and 6 h post operatively

Conclusion:-

Based on our study we conclude that

- Diclofenac Sodium is better than Paracetamol
  - provides longer duration post-operative analgesia. .
  - Better Visual Analogue Score
  - almost no adverse effects

SUMMARY:-

We have conducted a study on 60 paediatric patients of (5yrsto 12yrs)either sex undergoing elective surgical procedures under general anaesthesia to study and compare post-operative analgesic efficacy and side effects of paracetamol and diclofenac. All patients were randomly dividesd into two equal groups- group P to receive per rectal. paracetamol and group D to receive per rectal. diclofenac. Both the groups were comparable in demographic profile and surgical operations performed.

We observed that:-

1. Both the drugs were associated with cardiovascular stability throughout peri-operative period.
2. Though the VAS was comparable in both the groups but duration of analgesia was more with the diclofenac group.
3. The study has shown almost no side effects in both the groups.

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