"EFFECT OF PREOPERATIVE RECTAL DICLOFENAC SUPPOSITORY ON POST OPERATIVE ANALGESIC REQUIREMENT IN CLEFT PALATE REPAIR – A RANDOMIZED CLINICAL TRIAL"

By

Dr. ADARSH E. S.

DISSERTATION
submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D. ANAESTHESIOLOGY

Under the Guidance of
Dr . RAJESH MANE MD,DNB
Associate Professor,
DEPARTMENT OF ANAESTHESIOLOGY,
JAWAHARLAL NEHRU MEDICAL COLLEGE
BELGAUM, KARNATAKA

MAY - 2009

KLE UNIVERSITY, BELGAUM, KARNATAKA

DECLARATION

I hereby declare that this dissertation entitled **"EFFECT OF PREOPERATIVE RECTAL DICLOFENAC SUPPOSITORY ON POST OPERATIVE ANALGESIC REQUIREMENT IN CLEFT PALATE REPAIR – A RANDOMIZED CLINICAL TRIAL"** is a bonafide and genuine research work carried out by me under the guidance of **Dr .Rajesh Mane** **MD,DNB** Associate Professor, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum-590010.

Date: **Dr. ADARSH . E . S.**
Place:

KLE UNIVERSITY, BELGAUM, KARNATAKA

CERTIFICATE

This is to certify that the dissertation entitled **" EFFECT OF PREOPERATIVE RECTAL DICLOFENAC SUPPOSITORY ON POST OPERATIVE ANALGESIC REQUIREMENT IN CLEFT PALATE REPAIR – A RANDOMIZED CLINICAL TRIAL"** is a bonafide research work done by **Dr. ADARSH. E.S.**under my direct supervision and guidance in partial fulfillment of the requirement for the degree of **M.D. (ANAESTHESIOLOGY).**

Dr. Rajesh Mane **M.D.,DNB**
Associate Professor
Department of Anaesthesiology,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date :
Place : Belgaum

KLE UNIVERSITY, BELGAUM, KARNATAKA

CERTIFICATE

This is to certify that the dissertation entitled **"EFFECT OF PREOPERATIVE RECTAL DICLOFENAC SUPPOSITORY ON POST OPERATIVE ANALGESIC REQUIREMENT IN CLEFT PALATE REPAIR – A RANDOMIZED CLINICAL TRIAL"** is a bonafide research work done by **Dr. ADARSH.E.S.** under my supervision and under overall guidance of **Dr. RAJESH MANE** MD,DNB in partial fulfillment of the requirement for the degree of **M.D. (ANAESTHESIOLOGY).**

DR. Rajesh Powar **MS,M.Ch(BOM),DNB(Plastic)**
Professor and Head
Dept of Plastic and reconstructive surgery,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date :
Place:Belgaum

KLE UNIVERSITY, BELGAUM, KARNATAKA

ENDORSEMENT

This is to certify that the dissertation entitled **" EFFECT OF PREOPERATIVE RECTAL DICLOFENAC SUPPOSITORY ON POST OPERATIVE ANALGESIC REQUIREMENT IN CLEFT PALATE REPAIR – A RANDOMIZED CLINICAL TRIAL"** is a bonafide research work done by **Dr. ADARSH . E . S .** under the guidance of **DR. RAJESH MANE** **MD,DNB.** Associate Professor, Department of Anaesthesiology and co-guidance of **DR.RAJESH POWAR** **MS,M.Ch,DNB** ,Professor, Department of Plastic Surgery ,J. N. Medical College, Nehru Nagar, Belgaum-590010.

Dr. V. K . Dhulkhed **MD.DA**
Professor and Head,
Department of Anaesthesiology,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date:
Place: Belgaum

Dr. V. D. Patil **MD,DCH**
Principal,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date:
Place: Belgaum

KLE UNIVERSITY, BELGAUM, KARNATAKA

COPYRIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the KLE University, Belgaum, Karnataka shall have the rights to preserve, use and disseminate this dissertation in print or electronic format for academic / research purpose.

Date :

(**Dr. ADARSH. E.S.)**

Place : Belgaum

© KLE University, Belgaum, Karnataka

ACKNOWLEDGEMENT

First and foremost I would like to express my sincere gratitude and appreciation for my guide **Dr. Rajesh Mane.** **MD DNB,** Associate Professor, Department of Anaesthesiology, for his constant guidance, valuable suggestions, unparalleled encouragement and co-operation provided to me throughout the course of study. It has been a great pleasure and privilege to work under him. Without his immense professional insight and guidance I could have not completed this study.

I avail this opportunity to thank **Dr. V.K .Dhulkhed** MD. Professor and Head, Department of Anaesthesiology , for his keen interest, unparalleled encouragement and co-operation during this study.

I express my thanks to my co-guide **Dr Rajesh Powar** MS,M.Ch(Bom),DNB(Plastic) Professor and Head, Dept of Plastic & Reconstructive Surgery, KLESPKH & MRC, Belgaum, for the expertise ,encouragement and positive feedback, which has made it conceivable for me to expedite this dissertation.

I am deeply indebted to **Dr P.F.Kotur** MD. Senior Professor , Department of Anaesthesiology . His stature and knowledge has been highly inspirational all through my career as postgraduate.

I express my sincere gratitude to **Dr. V. D. Patil** **MD, DCH** Principal, J. N. Medical College, Belgaum, **Dr. M. V. Jali** **MD**, Director and Chief Executive, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum for allowing me to utilize the facilities in above institution for the dissertation.

I take this opportunity to thank **Dr. C. S. Sanikop** **MD,**

Dr. Suresh.S.N MD, **Dr. Lata Kulkarni** MD **, Dr. M. G.Dhorigol , Dr. Vandana Gogate** MD **, Dr .Vijay Umarani** MD, **Dr. Manjunath C Patil** MD**, Dr. Deepak C.J.** MD, **Dr. Kedareshewar** MD **Dr.Brijesh** and **Dr Maulik Mehta** for their kind support.

I sincerely thank**, Dr. G.C.Mirji** MD, **Dr Ananad Vagarali** MD**, Dr. Sharan Patil** MD, **Dr Shriram Sabde** D.A. D.N.B**.** and all other teachers of J. N. Medical College, Belgaum for their kind support and timely help during the study.

I sincerely thank **Mr M.D.Mallapur** MSc for his help in statistics and valuable guidance.I sincerely thank all my post graduate colleagues for their help in the study.

I express my sincere thanks to my friends **Dr.Sagar , Dr.Shivakumar, Dr.Shailesh, Dr. Ashish Alexander and Dr .Vishwas** for their constant help, support, encouragement and cooperation in designing my dissertation.

This would have not been possible without the co-operation and understanding of my patients involved in the study. I also thank the authors of numerous publications whose knowledge have been freely utilized in the preparation.

With deep sense of gratitude and affection, I am very thankful to my parents **,** brothers and my other elder family members who always have been a pillar of strength for me.

I thank all of our recovery nursing staff and plastic surgery ward staff for their continuous support they have rendered, during the course of this study.

Finally, I thank **Almighty** for all the blessings.

Dr . ADARSH . E.S.

LIST OF ABBREVATIONS

ASA – American Society of Anaesthesiologists

BT – Bleeding time

BP – Blood Pressure

CT – Clotting time

ECG - Electrocardiograph

EtCO2 – End tidal carbon dioxide

GI – Gastrointestinal

Group C – Conventional group

Group D – Diclofenac group

Hr – Hour

I.V – Intra venous

Inj – Injection

i.e – That is

IASP – International Association for the Study of Pain

kg – Kilogram

max – Maximum

mg – Milligram

min - Minutes

NIBP – Noninvasive Blood Pressure

NS – Non significant

NSAID – Non steroidal anti-inflammatory drug

P.G – Post Graduate

RAE – Ring Adair Elwin

S - Significant

S.D – Standard Deviation

SpO2- Oxygen saturation

µgm – Microgram

viz.. – namely , that is

ABSTRACT

Background

Inadequate analgesia in children besides its psychological effects, causes restlessness, excitability, tachycardia and increased oxygen consumption. Opioid analgesics used for analgesia are associated with sedation , respiratory depression and PONV. NSAIDs such as diclofenac is safe , effective and has shown to have an opioid sparing effect.

Objective

To evaluate the effectiveness of pre-operative rectal diclofenac (1mg/kg) in Cleft palate repair for post-operative analgesia and reduction in opioid requirements.

Study design

A randomized clinical trial

Methods

After obtaining approval from the institutional ethical committee, 60 children were allocated by computer generated randomization into two groups of 30 each; group D (Diclofenac group) and group C (Conventional group) . Children in group D and group C were similar in all aspects except for the fact that Group D children received 1mg/kg Diclofenac suppository after induction . Pain scores were evaluated using modification of objective pain scale by Hannallah and colleagues at frequent intervals for 6 hrs postoperatively by anaesthesiology P.G. or nursing staff in the recovery room who were blinded to the group. If the pain score was > 3 , rescue analgesic I.V fentanyl 0.5µgm/kg was administered. The pain scores at different intervals, number of doses and quantity of rescue analgesic required was noted. All the data collected was processed statistically .

Results

We observed that preoperative rectal diclofenac provided effective analgesia in immediate post-operative period as evidenced by reduced pain scores and reduced opioid requirement (P=0.00002) . There was no evidence of any increased perioperative bleeding in diclofenac group.

Conclusion

Preoperative rectal diclofenac reduces opioid consumption and provides good post-operative analgesia.

Keywords – Rectal diclofenac analgesia ; Cleft palate repair

CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

LIST OF PHOTOGRAPHS

INTRODUCTION

"For all the happiness mankind can gain , is not in pleasure but in rest from pain" the statement aptly describes the importance of analgesia in a patient with pain. Importance of pain relief also encompasses the paediatric age group.

A misconception very commonly endured is that a childs nervous system does not perceive pain. Children do experience and remember pain. Children have been under treated for pain because of the misconception that they neither suffer pain ,nor do they remember the painful experiences to the same degree that adults do. [1]

Pain in children is a complex phenomenon, as it is difficult to differentiate crying or restlessness due to pain from that of hunger or fear. Pain triggers complex biochemical and physiological stress responses and cause impairments in pulmonary , cardiovascular ,neuroendocrinal ,gastrointestinal ,immunological and metabolic functions. [2]

Cleft lip-palate is one of the most common congenital anomaly requiring surgical intervention at a very early stage of life. The incidence is reported to be 1 in 897 live births. [3] Surgical correction of palate involves considerable amount of tissue dissection and hence is proportionally associated with appreciable postoperative pain. Pain relief becomes all the more important as a quiet , alert child is required post operatively in these cases.

The common modes of analgesia for post operative pain includes opioids and non opioids like Non Steriodal Antiinflammatory Drugs (NSAID'S) , Paracetamol , Regional

techniques. So far opioids have been the mainstay of postoperative pain relief but recently nonopioids are being considered, because of the high incidence of nausea vomiting and also concerns about the risk of respiratory depression and sedation with opioids.

Among NSAIDs , diclofenac sodium is a effective and safe analgesic in children.[4] Eventhough there are controversies regarding its adverse effects like bleeding and GI disturbances in children, it has proved to be very efficient overall, the benefits outweighing the side effects. NSAIDs by virtue of their action not only reduce pain but also the inflammation. Diclofenac given preoperatively has also shown to provide Preemptive analgesia. [5]

In children, the choice of the route of administration is very important. The intramuscular injection evoke fear and anxiety in children. The oral formulation though tolerable is met with resistance and displeasure by children, especially those who have undergone surgery involving craniofacial region. Rectal Diclofenac suppository are available and are proved to be safe for use in children.[6]

Large number of cleft palate surgeries are being done every year in our institution. As per the existing protocol these children receive opioids (I.V fentanyl) for immediate postoperative pain relief. Hence, in the present study an attempt is being made to study the effect of preoperative rectal diclofenac suppository on postoperative analgesic requirement in cleft palate repair.

OBJECTIVES

The objectives of the present study are:

a. To determine the effectiveness of preoperative rectal diclofenac suppository (1mg/kg) on postoperative analgesia in Cleft palate repair.

b. To determine the reduction in opioid requirement in the immediate postoperative period (6hrs).

REVIEW OF LITERATURE

Ever since , it has been proven beyond doubt that infants and children do perceive pain as much as the adult, and the effects of pain on the child viz.. restlessness , psychosomatic effects , excitability , delayed discharge from hospital have been appreciated , efforts are being made towards effective post operative pain relief.

Various options , like regional blocks , oral tablets / syrups , rectal suppository, parentral opioids and patient / nurse controlled analgesia have been evaluated in paediatric population. Each option has its own advantages and disadvantages .

One such option is diclofenac sodium , a Non Steriodal Anti inflammatory drug which is available in oral , injectable and rectal suppository formulation. The analgesic efficacy and safety of diclofenac in adults is a proven fact. The use of diclofenac in paediatric population and its safety is less studied. Hence, the review of literature of diclofenac necessarily needs to be addressed in children with regards to its analgesic effect , safety, opioid sparing action and side effects like bleeding and exacerbation of asthma.

The existing literature on diclofenac addressing the above concerns is reviewed.

Hodsman N. B. A et al [7] in their study demonstrated that there was a mean post operative reduction of morphine by over one third and significant pain reduction upto 4 hrs after surgery in patients who had received Diclofenac sodium intramuscularly following abdominal surgery . As a secondary objective the study also concluded that there was no significant difference in platelet count pre and post operatively.

One of the commonest surgery for which a child presents is tonsillectomy. Post-tonsillectomy the child requires to be completely awake, pain free and calm. Various analgesics, opioids and nonopioids have been studied for analgesia in tonsillectomy. Bone M. E and Fell D [8] compared rectal diclofenac (2mg/kg) with intramuscular papavertum (0.2 mg/kg) or placebo for pain relief in children undergoing tonsillectomy . They demonstrated that intraoperative diclofenac offered satisfactory postoperative analgesia as compared with papavertum and resulted in awake and calm children during post operative period.

The efficacy, speed of recovery , sedation and nausea or vomiting was compared between diclofenac I.M. (1mg/kg) and pethidine (1mg/kg) after induction in patients undergoing tonsillectomy by Watters C.H and colleagues .[9] They concluded that rectal diclofenac proved to be equally effective analgesic and also the children who received rectal diclofenac were able to cooperate better and were less drowsy than those who received pethidine.

Paracetamol and diclofenac , two of the very commonly used nonopioid analgesics, have different modes of action. Paracetamol acts centrally and diclofenac acts at the periphery. Baer G.A and colleagues [4] did a study to compare postoperative pain and behavior following Adenoidectomy amongst preoperative rectal diclofenac (12.5 mg) and rectal paracetamol (125 mg) . The subjects received either rectal diclofenac or rectal paracetamol given along with rectal diazepam (0.5 mg/kg) before induction of anaesthesia. Pain was evaluated using seven criteria viz.. alertness, response to handling , anxiety , crying , restlessness, nausea vomiting and breathing pattern. The study concluded that the children in diclofenac group were less restless ($P < 0.03$) easier to

handle (p <0.01) and cried significantly less on arrival.There was no significant estimated blood loss.

In another study, Ejnell. H and colleagues [10] compared rectal diclofenac suppository (150-200 mg/day) with placebo in 40 patients for postoperative analgesia after Uvulopalatopharyngoplasty for 3 days. Consumption of rescue analgesic (Paracetamol suppository) based on pain as assessed by VAS and preoperative and postoperative bleeding and bleeding time were noted. The study concluded that consumption of rescue analgesic and VAS scores were significantly less in diclofenac group. Bleeding time and reported side effects did not differ between the two groups.

Caudal block is another frequently practiced and reliable mode of post operative analgesia in children following surgery below the umbilicus. Caudal block requires expertise in performing the block and is associated with complications if performed wrongly. In a study on children undergoing herniotomy as day cases, rectal diclofenac (2.5 mg/kg) was compared with caudal bupivacaine for post operative pain relief by Moores M. A and colleagues .[6] Pain was assessed as none , moderate and severe . The study revealed that except in immediate post operative period , rectal diclofenac provided analgesia comparable to that produced by caudal bupivacaine. Superior analgesia was evident in caudal group at 1 hr and only 60% of those who received rectal diclofenac were pain free at this time, although the proportion of pain free children increased later.

Another study in 39 ASA grade I and II children undergoing inguinal or penoscrotal surgery was conducted to evaluate the effect of combination of caudal block

(0.125% bupivacaine with adrenaline 1: 400000 at 1ml/kg) and rectally administered diclofenac (1mg/kg) for postoperative analgesia .[11] The results of the study was, need for postoperative analgesia (Paracetamol) was significantly greater in the children who received caudal block alone when compared with combination of caudal block with rectal diclofenac. There was no evidence of excessive bleeding in children who received diclofenac.

Paracetamol and diclofenac have different mechanism of action and their combination may prove synergistic or additive . Morton N.S and O'Brien .K [12] compared the analgesic efficacy of paracetamol suppository (15-20mg/kg) , diclofenac suppository (1mg/kg) and combination of both in 80 children aged between 5-13years who received PCA Morphine after appendicectomy. In the study cumulative morphine consumption was significantly reduced by concurrent administration of diclofenac but no additive effect of paracetamol was demonstrable with the doses used in this study. Analgesia was significantly improved with addition of diclofenac .

A large number of children with Asthma undergoing surgery are denied of diclofenac for safety concerns. Short J.A and colleagues[13] investigated the effect of diclofenac on the lung function of 70 children with a history of asthma. Peak flow and forced expiratory flow volume were measured and the patients were then given 1-1.5 mg/kg effervescent diclofenac orally . Spirometry was repeated at 10 , 20, 30 min and a 15% decrease in the results was considered a significant reduction in lung function. No patient demonstrated a consistent reduction in lung function of >15% during study , also there were no reports of wheezing or increased bronchodilator use after completion of the spirometry.

One of the key benefits attributed to diclofenac is its ability to reduce the cumulative opioid consumption .As a result problems inherent to opioid analgesics viz. sedation , respiratory depression , nausea or vomiting and retention of urine is minimized. A study on opioid sparing effect of rectal diclofenac (75mg/kg) following total abdominal hysterectomy was conducted in 40 ASA grade I and II patients , aged 20-60 yrs .[14] All patients were given a standardized anaesthesia and intravenous morphine via a patient controlled analgesia device and either diclofenac or placebo for postoperative analgesia. The study concluded that rectal diclofenac reduces morphine consumption ($p = 0.02$) , improves postoperative analgesia and reduces the incidence of adverse effects such as sedation and nausea.

In another study, Bhagat and colleagues [15] studied the adjunctive role of diclofenac to centrally acting analgesic tramadol for intraoperative and postoperative analgesia in ENT surgery. The study included diclofenac group who received diclofenac suppository 2mg/kg one hour prior to surgery and the other control group received placebo. The intraoperative analgesia in either group was by inj tramadol . The results of the study was that , patients in diclofenac group had adequate analgesia over 14hrs and only 4 hrs in the control group. The conclusion was that the use of preoperative rectal diclofenac has substantial effect as an adjunct intraoperative analgesic. Diclofenac considerably delays the onset of postoperative pain and is adequate as a sole analgesic for early postoperative period.

Recently, focus is towards the concept of Preemptive analgesia. Riad W and Moussa A [16] conducted a study in 108 patients posted for inguinal hernia repair to determine whether preoperative administration of rectal diclofenac (1mg/kg) and rectal

paracetamol (40mg/kg) decreased postoperative narcotic requirement compared to administration of each drug alone . Children were randomly assigned to receive either rectal diclofenac or paracetamol or their combination 1 hr prior to surgery. Pain was assessed using Wong and Baker pain scale. If the pain score was > 2 , inj morphine at a dose of 0.5 mg every 6 min with a maximum of 0.2 mg /kg was given . The total dose of morphine requirement and number of doses were noted . The study concluded that diclofenac is equally effective and the children who received rectal diclofenac-paracetamol combination experienced a lower pain score and a decreased need for morphine.

For children undergoing lower limb surgery regional techniques like caudal block have been used successfully. Gupta N and colleagues [17] compared caudal block with bupivacaine , rectal diclofenac and combination of both after induction of anaesthesia for post operative analgesia. Sixty children , randomized 20 in each group were included into study. Pain was assessed for 24hr post operatively using observational pain score in a blinded fashion. They concluded that rectal diclofenac in combination with caudal block provided good postoperative analgesia. Rectal diclofenac alone provided good analgesia extending upto 12hrs after 60 min of drug administration .

Diclofenac and the other NSAID's , because of their nonspecific action on the enzyme cyclo-oxygenase has a potential for increased post operative bleeding which has lead many to avoid them completely in the paediatric population resulting in suboptimal pain control. Heaney et al [18] assessed the effectiveness of preoperative rectal diclofenac (2mg/kg) on the blood clot strength in children undergoing Adenotonsillectomy. Blood was drawn for thromboelastograph analysis before administration , 1hr and 4hr after

administration of rectal diclofenac . The study concluded that diclofenac when given preoperatively does not adversely affect clot strength in immediate post operative period when the risk of primary haemorrhage is greatest.

Analgesia for Cleft palate repair so far has been predominantly with opioids , acetaminophen and NSAID'S . Cleft palate repair requires child to be awake , pain free and less crying postoperatively as chances of aspiration and increased bleeding is more with these events. Syladis .P, Trevor J, O'Neill [19] studied diclofenac analgesia for cleft palate surgery . The risk of post operative hemorrhage associated with the use of diclofenac was also assessed. Twenty consecutive children requiring repair of hard or soft palate were given single per rectum diclofenac (1mg/kg) following cleft palate repair , with additional doses every 12 hrs . Oral Paracetamol was prescribed for breakthrough pain at 15 mg/kg .The study concluded that twice daily rectal diclofenac suppository provided very good analgesia post cleft palate repair, obviating the need for opiates resulting in alert infants who fed well and were suitable for early discharge . Post operative bleeding complications were not reported .

Thus studies and existing literature on diclofenac sodium with regards to its effectiveness, safety and side effects in paediatric population opine that, it is

Safe and effective analgesic,

Suppository formulation is a tested mode acceptable for administration,

Also reduces the requirement of opioid during postoperative period and does not cause clinically significant postoperative bleeding though it inhibits platelet aggregation.

Hence, after reviewing the existing literature and existing practice of post operative analgesia for cleft palate repair in our institution (I.V fentanyl) and as there were few systematic study of its use in Cleft Palate repair surgeries, we decided to evaluate the effect of preoperative rectal diclofenac suppository on post operative analgesia in cleft palate repair.

BASIC SCIENCES

ANATOMICAL AND PHYSIOLOGICAL ASPECTS OF PAIN PERCEPTION

Pain is a complex sensation which is difficult to define and equally difficult to measure in an objective manner.

It has been defined by the International Association for the Study of Pain (IASP) 1986 as 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damages.

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.

The sensation of pain differs among individual patients as it is subjective to

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.

Pain can be represented as a VENN DIAGRAM

Figure I

PAIN THEORIES IN THE TWENTIETH CENTURY

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 nerve and tissue damage activates fibers that 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 components: the perception of pain and the reaction to pain.

Sensory Interaction Theory In 1959 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 (Melzack and Wall 1965, Wall 1978).

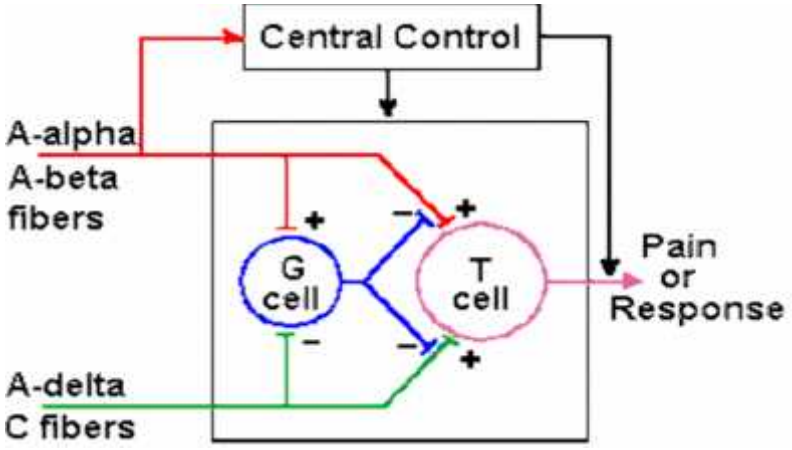


Figure II: Gate control theory

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 in lamina V of the dorsal horn and the still unidentified inhibitory cells, in laminae II and III. The essence of this theory is that large diameter fibers excite the I cells, which in 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 ending which responds 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 visceral. Their response differs however and they will produce pain of a dull, vague nature following distension, stretch or traction and will 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 . They are comprised of finely myelinated delta fibers 1-5 micrometer in diameter with conduction rate at 5-45 m/sec and the unmyelinated C fiber diameter 0.4 – 1.1 micro meters conducting at 0.5 – 2.0 m/sec. 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.

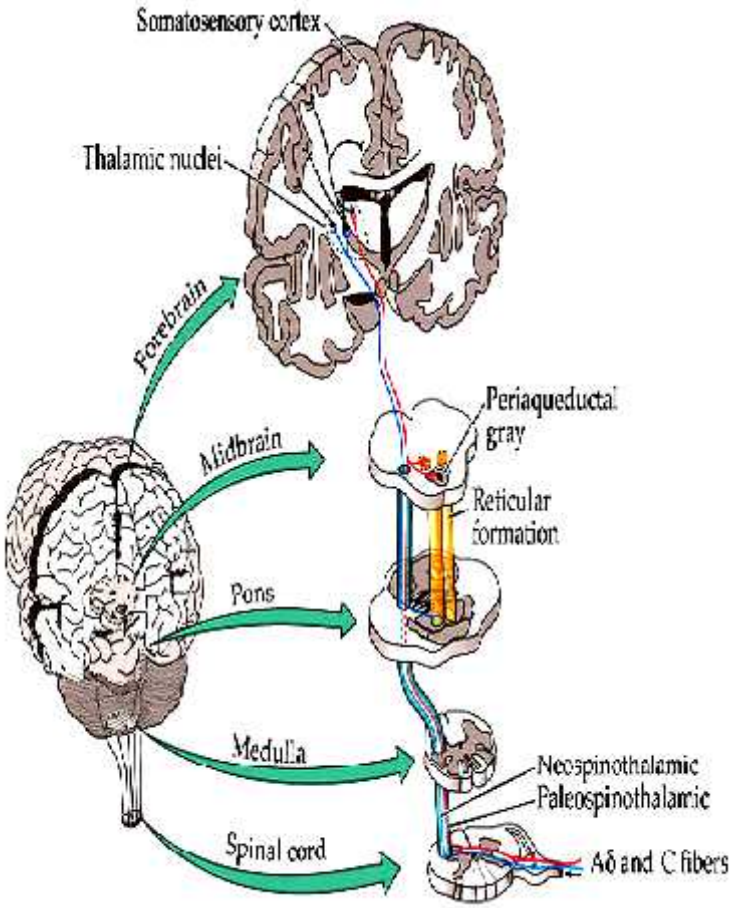


Fig III: Pain Pathway

Organization of pain pathways

The cell bodies of the primary pain afferents (i.e. the first order neurons) are located in the dorsal root ganglia. Central extensions of the primary neurons project, via the dorsal root, to the dorsal horn of the spinal cord and in the case of cranial pain afferents, to the nucleus of the trigeminal nerve. 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.

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 caudal tone or two adjacent segments ipsilaterally and some via the anterior commissure to the contralateral dorsal horn. 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 form 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 form 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/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 viz, pricking, cutting crushing, burning and freezing. However these stimuli are inadequate when applied to stomach and intestines where the local effects of an engorged or inflamed mucosa, distension or spasm of smooth muscle and traction on the mesenteric attachment produces pain. In skeletal muscle, pain is produced by ischemia (intermittent claudication), necrosis, hemorrhage, injuries to connective tissue sheaths and injection of irritating solutions. Prolonged contraction of the skeletal muscle produces an aching type of pain. Ischemia is also the most important cause of pain in cardiac muscle. Joints are insensitive to pricking, cutting and cautery, but pain is produced by inflammation of the synovial membrane and by exposure to hypertonic saline. Arteries are a source of pain when pierced by a needle, or involved in an inflammatory process. Distension and excessive pulsation of meningeal arteries resulting in stretching of the dura, produces headache.

Perception of pain

The threshold for the perceptions 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 vary from individual with the personality and character of the

individual. 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

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.

Loser, of multidisciplinary pain centre, University of Washington put forward a multifaceted model as depicted in this figure. 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.

Behaviour based 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."

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".

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.

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.

PAIN AS SELF-REPORTS ON MULTIPLE DIMENSIONS

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

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.

Pain in children is difficult to quantify. Various pain scales have been tested to assess pain in this age group. The pain scales which are used in children are

- Modification of the objective pain scale by Hannallah and colleagues,
- Wong and Baker (FACES) pain rating scale,
- The COMFORT pain scale for infants and children.
- Face-Legs-Activity-Cry-Consolability scale
- Visual analogue toy.

ACUTE POSTOPERATIVE PAIN

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.

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.

Adverse effect caused by post operative pain

Physiologic

Include pulmonary, cardiovascular, gastrointestinal and urinary dysfunction, impairment of muscle metabolism and function and neuroendocrine and metabolic changes.

Respiratory

Surgery including that of the upper abdomen or thorax produces a number of pulmonary changes, including reduced Vital capacity and Forced expiratory volume. Upper abdominal incisions result in reflex mediated increase in tone of abdominal muscles during expiration and in a decrease of diaphragmatic function. The results are reduced pulmonary compliance, muscle splinting and inability to breathe deeply or cough forcefully leading to hypoxia, hypercarbia, retention of secretions, atelectasis, and pneumonia. Increased muscle tone increases oxygen consumption and lactic acid production.

Cardiovascular

Pain causes stimulation of sympathetic neurons and subsequent tachycardia, increased stroke volume, cardiac work and myocardial oxygen consumption. The risk of myocardial ischaemia or infarction may be increased as is the risk of deep vein thrombosis when feat of aggravating pain results in reduced physical activity, venous stasis and platelet aggregations.

Gastrointestinal and urinary

Ileus, nausea, vomiting, hypomotility of the urethra and bladder and retention of urine can occur for a umber of reasons that include nociceptive impulses from viscera and somatic structure.

Neuroendocrine and metabolic

Suprasegemental reflex responses to pain, result in increased sympathetic tone, hypothalamic stimulation, increased catecholamine and catabolic hormone like cortisol, adrenocorticotrophic hormone, antidiuretic hormone, growth hormone, cyclic adenosine monophosphate, glucagon, aldosterone, renin, angiotensin 2 and decreased secretion of anabolic hormones insulin and testosterone. The effects of these changes include sodium and water retention and increased blood glucose, free fatty acids, ketone bodies, and lactate. Metabolism and oxygen consumption are increased and metabolic substrates are mobilized from storage depots. A catabolic state and negative nitrogen balance result, if the process continues.

Psychological

Postoperative pain is a major source of fear and anxiety for patient and if prolonged, leads to anger, resentment and lack of trust in the doctors and nurses who are perceived to be withholding pain relief. Pain leads to insomnia with further delayed recovery. Some patients may even try self medication which could be hazardous.

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

Diclofenac sodium

Diclofenac sodium is a Non Steriodal Antiinflammatory Drug (NSAID), a Phenyl acetic derivative with pronounced anti-inflamatory, analgesic, antirheumatic and antipyretic properties.

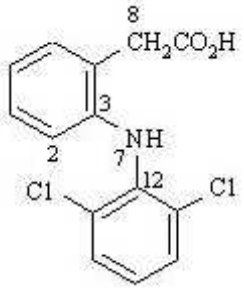


Figure IV

Pka = 4.0 , Molecular weight = 318.1

Faintly yellow white to light beige crystalline powder with no odour.

Mechanism of action :- The Analgesic and Antiinflammatory action of NSAID's are mainly due to cyclooxygenase enzyme inhibition, although decreased leukotreine and arachadonic acid production may also contribute . NSAIDs also have a central antinociceptive action , the mechanism for which is poorly understood.

Diclofenac inhibits both COX1 and COX 2 isoforms of Cyclooxygenase enzyme. The COX 2 enzyme is induced at sites of tissue injury and catalyzes prostaglandin formation (PGF2α and PGE2) from arachadonic acid and causes pain by generating action potential in nociceptive neurons . Inhibition of COX1 accounts to adverse effects viz. gastric

mucosal erosions , renal blood flow alteration and inhibition of experimentally induced platelet aggregation when administered in high doses.

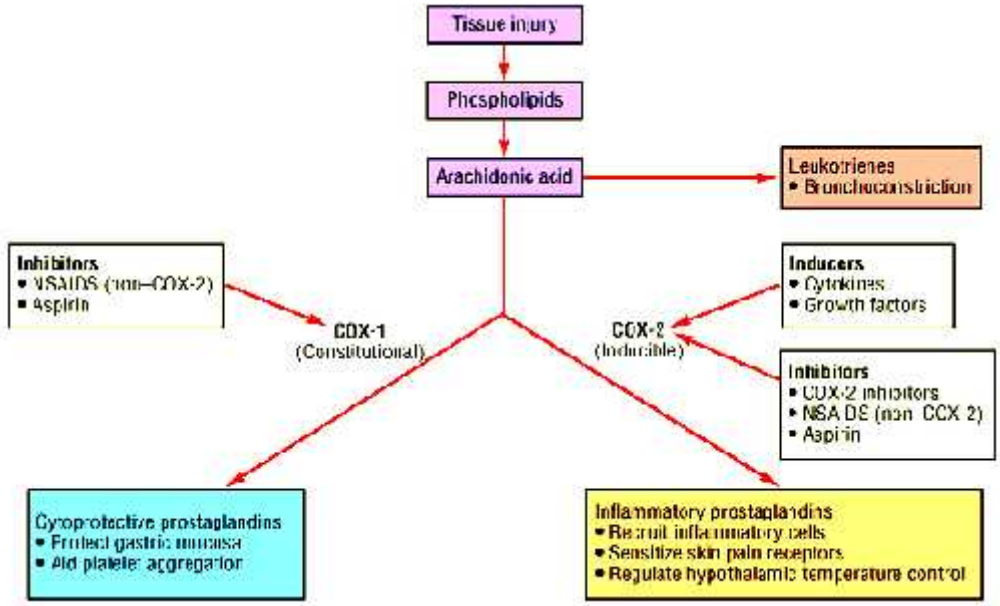


Figure V : **Tissue injury and its mediators**

Pharmacokinetics :- The drug is readily absorbed orally , rectally and intramuscularly.These constitute the main routes of systemic administration of Diclofenac . Recently , Diclofenac for slow intravenous administration has been made available. There is some presystemic elimination when administered orally

Bioavailabilty when administered orally is >90% and that by rectal route ranges from 20-90%. Diclofenac has a plasma half life of 1-2 hrs with a volume of distribution of 0.12/ltr/kg. It is upto 99.5% plasma protein bound, mainly to Albumin.

Metabolism :- Diclofenac undergoes extensive first pass metabolism primarily through 4' hydroxylation by cytochrome P4502C9 , although 5' hydroxylation by CYP3A4, CYP2C19, CYP2C8 and CYP2C18 also takes place**.** Upto 20-30 % is excreted in urine after an oral dose along with 10-20% through bile as glucuronide and sulphate conjugates.

The Rectal route is a suitable route for administration of diclofenac in children as it is associated with a higher relative bioavailabilty than enteric coated tablets and achieves maximum concentration earlier (50min rectal versus 108 min oral route) . This pharmacokinetic profile renders diclofenac suppository a suitable formulation for short duration surgery.

Therapeutic/ Clinical uses:-

Post operative pain relief

Rheumatoid arthritis, Osteoarthritis, Ankylosing Spondylitis.

Renal colic pain,

Acute gout , Juvenile Rheumatoid arthritis etc.

Precautions and warnings

Close medical supervision is mandatory in cases of diclofenac administration in gastro-intestinal ulceration.

Since bronchospasm has been reported with the use of NSAIDs, the drug should be used with caution in asthmatics.

Due to the importance of prostaglandins in maintaining renal blood flow, caution is required in patients with impaired cardiac or renal function, the elderly, patients being treated with diuretics and patients with substantial extracellular volume depletion. In patients with heart failure, hypertension or other conditions predisposing to fluid retention, it can cause retention of salt and water leading to oedema.

Platelet aggregation may be inhibited temporarily. Patients with haemostasis defects should therefore be carefully monitored.

Diclofenac should be used with caution in patients suffering from liver dysfunction. Initial elevations of liver enzymes seen with the drug are usually reversible. However, if they persist or worsens during the prolonged therapy, it should be discontinued.

Diclofenac should be avoided in pregnancy unless the benefits outweigh the potential risk to the foetus. This applies particularly to the last 3 months of pregnancy when, like other prostaglandin inhibitors, diclofenac may cause closure of the foetal ductal arteriosus, foetal renal impairment, inhibition of platelet aggregation and delayed labour and birth.

Diclofenac is detected in the breast milk following doses of 50mg every 8 hours, but the amounts are so small that no undesirable effects on the baby are seen.

Pharmacological preperations:-

Oral tablets

Rectal suppositories (12.5 mg/ 25mgmg/50mg/100mg strength)

Intramuscular and Intravenous injections

Gels for topical application**.**

RECTAL ROUTE

The rectal route has a rich blood supply and is drained by the superior , middle and inferior rectal veins . While the superior vein , which perfuses the upper part of the rectum drains into the portal vein and then subsequently into the liver, the middle and inferior rectal veins draining the lower part of the rectum open directly into the inferior venacava i.e into the systemic circulation. Thereby 50% of the drug administered by the Rectal route will bypass the liver. The potential for hepatic first pass metabolism is thus less for rectal administration than for the Oral dose.

In addition the local irritation of the drug when given orally, induces back diffusion of the acid into the gastric mucosa causing tissue damage,which is not seen with drugs administered via rectal route . Nevertheless, the adverse effects such as gastric irritation are not completely avoidable when given rectally ,since this also depends on the plasma concentration of the drug.

Thus the rectal route has many advantages viz..

Avoids the pain of intramuscular injection

Has easy acceptance by children

Avoids the problem associated with the drug being non-palatable for children

Bypases the liver, thereby offering better bioavailability

Avoids gastrointestinal disturbances

Has prolonged action ,as a result of sustained release.

For obvious reasons stated, diclofenac suppositories form a valuable tool for postoperative pain management . Marel C.D and colleagues [20] did a study on diclofenac and its metabolites' pharmacokinetics in children. They concluded that the rectum is a suitable route for diclofenac administration in children and is associated with a higher relative bioavailability than eneteric coated tablets and an earlier maximum concentration (50min versus 108 min). This pharmacokinetic profile renders diclofenac suppository a suitable formulation for short duration surgery.

MATERIALS AND METHODS

The present study titled **" Effect of Preoperative Rectal Diclofenac suppository on post operative analgesic requirement in Cleft palate repair – A Randomized Clinical trial "** was conducted in KLES Prabhakar Kore Hospital and MRC between December 2006 to January 2008.

After obtaining the Institutional Ethical committee clearance and informed consent the study was undertaken on 60 ASA grade 1 children between the age group of 9mths – 7 yrs of either sex posted for elective repair of Cleft Palate under general anaesthesia.

INCLUSION CRITERIA

I) Children undergoing Cleft palate repair between the age group of 9mths – 7 yrs.

II) ASA grade 1.

EXCLUSION CRITERIA

I) ASA grade 2 and above

II) Prolonged BT/CT

III) History suggestive of Kidney or Liver disease.

IV) History suggestive of allergy to aspirin/ related drugs

V) History suggestive of Bleeding disorders /Asthma/Anorectal anomaly

VI) Treatment with other analgesics/anticonvulsants / anticoagulant.

SAMPLE SIZE CALCULATION

Using the results of a previously conducted study and substituting the values in the below stated formula, a sample size of 10 in each group was arrived at . [17]

$$n = \frac{2\ (Z\alpha + Z\beta)^2\ (S_1^{\ 2}+S_2^{\ 2})}{(X_1-X_2)^{\ 2}}$$

Where , $Z\alpha = 1.65$, $Z\beta = 0.84$, Power =80%

S1= standard deviation of Diclofenac group

S2= standard deviation of placebo group

X1= mean of Diclofenac group.

X2 = mean of Conventional /Placebo group.

In our study a sample size of 60 (30 in each group) was taken.

DESIGN :- Randomized Clinical Trial.

METHOD

Each child was examined thoroughly and the patient /guardian was interviewed on the evening prior to the operation . Detailed history about any previous illness and any treatment received was elicited . A detailed physical examination including weight in kilogram and age in years/ months was noted.

Investigations like complete haemogram , bleeding time and clotting time were done. All parents/ guardians were informed regarding the procedure of anaesthesia and study intervention, its benefits and disadvantages in their vernacular language. A written consent of the same from the parents /guardians was obtained.

The children were kept nil by mouth for at least four hours prior to surgery. The children were then allocated into group D (Diclofenac suppository group) or group C (Conventional group) according to a computer generated randomized table.

All children were premedicated with intramuscular inj. glycopyrrolate 0.005mg/kg and inj. ketamine 5mg/kg in the recovery room and shifted to operating room after adequate sedation.

In the operating room, children were oxygenated with 100% oxygen with Jackson Rees modification of Ayres 'T' piece . Meanwhile a appropriate size intravenous line was secured and monitors were attached viz.. pulseoximeter, ECG monitor and NIBP.

All the children were induced with I.V. ketamine 1mg/kg and intubation was facilitated with I.V. suxamethonium 1-2 mg/kg . Intubation with appropriate sized uncuffed RAE orotracheal tube (south pole tube) was done and a throat pack was placed. The time of Induction was noted.

Rectal diclofenac suppository (1mg/kg) was inserted in lateral position following induction and intubation in group D children, while children belonging to group C received no suppository. The time of insertion of suppository was noted.

General anaesthesia was maintained in both the groups via a closed circuit with an oxygen : nitrous oxide mixture (50:50) along with I.V. fentanyl 1µgm/kg ,I.V. midazolam 0.05mg/kg and I.V. vecuronium 0.1mg/kg .Palate repair in all the patients was by Veau – Wardill – Kilner technique. Intraoperatively continuous monitoring of

heart rate , SpO2 , EtCO2 and blood pressure was done and any bleeding in excess of usual was noted . All children received i.v fluid Isolyte P as per standardized calculation.

At the end of the surgery , adequate reversal was done with I.V. glycopyrrolate 0.01mg/kg and I.V. neostigmine 0.05mg/kg .Haemostasis was inspected for and the throat pack was removed. Extubation was done after thorough oral suctioning.

Postoperatively in the recovery room , all the patients were monitored for

1) Haemodynamic parameters (PR , SpO2 , BP) every fifteen minutes for the first 90 minutes.
2) Pain was assessed by Anaesthesiology postgraduate and Nurse trained to use the Modification of Objective pain scale by Hannallah and colleagues[21] in the recovery room (table 1 & 2) . The person assessing the pain was blinded to the group . I.V. fentanyl 0.5µgm/kg was administered if the pain score was > 3.
3) The number and total dose of rescue analgesic (i.e I.V fentanyl 0.5µgm/kg) required was noted .
4) Observation for any bleeding in excess of usual was noted.

Table 1. PAIN SCORING (Modification of Objective pain scale by Hannallah & colleagues)

Name of doctor/nurse:-

Serial no.	Observation	Criteria	points
1	crying	No crying	0
		Crying but responds to TLC*	1
		Crying not responding to TLC*	2
2	movement	None	0
		Restlessness	1
		Thrashing	2
3	agitation	Asleep/calm	0
		Mild	1
		Hysterical	2

* TLC – tender loving care

pain defined by pain score > 3 points, rescue analgesia required

any other finding :-- increased bleeding yes/no

Table 2. Post Operative Pain Scoring

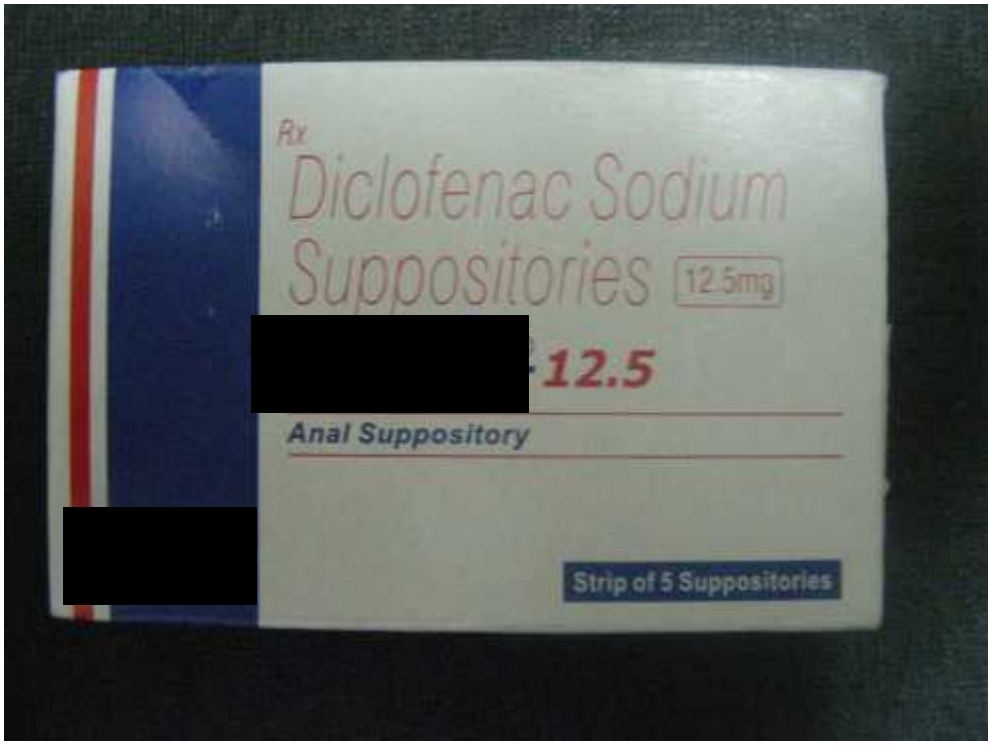
Time	Crying	Movement	Agitation	Total
O hrs				
1/2 hrs				
1 hrs				
1 $_{1/2}$ hrs				
2 hrs				
3 hrs				
4 hrs				
5 hrs				
6hrs				

All the data collected were tabulated in terms of Mean (S.D) .The data were compared between the groups with the following manner . Age , weight and duration of surgery were compared using the unpaired student t test.

Nonparametric Mann Whitney U test was used for comparing the mean (S.D) pain scores at different intervals. Comparison of number of children requiring rescue analgesic was done using Chi Square test. The comparison of total dose of fentanyl consumed (µgm) was done using unpaired Students t test.

P value < 0.05 was considered as statistically significant.

Photograph A



Photograph B

Diclofenac suppository

RESULTS AND OBSERVATIONS

The objective of the present study was to evaluate if preoperative Rectal diclofenac can reduce the postoperative requirement . The study was carried out in KLES Prabhakar Kore Hospital & MRC , Dept of Anaesthesiology , Belgaum, in between the period December 2006 to January 2008.

The study included 60 ASA grade 1 children in the age group of 9 months to 7 years, undergoing Cleft Palate repair . Each group consisted of 30 patients and were divided as group D (Diclofenac group ,n = 30) and group C (Conventional group ,n =30) by a computer generated randomization table.

Data was collected in both groups and observations of the analysed data are presented in the tabular form as follows.

DEMOGRAPHIC PROFILE

D group = Diclofenac group C group = Conventional group

Table 3, Table showing age ,weight and sex distribution in both the groups

Character	Diclofenac group	Conventional group	P Value
Age (Months)	33.60 ± 20.71	27.13 ± 17.18	0.1932 (NS)
Weight (kg)	10.31 ± 3.07	9.72 ± 2.67	0.4281 (NS)
Male : Female	20:10	15:15	

Students unpaired ‘t’ test.(P < 0.05 significant , NS = not significant)

The age, weight and sex ratio were comparable in both the groups.

Table 4 : **Table showing the duration of surgery in both the groups.**

Character	Group D	Group C	P value
Duration of surgery (min) Mean ±S.D	82.10 ± 19.08	80.77 ± 22.55	0.8056 (NS)

students unpaired 't' test.P < 0.05 significant, NS = not-significant.

Both the groups were comparable in terms of duration of surgery

Pain was assessed at intervals of 0 min (at the end of surgery) ,30 min, 60 min, 90 min, 2 hrs, 3 hrs, 4hrs, 5 hrs and 6 hrs postoperatively using Modification of Objective pain scale by Hannallah and colleagues by recovery room P.G/ nursing staff blinded to the group. A pain score of > 3, was considered to be significant and rescue analgesic, I.V. fentanyl 0.5µgm/kg was administered.

Table 5 , Table showing pain scores at different time in both the groups.

	Group D									**Group C**								
score	**0 min**	**30 min**	**60 min**	**90 min**	**2 hr**	**3 hr**	**4 hr**	**5 hr**	**6 hr**	**0 min**	**30 min**	**60 min**	**90 min**	**2 hr**	**3 hr**	**4 hr**	**5 hr**	**6 hr**
0	24	05	08	09	12	14	17	16	20	19	09	06	05	07	08	11	14	20
1	06	18	12	10	08	11	10	08	07	08	07	04	02	12	11	15	09	09
2	0	04	08	06	04	04	03	05	03	02	05	04	08	07	05	04	07	01
3	0	01	01	02	05	0	0	0	0	01	04	03	07	02	02	0	0	0
4	0	02	01	02	01	01	0	01	0	0	04	09	07	02	04	0	0	0
5	0	0	0	01	0	0	0	0	0	0	01	04	0	0	0	0	0	0
6	0	0	0	00	0	0	0	0	0	0	0	0	01	0	0	0	0	0
Total	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**

Table 6 : Table showing mean pain scores in the post operative period in the two groups.

Time	Group D Mean ± S.D	Group C Mean ± S.D	Mann-Whitney U test
0 min	0.2 ± 0.41	0.5 ± 0.78	0.2143(NS)
30 min	1.23 ± 1.01	1.67 ± 1.54	0.4464(NS)
60 min	1.17 ± 0.99	2.57 ± 1.79	0.0036(S)
90 min	1.37 ± 1.35	2.43 ± 1.52	0.0064(S)
2 hrs	1.17 ± 1.23	1.33 ± 1.12	0.4598(NS)
3 hrs	0.77 ± 0.94	1.43 ± 1.33	0.0519(NS)
4 hrs	0.53 ± 0.68	0.77 ± 0.68	0.1958(NS)
5 hrs	0.73 ± 0.98	0.79 ± 0.82	0.6009(NS)
6 hrs	0.43 ± 0.68	0.37 ± 0.56	0.8825 (NS)

At 0 hrs, i.e. soon after the operation when the child was brought to the recovery room . No children in the group D or group C had pain . The mean (S.D) pain scores in group D and group C were 0.2(±0.41) and 0.5 (± 0.78) respectively . There was no significant difference (P = 0.2143, Mann Whitney U test) with regards to pain immediately after the operation.

At 30 min, 2 children in group D (3.33%)and 5 children (8.33%) in group C had pain . The mean (S.D) pain scores in group D and group C were 1.23 (± 1.01) and 1.67 (±1.54) respectively . There was no significant difference in pain scores (P = 0.4464, Mann Whitney U test) at 30 min post operatively.

At 60 min, 1 child (1.66%) in group D and 13 (21.66%) children in group C had pain. The mean (S.D) pain scores at 60 min in group D and group C were 1.77 (±0.99) and 2.57 (± 1.79) respectively . There was a significant difference in pain scores at 60 min (P= 0.0036, Mann Whitney U test).

At 90 min , 3 children (4.99%) in group D and 8 children in group C (12.32 %) had pain. The mean (S.D) pain scores at 90 min in group D and group C were 1.37 (± 1.35) and 2.43 (± 1.52) respectively . There was a statistically significant reduced pain scores at 90 min in group D (P= 0.0064, Mann Whitney U test,).

At 2 hr, 1 child (1.66%) in group D and 2 children (3.33%) in group C had pain. The mean (S.D) pain scores in group D and group C at 2 hr were 1.17 (± 1.23) and 1.33 (± 1.12) respectively. There was no statistically significant difference in the pain scores between the groups at 2 hr (P = 0.4598, Mann Whitney U test).

At 3 hr, 1 child (1.66 %) in group D and 4 children (6.66%) in group C had pain. The mean (S.D) pain scores in group D and group C at 3 hr were 0.77 (± 0.94) and 1.43 (± 1.33) . There was no statistically significant difference in the pain scores at 3 hr between the groups (P= 0.0519 ,Mann Whitney U test).

At 4 hr , no child in group D and group C had pain. The mean (S.D) pain scores in group D and group C were 0.53 (± 0.68) and 0.77 (±0.68) . There was no statistically significant (P= 0.1958 ,Mann Whitney U test) difference in pain scores at 4 hr between the groups.

At 5 hr , 1 child (1.66%) in group D and no child in group C were assessed to have pain. The mean (S.D) pain scores in group D and group C at 5 hrs were 0.73 (± 0.98) and 0.79 (±0.82) respectively. There was no statistically significant difference in pain scores at 5 hr between the groups (P = 0.6009 , Mann Whitney U test)

At 6 hr , no child in either group had pain as assessed by the pain scale . The mean (S.D) pain scores in group D and group C at 6 hrs were 0.43 (±0.68) and 0.37 (± 0.56) respectively . There was no statistically significant difference in pain scores at 6 hr between the groups (P= 0.8825, Mann Whitney U test)

Table 7 : Table depicting number of cases requiring rescue analgesics in both the groups.

	Rescue analgesic		
Group	Yes	No	Total
Diclofenac	8 (26.66%)	22 (73.33%)	30
Conventional	24 (80.00%)	6 (20.00%)	30
	32	28	

P value by Chi Square test = 0.0001 (S)

Duration of adequate postoperative analgesia , taken from the completion of surgery till the pain score > 3 could not be assessed as the study was restricted for a follow up of 6 hrs postoperatively. Only 8 cases (26.66%) in group D required rescue analgesic (I.V. fentanyl) as compared to 24 cases (80%) in group C in the postoperative period of 6 hrs. There was a highly significant decrease in the number of children requiring rescue analgesic (P= 0.0001) in group D .

Table 8, Table depicting postoperative fentanyl consumption in both the groups

	Diclofenac	Conventional
Fentanyl consumption (µgm) , Mean ± S.D	1.67 ± 3.30	6.08 ± 4.03

P value = 0.00002 (S), Unpaired t test

The statistical analysis of postoperative I.V fentanyl consumption among the groups revealed that , the mean (S.D) fentanyl consumption was 1.67 (±3.30)µgm in group D and 6.08 (± 4.03) µgm in group C. There was a statistically significant reduced consumption of fentanyl in the diclofenac group (P= 0.00002).

Table 9 : Table depicting number of rescue analgesic doses required in both the groups

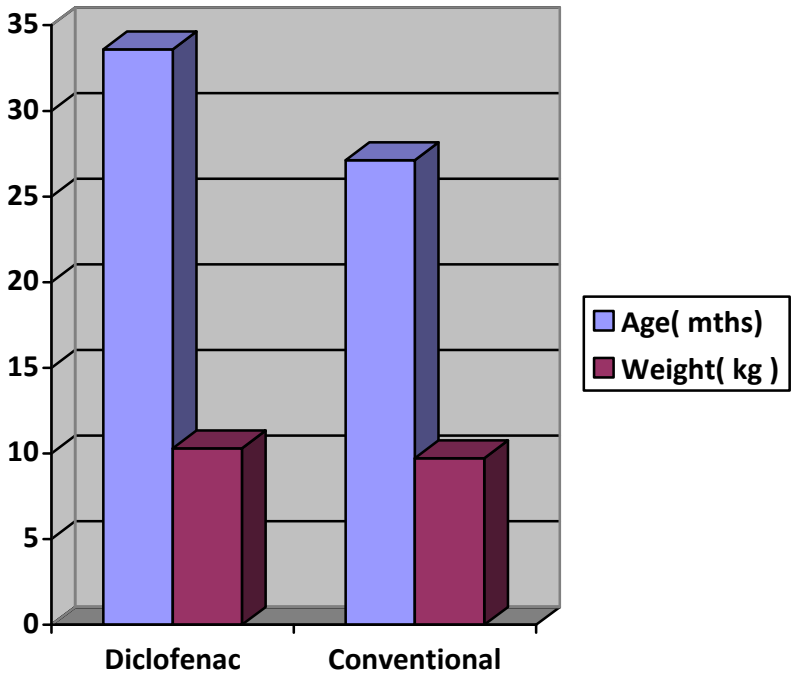
No. of doses	Diclofenac group	Conventional group
0	23 (76.66%)	6 (20%)
1	7 (23.33%)	19 (63.33%)
2	0	5 (16.66%)

5 out of 24 children in group D received a second dose of rescue analgesic as compared to group D where no child required a second dose of rescue analgesic.

Other observation like perioperative bleeding in excess of usual was not evident in any child receiving diclofenac.

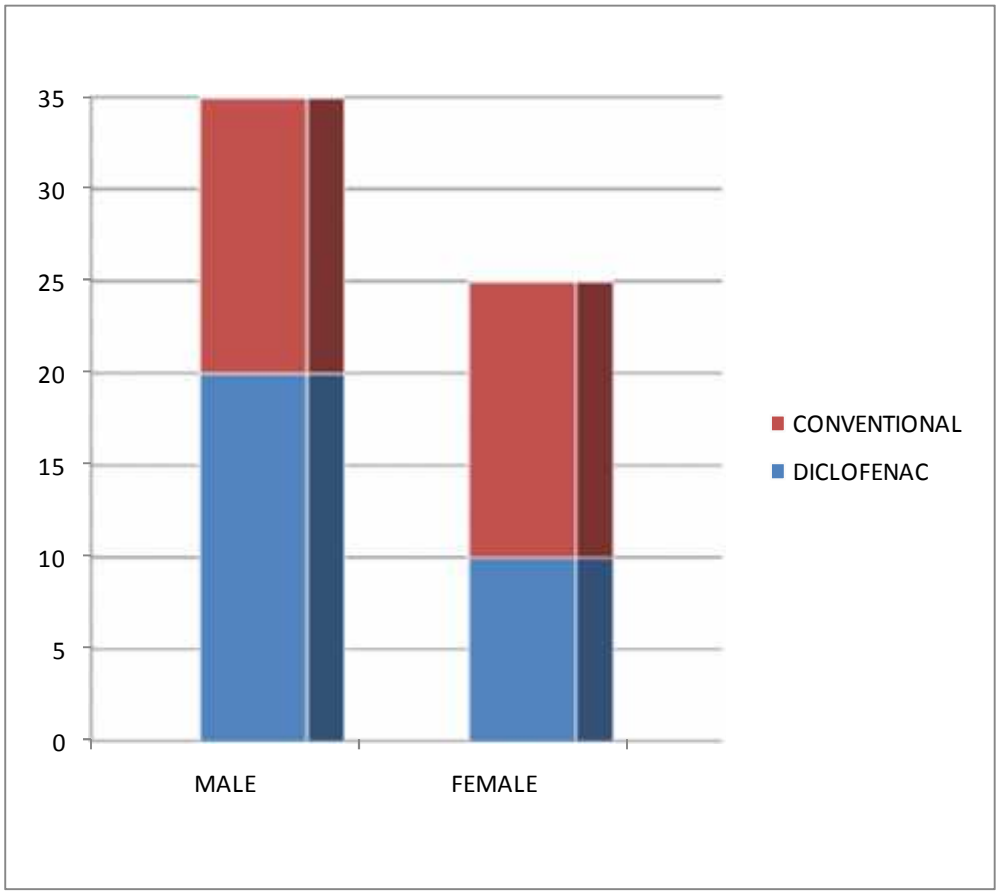
Graph 1

Age and Weight distribution in both the groups



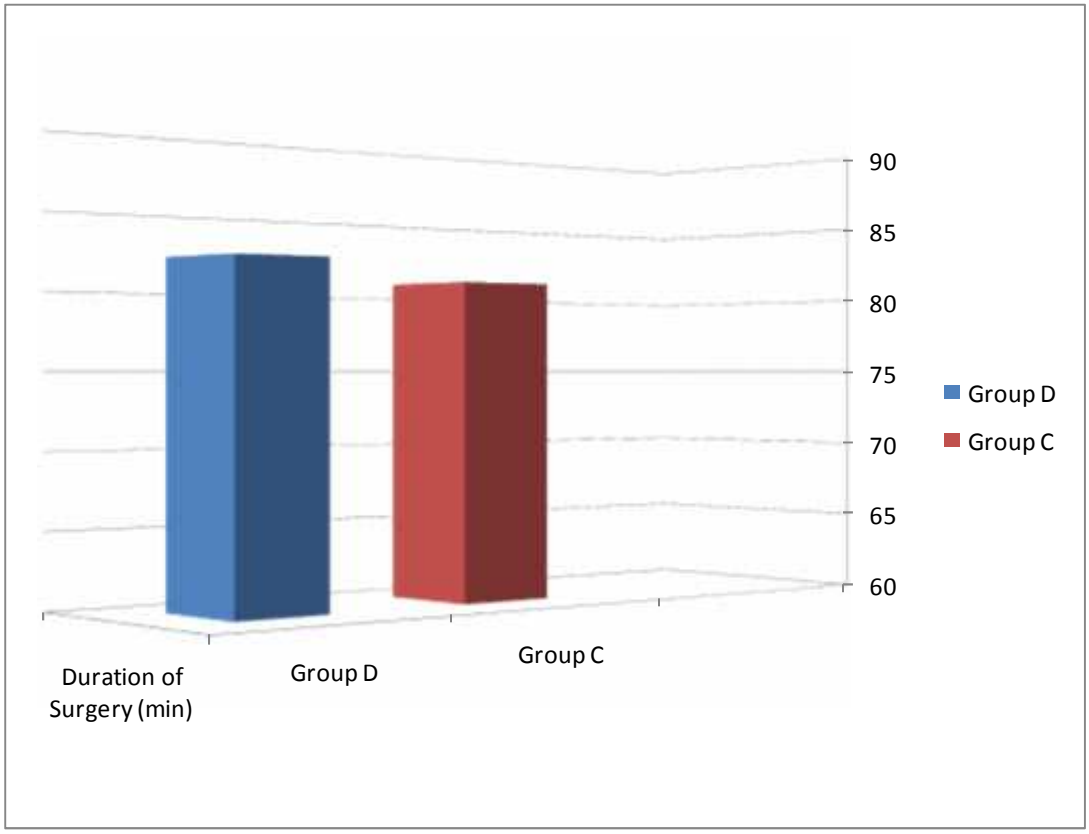
Graph 2

Sex ratio comparison in both the groups



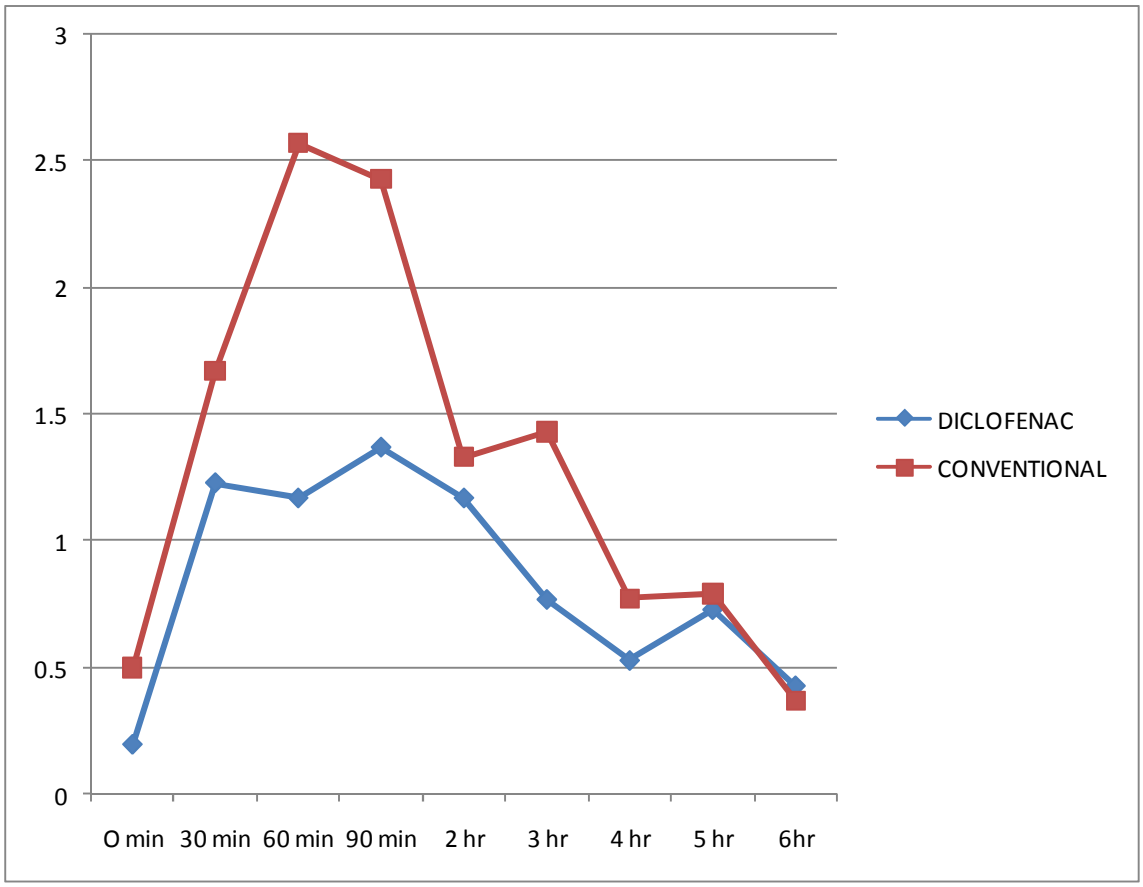
Graph 3

Mean duration of surgery in both the groups



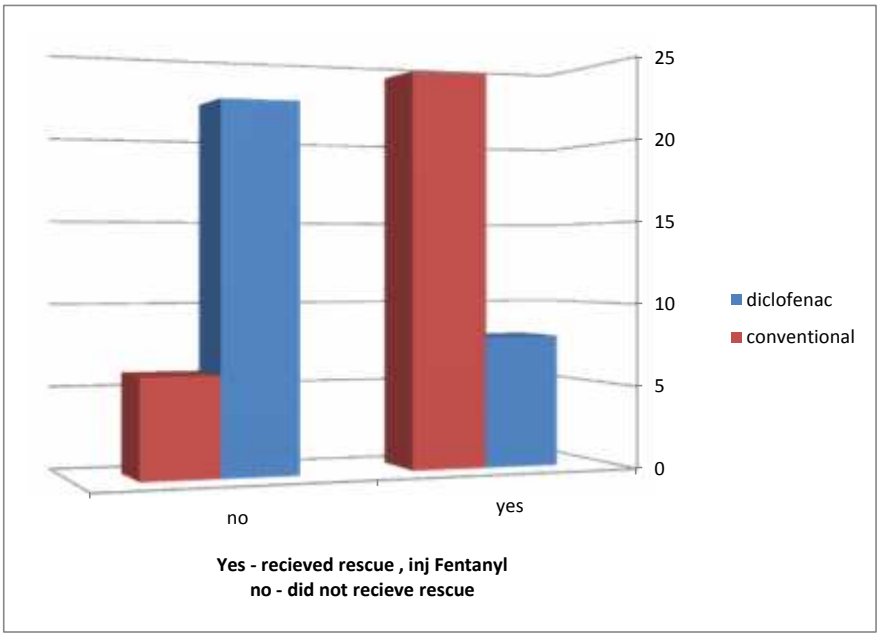
Graph 4

Graph depicting the mean pain scores in both the groups at different study intervals



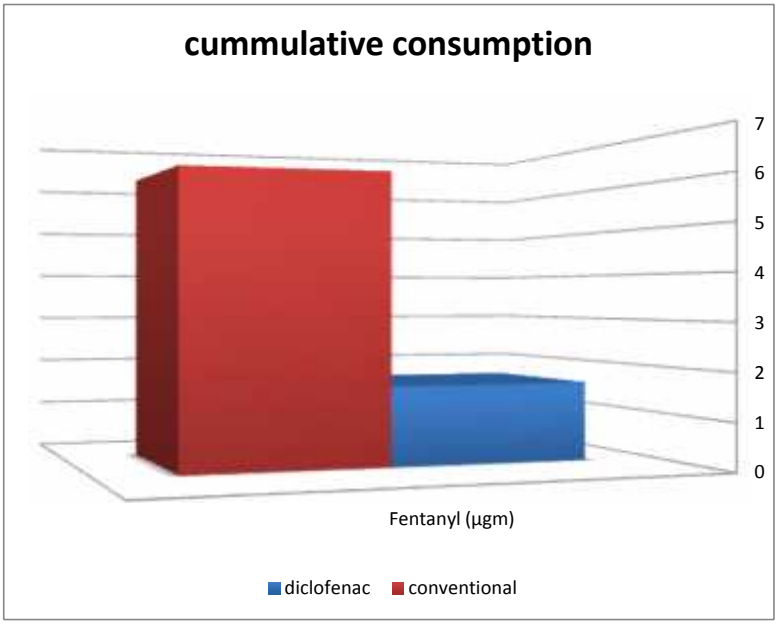
Graph 5

Graph depicting number of cases requiring rescue analgesic in both the groups



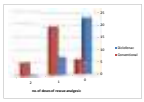
Graph 6

Graph depicting quantity of fentanyl consumed in both the groups



Graph 7

Graph depicting number of doses of rescue analgesic consumed in both the groups



DISCUSSION

"Pain like pleasure , is a passion of the soul , that is an emotion and not one of the senses" a statement that aptly personifies the views of two great philosophers ARSISTOTLE and PLATO. We as human beings are governed under the mastery of two very common feelings – Pain and Pleasure. When it comes to children the provision of pain relief after surgery is not only for the child's comfort but also a reassurative measure for the parents.

The prevention of pain and its control has innumerable benefits .Adequate pain relief is a humanitarian, moral and ethical responsibility of the Anaesthesiologist. It helps in reducing morbidity , helps in early weaning and discharge. Pain relief helps to reduce anxiety and provides a good sleep.

Adequate pain relief has been shown to restore the normal respiratory function by preventing atelectasis and infection. With good analgesia adverse effects due to sympathetic stimulation are prevented. Wound healing is better and so early mobilisation is possible . In children, adequate analgesia provides a calm and cooperative child in the postoperative period.

Despite the benefits, provison for pain relief in children remains neglected.

The American Academy of Paediatrics and American Pain Society (2001) states that there are barriers to the effective treatment of pain in children because of.

- The myth that children, especially infants do not feel pain the way adults do.

- Lack of assessment and reassessment for the presence of pain.

- Misunderstanding of how to conceptualize and quantify a subjective experience like pain.

- Fears of adverse effects of analgesic medications like respiratory depression.

A structured study design was formulated keeping in mind the above stated barriers.

The multimodal armamentarium to cater to the analgesic needs of the child includes – Non Steroidal Antinflammatory Drugs (NSAID) tailored to suit the individual needs of children. NSAIDs have become increasingly popular in the perioperative management of pain . In general , NSAIDs have been shown to be effective analgesics, as judged by either a reduction in pain scores and or Opioid sparing effect. [22,23]

Diclofenac , is one such NSAID which has been proved to be effective for postoperative analgesia in children. Given the pharmacokinetic and pharmacodynamic properties of diclofenac , nociceptor modulation necessitates their administration in advance of the anticipated time of analgesic requirement. [5]

Wall, suggested that the prophylactic use of analgesics may decrease their postoperative requirements by reducing noxious input and there by minimizing the hyperexcitable “WIND UP state” in the central nervous system. Hence, Pre emptive analgesia is defined as an antinociceptive treatment that prevents establishment of altered central processing of afferent input from injuries .[24]

Diclofenac, though available in injectable form, is not used frequently due to fear of pain on injection in children . The oral form has its own demerits since it is known to cause a variety of gastrointestinal disturbances.

Diclofenac administered rectally is safe and a convenient approach resulting in complete absorption and sustained release of drug providing early onset and long duration of postoperative analgesia. Diclofenac is safe in children above 6 months of age like other NSAIDs .[25,26]

Rectal suppositories of diclofenac are available in commercial preparations of 12.5 mg , 25mg, 50mg, and 100 mg. In our study we have used 12.5 mg and 25mg suppositories at a dose of 1mg/kg. The larger suppositories were divided or in the case of the smaller suppositories more than one were placed to meet the 1mg/kg dosage.

The rectal suppository which is absorbed in 30-60 min and achieves T max after 50min of insertion offers a simple maneuver to administer the drug, equaling the analgesic efficacy of the oral preparation. [27] In the process it bypasses the enteric system, where the danger of any NSAID lurks.

In the present study we have evaluated the effectiveness of preoperative rectal diclofenac suppository 1mg/kg in reducing the postoperative requirement of analgesics (I.V fentanyl) in children undergoing cleft palate repair in the immediate postoperative period (6hrs).

The study included 60 ASA grade 1 children aged between 9 months to 7 years , who were randomized into 2 groups, group D and group C based on computer generated randomisation table.

Group D – n=30, received rectal diclofenac 1mg/kg soon after induction and GA proceeded as per protocol.

Group C – n= 30, received GA as per the protocol.

The mean (S.D) age in the group D was 33.60 (±20.71) months and in group C was 27.13 (± 17.13) months , P value – 0.1932. The mean (S.D) weight in group D was 10.31 (±3.07) kg and in group C was 9.72 (± 2.67) , P value – 0.4281. Thus, children were comparable in characteristics such as age and weight. There was a comparable ratio of male to female in both groups.

The average duration of surgery for palate repair is about 60 min- 90 min approximately. In our study the mean (S.D) duration of surgery in group D was 82.10 ± 19.08 min and in group C was 80.77 ± 22.55 min, P- 0.8056. Thus , the duration of surgery was similar in both groups .

All cases were carried out under general anaesthesia with a standardised anaesthesia protocol. The children in group D and group C differed only with regards to the preoperative placement of rectal diclofenac suppository , otherwise both received drugs for general anaesthesia as per protocol .

The suppositories were inserted after the induction of anaesthesia and intubation with a view of Preemptive analgesia. Diclofenac suppository takes 30 – 60 min for onset of action with a t½ of 90 min to 120 min and the analgesic action lasts for 6-8 hrs. Hence, we expected that the analgesic effect of the drug to start during the surgery itself and extend into the immediate postoperative period.

Previous studies using rectal diclofenac convinced us to choose a rectal diclofenac dose of 1 mg/kg [28] , though it is less compared to few other studies. In most other studies children received a second dose of diclofenac after a period ranging from 8-12 hrs from the first dose .We however restricted our study to a single 1mg/kg dosage after induction as our primary objective was to study the reduction of opioid consumption in immediate post operative period i.e 6 hrs.

On comparing the pain scores between the two groups in our study there was no statistically significant difference between the two groups for the first 30 min (P0 = 0.2143 (NS), P30= 0.4464(NS)). This can be attributed to the residual effect of intraoperative analgesic (I.V fentanyl 1µgm/kg) .

At 60 min and 90 min , there was a significant reduction in pain scores in group D as compared with group C (P 60 = 0.0036 ,S; P 90 = 0.0064, S) . This can be attributed to analgesic action of diclofenac .

At 2,3, 4, 5 and 6 hrs there was no significant reduction in pain scores in group D as compared with group C (P2= 0.4598 NS, P3 = 0.0519 NS ,P 4= 0.1958 NS , P5 =0.6009 NS , P6 =0.8825,NS) . This may be attributed due to a significant majority of

children (upto 50%) in group C receiving rescue analgesic by 4 hrs postoperatively. Hence, they were subsequently pain free and did not have pain scores > 3.

It was observed that the children belonging to group D were more alert , calm and pain free beyond 6 hrs postoperatively,although the pain was not scaled as done during study period .

Hence, we conclude that rectal diclofenac (1mg/kg) was effective from 30 min postoperatively and extended to cover a period of upto 6 hrs as evidenced by the reduced pain scores. It can be further assumed that the analgesic action extended beyond 6 hrs, although a systematic assessment of pain was not carried out during this period.

This observation is supported by previous studies by Bone M E and D Fell [8] , who reported a duration of analgesia for 7.3 hrs . Other few studies have reported duration of analgesia extending upto a period of 12.45 hrs, [17] and 14 hrs [15] .

On comparing , the number of children receiving rescue analgesics in each group we noted that 8 children out of 30 in group D and 24 children out of 30 in group C required rescue analgesic (I.V fentanyl). This reduction in the number of children receiving rescue analgesic was significant (P=0.00001) in group D . Among 24 children in group C, 5 children received rescue analgesia twice in a period of 6hrs.

On comparing the quantity of I.V. fentanyl consumed in either groups, mean (S.D) in group D was 1.67±3.30µgm and group C was 6.08±4.03 µgm with a P value – 0.00002 which was highly significant.

Our study showed that preoperative rectal diclofenac significantly reduces the number of doses and the quantity of opioid required in the postoperative period. Our observation is also supported by previous studies by Moffat A C and colleagues who demonstrated a morphine sparing effect of diclofenac in upper abdominal surgeries [29] . Other studies have also demonstrated a 30 % reduction in postoperative reduction of opioid consumption. [30,31]

The children were also observed for perioperative blood loss.It was found that there was no significant bleeding in excess of usual in group D as assessed by the operating and recovery personnel.

We conclude that rectal diclofenac sodium is suited for preemptive approach and proves to be a efficient drug as part of balanced analgesia and helps to reduce consumption of opioids postoperative in the post operative period.

Future Scope

A combination of analgesics viz. NSAIDs , opioids together with regional techniques provide a balanced approach with minimal adverse effects and achieve a near total pain relief postoperatively in children. Hence, further studies are required in determining the ideal combination of these to achieve a better pain relief postoperatively with minimal adverse effects.

CONCLUSION

- Preoperative rectal diclofenac sodium was able to reduce opioid consumption in the postoperative period to a significant extent.
- Preoperative rectal diclofenac sodium provided good postoperative analgesia over a period of 6 hrs.
- There was no increased perioperative bleeding in diclofenac group.

Hence , rectal diclofenac sodium is a very good analgesic for postoperative analgesia in paediatric age group. It has a major role in providing preemptive analgesia and also being an integral component of balanced analgesia.

SUMMARY

The present study 'Effect of Preoperative Rectal Diclofenac on postoperative analgesic requirements in Cleft palate repair – A Randomized Clinical Trial' was carried out in the Department of Anaesthesiology , KLES Prabhakar Kore Hospital and MRC, Belgaum .

The study included 60 ASA grade 1 children between the age group of 9 months to 7 years divided into two groups consisting of 30 children each after randomisation by a computer generated randomisation table .

Group D – Rectal Diclofenac 1mg/kg.

Group C – Conventional group.

The suppository was inserted soon after the induction and intubation . Pain was assessed using modification of objective pain scale by Hannallah and colleagues by the r anaesthesiology PG/ nursing staff in the recovery room who were blinded to the groups.

Our study revealed that the children belonging to group D had a significant reduced pain scores over 6 hrs in the post operative period and also a significant reduction in requirement of rescue analgesic (I.V fentanyl) without any complications like excess bleeding.

BIBLIOGRAPHY

1) Gehdoo RP. Postoperative pain management in paediatric patients. Indian J.Anaesth 2004 ;48(5):406-414.

2) Gupta JL,Bhanagar SK, Srivastava JL.Aetiology and statistics in cleft lip and palate.Indian Journal of Plastic Surgery;6:99-107.

3) Rawal N , Sjostrand U, Christofferson E, Dalhstrom B, Arvile A, Rydman H.Comparison of intramuscular and epidural morphine for post operative analgesia in the grossly obese: influence on postoperative ambulation and pulmonary function. Anaesth Analg 1984;63.

4) Baer GA, Rorarius MGF, Kolehmainen S, Selin S.Effectiveness of paracetamol or diclofenac administered before operation on postoperative pain and behavior after adenoidectomy in small children. Anaesthesia 1992;47:1078-1080.

5) Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia II – recent advances and current trends. Can J Anaesth ; 48(11) : 1091-1101.

6) Moores MA, Wandless JG, Fell D.Paediatric post operative analgesia . A comparison of rectal diclofenac with caudal bupivacaine after inguinal herniotomy. Anaesthesia 1990 ; 45 :156-158.

7) Hodsman NBA, Burn J, Blyth A, Kenny GNC, Mc Ardle CS, Rotman H.The morphine sparing effects of diclofenac sodium following abdominal surgery. Anaesthesia 1987 ; 42: 1005-1008.

8) Bone ME, Fell D. A comparison of rectal diclofenac with intramuscular papavertum or placebo for pain relief following tonsillectomy. Anaesthesia 1988 ; 43 : 227-280 .

9) Watters CH, Patterson CC, Mathews HML, Campbell W. Diclofenac sodium for post tonsillectomy pain in children. Anaesthesia 1983 ; 43 : 641-643.

10) Ejnell H, Bjorkman R, Wahlander L, Hedner J. Treatment of postoperative pain with Diclofenac in Uvulopalatopharyngoplasty.Br J Anaesth 1992 ; 68 : 76-80 .

11) Gadiyar V, Gallagher TM, Crean PM, Taylor RH. The effect of a combination of rectal diclofenac and caudal bupivacaine on postoperative analgesia in children. Anaesthesia 1995 ; 50 : 820-822 .

12) Morton NS, O'Brein K.Analgesic efficacy of paracetamol and diclofenac in children receiving PCA morphine. Br J Anaesth 1999 ; 82(5): 715-717 .

13) Short JA, Barr CA, Palmer CD, Goddard JM, Stack CG, Primhak RA . Use of diclofenac in children with asthma . Anaesthesia 2000 ; 55 : 334-337 .

14) Ng A, Parker J, Toogood L, Cotton BR, Smith G. Does the opioid sparing effect of rectal diclofenac following total abdominal hysterectomy benefits the patient ?. Br J Anaesth 2002 ; 88(5) : 714-716 .

15) Bhagat H, Malhotra K, Tyagi C, Gangavar N, Pal N. Evaluation of preoperative rectal diclofenac for perioperative analgesia in ENT surgery . Indian J. Anaesth 2003 ; 47(6) : 463-466 .

16) Riad W, Moussa A. Pre-operative analgesia with rectal diclofenac and /or paracetamol in children undergoing inguinal hernia repair . Anaesthesia 2007 ; 62 : 1241- 1245.

17) Gupta N, Wakhloo R, Mehta A, Wali D, Gupta SD . Postoperative analgesia in children : Caudal block with bupivacaine , rectal diclofenac and combination of both. J.Anaesth Clin Pharmacol 2008 ; 24(3) : 321-324.

18) Heaney , Mairead , Looney , Yvonne , Mc Kinstry, Caleb , O'have , Brendan. Sequential clot strength analyses following diclofenac in paediatric tonsillectomy. Paediatric Anaesthesia 2007 ; 17(11) :1078-1082 .

19) Sylaidis P, O'Neill TJ. Diclofenac analgesia following Cleft palate surgery. Cleft Palate & Craniofac J 1998 ; 35 : 544-545 .

20) Marel CD, Anderson BJ, Romsing J, Jacqz. Aigrain E, Tibboel D. Diclofenac and metabolite pharmacokinetics in children . Paediatric Anaesthesia 2004 ;14(6) : 443-451 .

21) Hannallah RS, Broadman LM, Belman AB . Comparison of caudal and ilioinguinal , iliohypogastric nerve blocks for control of postorchiopexy pain in paediatric ambulatory surgery. Anaesthesiology 1987 ; 66 : 832-834 .

22) Dahl JB, Kehlet H . Nonsteriodal anti-inflammatory drugs: Rationale for use in severe postoperative pain. Br J Anaesthesia 1991 ;66 : 703-712 .

23) Kehlet H, Mather LE . The value of NSAIDs in the management of postoperative pain. Drugs 1992;44 (suppl 5): 1-63 .

24) Wall PD. The prevention of Postoperative pain .Pain 1988 ; 33 : 289-290.

25) Kokki H . Nonsteriodal inflammatory drugs for postoperative pain : a focus on children . Paediatric drugs 2003 ;5 : 103-123 .

26) Morris JL, Rosen DA, Rosen KR . Nonsteriodal anti-inflammatory agents in neonates . Paediatric drugs ; 5 : 385-405 .

27) Landsdrop D, Vree TB, Janssen TJ , Guelen PJM . Pharmacokinetics of rectal diclofenac and its hydroxyl metabolites in man . International Journal of Clinical Pharmacology therapy & toxicology 1990 ; 28 : 298-302 .

28) Morton NS, O'brien K . Analgesic efficacy of paracetamol and diclofenac in children receiving PCA morphine . Br J Anaesth 1999 ; 82(5) : 715-717.

29) Moffat AC, Kenny GNC, Prentice JW. Postoperative mefopam and diclofenac . Evaluation of their morphine sparing effect after abdominal surgery. Anaesthesia 1990 ; 45 : 302-305.

30) Lim NLSH, Lo WK, Chong JL, Pan AX. Single dose diclofenac suppository reduces post cesarean PCEA requirements . Can J Anaesth 2001 ; 48(4) : 383 – 386 .

31) Siddik SM, Aouad MT, Jalbout MI, Risk LB, Kamar GH, Baraka AS . Diclofenac and /or propacetamol for postoperative pain management after caesarean delivery in patients receiving patient controlled analgesia morphine. Regional Anaesthesia & Pain Medicine 2001 ; 26(4) : 310-315.

ANNEXURE - I

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr. / Mrs._____ we are requesting you to enroll your child in study titled **"Effect of Preoperative Rectal Diclofenac suppository on postoperative analgesic requirement in cleft palate repair – A Randomized Clinical Trial"** conducted by DR.ADARSH E. S, postgraduate student in M.D ANAESTHESIOLOGY, under the guidance of DR RAJESH MANE, Associate Professor Dept of Anaesthesiology and Co-guidance of DR .RAJESH POWAR, Professor and Head , Dept of Plastic surgery ,JNMC, Belgaum under KLE University , Belgaum.

Respected sir/madam we request you to enroll your child to participate in our study as your child is eligible for participating in the study. During the study you will be asked some questions regarding your child's present, past medical history and you are supposed to answer to the best of your knowledge.

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

OBJECTIVE :The purpose of research is to evaluate whether preoperative Rectal Diclofenac suppository (1mg/kg)can reduce postoperative requirement of analgesics (I.V Fentanyl 0.5µgm/kg)

PROCEDURE INVOLVED:

If you agree to enroll your child in my study, I will ask your child's present , past and family history. then the child will be clinically examined in detail & investigation like haemoglobin %, bleeding time ,clotting time.will be done.

RISKS AND BENEFITS:

Diclofenac affects platelet aggregation and increases bleeding time, but this increase in bleeding time is within the upper range of normal bleeding time, which should not cause any bleeding problem following surgery. Other risk is with route of delivery of drug which may cause mild discomfort.

Benefit gained by enrolling your child in the study: your child will receive adequate post operative pain relief , will be free of side effects of opioids, will become alert much early which may help facilitate early feeding.

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

PRIVACY AND CONFIDENTIALITY:

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

1.In emergency to protect your child's rights and welfare.

2.If required by law.

FINANCIAL INCENTIVES FOR PARTICIPATION:

No incentives will be provided on participating in the study

AUTHORIZATION TO PUBLISH RESULTS:

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

COMPENSATION:

In the event of injury related to the study, treatment will be made available through KLESPK Hospital and MRC ,BELGAUM. There is no compensation or payments for such medical treatment by law.If the child is injured you may contact DR.ADARSH . PG M.D. ANAESTHESIOLOGY. KLESPK Hospital and MRC, BELGAUM. PH No.9844243227.

QUESTIONS:

In case you have any questions related to the study, you can contact Investigator - Dr ADARSH E.S ,(Phone No. 9844243227], co-investigator-DR RAJESH MANE ,DEPT OF ANAESTHESIOLOGY.

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

CONSENT STATEMENT

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

Subjects name_____

Parent/ guardian name_____

Signature or the Left Thumb print of Parent or legally authorized representative

_____ _____

Witness Name_____ Signature_____

Investigators Name _____ Signature_____

Date_____

Place_____

ANNEXURE - II

PROFORMA

"Effect of Preoperative Rectal Diclofenac suppository on postoperative analgesic requirement in cleft palate repair – A Randomized Clinical Trial"

INVESTIGATOR:- DR ADARSH E.S. GUIDE:- DR .RAJESH MANE

CO-GUIDE:-DR.RAJESH POWAR

Name of the Patient: _____

Age of the patient: _____ Years weight:- _____ kgs

Sex of the patient: Male/Female I.P. No.: _____

Address:-

Anaesthesiologist:- _____ Surgeon:- _____

Preanaesthetic Evaluation:-

Chief complaints:-1)

2)

3)

past history :-

h/o allergy to aspirin/related drugs

h/s/o bleeding disorders

h/s/o asthma

h/s/otreatment with anticoagulant drug/other analgesics or anticonvulsants

h/s/o passing loose stools in immediate past/anorectal complaints

h/o any major illness

Family history:-

General physical examination:-

Pallor/icterus/clubbing/cyanosis/lymphadenopathy/edema

Vitals- PR/HR:- **B.P/C.F.T:-**

Head toe examination:-

Systemic examination:-

Respiratory system:-

Cardiovascular system:-

Central nervous system:-

Per abdomen:-

Air way and spine assessment:-

Investigations :- Hb%_____

Bleeding time _____

Clotting time _____

Others if any

ASA Grading:-

Diagnosis :-_____

Proposed surgery:- _____

Inclusion criteria:-

1)patients undergoing palate repair between age group of nine months to seven years

2) ASA grade 1

Exclusion criteria:-

1) ASA grade 2 and above
2) prolonged BT/CT
3) h/s/o kidney or liver disease
4) h/s/o allergy to aspirin/ related drugs
5) h/s/o bleeding disorders/asthma
6) h/s/o anorectal/gastric complaints
7) h/o treatment with other analgesics anticonvulsant/anticoagulant

Date of surgey :-

From :-_____ to _____

METHOD:- After having met inclusion and exclusion criteria, having obtained informed consent from parent or gaurdian

Subjects are allocated into group D (Diclofenac suppository group) or group P(placebo suppository group) according to computer generated randomized table. Pre operative parameters PR/B.P are noted.

Study subject is premedicated with I.M glycopyrrolate 0.005 mg/kg, I.M ketamine 5 mg/kg. once the child is sedated the child is shifted to operating room. Child is pre oxygenated with 100% oxygen mean while i.v. line is secured with a proper size cannula, monitors attached viz.. pulseoximeter ,NIBP, ECG monitor**.**

The child is induced with I.V. Ketamine 1 mg/kg followed by intubating dose of Suxamethonium 1-2mg/kg ,then intubated with an adequate size RAE orotracheal tube(south pole tube) with the help of appropriate size laryngoscope. Tube is then fixed ,throat pack is inserted.

Rectal diclofenac(1 mg/kg) is inserted based on group the subject belongs to.

General anaesthesia maintained on Oxygen , Nitrous oxide (50:50)

I.V vecuronium 0.1 mg/kg, I.V fentanyl 1mcg/kg, I.V midazolam 0.05 mg/kg. intra operative PR ,B.P, monitored every 15 min.

Reversed adequately with I.V gycopyrrolate 0.01mg/kg and I.V neostigmine 0.03-0.05 mg/kg. Throat pack removed , haemostasis inspected for and extubated after thorough oral suctioning.

Time of induction:-_____

Time of insertion of suppository:-_____

Time of start of procedure:-_____ completion :-_____--

OBSERVATIONS:-

Intraoperative haemodynamic parameters :-

time	0 min	15 min	30 min	45 min	60 min	75 min	90 min
P.R							
B.P							

Post operative haemodynamic parameters :-

time	0 min	15 min	30 min	45 min	60 min	75 min	90 min
P.R							
B.P							

Post Operative Pain Scoring:-

time	crying	movement	agitation	total
O hrs				
1/2 hrs				
1 hrs				
1 $_{1/2}$ hrs				
2 hrs				
3 hrs				
4 hrs				
5 hrs				
6hrs				

Number of rescue analgesic* doses given:-

*** rescue analgesic- I.V fentanyl (0.5µgm/kg)**

PAIN SCORING(hannallah pain scale):-

Name of doctor/sister:-

Serial no..	observation	criteria	points
1	crying	No crying	0
		Crying but responds to TLC*	1
		Crying not responding to TLC*	2
2	movement	None	0
		Restlessness	1
		Thrashing	2
3	agitation	Asleep/calm	0
		Mild	1
		Hysterical	2

* TLC – tender loving care

pain defined by pain score > 3 points, rescue analgesia required

any other finding :-- increased bleeding yes/no

date of study:- **Anaesthesiologist:-**

Signature:-

CONVENTIONAL GROUP

Sl. No..	Date	Age (yrs/ mth)	Age(mths)	M/F	Weight	Duration	Rescue (No..Doses)	Dose (mic) Fentanyl	0hrs	30min	60min	90min	2hrs	3hrs	4hrs	5hrs	6hrs
1	20-12-06	4yr	48	M	9.5	110	1	5	0	1	4	1	1	2	0	1	1
2	21-12-06	1yr2m	14	F	8.5	90	1	5	1	0	2	4	1	2	1	0	0
3	12-01-07	1YR1M	13	F	9.4	108	1	5	0	0	1	3	0	4	2	0	0
4	19-01-07	1yr6m	18	M	10	70	1	5	0	3	4	2	0	1	2	2	2
5	24-01-07	1yr1m	13	M	9.7	45	1	5	0	1	2	4	1	1	2	1	1
6	30-01-07	1yr16d	18	F	10	60	0	0	0	0	3	0	0	0	2	2	1
7	31`/01/07	1yr6m	18	M	9	110	1	10	0	0	1	4	1	1	1	2	1
8	02-02-07	4yr	48	F	11	70	1	10	1	3	4	0	1	2	0	1	0
9	03-02-07	1y6m	18	M	9	55	1	10	0	3	4	3	4	1	1	2	0
10	15-02-07	2yr	24	F	6	80	2	5	0	4	5	2	0	1	1	0	0
11	24-02-07	2yr6m	30	F	10	85	0	0	0	0	1	0	2	0	0	2	1
12	26-02-07	1yr1m	13	F	8.5	100	1	5	0	1	2	0	0	4	1	1	0
13	28-02-07	1yr4m	16	M	9	105	1	5	0	0	3	4	1	0	1	1	0
14	20-03-07	2yr6m	30	M	10	60	0	0	0	0	1	2	0	1	1	0-	1
15	31-03-07	4yr	48	F	14	55	2	5	1	4	0	6	2	0	0	0	0
16	04-04-07	4yr	48	F	14	110	0	0	0	0	0	3	3	3	1	0	0
17	05-04-07	1yr6m	18	M	6.5	120	1	5	1	4	0	3	0	0	0	0	1
18	11-04-07	1yr6m	18	F	9	70	0	0	0	1	0	0	3	2	0	1	0
19	17-04-07	1yr4m	16	F	7.5	90	1	5	0	1	4	2	1	1	1	0	0
20	23-04-07	1yr6m	18	F	7	35	0	0	0	1	0	2	1	3	1	2	0
21	24-04-07	1yr6m	18	M	8.5	60	1	7.5	0	1	0	2	1	4	1	2	0
22	05-06-07	3yr6m	42	M	11	80	1	10	2	4	4	3	2	1	1	0	0
23	03-07-07	2yr6m	30	M	10	85	2	10	1	3	5	4	2	1	1	0	0
24	11-07-07	1yr6m	18	M	6	85	2	10	1	2	5	4	2	1	0	0	0
25	19-07-07	1yr7m	19	M	10	90	1	10	0	0	5	3	4	2	0	1	1
26	20-07-07	1yr1m	13	M	8.5	105	2	5	0	2	3	4	2	4	1	0	0
27	13-08-07	7yr	84	F	20	85	1	15	1	2	4	2	2	1	1	0	0
28	14-08-07	5yr	60	F	11	40	1	10	2	2	4	3	1	0	0	1	1
29	14-08-07	1yr1m	13	M	9	80	1	10	1	2	4	2	1	0	0	1	0
30	21-08-07	2yr6m	30	F	10	85	1	10	3	5	2	1	1	0	0	0	0
MEAN		2.26	27.13		9.72	80.77	29	6.08	0.50	1.67	2.57	2.43	1.33	1.43	0.77	0.79	0.37
S.D.		1.43	17.18		2.67	22.55		4.03	0.78	1.54	1.79	1.52	1.12	1.33	0.68	0.82	0.56

DICLOFENAC GROUP

Sl no..	Date	Age(yrs,mths)	Age(mths)	M/F	Weight(kg)	Duration(min)	Rescue(no.. of dose)	Dose (mic)	PAIN SCORES								
									0hrs	30min	60min	90min	2hrs	3hrs	4hrs	5hrs	6hrs
1	09-12-06	7yrs	84	F	8	110	0	0	0	1	2	3	3	0	0	1	1
2	08-01-07	1y3m	15	M	8	90	1	5	0	0	1	3	2	2	2	4	2
3	08-01-07	1y9m	21	M	8	110	0	0	0	0	1	1	4	0	1	1	2
4	16-01-07	2yr	24	M	8	115	1	5	0	3	0	1	3	4	1	0	1
5	23-01-07	3yr	36	F	13	55	0	0	0	1	1	0	3	0	1	2	0
6	07-02-07	7yr	84	M	21	85	1	10	0	4	1	0	1	2	0	1	0
7	05-03-07	3yr	36	M	10	120	1	10	0	1	4	4	0	1	2	1	1
8	28-03-07	11m	11	M	9	110	1	5	0	1	0	4	0	1	2	0	1
9	31-03-07	1yr	12	M	7.5	55	1	5	0	1	1	5	2	1	0	0	0
10	14-04-07	1y3m	15	M	9	62	0	0	0	2	0	1	3	1	1	2	2
11	14-04-07	4yr	48	M	6.5	70	0	0	0	1	3	1	1	0	0	2	0
12	19-04-07	1y6m	18	M	11	80	0	0	0	1	2	2	2	2	1	1	0
13	26-04-07	3yr	36	M	14	95	0	0	0	0	1	2	0	0	0	0	0
14	27-04-07	1y5m	17	M	10	93	0	0	1	2	1	0	0	1	1	0	0
15	18-05-07	2y6m	30	M	10	75	1	10	0	4	2	1	1	0	1	2	1
16	07-06-07	5yr	60	F	14	75	0	0	0	2	2	1	0	0	1	2	1
17	14-06-07	1y6m	18	M	8.5	100	0	0	0	1	1	0	0	1	0	0	0
18	21-06-07	2yr	24	M	10	75	0	0	0	0	1	2	0	1	0	0	0
19	03-07-07	1y5m	17	F	8.5	80	0	0	1	0	1	2	0	0	0	1	0
20	11-07-07	4y6m	54	F	14	50	0	0	1	1	1	0	1	1	0	0	0
21	12-07-07	1yr	12	F	10	80	0	0	1	1	2	1	0	0	0	1	1
22	17-07-07	4yr	48	M	14	85	0	0	0	2	2	1	0	0	1	1	0
23	02-08-07	1y6m	18	F	7.5	93	0	0	0	1	1	0	0	1	0	0	0
24	02-08-07	2yr	24	M	7.5	65	0	0	0	1	0	0	0	2	1	0	0
25	08-08-07	3yr	36	M	10	75	0	0	0	1	0	0	1	1	0	0	0
26	09-08-07	3yr	36	F	9	85	0	0	0	1	0	1	2	0	0	0	0
27	13-08-07	5yr	60	M	10	80	0	0	1	1	0	0	3	1	0	0	0
28	20-08-07	5yr	60	M	15	65	0	0	0	1	0	2	1	0	0	0	0
29	21-08-07	1yr	12	F	8.4	50	0	0	0	1	2	1	1	0	0	0	0
30	20-01-08	3y6m	42	F	10	80	0	0	1	1	2	2	1	0	0	0	0
Mean		2.80	33.60		10.31	82.10	7	1.67	0.20	1.23	1.17	1.37	1.17	0.77	0.53	0.73	0.43
S.D		1.73	20.71		3.07	19.08		3.30	0.41	1.01	0.99	1.35	1.23	0.94	0.68	0.98	0.68