COMPARISON OF TRANSDERMAL DICLOFENAC PATCH WITH ORAL DICLOFENAC AS AN ANALGESIC MODALITY IN MANAGEMENT OF POSTOPERATIVE PAIN

THESIS

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of

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In the subject of

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By

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"COMPARISON OF TRANSDERMAL DICLOFENAC PATCH WITH ORAL DICLOFENAC AS AN ANALGESIC MODALITY IN MANAGEMENT OF POSTOPERATIVE PAIN"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. Rashmi Agarwal** in the Department of Oral and Maxillofacial Surgery, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh.

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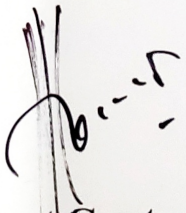
This is to certify that the dissertation entitled **"COMPARISON OF TRANSDERMAL DICLOFENAC PATCH WITH ORAL DICLOFENAC AS AN ANALGESIC MODALITY IN MANAGEMENT OF POSTOPERATIVE PAIN"** has been undertaken by the candidate **Dr. Dube Yati Harikishore,** herself in this department. The candidate fulfils all the conditions necessary for the submission of this thesis.

Recommendation of Head of Department



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This is to certify that the dissertation entitled **"COMPARISON OF TRANSDERMAL DICLOFENAC PATCH WITH ORAL DICLOFENAC AS AN ANALGESIC MODALITY IN MANAGEMENT OF POSTOPERATIVE PAIN"** is an original bonafide research work done by **Dr. Dube Yati Harikishore,** in partial fulfillment of the requirement for the degree of Master of Dental Surgery (M.D.S) in the speciality of Oral and Maxillofacial Surgery under my supervision.

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CERTIFICATE

This is to certify that the dissertation entitled **"COMPARISON OF TRANSDERMAL DICLOFENAC PATCH WITH ORAL DICLOFENAC AS AN ANALGESIC MODALITY IN MANAGEMENT OF POSTOPERATIVE PAIN"** has been undertaken by the candidate **Dr. Dube Yati Harikishore,** under direct supervision and guidance of **Dr. Rashmi Agarwal** in the Department of Oral and Maxillofacial Surgery, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh.

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अखण्डमण्डलाकारं व्याप्तं येन चराचरं।

तत्पदं दर्शितं येन तस्मै श्रीगुरुवे नमः।।

Salutation to the noble Guru, who has made it possible to realize the state which pervades the entire cosmos, everything animate and inanimate.

अनेकजन्मसंप्राप्त कर्मबन्धविदाहिने।

आत्माज्ञानप्रदानेन तस्मै श्रीगुरुवे नमः।।

Salutation to the noble Guru, who by bestowing the knowledge of the self burns up the bondage created by accumulated actions of innumerable births.

मन्नाथः श्रीजगन्नाथः मद्गुरुः श्रीजगद्गुरुः।

मदात्मा सर्वभूतात्मा तस्मै श्रीगुरुवे नमः।।

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- Dr Yati Dube

CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

LIST OF ANNEXURES

LIST OF ABBREVIATIONS

NSAIDs	-	Non Steroidal Anti Inflammatory Drugs
VAS	-	Visual Analog Scale
VDS	-	Visual Descriptive Scale
NRPS	-	Numerical Rating Pain Scale
WB-FPS	-	Wong Baker Facial Pain Scale
OD	-	Once Daily (Omne in die)
BD	-	Twice daily (bis in die)
TID	-	Thrice daily (ter in die)
TDS	-	Thrice daily (ter die sumendum)
gm	-	Gram
mg	-	Milligram
µg	-	Microgram
ng	-	Nanogram
l	-	Litre
ml	-	Milliliter
Mm	-	Millimeter
Inj.	-	Injection
po	-	per os
hrs	-	Hours

ABSTRACT

ABSTRACT

Aim:

To compare the efficacy of transdermal Diclofenac patch with oral Diclofenac tablet in the management of postoperative pain.

Methodology:

The study was performed on 50 patients of both sexes aged between 14 -70 years reporting to the out-patient department (OPD) of BBDCODS, Lucknow. The surgical intervention viz. extraction, minor surgery and major surgery were undertaken post case-history and diagnosis. After the procedure, study medications according to the randomly allotted groups were given which included Tab. Diclofenac (Group-A) 100 mg od for 3 consecutive days and transdermal Diclofenac patch (Group-B) 100 mg applied on the arm for 3 consecutive days which was changed every 24 hrs. Then post-operative pain was evaluated based on VAS, VDS, NRPS and WB-FPS every 3 hrs, 6 hrs, 12 hrs and 24 hrs for 3 consecutive days.

Results:

Both the Tab. Diclofenac and transdermal Diclofenac patch caused significant reduction in pain scores with time. Though mean pain scores used like VAS, VDS, NRPS and WB-FPS for transdermal Diclofenac patch was lesser than the mean pain scores of Tab. Diclofenac but the difference was not statistically significant.

Conclusion:

Based on the findings from present study, it can be concluded that both Tab. Diclofenac and transdermal Diclofenac patch are equally effective in management of postoperative pain. Transdermal Diclofenac patch with its various advantages of transdermal delivery system can be used as an alternative to Oral Diclofenac in the management of postoperative pain.

INTRODUCTION

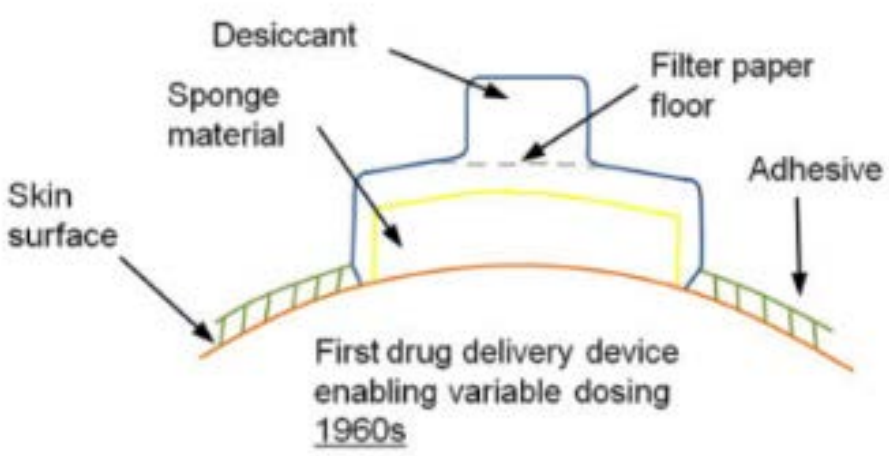
INTRODUCTION

The International Association for Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with either actual or potential tissue damage, or described in terms of such damage.” [1] The most perennial indication of surgery and patients seeking medical attention is pain relief. It causes post-operative impediment leading to poor mobility, increased arterial pressure, myocardial work resulting in increased morbidity. Damage tissue invokes pain that causes activation of somatosensory system that leads to increased responsiveness of central and peripheral pain pathways. [2, 32, 33]

Numerous routes for administration of analgesic drugs are oral, parenteral, inhalational and transdermal. Oral route cues first pass metabolism and only 50% of absorbed drug appears in systemic circulation and attains high plasma concentration with substantial corollaries involving gastrointestinal tract while administration of parenteral drug can be painful and leads to corollaries due to abrupt increase of drug in plasma. [3, 4]

The most commonly used pain medications are NSAIDs. However, indiscreet usage of NSAIDs has driven many adverse effects. [5, 6] The most frequently prescribed NSAID exhibiting anti-inflammatory, analgesic and anti-pyretic action is Diclofenac. The mechanism by which NSAIDs act is by inhibiting cyclo-oxygenase 1 and 2 (COX-1 and COX-2) which are prime enzymes in prostaglandin synthesis. By inhibiting the COX enzymes, prostaglandins produced thereby are fewer which help in easing of pain and inflammation. Diclofenac 100mg is recurrently used once daily for 3-5 days. [34]

Lately, transdermal patches have been developed as pioneering topical delivery system postulating sustained drug delivery. Important components associated with transdermal delivery are the defined delivery system in dose, area, vehicle and device; the quantification of the time course of absorption into urine; and the application of pharmacokinetic principles to quantify the resulting drug delivery kinetics. It is a medicated adhesive patch applied over the skin so as to release precise dosage of medicine with predetermined release rate in the blood stream. The application of transdermal delivery is restricted due to the substantial barrier to penetration across the skin which is associated principally with the outermost stratum corneum layer of the epidermis. [6]



Transderm SCOP was the first transdermal system to be approved by FDA in 1979 for motion-sickness. Dale Wurster's contribution to the early understanding of transdermal delivery is highly accredited (Roberts, 2013). Diclofenac patch was officially approved for usage in 1993 in Europe. It has been used in plethora of cases ranging from hysterectomy, lower limb surgery, ankle sprain, third molar extraction, etc. [7]

The size of the patch used in this study was 37.5 sq cm. Diffusion of topical diclofenac occurs into the subdermal tissue. The small lipophilic molecules are proficient of rapid diffusion through the skin and dispenses in blood, muscle, interstitial tissue and synovial fluid. In presence of 1.16% diethylamine salt (1% diclofenac sodium), absorption transpires continually through the underlying dermis, and subcutaneous tissue to a depth of 3 – 4 mm. Plasma concentrations are less than tissue concentrations, thereby, plummeting the probability of systemic corollaries. In one study, plasma levels achieved by transdermal patch ranged between 20-50 ng/ml, which was lesser when compared to the oral route, but these levels were sustained for a longer time. [8, 9]

The therapeutically attainable plasma concentrations (C_{55}) is defined by the rate of delivery of a drug from a patch through the skin (R_0) divided by the systemic clearance (Cl) [59]

$$\text{i.e. } C_{55} = \frac{R_0}{Cl} = \frac{J_{skin} \times A}{Cl}$$

where, J_{skin} is the per unit area transdermal drug flux

A is the area of application (Roberts and Walters, 1998).

AIM & OBJECTIVES

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AIM

To compare the efficacy of transdermal Diclofenac patch with oral Diclofenac tablet in management of postoperative pain.

OBJECTIVES

1. To evaluate postoperative pain relief in patients with transdermal Diclofenac patch and oral Diclofenac tablet.
2. To evaluate incidence of adverse drug reactions of transdermal patch to its oral counterpart.
3. To compare both the groups.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

- **Despande et al. (1991)** [6] conducted an evaluation between Diclofenac Transdermal Patch Vs Transdermal EMLA cream for attenuation of pain of venous cannulation. They testified that pain intensity diminished during cannulation with Transdermal Diclofenac Patch as revealed by VAS score and contracted hemodynamic stress response but wasn't superior to EMLA cream.

- **Sanford H Roth et al. (1992)** [7] assessed the efficacy and safety of topical Diclofenac solution (pennsaid) in treatment of primary osteoarthritis of knee in a double blinded vehicle controlled clinical trial in 326 patients and were randomized to receive 40 drops of topical Diclofenac solution 4 times daily for 12 weeks. 3 outcomes were assessed on WOMAC pain and physical function subscales and positive results were in favour of its usage.

- **Bailey et al. (1993)** [8] evaluated in a double blinded study with 136 patients to compare the efficacy of Diclofenac 50mg tid and aspirin 600mg in management of post-operative pain third molar extractions. Decrease in pain intensity was seen in Diclofenac dispersible tablets and inferred that Aspirin as well as Diclofenac dispersible tablets are equipotentially efficient in post extraction pain. Diclofenac was found to be superlative to soluble aspirin with respect to the mouth-opening extent achieved after extraction of impacted third molars.

- **Assandri et al. (1993)** [9] assessed permissibility and pharmacokinetic profile for Diclofenac Hydroxyethyl pyrolidone together in animals and volunteers deduced that post application flexor patch delivered Diclofenac at constant level into plasma upto 12 hours. They testified that peak plasma concentration of Diclofenac post patch application was nearly 15 ng ml^{-1} which was much lower than that reached by oral administration which was nearly 1500 ng ml^{-1}. The levels reached with topical gel or cream application with estimated absorbed dose of 5-10 mg per application was noticed to be acceptable for the foreseen therapeutic use with no objectionable corollary.

- **Muller et al. (1997)** [10] in a study on 20 individuals to define the concentration of Diclofenac in tissue layers post-topical application was conducted. The use of microdialysis probe into skin 3.9mm and 9.3mm respectively to assess the concentration in the superficial and deep layers post application of the 300mg single dose transdermal patch was done. The infiltration of transdermal Diclofenac patch was found to be unpredictable after single dose.

- **Arora P, Mukherjee B (2002)** [11] testified the design, development, physicochemical and in-vitro, in-vivo evaluation of transdermal patches comprising Diclofenac diethylammonium salt with polymers like polyvinyl pyrollidone and ethyl cellulose. On the basis of in-vivo and in-vitro studies conducted on rat, it was inferred that polyvinyl pyrollidone : ethyl cellulose 1:2

showed superlative permeation properties in combination with pain relief in ratio of 1:4.

- **Predel et al. (2003)** [12] examined the assurance of transdermal Diclofenac patch 140 mg in handling sports injuries in 120 patients in a study for evaluation of tenderness to pressure for 7 days b.d. They inferred that Diclofenac 140 mg patch for acute traumatic blunt soft tissue injuries is a finer option as there was reduced pain score and inferred that the Diclofenac patch was effective, well tolerated and testified no significant corollary in contrast to placebo.

- **Joshi et al. (2004)** [13] conducted a study in 119 subjects requiring surgical extraction of third molar under anesthesia as daycare surgery and effectiveness of Diclofenac sodium 100mg, Ibuprofen 600mg, Paracetamol 1gm with Codeine 60mg and placebo when given preoperatively were equated. Visual analog scale and verbal rating scale were utilized for assessing post-operative pain at 15 minutes, 30 minutes, 1hour, 3 hours, 6 hours and 24 hours. Median time of requisition of supplementary post-operative analgesics was less for placebo in comparison to Diclofenac group. The inference drawn was that equi-potential efficacy was noted in case of single preoperative dose of all others in comparison to Codeine 60mg in management of post-operative pain.

- **Mason et al. (2004)** [14] conducted a meta-analysis in 22 double blinded placebo controlled trial which were selected from database for the efficacy of topical NSAIDS and transdermal Diclofenac patch for acute pain and inferred

that transdermal preparation caused minimal corollary and emphasized the usage of transdermal Diclofenac patch in sports related injuries and osteoarthritis.

- **Niethard Fu et al. (2005)** [15] in a double blinded placebo controlled study conducted in 238 patients wherein usage of transdermal Diclofenac gel for osteoarthritis of knee was performed. In the first week, mild difference was seen in pain relief between placebo and Diclofenac gel and in the second week, peak difference was noted. The inference drawn was that transdermal Diclofenac gel was superlative in pain control and dearth of side effects was noted in managing the osteoarthritis pain management.

- **Lopez Carriches C, Martinez Gonzalez JM, Donado Rodriguez (2005)** [16] conducted a study on 73 patients for the management of trismus post lower third molar extraction by comparing the efficacy between Methylprednisolone 4mg TDS and Diclofenac sodium 50mg TDS. The assessment of trismus was done by three measurements tragus to angle of the mouth, tragus to pogonion and corner of the eye to angle of the mouth. The inference drawn was that oral Diclofenac sodium and Methylprednisolone were equipotentially effective in terms of anti-inflammatory efficacy for controlling post-operative trismus post lower third molar extractions.

- **Bamgbose BO et al. (2006)** [17] in a study on 150 subjects for management of post-operative pain, swelling and trismus post-surgical extraction of third

molars wherein efficacy of Dexamethasone 8mg I.M. v/s Acetaminophen 1000mg P.O. and monotherapy with diclofenac K 50mg PO was done. Evaluation of swelling by measuring tragus to gonion and from tragus to opposite tragus was done and post-operative pain was evaluated in pain intensity scale. Pain was absent in patients taking Diclofenac and Dexamethasone in comparison to other group while swelling was diminished in group with Diclofenac and Dexamethasone and in the group with Dexamethasone. The inference drawn was that the combination of Diclofenac potassium and Dexamethasone provided add-on advantage from swelling instead of singular handling of pain management.

- **Baboota S, Shakeel F and Kohli K (2006)** [18] evaluated the transdermal Diclofenac formulations with permeability enhancers like olesan oil and Dimethyl sulfoxide and polymers like carbopol-940, polyvinyl alcohol (PVA), hydroxyl propyl methyl cellulose-K(4) M, hydroxy propyl cellulose-M, and sodium carboxy methyl cellulose. These preparations underwent various changes physiochemically and skin permeation studies done in-vitro. The superior permeability was found to be seen in Carbopol polymer and Poly vinyl alcohol polymer in comparison to Volteran gel of Diclofenac.

- **Agarwal et al. (2006)** [19] in a study on 450 patients who underwent elective surgery to evaluate the efficacy of EMLA patch with transdermal Diclofenac patch for intravenous cannulation pain wherein 3 groups were created viz group 1 was control group with placebo patch, group 2 was EMLA cream and group 3

was Diclofenac patch with the preparations used at cannulation site an hour prior to cannulation with evaluation done in VAS. The inference drawn was that Diclofenac patch and EMLA are equipotentially effective in the management of venous cannulation pain with transdermal Diclofenac patch having minimal corollary.

- **Alessandri et al. (2006)** [20] in a study on 120 patients for the management of laproscopic gynaecological surgeries that was divided into 2 groups, one study group being transdermal group and other control group being placebo where application was on the incision site post-surgery. Evaluation of post-operative pain intensity was done at 6 hours, 12 hours and 24 hours. No peculiar difference in pain intensity was noted between the 2 groups at 6 hours but mean pain intensity in study group at 12 hours and at 24 hours was less in comparison to control group. The rate of discharge in patients receiving transdermal Diclofenac patch with standard analgesic in comparison to a standard analgesic alone was similar.

- **Minghetti P et al. (2007)** [21] evaluated the penetration of various salts of Diclofenac in skin like Diclofenac sodium, Diclofenac potassium, Diclofenac diethylamine, Diclofenac epolamine and inferred that superlative preparation of Diclofenac was found to be aqueous preparation with organic base.

- **Funk et al. (2008)** [32] in a study on 31 subjects evaluated the efficacy of transdermal Diclofenac hydroxyl pyrolidone with oral Diclofenac in post

arthroscopic pain management in shoulder joint with 2 groups divided viz, group 1 with 17 patients wherein post-operative medication was oral Diclofenac sodium with Codeine and Paracetamol combination and group 2 included 14 patients who procured transdermal Diclofenac hydroxy pyrolidone in combination with Codeine, Paracetamol. Evaluation of post-operative pain in Visual analog scale for the first 48 hours was done with mean pain score in group 1 being higher than group 2 with the inference being both forms depicting equi-potential analgesic efficacy.

- **Bachalli PS, Nandakumar H, Srinnath N (2009)** [3] assessed pain control following surgical extraction of mandibular impacted third molar in 20 subjects wherein transdermal Diclofenac patch 100mg against oral Diclofenac 100mg OD was prescribed and deduced that oral Diclofenac had slightly more promising efficacy than transdermal counterpart in the first post-operative day whereas both the forms of Diclofenac had similar effectiveness in second and third post-operative days and inferred the usage of transdermal Diclofenac patch as a substitute for its oral counterpart was a finer option for the management of post-operative pain.

- **Hsieh et al. (2010)** [33] conducted a trial to evaluate the efficacy and corollary of transdermal Diclofenac patch in management of myofacial pain syndrome of trapezius wherein Diclofenac sodium patch was compared with control Menthol patches and treatment to control ratio was 2:1 with safety parameters and efficacy being assessed at the operative day, day 4 and day 8. The inference was that greater pain reduction and early mobilization of involved muscles in Diclofenac patch group in comparison to control wherein skin irritation and

erythema was seen. Diclofenac sodium patch was considered superior to placebo with plummeting VAS scores and refining functional outcomes with no significant corollary.

- **Lionberger DR and Brennan MJ (2010)** [22] published a review by collecting data from Medline (1978 - 2008) regarding pain control in relation to the soft tissue injury by Diclofenac epolamine, inference drawn was that topical NSAID in contrast to placebo was clinically effective in treating acute pain from soft tissue contusions, strains, sprains.

- **Krishna R, Natraj MS (2012)** [23] in a study on 60 subjects compared the efficacy of pre-emptive post-operative analgesia in lower limb surgeries under subarachnoid block wherein single dose of transdermal Diclofenac patch 100mg (study group) given at the beginning of the surgery was compared with injection Diclofenac 75mg (control group) given 30 minutes before the end of the surgery with pain evaluation done by VAS in two hours and six hours. Rescue analgesia was given in patients with VAS score greater than or equal to 7. The inference drawn was that efficacy of transdermal Diclofenac patch and intramuscular Diclofenac was similar in management of acute post-operative pain without any corollary.

- **Bhaskar H, Kapoor P, Ragini (2013)** [24] conducted a cross over efficacy trial in 20 subjects wherein the analgesic modality was evaluated post orthodontic extraction in which transdermal Diclofenac patch 100mg and oral Diclofenac were compared in verbal pain intensity scale and pain relief scale. Paracetamol was

prescribed as the emergency medication for patients with transdermal patch. The inference drawn was that gradual decrease in pain relief from both forms of Diclofenac from day 1 to day 3 was noted and transdermal form was considered as a superlative option for providing potent analgesia with added advantage of improved patient compliance.

- **Khalili S et al. (2014)** [25] in a study in 90 patients compared transdermal Diclofenac and EMLA for venous cannulation undergoing elective surgery. VAS revealed mean score to be highest in placebo, higher in EMLA and least for transdermal Diclofenac and inferred that equi-potential efficacy with respect to transdermal Diclofenac and EMLA.

- **Tejaswi DV, Prabhuji ML, Khaleelahmed S. (2014)** [34] comparatively evaluated the analgesic efficacy and patient tolerability of the transdermal patch vs Oral Diclofenac following root coverage procedures with subepithelial connective tissue graft in 20 subjects in whom following the surgical procedure on the control sites, oral Diclofenac sodium 100 mg QD for 3 days was administered and on the contralateral test site, a transdermal patch was applied for 24 hours for 3 post-operative days. Significant reduction in pain intensity was observed only in the test (transdermal patch) group at the 2-hour and 4- hour postsurgical intervals with reduction deemed not statistically significant post 4-hour interval. They concluded transdermal patch was effective in the post-operative pain control following root coverage procedures with no GI complications.

- **Reddy RP et al. (2015)** [26] in a study in 60 patients compared the efficacy of transdermal and intramuscular Diclofenac in inguinal hernia mesh repair surgeries. Intramuscular Diclofenac 75mg and transdermal Diclofenac diethylamine was given an hour post initiation of spinal anesthesia. VAS was used to assess post operative pain after 2hours, 4hours, 6hours, 12hours, 18hours and 24hours with rescue medication being butrophanol 2mg. The inference drawn was that transdermal Diclofenac was more superior in management of post-operative pain.

- **Krishnan S et al. (2015)** [27] in a study including 40 patients with unsalvagable non-tender molar teeth which were divided into case and control compared the transdermal Diclofenac and oral Diclofenac efficacy in the management of post extraction pain where evaluation of post-operative pain was done in 6 hours, 12 hours in VAS. They inferred that efficacy of transdermal Diclofenac patch in comparison to oral Diclofenac sodium tablet in control of post-operative pain following extraction was same.

- **Barrows NR et al. (2015)** [28] conducted a study on 50 patients by application of patch of transdermal delivery of Diclofenac potassium of size 5-6 microns with carrier being acted upon by natural rubber latex biomembrane and inferred that Diclofenac releases 20% of Diclofenac for duration of 9 days with positive turn-out in favour of patch usage in management of pain post elective surgery.

- **Bhargava GS, Sidhu AS, Bansal D, Bhatia AS (2015)** [29] in a study incorporating 100 subjects for the management of post-operative pain after abdominal

surgeries with transdermal Diclofenac patch placed an hour prior to the end of the surgery and Diclofenac intramuscular injection. Post-operative pain was evaluated in VAS in immediate post-operative period, post 4 hours, 8 hours, 12 hours and 24 hours. Mean time first supplement of analgesia for transdermal Diclofenac group was 7.21 hours and for oral Diclofenac was 7.43 hours. The inference was that the efficacy of transdermal Diclofenac patch and Diclofenac intramuscular injection is analogous in providing post-operative analgesia.

- **Narzaree P, Griwan MS, Sign J (2016)** [30] compared the efficacy of transdermal Diclofenac and intramuscular Diclofenac for management of post-operative pain in inguinal hernia surgery wherein transdermal patch was applied 3hours prior to surgery and two doses of Diclofenac intramuscular injection was given at 2hours and 12 hours post surgery. VAS and verbal rating scale was used to evaluate every 6 hours for 24 hours and Tramadol 50mg slow intravenous infusion was administered in subjects with pain score of 5. They inferred that when applied three hours prior to surgery transdermal Diclofenac was found to be equi-efficient with intra muscular Diclofenac.

- **Verma R, Kumar S, Goyal A, Ajay C. (2016)** [31] in a study including 60 patients requiring lower limb surgeries, 2 groups were created wherein group D received transdermal Diclofenac diethylamine 100mg and group K received transdermal Ketoprufen 20mg were compared. Post-operative pain in VAS at immediate, l hour, 2hours, 4hours, 8hours, 12hours, 16hours, 20hours, 24hours was evaluated. Injection Tramadol 100mg was administered in patients with pain score more than or equal to four. Post-operative VAS in group K was significantly low in

comparison to group D with rescue analgesia procured by 11 patients in group D and 3 patients in group K with inference that both the forms have equi-efficacy in post operative pain management in orthopedic surgeries.

- **Kumar V, Gupta S, Verma R (2017)** [35] evaluated the role of transdermal Diclofenac nupatch in post-operative pain management wherein pain intensity and pain relief showed that the efficacy of transdermal Diclofenac patch was excellent in 34 patients and good in 38 patients, fair in 27 patients and poor in a patient with no rescue medicine usage in 34 patients while it was used in 66 patients with the inference that transdermal patches reduces the corollary as it bypasses the first pass metabolism and achieves a constant and controlled drug release.

- **Chandrasekhran B.M et al. (2018)** [36] evaluated the analgesic efficacy of transdermal patch (NuPatch®) and oral Diclofenac sodium during post-operative period in patient undergoing quadrant periodontal flap surgery. 2 groups were formed viz Group I (30 quadrants) - Diclofenac sodium 50 mg b.i.d for three days. Group II (30 quadrants) - NuPatch® 100 mg once daily for 3 days applied on the deltoid region. Pain intensity and pain relief were assessed postoperatively at 2, 6, and 12 hours on the same day and on 2nd and 3rd day using Numerical Rating Scale and VAS which was significantly reduced post first day in group II. Adverse reaction viz gastric irritation in group I and no corollaries in group II were noted and inferred usage of transdermal Diclofenac patch as a finer option for mild to moderate pain.

- **Diwan V et al. (2019)** [37] studied comparative evaluation of transdermal Diclofenac patch with oral Diclofenac sodium as an analgesic drug following

periodontal flap surgery in 20 patients wherein transdermal Diclofenac patch was applied on the right arm following surgery of a quadrant and 100 mg oral Diclofenac sodium b.d. was prescribed following surgery of the subsequent quadrant. The post-operative pain was recorded on VA and pain intensity scale 24hour after the surgery. Inference was that Diclofenac sodium administered transdermally has equi-efficacy in comparison to oral counterpart.

- **Talani S. et al. (2020)** [38] assessed efficacy of transdermal Diclofenac patch versus oral Diclofenac tablet as an analgesic modality post premolar extractions in orthodontic patients with 33 symmetrical pairs of indicated premolars (either first or second) with each patient been given either transdermal Diclofenac sodium patch 100mg od or oral Diclofenac tablet 50mg b.d. post 3 days of extraction. Inference drawn was that transdermal Diclofenac patch acts as a potent analgesic modality for management of mild – moderate pain intensity with lower incidence of systemic adverse effects but cost and availability limits its usage.

MATERIAL & METHODS

MATERIAL AND METHODS

Materials and Instruments:

1. Oral Diclofenac tablet (100mg SR)
2. Transdermal Diclofenac patch

Place of the study where it is conducted:

The study will be conducted in patients reporting to the OPD of Oral and Maxillofacial Surgery Department, BBDCODS, Lucknow.

Study subjects:

14-70 years old subjects reporting to the OPD of Oral and Maxillofacial Surgery Department, BBDCODS, Lucknow.

Study Sample and size:

50 patients with oral Diclofenac as analgesic modality and 50 patients with Diclofenac transdermal patch as analgesic modality for management of pain shall be included in the study with total sample of 100.

Eligibility Criteria:

Inclusion criteria

- Age group 14-70 years
- Both genders.
- Participants without known systemic illness.
- Participants without any history of adverse reaction to NSAID.
- Extraction of teeth

- Minor oral surgery.
- Major oral surgery

Exclusion Criteria

- Participants more than 70 years of age and less than 14 years of age.
- Participants with known systemic illness: History of CVS disease, Asthma, Peptic ulcers, Urticaria.
- Subjects who are on nephrotoxic agents like aminoglycosides.
- Impaired renal/hepatic function.
- Impaired coagulation, bleeding disorder.
- Previous history of reaction to NSAID.

Sampling Method:

A prospective, randomized, single centre study will be performed among patients reporting to the out-patient department (OPD) of Oral and Maxillofacial Surgery Department, BBDCODS, Lucknow.

Total of 100 patients will be divided into 2 groups:

1. Group A – Oral Diclofenac as an analgesic modality for management of postoperative pain.
2. Group B – Transdermal Diclofenac patch as an analgesic modality for management of postoperative pain.

Methodology:

A prospective, randomized, single centre study will be performed among patients reporting to the out-patient department (OPD) of Oral and Maxillofacial Surgery Department, BBDCODS, Lucknow. After proper case history recording and diagnosis, appropriate procedure will be carried out (Extraction, Minor oral surgery, Major oral surgery). 100 patients will be randomly divided into 2 main groups – Group A will be given oral Diclofenac group as an analgesic modality postoperatively and Group B will be given transdermal Diclofenac patch as an analgesic modality postoperatively. For Group A patients, oral Diclofenac 100mg will be prescribed which has to be taken once for 3 days. For Group B patients, transdermal Diclofenac patch 100mg will be applied onto the arm of the patient which will be changed 24 hours later.

Postsurgical pain assessment: Pain will be the primary variable which will be assessed.

Post-operative pain will be assessed by the following:

- Visual Analog Scale**:**

  VAS is most commonly a straight 10cm line without demarcations that has the words “no pain” at the left-most end and “worst pain imaginable” at the right-most end. Patient is required to mark the 10 cm line at a point that corresponds to the level of pain intensity he or she presently feels.

- Verbal Descriptor Scale**:**

  Verbal descriptor scale is a list of words, ordered in terms of severity from least to most which describes the amount of pain that a patient may be experiencing. Patients are asked to either circle or state the word that best describes their pain intensity at that moment in time.

- Numerical Rating Pain Scale**:**

  The numerical rating scale offers the individual in pain to rate their pain score. User has the option to verbally rate their scale from 0 to 10 or to place a mark on a line indicating their level of pain. 0 indicates the absence of pain, while 10 represents the most intense pain.

- Wong Baker Faces Pain Scale**:**

  Adults who have difficulty using the numbers on the visual/numerical rating scales can be assisted with the use of the 6 facial expressions suggesting

various pain intensities asking the patient to choose the face that best describes how they feel. It combines pictures and numbers to allow pain to be rated by the user. Faces range from a smiling face to a sad, crying face. Numerical rating is assigned to each face, of which there are 6 total.

- Pain questionnaire and drug adverse effect questionnaire**:**

  It includes questions asked to the patient regarding pain intensity, pain rate and interference of pain with regular activities. There are also questions asked about any side effects that occur after application of patch or after intake of tablet.

PROPERTIES INFLUENCING TRANSDERMAL DELIVERY [34 – 39]

- Medicament release from the vehicle.
- Penetration through the skin barrier.
- Pharmacological response activation.

KINETICS OF TRANSDERMAL PERMEATION [40 – 43]

- Absorption by stratum corneum.
- Drug penetration via viable epidermis.
- Drug uptake by the capillary network in the dermal papillary layer.

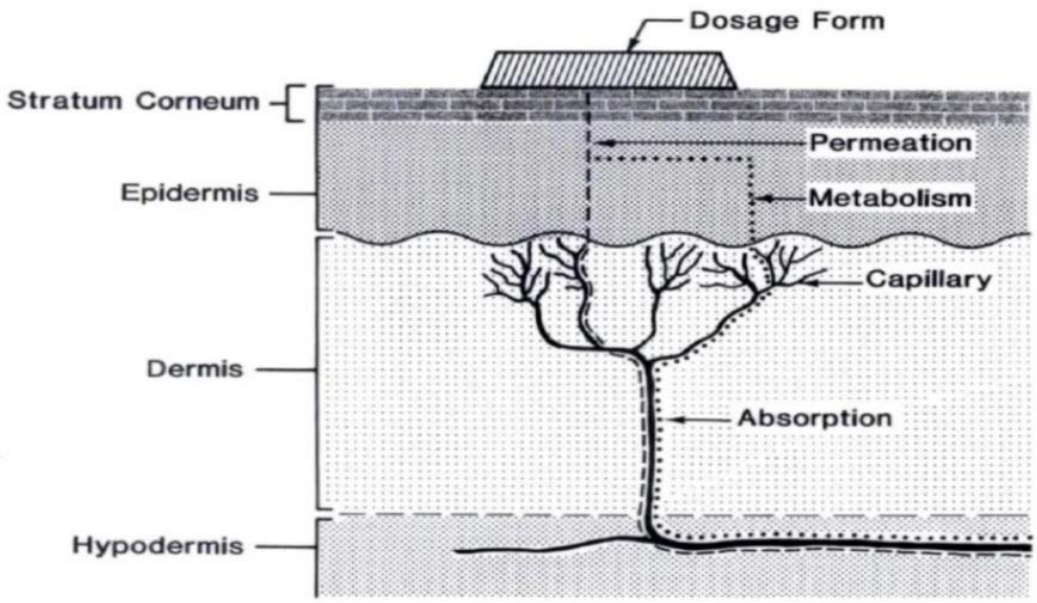


Figure: Kinetics of Transdermal patch

DESIRABLE FEATURES FOR TRANSDERMAL PATCHES [44 – 49]

- Non-intrusive
- Avoidance of first pass metabolism of drugs and typically follows Zero order delivery
- Painless system of drug delivery
- Extended duration of action
- Incessant pain relief
- Uncomplicated elimination of drug delivery during toxicity
- Lesser corollaries and therapeutic failures
- Patient affable usage due to simplified medication regimen and easy application.

COMPONENTS OF TRANSDERMAL PATCHES [50, 51]

- Liner :

  It shields the patch throughout storage. The liner is detached preceding usage.

- Drug :

  Direct contact of drug solution with release liner

- Adhesive :

  Contributes in adherance of components of the patch along with adherence of patch to the skin

- Membrane :

  Controls release of drug from reservoir and multi-layer patches

- Backing :

  Shields the patch from outer environment

Constituents of Transdermal delivery system encompasses:

Polymer Matrix -

Polymer controls drug release from the device. [52, 53]

a) Natural Polymers: Eg. Gelatin, Waxes, Proteins, Gums and their derivatives

b) Synthetic Elastomers: Eg. Silicone rubber, Nitrile, Acrylonitrile

c) Synthetic Polymers: Eg. Polyvinyl alcohol, Polyethylene, Polypropylene

Drug [54 – 56] **-**

- Molecular weight of the drug must be less than approximately 1000 daltons.

- It must have affinity for both – lipophilic and hydrophilic phases.
- It must have low melting point. (less than 200^{o} C)
- It must be non-ionic, potent, short half life and be non-irritating.

Permeation Enhancers -

They augment skin permeability by altering skin as a barrier to the flux of an anticipated penetrant. [57, 58]

a) Solvents

They increase penetration by swallowing the polar pathway and/or by fluidizing lipids.

Eg: Methanol, dimethyl sulfoxide, 2 pyrrolidone, propylene glycol

b) Surfactants

They enhance polar pathway transport of hydrophilic drugs. The capability of a surfactant to modify penetration is a function of the polar head group and the hydrocarbon chain length.

Eg : Sodium lauryl sulphate, Sodium taurocholate

c) Miscellaneous chemicals

Eg : urea (hydrating and keratolytic agent)

Other Excipients –

a) Adhesives: [60]

- must adhere to the skin and effortlessly removed.
- must not dispense an unwashable residue on the skin.
- must not irritate or sensitize the skin.

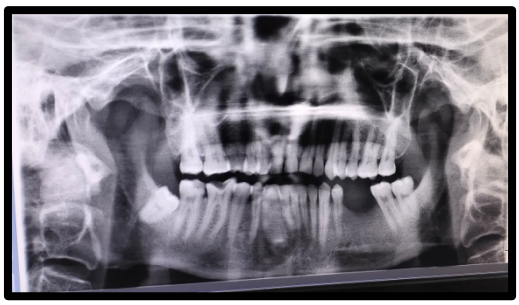
b) Backing membrane:

These are flexible and offer a decent bond to the drug reservoir, prevent drug from parting the dosage form through the top and admits printing. It is impermeable substance which protects the product during usage. [61, 62]

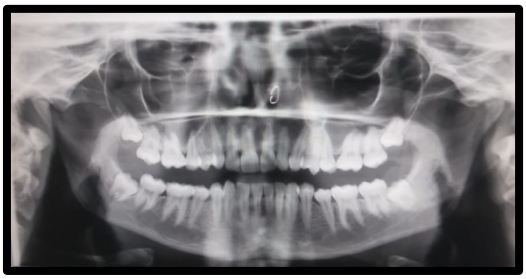
eg. plastic backing with absorbent pad.

Figure – 1: Diclofenac Transdermal Patch

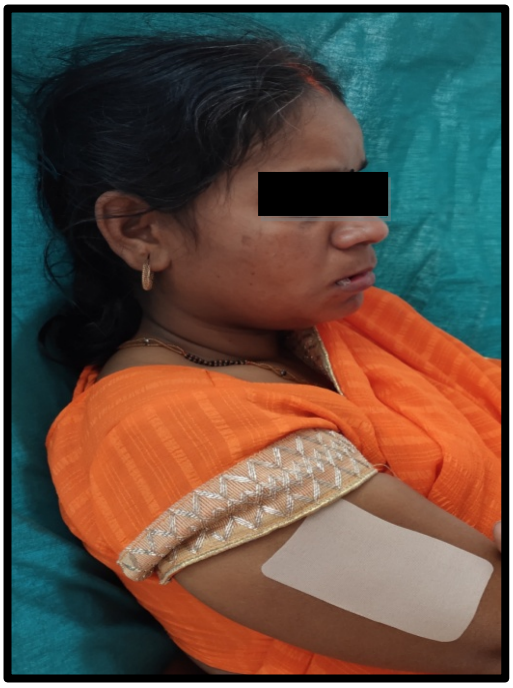
Figure – 2: Diclofenac prolonged release Tablets

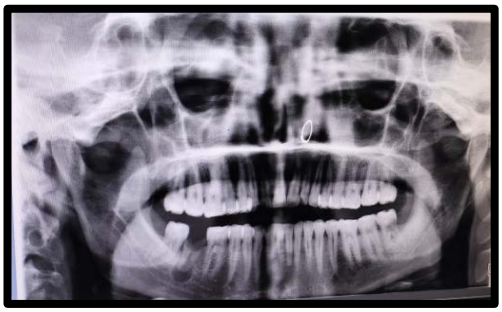


Patient - 1 **OPG**



Patient – 2 **OPG**





Patient – 3 **OPG**

Figure – 3: Transdermal patch applied on the Right arm of the patient

OBSERVATIONS AND RESULTS

OBSERVATIONS AND RESULTS

Statistical analysis:

The data was analyzed by Data Analysis tool of Excel and Statistical Package for Social Sciences (SPSS) software. Unpaired t – test was applied to find the statistical significance between the 2 groups. ANOVA test followed by Post-hoc test applied to find statistical significance between the groups. p value less than 0.05 ($p<0.05$) was considered statistically significant.

Table – 1: Mean VAS scores of the groups at different time period

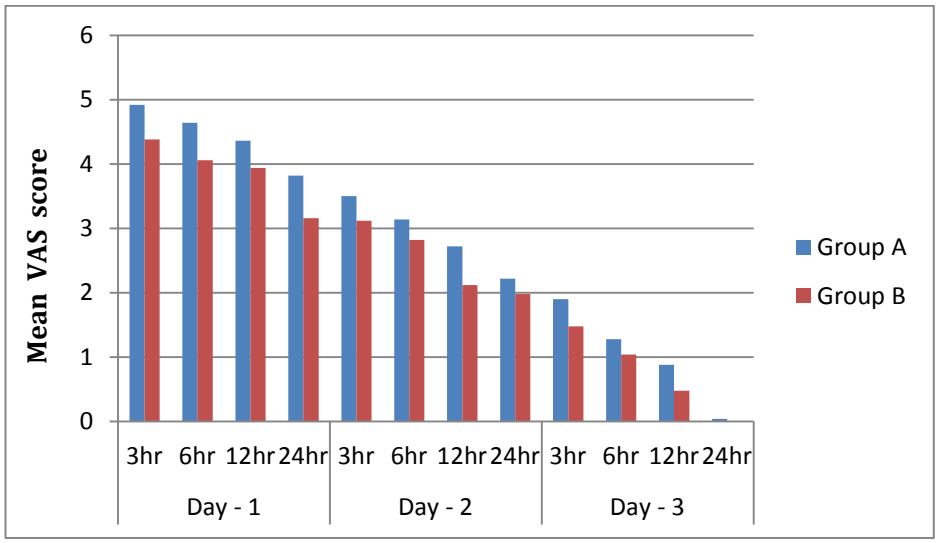
	VAS score (Mean ± SD)			
Day - 1	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	4.92 ± 0.27	4.64 ± 0.48	4.36 ± 0.53	3.82 ± 0.63
Group - B	4.38 ± 0.49	4.06 ± 0.24	3.94 ± 0.37	3.16 ± 0.37
Day - 2	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	3.50 ± 0.51	3.14 ± 0.61	2.72 ± 0.57	2.22 ± 0.58
Group - B	3.12 ± 0.33	2.82 ± 0.44	2.12 ± 0.33	1.98 ± 0.32
Day - 3	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	1.90 ± 0.36	1.28 ± 0.50	0.88 ± 0.33	0.04 ± 0.20
Group – B	1.48 ± 0.54	1.04 ± 0.20	0.48 ± 0.50	0.00 ± 0.00

Interpretation:

In Group – A, mean VAS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 4.92, 4.64, 4.36 and 3.82 respectively and Day-2 scores were 3.50, 3.14, 2.72 and 2.22 respectively and Day-3 scores were 1.90, 1.28, 0.88 and 0.04 respectively.

In Group – B, mean VAS score for Day-1 at 3hrs, 6hrs, 12hrs and 24hrs were 4.38, 4.06, 3.94 and 3.16 respectively and Day-2 scores were 3.12, 2.82, 2.12 and 1.98 respectively and Day-3 scores were 1.48, 1.04, 0.48 and 0.00 respectively.

Graph – 1: Mean VAS scores of the groups at different time period



Interpretation:

In Group – A, mean VAS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 4.92, 4.64, 4.36 and 3.82 respectively and Day-2 scores were 3.50, 3.14, 2.72 and 2.22 respectively and Day-3 scores were 1.90, 1.28, 0.88 and 0.04 respectively.

In Group – B, mean VAS score for Day-1 at 3hrs, 6hrs, 12hrs and 24hrs were 4.38, 4.06, 3.94 and 3.16 respectively and Day-2 scores were 3.12, 2.82, 2.12 and 1.98 respectively and Day-3 scores were 1.48, 1.04, 0.48 and 0.00 respectively.

Table – 2: Mean VDS scores of the groups at different time period

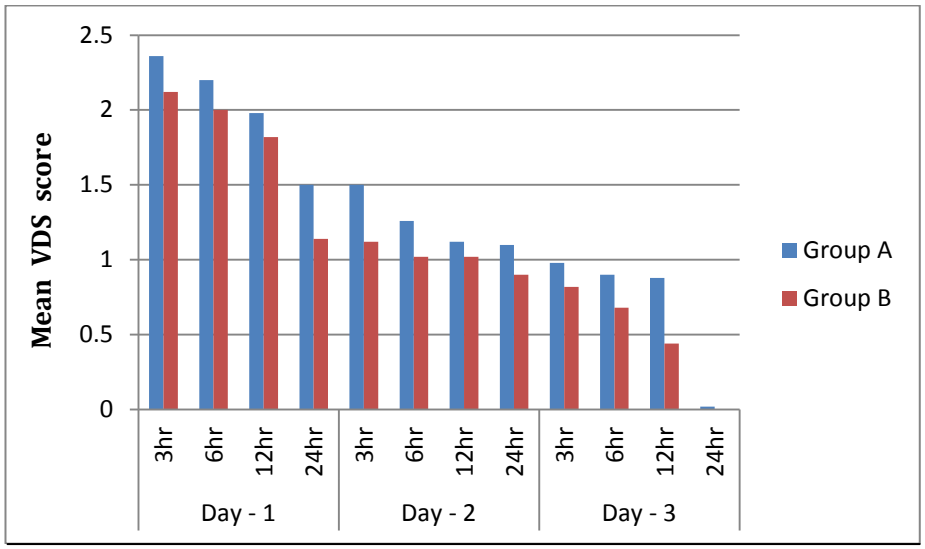
	VDS score (Mean ± SD)			
Day - 1	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	2.36 ± 0.48	2.20 ± 0.40	1.98 ± 0.14	1.50 ± 0.51
Group - B	2.12 ± 0.33	2.00 ± 0.20	1.82 ± 0.39	1.14 ± 0.35
Day - 2	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	1.50 ± 0.51	1.26 ± 0.44	1.12 ± 0.33	1.10 ± 0.30
Group - B	1.12 ± 0.33	1.02 ± 0.14	1.02 ± 0.14	0.90 ± 0.20
Day - 3	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	0.98 ± 0.14	0.90 ± 0.30	0.88 ± 0.33	0.02 ± 0.14
Group - B	0.82 ± 0.39	0.68 ± 0.47	0.44 ± 0.50	0.00 ± 0.00

Interpretation:

In Group – A, mean VDS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 2.36, 2.20, 1.98 and 1.50 respectively and Day-2 scores were 1.50, 1.26, 1.12 and 1.10 respectively and Day-3 scores were 0.98, 0.90, 0.88 and 0.02 respectively.

In Group – B, mean VDS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 2.12, 2.00, 1.82 and 1.14 respectively and Day-2 scores were 1.12, 1.02, 1.02 and 0.90 respectively and Day-3 scores were 0.82, 0.68, 0.44 and 0.00 respectively.

Graph – 2: Mean VDS scores of the groups at different time period



Interpretation:

In Group – A, mean VDS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 2.36, 2.20, 1.98 and 1.50 respectively and Day-2 scores were 1.50, 1.26, 1.12 and 1.10 respectively and Day-3 scores were 0.98, 0.90, 0.88 and 0.02 respectively.

In Group – B, mean VDS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 2.12, 2.00, 1.82 and 1.14 respectively and Day-2 scores were 1.12, 1.02, 1.02 and 0.90 respectively and Day-3 scores were 0.82, 0.68, 0.44 and 0.00 respectively.

Table – 3: Mean NRPS scores of the groups at different time period

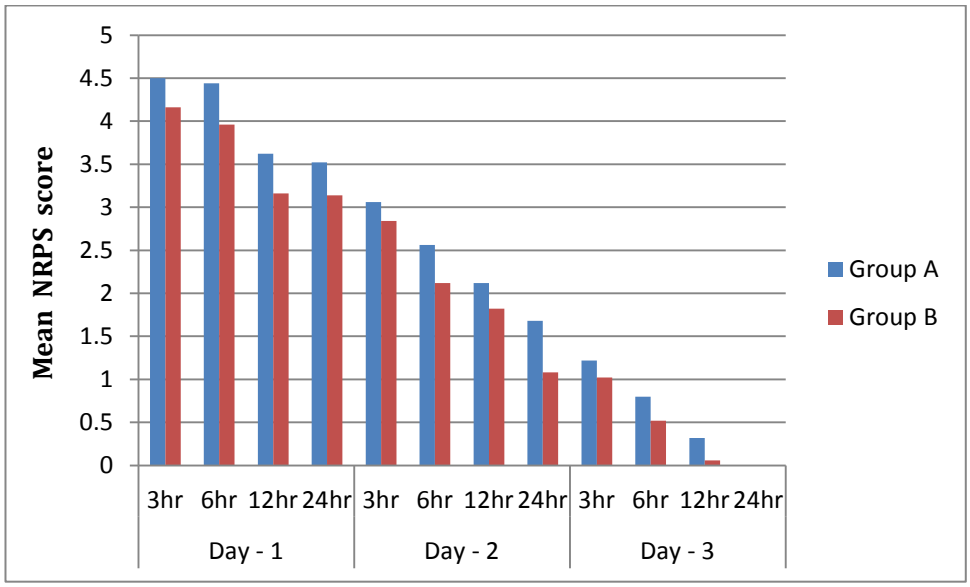
	NRPS score (Mean ± SD)			
Day - 1	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	4.50 ± 0.51	4.44 ± 0.50	3.62 ± 0.57	3.52 ± 0.50
Group - B	4.16 ± 0.37	3.96 ± 0.28	3.16 ± 0.37	3.14 ± 0.35
Day - 2	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	3.06 ± 0.51	2.56 ± 0.50	2.12 ± 0.52	1.68 ± 0.55
Group - B	2.84 ± 0.37	2.12 ± 0.33	1.82 ± 0.39	1.08 ± 0.27
Day - 3	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	1.22 ± 0.42	0.80 ± 0.40	0.32 ± 0.47	0.02 ± 0.14
Group - B	1.02 ± 0.14	0.52 ± 0.54	0.06 ± 0.24	0.00 ± 0.00

Interpretation:

In Group – A, mean NRPS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 4.50, 4.44, 3.62 and 3.52 respectively and Day-2 scores were 3.06, 2.56, 2.12 and 1.68 respectively and Day-3 scores were 1.22, 0.80, 0.32 and 0.02 respectively.

In Group – B, mean NRPS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 4.16, 3.96, 3.16 and 3.14 respectively and Day-2 scores were 2.84, 2.12, 1.82 and 1.08 respectively and Day-3 scores were 1.02, 0.52, 0.06 and 0.00 respectively.

Graph – 3: Mean NRPS scores of the groups at different time period



Interpretation:

In Group – A, mean NRPS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 4.50, 4.44, 3.62 and 3.52 respectively and Day-2 scores were 3.06, 2.56, 2.12 and 1.68 respectively and Day-3 scores were 1.22, 0.80, 0.32 and 0.02 respectively.

In Group – B, mean NRPS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 4.16, 3.96, 3.16 and 3.14 respectively and Day-2 scores were 2.84, 2.12, 1.82 and 1.08 respectively and Day-3 scores were 1.02, 0.52, 0.06 and 0.00 respectively.

Table – 4: Mean WB-FPS scores of the groups at different time Period

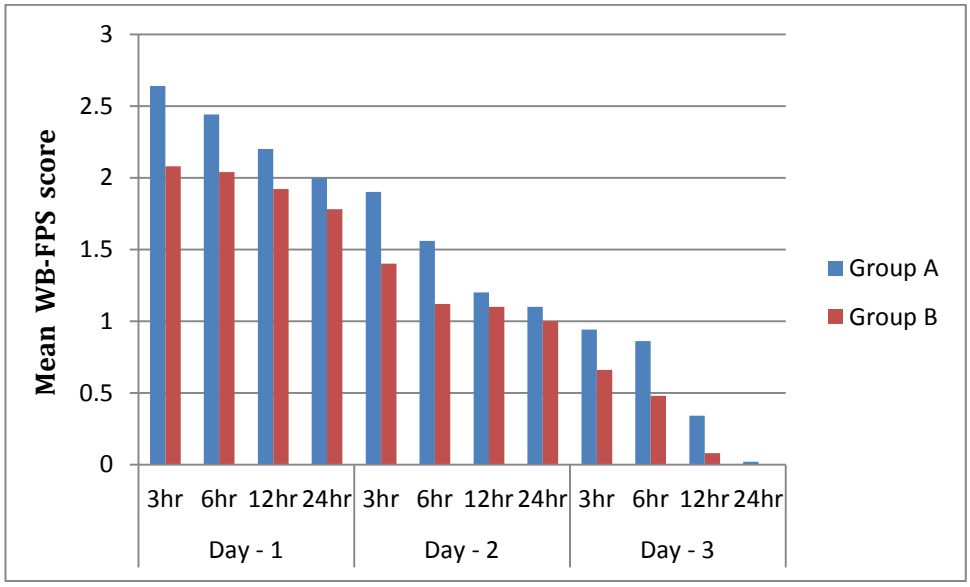
	WB-FPS score (Mean ± SD)			
Day - 1	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	2.64 ± 0.48	2.44 ± 0.50	2.20 ± 0.40	2.00 ± 0.00
Group - B	2.08 ± 0.27	2.04 ± 0.20	1.92 ± 0.27	1.78 ± 0.42
Day - 2	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	1.90 ± 0.30	1.56 ± 0.50	1.20 ± 0.40	1.10 ± 0.20
Group - B	1.40 ± 0.50	1.12 ± 0.33	1.10 ± 0.20	1.00 ± 0.10
Day – 3	**3hrs**	**6hrs**	**12hrs**	**24hrs**
Group – A	0.94 ± 0.24	0.86 ± 0.35	0.34 ± 0.48	0.02 ± 0.14
Group - B	0.66 ± 0.48	0.48 ± 0.50	0.08 ± 0.27	0.00 ± 0.00

Interpretation:

In Group – A, mean WB-FPS score for Day-1 at 3hrs, 6hrs, 12hrs and 24hrs were 2.64, 2.44, 2.20 and 2.00 respectively and Day-2 scores were 1.90, 1.56, 1.20 and 1.10 respectively and Day-3 scores were 0.94, 0.86, 0.34 and 0.02 respectively.

In Group – B, mean WB-FPS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 2.08, 2.04, 1.92 and 1.78 respectively and Day-2 scores were 1.40, 1.12, 1.10 and 1.00 respectively and Day-3 scores were 0.66, 0.48, 0.08 and 0.00 respectively.

Graph – 4: Mean WB-FPS scores of the groups at different time period



Interpretation:

In Group – A, mean WB-FPS score for Day-1 at 3hrs, 6hrs, 12hrs and 24hrs were 2.64, 2.44, 2.20 and 2.00 respectively and Day-2 scores were 1.90, 1.56, 1.20 and 1.10 respectively and Day-3 scores were 0.94, 0.86, 0.34 and 0.02 respectively.

In Group - B, mean WB-FPS score for Day-1 at 3hrs , 6hrs, 12hrs and 24hrs were 2.08, 2.04, 1.92 and 1.78 respectively and Day-2 scores were 1.40, 1.12, 1.10 and 1.00 respectively and Day-3 scores were 0.66, 0.48, 0.08 and 0.00 respectively.

Table-5: Comparison of mean scores of different pain scales between the groups at 3 hrs on Day – 1

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	4.92 ± 0.27	2.36 ± 0.48	4.50 ± 0.51	2.64 ± 0.48
Group – B	4.38 ± 0.49	2.12 ± 0.33	4.16 ± 0.37	2.08 ± 0.27
p – value	**0.08**	**0.26**	**0.09**	**0.06**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 1 for 3hr VAS, VDS, NRPS and WB-FPS scores were 4.92, 2.36, 4.50 and 2.64 respectively. In Group – B, the mean Day – 1 for 3hr VAS, VDS, NRPS and WB-FPS scores were 4.38, 2.12, 4.16 and 2.08 respectively. The differences in mean Day – 1 for 3hr pain scores were not statistically significant.

Table - 6: Comparison of mean scores of different pain scales between the groups at 6 hrs on Day – 1

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	4.64 ± 0.48	2.20 ± 0.40	4.44 ± 0.50	2.44 ± 0.50
Group – B	4.06 ± 0.24	2.00 ± 0.20	3.96 ± 0.28	2.04 ± 0.20
p – value	**0.09**	**0.48**	**0.12**	**0.35**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 1 for 6hr VAS, VDS, NRPS and WB-FPS scores were 4.64, 2.20, 4.44 and 2.44 respectively. In Group – B, the mean Day – 1 for 6hr VAS, VDS, NRPS and WB-FPS scores were 4.06, 2.00, 3.96 and 2.04 respectively. The differences in mean Day – 1 for 6hr pain scores were not statistically significant.

Table - 7: Comparison of mean scores of different pain scales between the groups at 12 hrs on Day – 1

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	4.36 ± 0.53	1.98 ± 0.14	3.62 ± 0.57	2.20 ± 0.40
Group – B	3.94 ± 0.37	1.82 ± 0.39	3.16 ± 0.37	1.92 ± 0.27
p – value	**0.06**	**0.65**	**0.10**	**0.13**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 1 for 12hr VAS, VDS, NRPS and WB-FPS scores were 4.36, 1.98, 3.62 and 2.20 respectively. In Group – B, the mean Day – 1 for 12 hr VAS, VDS, NRPS and WB-FPS scores were 3.94, 1.82, 3.16 and 1.92 respectively. The differences in mean Day – 1 for 12hr pain scores were not statistically significant.

Table - 8: Comparison of mean scores of different pain scales between the groups at 24 hrs on Day – 1

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	3.82 ± 0.63	1.50 ± 0.51	3.52 ± 0.50	2.00 ± 0.00
Group – B	3.16 ± 0.37	1.14 ± 0.35	3.14 ± 0.35	1.78 ± 0.42
p – value	**0.07**	**0.11**	**0.07**	**0.71**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 1 for 24hr VAS, VDS, NRPS and WB-FPS scores were 3.82, 1.50, 3.52 and 2.00 respectively. In Group – B, the mean Day – 1 for 24hr VAS, VDS, NRPS and WB-FPS scores were 3.16, 1.14, 3.14 and 1.78 respectively. The differences in mean Day – 1 for 24hr pain scores were not statistically significant.

Table - 9: Comparison of mean scores of different pain scales between the groups at 3 hrs on Day – 2

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	3.50 ± 0.51	1.50 ± 0.51	3.06 ± 0.51	1.90 ± 0.30
Group – B	3.12 ± 0.33	1.12 ± 0.33	2.84 ± 0.37	1.40 ± 0.50
p – value	**0.14**	**0.13**	**0.27**	**0.08**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 2 for 3hr VAS, VDS, NRPS and WB-FPS scores were 3.50, 1.50, 3.06 and 1.90 respectively. In Group – B, the mean Day – 2 for 3hr VAS, VDS, NRPS and WB-FPS scores were 3.12, 1.12, 2.84 and 1.40 respectively. The differences in mean Day – 2 for 3hr pain scores were not statistically significant.

Table - 10: Comparison of mean scores of different pain scales between the groups at 6 hrs on Day – 2

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	3.14 ± 0.61	1.26 ± 0.44	2.56 ± 0.50	1.56 ± 0.50
Group – B	2.82 ± 0.44	1.02 ± 0.14	2.12 ± 0.33	1.12 ± 0.33
p – value	**0.18**	**0.57**	**0.07**	**0.06**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 2 for 6hr VAS, VDS, NRPS and WB-FPS scores were 3.14, 1.26, 2.56 and 1.56 respectively. In Group – B, the mean Day – 2 for 6hr VAS, VDS, NRPS and WB-FPS scores were 2.82, 1.02, 2.12 and 1.12 respectively. The differences in mean Day – 2 for 6hr pain scores were not statistically significant.

Table - 11: Comparison of mean scores of different pain scales between the groups at 12 hrs on Day – 2

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	2.72 ± 0.57	1.12 ± 0.33	2.12 ± 0.52	1.20 ± 0.40
Group – B	2.12 ± 0.33	1.02 ± 0.14	1.82 ± 0.39	1.10 ± 0.20
p – value	**0.08**	**0.71**	**0.10**	**0.72**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 2 for 12hr VAS, VDS, NRPS and WB-FPS scores were 2.72, 1.12, 2.12 and 1.20 respectively. In Group – B, the mean Day – 2 for 12hr VAS, VDS, NRPS and WB-FPS scores were 2.12, 1.02, 1.82 and 1.10 respectively. The differences in mean Day – 2 for 12hr pain scores were not statistically significant.

Table - 12: Comparison of mean scores of different pain scales between the groups at 24 hrs on Day – 2

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	2.22 ± 0.58	1.10 ± 0.30	1.68 ± 0.55	1.10 ± 0.20
Group – B	1.98 ± 0.32	0.90 ± 0.20	1.08 ± 0.27	1.00 ± 0.10
p – value	**0.51**	**0.16**	**0.13**	**0.48**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 2 for 24hr VAS, VDS, NRPS and WB-FPS scores were 2.22, 1.10, 1.68 and 1.10 respectively. In Group – B, the mean Day – 2 for 24hr VAS, VDS, NRPS and WB-FPS scores were 1.98, 0.90, 1.08 and 1.00 respectively. The differences in mean Day – 2 for 24hr pain scores were not statistically significant.

Table - 13: Comparison of mean scores of different pain scales between the groups at 3 hrs on Day – 3

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	1.90 ± 0.36	0.98 ± 0.14	1.22 ± 0.42	0.94 ± 0.24
Group – B	1.48 ± 0.54	0.82 ± 0.39	1.02 ± 0.14	0.66 ± 0.48
p – value	**0.09**	**0.65**	**0.61**	**0.41**

(p>0.05 not significant on comparison of Group - A with Group - B)

Interpretation:

In Group – A, the mean Day – 3 for 3hr VAS, VDS, NRPS and WB-FPS scores were 1.90, 0.98, 1.22 and 0.94 respectively. In Group – B, the mean Day – 3 for 3hr VAS, VDS, NRPS and WB-FPS scores were 1.48, 0.82, 1.02 and 0.66 respectively. The differences in mean Day – 3 for 3hr pain scores were not statistically significant.

Table - 14: Comparison of mean scores of different pain scales between the groups at 6 hrs on Day – 3

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	1.28 ± 0.50	0.90 ± 0.30	0.80 ± 0.40	0.86 ± 0.35
Group – B	1.04 ± 0.20	0.68 ± 0.47	0.52 ± 0.54	0.48 ± 0.50
p – value	**0.57**	**0.36**	**0.16**	**0.07**

(p>0.05 no significant compared Group - A with Group – B)

Interpretation:

In Group – A, the mean Day – 3 for 6hr VAS, VDS, NRPS and WB-FPS scores were 1.28, 0.90, 0.80 and 0.86 respectively. In Group – B, the mean Day – 3 for 6hr VAS, VDS, NRPS and WB-FPS scores were 1.04, 0.68, 0.52 and 0.48 respectively. The differences in mean Day – 3 for 6hr pain scores were not statistically significant.

Table - 15: Comparison of mean scores of different pain scales between the groups at 12 hrs on Day – 3

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	0.88 ± 0.33	0.88 ± 0.33	0.32 ± 0.47	0.34 ± 0.48
Group – B	0.48 ± 0.50	0.44 ± 0.50	0.06 ± 0.24	0.08 ± 0.27
p – value	**0.09**	**0.07**	**0.42**	**0.38**

(p>0.05 not significant on comparison of Group - A with Group – B)

Interpretation:

In Group – A, the mean Day – 3 for 12hr VAS, VDS, NRPS and WB-FPS scores were 0.88, 0.88, 0.32 and 0.34 respectively. In Group – B, the mean Day – 3 for 12hr VAS, VDS, NRPS and WB-FPS scores were 0.48, 0.44, 0.06 and 0.08 respectively. The differences in mean Day – 3 for 12hr pain scores were not statistically significant.

Table - 16: Comparison of mean scores of different pain scales between the groups at 24 hrs on Day – 3

Groups	VAS (Mean ± SD)	VDS (Mean ± SD)	NRPS (Mean ± SD)	WB-FPS (Mean ± SD)
Group – A	0.04 ± 0.20	0.02 ± 0.14	0.02 ± 0.14	0.02 ± 0.14
Group – B	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
p – value	**0.89**	**0.92**	**0.92**	**0.92**

(p>0.05 not significant on comparison of Group - A with Group – B)

Interpretation:

In Group – A, the mean Day – 3 for 24hr VAS, VDS, NRPS and WB-FPS scores were 0.04, 0.02, 0.02 and 0.02 respectively. In Group – B, the mean Day – 3 for 24hr VAS, VDS, NRPS and WB-FPS scores were 0.00, 0.00, 0.00 and 0.00 respectively. The differences in mean Day – 3 for 24hr pain scores were not statistically significant.

Table-17: Comparison of mean pain score values within the Group – A at different time periods Day –1

Day-1 Score	Group – A							
	VAS (Mean±SD)	**p value**	**VDS (Mean±SD)**	**p value**	**NRPS (Mean±SD)**	**p value**	**WB-FPS (Mean±SD)**	**p value**
3hr	4.92 ± 0.27		2.36 ± 0.48		4.50 ± 0.51		2.64 ± 0.48	
6hr	4.64 ± 0.48*	0.000	2.20 ± 0.40		4.44 ± 0.50		2.44 ± 0.50	
12hr	4.36 ± 0.53*#	0.006	1.98 ± 0.14*#	0.000	3.62 ± 0.57*#	0.000	2.20 ± 0.40*	0.000
24hr	3.82±0.63*#@	0.000	1.50 ± 0.51*#	0.001	3.52 ± 0.50*#	0.000	2.00±0.00*#@	0.000

(*p<0.05 significant compared 3 hrs with other time periods.
#p<0.05 significant compared 6 hrs with other time periods.
@p<0.05 significant compared 12 hrs with 24 hrs)

Interpretation:

The mean Day-1 VAS scores at 3, 6, 12 and 24 hr in Group-A were 4.92, 4.64, 4.36 and 3.82 respectively. The mean Day-1 VDS scores at 3, 6, 12 and 24 hr in Group-A were 2.36, 2.20, 1.98 and 1.50 respectively. The mean Day-1 NRPS scores at 3, 6, 12 and 24 hr in Group-A were 4.50, 4.44, 3.62 and 3.52 respectively. The mean Day-1 WB-FPS scores at 3, 6, 12 and 24 hr in Group-A were 2.64, 2.44, 2.20 and 2.00 respectively. The differences in mean pain score between 3 hr and 12 hr; 3 hr and 24 hr; 6 hr and 24 hr were statistically significant.

Table-18: Comparison of mean pain score values within the Group – B at different time periods Day –1

Day-1 Score	Group – B							
	VAS (Mean±SD)	p value	VDS (Mean±SD)	p value	NRPS (Mean±SD)	p value	WB-FPS (Mean±SD)	p value
3hr	4.38 ± 0.49		2.12 ± 0.33		4.16 ± 0.37		2.08 ± 0.27	
6hr	4.06 ± 0.24*		2.00 ± 0.20		3.96 ± 0.28*	0.003	2.04 ± 0.20	
12hr	3.94 ± 0.37*	0.000	1.82 ± 0.39*#	0.000	3.16 ± 0.37*#	0.000	1.92 ± 0.27*	0.004
24hr	3.16±0.37*#@	0.000	1.14±0.35*#@	0.000	3.14 ± 0.35*#		1.78 ± 0.42*#	0.000

(*p<0.05 significant compared 3 hrs with other time periods.
#p<0.05 significant compared 6 hrs with other time periods.
@p<0.05 significant compared 12 hrs with 24 hrs)

Interpretation:

The mean Day-1 VAS scores at 3, 6, 12 and 24 hr in Group-B were 4.38, 4.06, 3.94 and 3.16 respectively. The mean Day-1 VDS scores at 3, 6, 12 and 24 hr in Group-B were 2.12, 2.00, 1.82 and 1.14 respectively. The mean Day-1 NRPS scores at 3, 6, 12 and 24 hr in Group-B were 4.16, 3.96, 3.16 and 3.14 respectively. The mean Day-1 WB-FPS scores at 3, 6, 12 and 24 hr in Group-B were 2.08, 2.04, 1.92 and 1.78 respectively. The differences in mean pain score between 3hr and 12hr; 3hr and 24hr; 6hr and 24hr were statistically significant.

Table-19: Comparison of mean pain score values within the Group – A at different time periods Day –2

Day-2 Score	Group – A							
	VAS (Mean±SD)	**p value**	**VDS (Mean±SD)**	**p value**	**NRPS (Mean±SD)**	**p value**	**WB-FPS (Mean±SD)**	**p value**
3hr	3.50 ± 0.51		1.50 ± 0.51		3.06 ± 0.51		1.90 ± 0.30	
6hr	3.14 ± 0.61*	0.001	1.26 ± 0.44		2.56 ± 0.50*	0.000	1.56 ± 0.50*	0.001
12hr	2.72 ± 0.57*#	0.001	1.12 ± 0.33*		2.12 ± 0.52*#	0.001	1.20 ± 0.40*#	0.001
24hr	2.22±0.58*#@	0.000	1.10 ± 0.30*	0.000	1.68±0.55*#@	0.000	1.10 ± 0.20*#	

(*p<0.05 significant compared 3 hrs with other time periods.
#p<0.05 significant compared 6 hrs with other time periods.
@p<0.05 significant compared 12 hrs with 24 hrs)

Interpretation:

The mean Day-2 VAS scores at 3, 6, 12 and 24 hr in Group-A were 3.50, 3.14, 2.72 and 2.22 respectively. The mean Day-2 VDS scores at 3, 6, 12 and 24 hr in Group-A were 1.50, 1.26, 1.12 and 1.10 respectively. The mean Day-2 NRPS scores at 3, 6, 12 and 24 hr in Group-A were 3.06, 2.56, 2.12 and 1.68 respectively. The mean Day-2 WB-FPS scores at 3, 6, 12 and 24 hr in Group-A were 1.90, 1.56, 1.20 and 1.10 respectively. The differences in mean pain score between 3hr and 12hr; 3hr and 24hr were statistically significant.

Table-20: Comparison of mean pain score values within the Group – B at different time periods Day –2

Day-2 Score	Group – B							
	VAS (Mean±SD)	p value	VDS (Mean±SD)	p value	NRPS (Mean±SD)	p value	WB-FPS (Mean±SD)	p value
3hr	3.12 ± 0.33		1.12 ± 0.33		2.84 ± 0.37		1.40 ± 0.50	
6hr	2.82 ± 0.44*	0.001	1.02 ± 0.14		2.12 ± 0.33*	0.000	1.12 ± 0.33*	0.001
12hr	2.12 ± 0.33*#	0.000	1.02 ± 0.14		1.82 ± 0.39*#	0.000	1.10 ± 0.20*	
24hr	1.98 ± 0.32*#		0.90 ± 0.20*	0.002	1.08±0.27*#@	0.000	1.00 ± 0.10*#	0.007

(*p<0.05 significant compared 3 hrs with other time periods.
#p<0.05 significant compared 6 hrs with other time periods.
@p<0.05 significant compared 12 hrs with 24 hrs)

Interpretation:

The mean Day-2 VAS scores at 3, 6, 12 and 24 hr in Group-B were 3.12, 2.82, 2.12 and 1.98 respectively. The mean Day-2 VDS scores at 3, 6, 12 and 24 hr in Group-B were 1.12, 1.02, 1.02 and 0.90 respectively. The mean Day-2 NRPS scores at 3, 6, 12 and 24 hr in Group-B were 2.84, 2.12, 1.82 and 1.08 respectively. The mean Day-2 WB-FPS scores at 3, 6, 12 and 24 hr in Group-B were 1.40, 1.12, 1.10 and 1.00 respectively. The differences in mean pain score between 3hr and 24hr were statistically significant.

Table-21: Comparison of mean pain score values within the Group – A at different time periods Day –3

Day-3 Score	Group – A							
	VAS (Mean±SD)	**p value**	**VDS (Mean±SD)**	**p value**	**NRPS (Mean±SD)**	**p value**	**WB-FPS (Mean±SD)**	**p value**
3hr	1.90 ± 0.36		0.98 ± 0.14		1.22 ± 0.42		0.94 ± 0.24	
6hr	1.28 ± 0.50*	0.000	0.90 ± 0.30		0.80 ± 0.40*	0.000	0.86 ± 0.35	
12hr	0.88 ± 0.33*#	0.000	0.88 ± 0.33		0.32 ± 0.47*#	0.000	0.34 ± 0.48*#	0.000
24hr	0.04±0.20*#@	0.000	0.02±0.14*#@	0.000	0.02±0.14*#@	0.000	0.02±0.14*#@	0.000

(*p<0.05 significant compared 3 hrs with other time periods.
#p<0.05 significant compared 6 hrs with other time periods.
@p<0.05 significant compared 12 hrs with 24 hrs)

Interpretation:

The mean Day-3 VAS scores at 3, 6, 12 and 24 hr in Group-A were 1.90, 1.28, 0.88 and 0.04 respectively. The mean Day-3 VDS scores at 3, 6, 12 and 24 hr in Group-A were 0.98, 0.90, 0.88 and 0.02 respectively. The mean Day-3 NRPS scores at 3, 6, 12 and 24 hr in Group-A were 1.22, 0.80, 0.32 and 0.02 respectively. The mean Day-3 WB-FPS scores at 3, 6, 12 and 24 hr in Group-A were 0.94, 0.86, 0.34 and 0.02 respectively. The differences in mean pain score between 3hr and 24hr; 6hr and 24hr; 12hr and 24hr were statistically significant.

Table-22: Comparison of mean pain score values within the Group – B at different time periods Day –3

Day-3	Group – B							
Score	**VAS (Mean±SD)**	**p value**	**VDS (Mean±SD)**	**p value**	**NRPS (Mean±SD)**	**p value**	**FPS (Mean±SD)**	**p value**
3hr	1.48 ± 0.54		0.82 ± 0.39		1.02 ± 0.14		0.66 ± 0.48	
6hr	1.04 ± 0.20*	0.000	0.68 ± 0.47		0.52 ± 0.54*	0.000	0.48 ± 0.50	
12hr	0.48 ± 0.50*#	0.000	0.44 ± 0.50*	0.000	0.06 ± 0.24*#	0.000	0.08 ± 0.27*#	0.000
24hr	0.00±0.00*#@	0.000	0.00±0.00*#@	0.000	0.00 ± 0.00*#		0.00 ± 0.00*#	0.000

(*p<0.05 significant compared 3 hrs with other time periods.
#p<0.05 significant compared 6 hrs with other time periods.
@p<0.05 significant compared 12 hrs with 24 hrs)

Interpretation:

The mean Day-3 VAS scores at 3, 6, 12 and 24 hr in Group-B were 1.48, 1.04, 0.48 and 0.00 respectively. The mean Day-3 VDS scores at 3, 6, 12 and 24 hr in Group-B were 0.82, 0.68, 0.44 and 0.00 respectively. The mean Day-3 NRPS scores at 3, 6, 12 and 24 hr in Group-B were 1.02, 0.52, 0.06 and 0.00 respectively. The mean Day-3 WB-FPS scores at 3, 6, 12 and 24 hr in Group-B were 0.66, 0.48, 0.08 and 0.00 respectively. The differences in mean pain score between 3hr and 12hr; 3hr and 24hr; 6hr and 24hr were statistically significant.

There were no side-effects according to questionnaire given to each participant in both the groups.

DISCUSSION

DISCUSSION

The Latin word “peona” means pain which translates into punishment. The prevention of central sensitization seems to be an effective way in controlling pain post - operatively. [15] Gastric irritation is a known side effect of NSAIDs. The bioavailability decreases when enteral route is employed and maintenance of a steady plasma level of the drug is thereby achieved by repetitive administration of the drug. Routes which bypass first - pass mechanism viz. intra-venous, intra-osseous and intra-muscular are painful on application. [26] The transdermal drug delivery system is an effective route which camouflages the disadvantages of oral route. [34]

Pain evaluation is always subjective, but can be evaluated in various scales like VAS, VDS, NRPS and WB-FPS. In this comparative study, the efficacy of Diclofenac tablet and Diclofenac transdermal patch in management of post-operative pain is compared. The parameters evaluated for post-operative pain score are VAS, VDS, NRPS and WB-FPS at an interval of 3hr, 6hr, 12hr and 24hr for 3 consecutive days.

Post-operative pain:

On Day – 1, the mean pain score in all the pain scales like VAS, VDS, NRPS and WB-FPS were reduced with time in both the groups which was statistically significant. This result was in compliance with **Bhaskar et al** [24], where he had inferred on comparing post-operative pain, the mean pain score reduced with time in both the groups. Though the mean 3hr, 6hr, 12hr and 24hr pain scores in all the scales seems to be lesser in Group – B (Diclofenac patch) when compared to Group – A (Diclofenac tablet) the p value was not statistically significant. The result obtained in this study was not incompliance with the previous study by **Bachalli PS et al**.[3] where on comparing Diclofenac patch with tablet, the Diclofenac tablet was more effective in managing the postoperative pain in first 24hrs. This disparity was due to the fact that the analgesics in this study were given preemptively.

On Day – 2, the mean 3hr, 6hr, 12hr and 24hr pain score in all the pain scales seems to be lesser in Group-B (Diclofenac patch) when compared to Group-A (Diclofenac tablet) the p-value was not statistically significant. This result was similar to the result obtained by **Bachalli PS et al.**[3] which states that the transdermal Diclofenac and Oral Diclofenac are equally efficacious in managing the postoperative pain on Day – 2. The mean pain score in all the pain scales like VAS, VDS, NRPS and WB-FPS reduced with time in both the groups which was statistically significant. The reduction of mean NRPS score was significant in both groups (Diclofenac tablet and Diclofeanc patch). In other scales like VAS, VDS, WB-FPS the difference in pain score between

12hr and 24hr were not significant and the difference in mean pain scores between 3hr and 24hr were significant in both the groups.

On Day – 3, the mean 3hr, 6hr, 12hr and 24hr pain scores in all the scales seems to be lesser in Group-B (Diclofenac patch) when compared to Group-A (Diclofenac tablet) the p-value was not statistically significant. The mean pain scores in all the pain scales like VAS, VDS, NRPS and WB-FPS reduced with time in both the groups and the reduction were statistically significant in both groups (Diclofenac tablet and Diclofenac patch). This result was in accordance with **Bhaskar et al.** [24], where on comparing post-operative pain, the mean pain score reduced with time in both the groups.

In the current study, no patients required an emergency medication in both Group-A and Group-B although in a comparative interventional study of **Baskhar et al**. [24] about one out of twenty patients required emergency Tab. Paracetamol as an emergency medication inspite of transdermal patch. This disparity can be explained by preemptive consumption of analgesic.

In this study both Diclofenac tablet and transdermal Diclofenac reduces the pain score on all 3 days without letting the patient to go for an emergency pain medication. Though the mean pain scores for the patients in Group-A (transdermal patch) was lesser than in Group-B (Diclofenac tablet), the differences between them were not statistically significant. Thus leading to the conclusion of equal efficacy of the two medication in management of postoperative pain. The results were similar to the study by **Krishnan et al.** [27]

who compared the efficacy of transdermal Diclofenac and Oral Diclofenac in third molar extraction.

In this study no patients had side effects like gastric irritation from the tablet Diclofeanac, unlike the study conducted by **Bhaskar et al** [24] where he reported that two of twenty patients had gastric irritation. This confutation can be explained by the inclusion of Tab. Pantoprazole 40mg OD prescribed along with tablet Diclofenac 100mg OD. None of the patients reported any allergic or corollaries of Diclofenac patch, as the patients allergic to Diclofenac were excluded from the study.

CONCLUSION

CONCLUSION

Pain is usually the chief complaint of patient which requires to be addressed primarily. In postoperative pain management advancement in pharmacology, techniques such as usage of sustained delivery system and its knowledge are making major inroads in achieving this initiative. Most commonly used pharmacological agent in post-operative pain management are NSAIDs viz. Diclofenac, Paracetamol, Ibuprofen, used either orally or parenterally.

In this study, Diclofenac has been used in Tablet and Transdermal forms. The purpose of the abovementioned study was to compare the efficacy of Oral Diclofenac with Transdermal patch of Diclofenac in management of postoperative pain. It was designed as comparative interventional study with sample size of 50 in each group. The selection of the cases was based on fulfilment of inclusion and exclusion criteria. Thereafter patients were randomly divided into 2 groups i.e. Group-A (Oral Diclofenac) and Group-B (transdermal patch of Diclofenac). After surgical interventional procedure, drug was administered according to the allocated groups and then pain was scaled based on following modalities viz. VAS, VDS, NRPS and WB - FPS at an interval of 3hrs, 6hrs, 12hrs and 24hrs for 3 consecutive days.

On Day – 1, the mean pain score of all the scales decreased with time significantly in both the groups. The Group-B mean pain score at 3hr, 6hr, 12hr and 24hr was lesser than the mean pain scores of Group-A. But the difference was not statistically significant.

On Day – 2, the mean pain score of NRPS decreased with time significantly in both the groups. The Group-B mean pain score at 3hr, 6hr, 12hr and 24hr was lesser than the mean pain scores of Group-A. But the difference was not statistically significant.

On Day – 3, the mean pain score of all the scales decreased with time significantly in both the groups. The Group-B mean pain score at 3hr, 6hr, 12hr and 24hr was lesser than the mean pain scores of Group-A. But the difference was not statistically significant.

Thus according to statistical analysis of this study, it is proved that the Transdermal Diclofenac and Oral Diclofenac are equally effective in management of postoperative pain.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Sivrikaya GU. Multimodal analgesia for postoperative pain management. In: Racz G, editor. Pain management – current issues and opinions. Croatia: In Techpublishers; 2009. p. 177-210.
2. Woolf CJ, Chong MS. Preemptive analgesia-treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg 1993;77:362-79.
3. Bachalli PS, Nandakumar H, Srinath N. A comparitive study of diclofenac transdermal patch against oral diclofenac for pain control following removal of mandibular impacted third molars. J Maxillofac Oral Surg 2009; 8(2): 167-72.
4. Naesdal J, Brown K.NSAID - associated Adverse effects and Acid Control in Preventing Them: A review of current treatment options. Drug 2006;29:119-32.
5. Mandell BF. General tolerability and use of non-steroidal anti-inflammatory drugs. Am J Med 1999;107:72-6.
6. Bhowmik D, Duraivel S, Kumar KPS. Recent Trends in Challenges and Opportunitiesin Transdermal Drug Delivery System. Pharma Innov J 2012;1(10):9-23

7. Patel D, Chaudhary SA, Parmar B, Bhura N. Transdermal Drug Delivery System: A Review. Pharma Innov J 2012; 1(4): 78-88

8. Bailey BMW, Zaki G, Rotman H, Woodwards RT. A double-blind comparative study of soluble aspirin and dictofenac dispersible in the control of postextraction pain after removal of impacted third molars. Int J Oral Maxillofac Surg 1993; 22. 238-41

9. Assandri A, Canali S, Giachetti C. Local tolerability and pharmacokinetic profile ofa new transdermal delivery system, DHEP plaster. Drugs Exp Clin Res 1993;19:89-6.

10. Muller M, Mascher H, Kikuta C. Diclofenac concentrations in defined tissue layers after topical administration. Clin Pharmacol Ther 1997;62(3):293-9.

11. Arora P, Mukherjee B. Design, development, physicochemical, and in vitro and in vivo evaluation of transdermal patches containing diclofenacdiethylammonium salt. J Pharm Sci 91:2089-96.

12. Predel HG, Koll R, Pabst H. Diclofenac patch for topical treatment of acute impact injuries: a randomized double blind placebo controlled multicenter study. Br J Sports Med 2004; 38(3); 318-323.

13. Joshi A, Parara E, Macfarlane TV. A double- blind randomized controlled clinical trial of the effect of preoperative ibuprofen, diclofenac, paracetamol with codeine and placebo tablet for relief of postoperative pain after removal of impacted third molars. Br J Oral Maxillofac Surg 2004; 42(4): 299-306.

14. Mason L, Moore RA, Edward JE, Derry S, McQuay HU. Topical NSAIDs for acute pain: A meta analysis. BMC Family Practice 2004;5:10.

15. Niethard FU, Gold MS, Solomon GS, Liu JM, Unkauf M, Albrecht HH, Elkik F.Efficacy of topical diclofenac diethylamine gel in osteoarthritis of the knee. J Rheumatol. 32: 2384-92.

16. Carriches CL, Gonzalez JM, Rodriguez MD. The use of methylprednisolone versus diclofenac in the treatment of inflammation and trismus after surgical removal of lower third molars. Med Oral Patol Oral Cir Bucal 2006;11:E440-5.

17. Bamgbose BO, Akinwande JA, Adeyemo WL. A prospective, randomized, open label, pilot clinical trial comparing the effects of dexamethasone coadministered with Diclofenac potassium or acetaminophen and Diclofenac potassium monotherapy after third molar extraction in adults. Curr Ther Res Clin Exp 2006;67:230-40.

18. Baboota S, Shakeel F, Kohli K. Formulation and evaluation of once-a-day transdermal gels of diclofenac diethylamine. Methods Find. Exp Clin Pharmacol.28:109-114.

19. Agarwal A, Goutham S, Gupta D, Singh U. Transdermal diclofenac vs eutectic mixture of local anesthetics for venous cannulation pain. CAN J ANESTH 2007;54(3):196-200.

20. Alessandri F, Lijoi D, Mistrangela E. Topical diclofenac patch for postoperative wound pain in laparoscopic gynecologic surgery: a randomized study. J Minim Invasive Gynecol 2006;13(3):195-200.

21. Minghetti P, Cilurzo F, Casiraghi A, Montanari L, Fini A. Ex vivo study of transdermal permeation of four diclofenac salts from different vehicles. J Pharm Sci 2007;96:814-23.

22. Lionberger DR, Brennan MJ. Topical nonsteroidal anti-inflammatory drugs for the treatment of pain due to soft tissue injury: diclofenac epolamine topical patch. J Pain Res 2010; 10(3): 223–33.

23. Krishna R, Nataraj MS. Efficacy of single dose transdermal diclofenac patch as pre-emtive post operative analgesia: a comparison with intramuscular diclofenac. South Afr J Anaesth Analg 2012; 18(14):194-7.

24. Bhaskar H, Kapoor P, Ragini. Comparison of transdermal diclofenac patch with oral diclofenac as an analgesic modality following multiple premolar extractions in orthodontic patients: A cross over efficacy trial. Contemp Clin Dent 2010;1(3):158-163.

25. Khalili S et al. The effectiveness of diclofenac gel and eutectic mixture of local anesthetic cream on vein puncture pain severity with vein catheter in patient undergoing cesarean section: A randomized, double-blind, placebo-controlled trial. Int J Appl Basic Med Res 2014;4:46-9.

26. Reddy RP, Rajashekar SB, Karthik US. Comparing the Effectiveness of Transdermal Diclofenac Patch and Inramuscular Diclofenac Injection in Postoperative Pain Relief after Inguinal Hernia Mesh Repair: A Randomised Study in the Department of General Surgery. Journal of Evidence based Medicine and Healthcare 2015;2(34):5286-92.

27. Krishnan S. Transdermal diclofenac patch for control of post-extraction pain, pilot randomized controlled double blind study. J Maxillofac Oral Surg 2015; 19(1): 5-12.

28. de Barros, Chagas PAM, Borges FA, et al. Diclofenac Potassium Transdermal Patches Using Natural Rubber Latex Biomembranes as Carrier. Journal of Materials [Internet]. 2015. doi:10.1155/2015/807948

29. Bhargava GS, Sidhu AS, Bansal D, Bhatia AS. Comparative study in management of post operative pain with diclofenac patch versus diclofenacinjection, CIB tech J Surg 2015; 4(1):10-15.

30. Narzaree P, Griwan MS, Sign J. Efficacy and safety of transdermal diclofenac patch versus intramuscular diclofenac injections in postoperative patients ofinguinal hernia. Int J Basic Clin Pharmacol. 2016 Apr;5(2):447-452.

31. Verma R, Kumar S, Goyal A, Ajay C. Comparison of single dose transdermal patches of diclofenac and ketoprofen for postoperative analgesia in lower limb orthopaedic surgery. Int J Res Med Sci 2016;4(3):718-21.

32. Carr DB, Goudas LC. Acute pain. Lancet 1999;353(12):2051-8.

33. Woolf CJ. Evidence for a central component of post injury pain hypersensitivity. Nature 1983;308:366-368.

34. Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia: physiological pathways and pharmacological modalities. Can J Anaesth 2001; 48: 1000-10.

35. Roelofse et al. Analgesic and Anti-inflammatory Efficacy of Tenoxicam and Diclofenac Sodium. Anesth Prog 1996;43:103-7.

36. Nazar MN, Puthiriraj V. Analgesics following Mandibular Third Molar Surgery. Int J of Pharmaceutical Clin Res 2014;6(1):13-9.

37. Ong, Seymour. Maximizing the Safety of Nonsteroidal Anti-inflammatory Drug Use for Postoperative Dental Pain: An Evidence-based Approach. Anesth Prog 2003;50:62-74

38. Shah R, Mahajan A, Shah N, Dadania AP. Preemptive analgesia in third molar impaction surgery. Nat J Maxillofac Surg 2012; 3(2): 144-7.

39. Zanzane MD, Geeverghese R. Use of transdermal patches as drug delivery system: global scenario. World J Pharmaceutical Res 2015; 4(3): 1809-23.

40. Shobha D, Jajee P. Comparative Evaluation of Efficacy of Transdermal Diclofenac Patch. Eutectic Mixture of Local Anaesthetic Cream and Placebo for Venous Cannulation Pain and Attenuation of Hemodynamic Response. Int J Sci Res 2014;3(2):17-21.

41. Zuniga JR et al. Analgesic Safety and Efficacy of Diclofenac Sodium Softgelson Postoperative Third Molar Extraction Pain. J Oral and Maxillofac Surg 2004; 62(7): 806-15.

42. Bookman AAM, Williams KSA, Shainhouse JZ. Effect of a topical diclofenac solution for relieving symptoms of primary osteoarthritis of the knee: a randomized controlled trial. JAMC 2004;171(4):333-8.

43. Bruhlmann P, Michel B M. Topical diclofenac patch in patients with knee osteoarthritis: A randomized, double-blind, controlled clinical trial. Clinical and Experimental Rheumatology 2003;21:193-8.

44. Kotecha B, Oleary G, Bradburn J, Darowski M, Gwinnutt CL. Pain relief after tonsillectomy in adults: intramuscular diclofenac and papaveretum compared. Clinical Otolaryngology & Allied Sciences 1991;16: 345-9.

45. Power I, Chambers WA, Greer IA, Ramage D, Simon E. Platelet function after intramuscular diclofenac. Anaesthesia 1990;45:916-9.

46. Huskisson EC, Bryans R. Diclofenac sodium in the treatment of painful stiff shoulder. Current Medical Research and Opinion 1983;8(5)

47. Haynes RJ, Walker S, Kirkpatrick JNP. Topical diclofenac relieves pain from corneal rust ring. Eye 1996;10:443-6.

48. Salmann AR. The history of diclofenac. Am J Med 1986; 80(4):29-33.

49. Helfgott SM, Sandberg-Cook J, Zakim D, Nestler J. Diclofenac-Associated Hepatotoxicity. JAMA. 1990;264(20):2660-2662.

50. Karachalios GN, Fotiadou A, Chrisikos N, Karabetsos A, Kehagioglou, K. Treatment of Acute Migraine Attack With Diclofenac Sodium: A Double-Blind Study. Headache: The Journal of Head and Face Pain 1992;32:98-100.

51. Gebauer K, Brown P, Varigos G. Topical diclofenac in hyaluronan gel for the treatment of solar keratoses. Australasian Journal of Dermatology 2003;44:40-43.

52. Baert, Filip, Hart, John, Blackstone, Michael O. A Case of Diclofenac-Induced Colitis with Focal Granulomatous Change. American Journal of Gastroenterology 1995;90(10):1871-3.

53. Dunk AA, Walt RP, Jenkins WJ, Sherlock SS. Diclofenac hepatitis. BritishMedical Journal 1982;284(6329):1605-6.

54. Romano A, Pietrantonio F, Di Fonso M, Garcovich A, Chiarelli C, Venuti A, Barone C. Positivity of patch tests in cutaneous reaction to diclofenac. Allergy 1994;49:57-9.

55. Verstraeten A, Bakshi R. Diclofenac Potassium for the Treatment of Traumatic Joint Distortions: An Open Multicentre Study. J Int Med Res 1991;19(2) 165-170.

56. Hodsman NBA, Burns J, Blyth A, Kenny GNC, McArdle CS, Rotman H. The morphine sparing effects of diclofenac sodium following abdominal surgery. Anaesthesia 1987; 42:1005-8.

57. Mastrolonardo M. Topical diclofenac 3% gel plus cryotherapy for treatment of multiple and recurrent actinic keratoses. Clinical and Experimental Dermatology2009;34:33-35.

58. Sen I, Mitra S, Gombar KK. Fatal anaphylactic reaction to oral diclofenac sodium**.** Canadian Journal of Anaesthesia 2001;48: 421-421

59. Preetha JP, Karthika K, Rekha NR, Elshafie K. Formulation and evaluation of in situ ophthalmic gels of diclofenac sodium.Journal of Chemical and Pharmaceutical Research 2010;2(3):528-35

60. Jonker MJ, Bruynzeel DP. Anaphylactic reaction elicited by patch testing with diclofenac. Contact Dermatitis 2003;49:114-5.

61. AL-Waili NS. Diclofenac sodium in the treatment of primary nocturnal enuresis: double-blind crossover study. Clinical and Experimental Pharmacology and Physiology 1986;13:139-142.

62. Tiwari AK, Tomar GS, Ganguly S, Kapoor MC. Kounis syndrome resulting from anaphylaxis to diclofenac. Indian J Anaesth 2013;57:282-4.

63. Schnitzer TJ. Update on guidelines for the treatment of chronic musculoskeletal pain. Clin Rheumatol 2006;25 Suppl 1:S22-9.

64. Santos J, Alarcão J, Fareleira F, Vaz-Carneiro A, Costa J. Tapentadol for chronic musculoskeletal pain in adults. Cochrane Database Syst Rev 2015;5:CD009923.
65. Derry S, Moore RA, Rabbie R. Topical NSAIDs for chronic musculoskeletal pain in adults. Cochrane Database Syst Rev 2012;9:CD007400.
66. Dieppe P. Chronic musculoskeletal pain. BMJ 2013;346:f3146.
67. Chopra A. Disease burden of rheumatic diseases in India : COPCORD perspective. Indian J Rheumatol 2015;10:70-7.
68. Blower AL, Brooks A, Fenn GC, Hill A, Pearce MY, Morant S, et al. Emergency admissions for upper gastrointestinal disease and their relation to NSAID use. Aliment Pharmacol Ther 1997;11:283-91.
69. Moore N, Pollack C, Butkerait P. Adverse drug reactions and drug-drug interactions with over-the-counter NSAIDs. Ther Clin Risk Manag 2015;11:1061-75.
70. Gorelick PB, Weisman SM. Risk of hemorrhagic stroke with aspirin use: An update. Stroke 2005;36:1801-7.
71. McCarberg BH, Argoff CE. Topical diclofenac epolamine patch 1.3% for treatment of acute pain caused by soft tissue injury. Int J Clin Pract 2010;64:1546-53.
72. Bachalli PS, Nandakumar H, Srinath N. A comparitive study of diclofenac transdermal patch against oral diclofenac for pain control following removal of mandibular impacted third molars. J Maxillofac Oral Surg 2000;8:167-72.

73. Bhaskar H, Kapoor P, Ragini. Comparison of transdermal diclofenac patch with oral diclofenac as an analgesic modality following multiple premolar extractions in orthodontic patients: A cross over efficacy trial. Contemp Clin Dent 2000;1:158-63.
74. Banning M. Topical Diclofenac: Clinical Effectiveness and Current uses in Osteoarthritis of the Knee and Soft Tissue Injuries. Expert Opinion Pharmacotherapy 2008;9:2921-9.
75. Hsieh LF, Hong CZ, Chern SH, Chen CC. Efficacy and side effects of diclofenac patch in treatment of patients with myofascial pain syndrome of the upper trapezius. J Pain Symptom Manage 2010;39:116-25.
76. Mu R, Bao CD, Chen ZW, Zheng Y, Wang GC, Zhao DB, et al. Efficacy and safety of loxoprofen hydrogel patch versus loxoprofen tablet in patients with knee osteoarthritis: A randomized controlled non-inferiority trial. Clin Rheumatol 2016;35:165-73.
77. Uhl RL, Roberts TT, Papaliodis DN, Mulligan MT, Dubin AH. Management of chronic musculoskeletal pain. J Am Acad Orthop Surg 2014;22:101-10.
78. Rowbotham MC. What is a “clinically meaningful” reduction in pain? Pain 2001;94:131-2.
79. Brühlmann P, Michel BA. Topical diclofenac patch in patients with knee osteoarthritis: A randomized, double-blind, controlled clinical trial. Clin Exp Rheumatol 2003;21:193-8.

80. Goei Thè HS, Lund B, Distel MR, Bluhmki E. A double-blind, randomized trial to compare meloxicam 15 mg with diclofenac 100 mg in the treatment of osteoarthritis of the knee. Osteoarthritis Cartilage 1997;5:283-8.
81. Reddy PR, Rajashekar SB, Karthik US. Comparing the effectiveness of transdermal diclofenac patch and inramuscular diclofenac injecton in postoperative pain relief after inguinal hernia mesh repair: A randomised study in the department of general surgery. J Evid Based Med Heathc 2015;2:5286-92.
82. Lister BJ, Poland M, DeLapp RE. Efficacy of nabumetone versus diclofenac, naproxen, ibuprofen, and piroxicam in osteoarthritis and rheumatoid arthritis. Am J Med 1993;95:2S-9S.
83. Goyal A, Kumar S, Nagpal M, Singh I, Arora S (2011) Potential of Novel Drug Delivery Systems for Herbal Drugs. Indian Journal of pharmaceutical Research and Education 45(3): 225-235.
84. Archer HK, Pettit MS (1997) Analgesic and antiphlogistic compositions and therapeutic wrap for topical delivery.
85. Ghulaxe C, Verma R (2015) A review on transdermal drug delivery system. The Pharma Innovation Journal 4(1): 37-43.
86. Rathore B, Mahidi AA, Paul BN, Saxena PN, Das SK (2007) Indian herbal medicines: possible potent therapeutic agents for rheumatoid arthritis. Journal of Clinical Biochemistry and Nutrition. 41(1): 12-17.

87. Park YG, Ha CW, Han D, Bin S, Kim HC, et al. (2013) A prospective, randomized, double-blind, multicenter comparative study on the safety and efficacy of Celecoxib and GCSB-5,dried extracts of six herbs, for the treatment of of osteoarthritis of knee joint. J Ethnopharmacol 149(3): 816-824.
88. Sahoo BJ, Mishra AN (2013) Formulation and evaluation of transdermal patches of diclofenac. World Journal of Pharmacy and Pharmaceutical Sciences 2(6): 4965-4971.
89. Gowda DV, Rajesh N, Somashekhara CN, Siddaramaiah (2010) Development and evaluation of Aceclofenac loaded transdermal film. International Journal of Pharmtech Research 2(4): 2224-2233.
90. Patel RP, Patel G, Baria A (2009) Formulation and evaluation of transdermal patch of Aceclofenac. International Journal of Drug Delivery 1: 41-51.
91. Gaikwad AK (2013) Transdermal drug delivery system: formulation aspects and evaluation. J Pharm Sci 1(1): 1-10.
92. Santosh G, Dhaval P, Mantesh K, Ajay S, Vital V (2009) Formulation and evaluation of matrix type transdermal patches of Glibenclamide. Int J of Pharmaceutical Sciences and Drug Research 1(1): 46-50.
93. Kumar SS, Behury B, Sachinkumar P (2013) Formulation and evaluation of transdermal patch of Stavudine. J Pharm Sci 12(1): 63-69.
94. Prabhakar P, Shah S, Gundad (2011) Formulation development and investigation of Domperidone transdermal patches. Int J of Pharm Investig 1(4): 240-246.

95. Jadhav RT, Kasture PV, Gattani SG, Surana SJ (2009) Formulation and evaluation of transdermal films of diclofenac sodium. Int.J. Pharmtech Res 1(4): 1507-1511.

96. Murthy SN, Rani S, Hiremath R (2001) Formulation and evaluation of controlled release transdermal patches of theophylline-salbutamol sulphate. Indian Journal of Pharmaceutical Education and Research 27(2): 1057-1062.

97. Saxena M, Mutalik S, Reddy MS (2006) Formulation and evaluation of transdermal patches of metoclopramide hydrochloride. Indian drugs 43(9): 740-745.

98. Mali AD, Bathe R, Patil M (2015) An updated review on transdermal drug delivery systems. International Journal of Advances in Scientific Research 1(06): 244-254.

99. Darwhekar G, Jain DK, Patidar PK (2011) Formulation and evaluation of transdermal drug delivery system of Clopidogrel bisulfate. Asian Journal of Pharmacy and Life Science 1(3): 26.

100. Prajapati ST, Patel CG, Patel CN (2011) Formulation and Evaluation of transdermal Patch of repaglinide. ISRN Pharma 2: 65-78.

101. Priyanka K, Abhishek S, Aman, Pooja P, Bhawna C. Formulation and Evaluation of Transdermal Patch of Diclofenac Sodium. Glob J Pharmaceu Sci. 2018; 4(4): 555647

102. Shinde VA, Kalikar M, Jagtap S, Dakhale GN, Bankar M, Bajait CS, et al. Comparison of efficacy and safety of oral diclofenac versus transdermal diclofenac patch in chronic musculoskeletal pain: A randomized, open-label trial. J Pharmacol Pharmacother 2017;8:166-71.

103. Lu K, Wang HZ, Gao YZ, Zhu J. Development and evaluation of aceclofenac loaded lipospheres for the treatment of osteoarthritis. J Biomater Tissue Eng 2015; 5: 504-508.

104. Ahlström U, Bakshi R, Nilsson P, Wåhlander L. The analgesic efficacy of diclofenac dispersible and ibuprofen in postoperative pain after dental extraction. European journal of clinical pharmacology. 1993 Jul;44(6):587-8.

105. Bakshi R, Jacobs LD, Lehnert S, Picha B, Reuther J. A double-blind, placebo-controlled trial comparing the analgesic efficacy of two formulations of diclofenac in postoperative dental pain. Current therapeutic research. 1992 Sep 1;52(3):435-42.

106. Bakshi R, Frenkel G, Dietlein G, Meurer-Witt B, Schneider B, Sinterhauf U. A placebo-controlled comparative evaluation of diclofenac dispersible versus ibuprofen in postoperative pain after third molar surgery. The Journal of Clinical Pharmacology. 1994 Mar;34(3):225-30.

107. Chang DJ, Desjardins PJ, Chen E, Polis AB, McAvoy M, Mockoviak SH, Geba GP. Comparison of the analgesic efficacy of rofecoxib and enteric-coated diclofenac sodium in the treatment of postoperative dental pain: a randomized, placebo-controlled clinical trial. Clinical therapeutics. 2002 Apr 1;24(4):490-503.

108. Cooper SA, Cowan A, Tallarida RJ, Hargreaves K, Roszkowski M, Jamali F, Borenstein M, Lucyk D, Fielding AF, Smith B, Feng D. The Analgesic Interaction of Misoprostol with Nonsteroidal Anti-Inflammatory Drugs. American Journal of Therapeutics. 1996 Apr 1;3(4):261-7.

109. Desjardins PJ, Black PM, Daniels S, Bird SR, Fitzgerald BJ, Petruschke RA, Tershakovec A, Chang DJ. A randomized controlled study comparing rofecoxib, diclofenac sodium, and placebo in post-bunionectomy pain. Current medical research and opinion. 2004 Oct 1;20(10):1523-37.

110. Hebertson RM, Storey N. The comparative efficacy of diclofenac potassium, aspirin, and placebo in the treatment of patients with pain following gynecologic surgery. Todays Therapeutic Trends. 1995;12:33.

111. Hersh EV, Levin LM, Adamson D, Christensen S, Kiersch TA, Noveck R, Watson II G, Lyon JA. Dose-ranging analgesic study of prosorb® diclofenac potassium in postsurgical dental pain. Clinical therapeutics. 2004 Aug 1;26(8):1215-27.

112. Hofele CM, Gyenes V, Daems LN, Stypula-Ciuba B, Wagener H, Siegel J, Edson K, STUDY GROUP. Efficacy and tolerability of diclofenac potassium sachets in acute postoperative dental pain: a placebo-controlled, randomised, comparative study vs. diclofenac potassium tablets. International journal of clinical practice. 2006 Mar;60(3):300-7.

113. Kubitzek F, Ziegler G, Gold MS, Liu JM, Ionescu E. Analgesic efficacy of low-dose diclofenac versus paracetamol and placebo in postoperative dental pain. Journal of orofacial pain. 2003 Jul 1;17(3).

114. Nelson SL, Brahim JS, Korn SH, Greene SS, Suchower LJ. Comparison of single-dose ibuprofen lysine, acetylsalicylic acid, and placebo for moderate-to-severe postoperative dental pain. Clinical therapeutics. 1994 May 1;16(3):458-65.

115. Olson NZ, Sunshine A, Zighelboim I, DeCastro A. Onset and duration of analgesia of diclofenac potassium in the treatment of postepisiotomy pain. American journal of therapeutics. 1997 Jul 1;4(7-8):239-46.

116. Torres LM, Cabrera J, Martinez J, Calderón E, Fernández S, Chaves J. The specific COX-2 inhibitor valdecoxib provides effective analgesia after inguinal hernia surgery. Revista Espanola de Anestesiologia y Reanimacion. 2004 Dec 1;51(10):576-82.

117. Zuniga JR, Phillips CL, Shugars D, Lyon JA, Peroutka SJ, Swarbrick J, Bon C. Analgesic safety and efficacy of diclofenac sodium softgels on postoperative third molar extraction pain. Journal of oral and maxillofacial surgery. 2004 Jul 1;62(7):806-15.

118. Apaydin A, Ozyuvaci H, Ordulu M, Disci R. Postoperative pain relief by single dose diclofenac kalium and etodolac. A comparative clinical study. Ağrı (Algoloji) Derneği'nin Yayın organıdır= The Journal of the Turkish Society of Algology. 1994;6(4):28-34.

119. Carlos DE. COMPARATIVE-STUDY OF THE EFFICACY OF DICLOFENAC NA, MEPERIDINE HCL AND NALBUPHINE HCL IN POSTOPERATIVE ANALGESIA. Philippine Journal of Internal Medicine. 1984 Jan 1;22(1):51-5.

120. Dorfmann H. Controlled therapeutic trial of diclofenac in meniscectomy under arthroscopy. Revue du Rhumatisme et des Maladies Osteo-articulaires. 1991 Jan 1;58(1):59-61.

121. El-Tanany H, Boghdady W. A double blind comparative study of Diclofenac-K and Glafenine in the management of acute dental pain. Cairo Dental Journal. 1993;9(2):117-20.

122. Fineschi G, Tamburrelli FC, Francucci BM, Pisati R. Oral diclofenac dispersible provides a faster onset of analgesia than intramuscular ketorolac in the treatment of postoperative pain. Clinical drug investigation. 1997 Jan;13(1):1-7.

123. Frezza R, Bolognesi P, Bernardi F. Comparison of the action of 3 non-steroidal anti-inflammatory agents in the control of post-operative pain. Effectiveness of NSAID against pain. Attualita dentale. 1985 Nov 24;1(30):40-2.

124. Canaro Garcia D, Espinosa JD, Marti ML. Analgesic efficacy of both lisine clonixinate and diclofenac for the postsurgical pain during ambulatory surgery. Prensa Medica Argentina. 1997;84:1061-5.

125. Henrikson PA, PA H, LA W. Absorption and effect of diclofenac-sodium after surgical removal of a lower wisdom tooth. 1982; 31(1):20–6.

126. Hultin M, Olander KJ. A clinical trial of the analgesic properties of Voltaren (diclofenac sodium). Scandinavian Journal of Rheumatology. 1978 Jan 1;7(sup22):42-5.

127. Iqbal KM, Gour KB. Assessment of post operative analgesia: A comparative study of Pethidine and Diclofenac sodium. Journal of Bangladesh College of Physicians and Surgeons. 1986;4(1):1-7.

128. Iwabuchi T, Soma S. Use of Voltaren for relief of post-extraction pain. Shikai Tenbo - Dental outlook. 1980 Feb 1;55(2):367-70.

129. De Joubert JJ. An assessment of the efficacy and tolerability of Voltaren in the treatment of inflammation after extraction of teeth. The Journal of the Dental Association of South Africa= Die Tydskrif van die Tandheelkundige Vereniging van Suid-Afrika. 1977 Oct;32(10):581-3.

130. Kittaka S, Aizawa H, Tokue I, Suge Y. Efficacy of GP-45,840 on after-pains. Medical Consultation and New Remedies. 1972;9:1123-34.

131. Mayer M, Weiss P. Antiphlogistic and analgesic effect of diclofenac sodium after maxillofacial interventions in a double-blind trial. Deutsche Zahnarztliche Zeitschrift. 1980 May 1;35(5):559-63.

132. Vigneron JR, Thys R. Study of the anti-inflammatory and analgesic actions of diclofenac in traumatology and orthopedic surgery. Revue Medicale de Liege. 1977 Jan 1;32(1):10-4.

133. Zhang SL, Meng ZY, Xu JH, Shou BQ. Analgesic efficacy of diclofenac potassium in dental pain trial. Journal of Medical Postgraduate. 2000;13:24-5.

134. Wuolijoki E, Oikarinen VJ, Ylipaavalniemi P, Hampf G, Tolvanen M. Effective postoperative pain control by preoperative injection of diclofenac. European journal of clinical pharmacology. 1987 May;32(3):249-52.

135. Barden J, Edwards J, Moore RA, McQuay HJ. Single dose oral diclofenac for postoperative pain. The Cochrane database of systematic reviews. 2004 Jan 1(2):CD004768.

136. Collins SL, Moore RA, McQuay HJ, Wiffen PJ. Oral ibuprofen and diclofenac in post-operative pain: a quantitative systematic review. European Journal of Pain. 1998 Jan 1;2(4):285-91.

137. Riess W, Stierlin H, Degen P, Faigle JW, Gerardin A, Moppert J, Sallmann A, Schmid K, Schweizer A, Sulc M, Theobald W. Pharmacokinetics and metabolism of the anti-inflammatory agent Voltaren. Scandinavian Journal of Rheumatology. 1978 Jan 1;7(sup22):17-29.

138. Hinz B, Rau T, Auge D, Werner U, Ramer R, Rietbrock S, Brune K. Aceclofenac spares cyclooxygenase 1 as a result of limited but sustained biotransformation to diclofenac. Clinical Pharmacology & Therapeutics. 2003 Sep;74(3):222-35.

139. Brundig P, Börner RH, Haerting R, Janitzky V, Schlichter A. Glycose aminoglycane excretion and concentration in the urine of patients with frequently recurrent calcium-oxalate lithiasis prior to and following Diclofenac-Na therapy. Urological Research. 1990 Feb;18(1):21-4.

140. Herculano RD, Silva CP, Ereno C, Guimaraes SA, Kinoshita A, Graeff CF. Natural rubber latex used as drug delivery system in guided bone regeneration (GBR). Materials Research. 2009 Jun;12(2):253-6.

141. Sader SL, Coutinho Netto J, Barbieri Neto J, MAZZETTO SA, ALVES JR P, Vanni JC, Sader AA. Substituição parcial do pericárdio de cães por membrana de látex natural. Brazilian Journal of Cardiovascular Surgery. 2000;15:338-44.

142. Zhang Y, Cun D, Kong X, Fang L. Design and evaluation of a novel transdermal patch containing diclofenac and teriflunomide for rheumatoid arthritis therapy. Asian Journal of pharmaceutical sciences. 2014 Oct 1;9(5):251-9.

143. Kendall MJ, Thornhill DP, Willis J. Factors affecting the pharmacokinetics of diclofenac sodium (Voltarol). Rheumatology and Rehabilitation. 1979 Jan 1:38-46.

144. Aielo PB, Borges FA, Romeira KM, Miranda MC, Arruda LB, L Filho PN, Drago BD, Herculano RD. Evaluation of sodium diclofenac release using natural rubber latex as carrier. Materials Research. 2014;17:146-52.

145. Ray SD, Ghosal K, Ghosal I, Ghosh D. Alginate/hydrophobic HPMC (60L) particulate systems: new matrix for controlled release of diclofenac potassium. Latin American Journal of Pharmacy. 2011;30.

146. Wang LY, Gu YH, Zhou QZ, Ma GH, Wan YH, Su ZG. Preparation and characterization of uniform-sized chitosan microspheres containing insulin by membrane emulsification and a two-step solidification process. Colloids and Surfaces B: Biointerfaces. 2006 Jul 1;50(2):126-35.

147. Dias Murbach H, Jaques Ogawa G, Azevedo Borges F, Romeiro Miranda MC, Lopes R, Roberto de Barros N, Guedes Mazalli AV, Gonçalves da Silva R, Ferreira Cinman JL, de Camargo Drago B, Donizetti Herculano R. Ciprofloxacin release using natural rubber latex membranes as carrier. International Journal of Biomaterials. 2014 Dec 22;2014.

148. Semalty A, Semalty M, Singh D, Rawat MS. Development and physicochemical evaluation of pharmacosomes of diclofenac. Acta Pharmaceutica. 2009 Sep 1;59(3):335-44.

149. Maswadeh H, Abdulhalim A, Demetzos C. Improvement of encapsulation efficiency of diclofenac sodium in to uncoated and chitosan-coated liposomes. Indian journal of pharmaceutical sciences. 2004;66(5):607.

150. Langer R, Folkman J. Polymers for the sustained release of proteins and other macromolecules. Nature. 1976 Oct;263(5580):797-800.

151. Kumar A, Mohan L, Shinde P, Chang HY, Nagai M, Santra TS. Mechanoporation: Toward single cell approaches. InHandbook of Single-Cell Technologies 2021 Oct 29 (pp. 31-59). Singapore: Springer Singapore.

ANNEXURE

BABU BANARASI DAS COLLEGE OF DENTAL SCIENCES
(FACULTY OF BBD UNIVERSITY), LUCKNOW

INSTITUTIONAL RESEARCH COMMITTEE APPROVAL

The project titled **"Comparison of Transdermal Diclofenac Patch with Oral Diclofenac as an Analgesic Modality in Management of Post Operative Pain"** submitted by **Dr Dube Yati Harikishore** Post graduate student from the **Department of Oral & Maxillofacial Surgery** as part of MDS Curriculum for the academic year 2019-2022 with the accompanying proforma was reviewed by the Institutional Research Committee present on **19th December 2019** at BBDCODS.

The Committee has granted approval on the scientific content of the project. The proposal may now be reviewed by the Institutional Ethics Committee for granting ethical approval.

Prof. Vandana A Pant
Co-Chairperson

Prof. B. Rajkumar
Chairperson

Babu Banarasi Das University
Babu Banarasi Das College of Dental Sciences,
BBD City, Faizabad Road, Lucknow – 226028 (INDIA)

Dr. Lakshmi Bala
Professor and Head Biochemistry and
Member-Secretary, Institutional Ethics Committee

Communication of the Decision of the VIII[th] Institutional Ethics Sub-Committee

IEC Code: 30 **BBDCODS/03/2020**

Title of the Project: Comparison of Transdermal Diclofenac Patch with Oral Diclofenac as an Analgesic Modality in Management of Post Operative Pain.

Principal Investigator: Dr. Dube Yati Harikishore **Department:** Oral & Maxillofacial Surgery

Name and Address of the Institution: BBD College of Dental Sciences Lucknow.

Type of Submission: New, MDS Project Protocol

Dear Dr. Dube Yati Harikishore,

The Institutional Ethics Sub-Committee meeting comprising following four members was held on 18[th] March, 2020.

1.	Dr. Lakshmi Bala Member Secretary	Prof. and Head, Department of Biochemistry, BBDCODS, Lucknow
2.	Dr. Amrit Tandan Member	Prof. & Head, Department of Prosthodontics and Crown & Bridge, BBDCODS, Lucknow
3.	Dr. Sahana S. Member	Reader, Department of Public Health Dentistry, BBDCODS, Lucknow
4.	Dr. Sumalatha M.N. Member	Reader, Department of Oral Medicine & Radiology, BBDCODS, Lucknow

The committee reviewed and discussed your submitted documents of the current MDS Project Protocol in the meeting.

The comments were communicated to PI thereafter it was revised.

Decisions: The committee approved the above protocol from ethics point of view.

Forwarded by:

Lakshmi Bala 18/03/20

(Dr. Lakshmi Bala)
Member-Secretary
IEC

Member-Secretary
Institutional Ethic Committee
BBD College of Dental Sciences
BBD University
Faizabad Road, Lucknow-226028

(Dr. B. Rajkumar)
Principal
BBDCODS

PRINCIPAL
Babu Banarasi Das College of Dental Sciences
(Babu Banarasi Das University)
BBD City, Faizabad Road, Lucknow-226028

ANNEXURE

Statistical formula used:

1. **Mean:**

   The individual observations were first added together and then divided by the number of observation. The operation of adding together or summation is denoted by the sign Σ.

   The individual observation is denoted by a sign X, number of observation is denoted by n, and the mean by $\bar{X}$

   $$\bar{X} = \Sigma X/\text{No. of observation (n)}$$

2. **Standard Deviation**:

   It is denoted by a greek letter σ.

   If the sample is >30 then-

   $$\sigma=\sqrt{\sum\left(\frac{x-x}{n}\right)^2}$$

   If sample is < 30 then-

   $$\sigma=\sqrt{\sum\left(\frac{x-x}{n-1}\right)^2}$$

3. **Student t – test**:

   A t-test is most commonly applied when the test statistic would follow a normal distribution if the value of the scaling term in the test statistic were known. When the scaling term is unknown and is replaced by an estimate based on the data, the test statistics (under certain condition) follow a student t distribution. The t- test

can be used for example, to determine if two sets of data are significantly different from each other.

4. **Level of significance**:

$p > 0.05$	Not significant
$p < 0.05$	Significant
$p < 0.01$	Highly significant
$p < 0.001$	Very highly significant

Babu Banarasi Das College of Dental Sciences
(Babu Banarasi Das University)
BBD City, Faizabad Road, Lucknow – 227105 (INDIA)

Consent Form (English)

Title of the Study ……..

Study Number……..
Subject's Full Name…….
Date of Birth/Age ……
Address of the Subject…….
Phone no. and e-mail address……
Qualification ……
Occupation: Student / Self Employed / Service / Housewife /Other
(Please tick as appropriate)
Annual income of the Subject……
Name and of the nominees(s) and his relation to the subject.....(For the purpose of compensation in case of trial related death).

1. I confirm that I have read and understood the Participant Information Document dated……..for the above study and have had the opportunity to ask questions. **OR** I have beenexplained the nature of the study by the Investigator and had the opportunity to ask questions.
2. I understand that my participation in the study is voluntary and given with free will without any duress and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the project, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided sucha use is only for scientific purpose(s).
5. I permit the use of stored sample (tooth/tissue/blood) for future research. **Yes [ ] No [ ]**
   Not Applicable [ ]
6. I agree to participate in the above study. I have been explained about the complications and side effects, if any, and have fully understood them. I have also read and understood the participant/volunteer's Information document given to me.

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:……..
Signatory's Name……. Date …….
Signature of the Investigator…… Date……..
Study Investigator's Name..... Date……..
Signature of the witness…… Date……..
Name of the witness……
Received a signed copy of the PID and duly filled consent form
Signature/thumb impression of the subject or legally Date……

Acceptable representative

Babu Banarasi Das College of Dental Sciences

(Babu Banarasi Das University)

BBD City, Faizabad Road, Lucknow – 227105 (INDIA)

सहमति पत्र

अध्ययन शीर्षक.....

अध्ययन संख्या.....

प्रतिभागी के पूर्ण नाम.....

जन्म तिथि / आयु.....

प्रतिभागी का पता .....

फोन नं. और ई-मेल पता .....

योग्यता .....

व्यवसाय: छात्र / स्व कार्यरत / सेवा / ग्रहिणी .....

अन्य (उचित रुप मे टिक करें) .....

प्रतिभागी की वार्षिक आय .....

प्रत्याशीयो के नाम और प्रतिभागी से संबंध...(परीक्षण से संबंधित मौत के मामले मे मुआवजे के प्रयोजन के लिए)

1. मेरी पुष्टि है कि मैने अध्ययन हेतु सुचना पत्र दिनांक ..... को पढ व समझ लिया तथा मुझे प्रश्न पुछने या मुझे अध्ययन अन्वेषक ने सभी तथ्यों को समझा दिया है तथा मुझे प्रश्न पुछने के समान अवसर प्रदान किए गये।

2. मैंने यहाँ समझ लिया कि अध्ययन में मेरी भागीदारी पूर्णत: स्वैच्छिक है और किसी भी दबाव के बिना स्वतंत्र इच्छा के साथ दिया है किसी भी समय किसी भी कारण के बिना , मेरे इलाज या कानूनी अधिकारो को प्रभावित किए बिना , अध्ययन में भाग न लेने के लिए स्वतंत्र हुँ ।

3. मैंने यह समझ लिया है कि अध्ययन के प्रायोजक , प्रायोजक की तरफ से काम करने वाले लोग, आचार समिति और नियामक अधिकारियों को मेरे स्वास्थ्य रिकार्ड को वर्तमान अध्ययन या आगे के अध्ययन के सन्दर्भ देखने के लिए मेरी अनुमति की जरूरत नही है, चाहे मैने इस अध्ययन से नाम वापस ले लिया है। हॉलाकि मै यह समझता हुँ कि मेरी पहचान को किसी भी तीसरे पक्ष या प्रकाशित माध्यम में नही दी जायेगी।

4. मै इससे सहमत हूँ कि कोई भी डेटा या परिणाम जो इस अध्ययन से प्राप्त होता है उसका वैज्ञानिक उद्देश्य (ओं) के उपयोग के लिए मेरी तरफ से कोई प्रतिबंध नही है।

5. भविष्य के अनुसंधान के लिए भंडारित नमूना (ऊतक/रक्त) पर अध्ययन के लिए अपनी सहमति देता हुँ।

हॉ [ ] नही [ ] अनउपयुक्त [ ]

6. मै परीक्षण की अनुमति देता हुँ। मुझे इसके द्वारा यदि कोई परेशानी होती है, इसके बारे में जानकारी दे दी गई है। मैने रोगी जानकारी सूचना पत्र को पढ तथा समझ लिया है।

प्रतिभागी / कानूनी तौर पर स्वीकार्य प्रतिनिधि का हस्ताक्षर (या अंगूठे का निशान.....

हस्ताक्षरकर्ता का नाम..... दिनांक .....अन्वेषक के

हस्ताक्षर ..... दिनांक .....

अध्ययन अन्वेषक का नाम .....

गवाह के हस्ताक्षर ..... दिनांक .....गवाह के

नाम .....

मैनें पीआईडी और विधिवत भरे सहमति फार्म का एक हस्ताक्षर की नकल प्राप्त की.

प्रतिभागी कानूनी तौर पर प्रतिनिधि का हस्ताक्षर/ अंगूठे का निशान ..... दिनांक.....

Babu Banarasi Das College of Dental Sciences

(Babu Banarasi Das University)

BBD City, Faizabad Road, Lucknow – 227105 (INDIA)

Participant Information Document (PID)

1. **Study Title**

To compare the efficacy of transdermal Diclofenac patch with oral Diclofenac tablet in management of postoperative pain.

2. **Invitation Paragraph**

You are being invited to take part in a research study, therefore, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information. It is upto you to decide whether or not you wish to take part.

3. **What is the purpose of the study?**

To compare the efficacy of transdermal Diclofenac patch with oral Diclofenac tablet in management of postoperative pain.

4. **Why have you been chosen?**

The study comprises of 100 participants and you have been chosen for this study as you have fulfilled the desired inclusion criteria.

5. **Why would you take part?**

Your participation in the research is entirely voluntary. If you do, you will be given this information sheet and will be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time without giving a reason.

6. **What will happen to you if you take part?**

You will be involved in my study for 3 consecutive days or till the pain relieves (whichever is earlier). Reporting of pain has to be done every 3hrs, 6hrs, 12hrs and 24hrs for 3 consecutive days post-operatively. Post the required procedure, a transdermal patch will be applied on the right arm which has to be changed after 24hrs for the transdermal patch group and only oral form of medication will have to be consumed for the participants

involved in the tablet group. Reporting of pain has to be done by participants of each group. Any adverse effects due to transdermal patch or medication has to be reported immediately. The study is being conducted to relieve the pain post-operatively without any undue side effects.

7. What do I have to do?

You can have your regular lifestyle and you will have to follow the post-operative instructions given post procedure like avoiding spitting, eating soft food, maintaining proper oral hygiene, warm saline rinses post 24 hours of the minor procedure, following prescribed medication, in case of patch application changing the patch after 24hours.

8. What is the procedure that is being tested?

It's a post-operative procedure done by either consumption of medication or application of the patch (according to the group the patient is allocated to) to reduce pain post-operatively.

9. What are the interventions for the study?

There are no interventions, risk related to the study. There is benefit to the volunteer as he/she will be relieved of pain post procedure without any undue side effects.

10. What are the side effects of taking part?

Side effects are rare if at all like (for patch group) : Redness, urticaria at the site of application

(for tablet group) : Gastric irritation

If at all anything undue is experienced, report it to the undersigned immediately.

11. What are the possible disadvantages and risks of taking part?

There are no disadvantages of the study other than the side effects associated with patch or the tablet which is rare and already mentioned above.

12. What are the possible benefits of taking part?

As medication which is given post-operatively can cause gastric irritation, patch applied can relieve the same by avoiding it and due to non-intrusive nature, painless system of drug delivery with extended duration of action, easy appliaction, incessant pain relief can be achieved.

13. What if new information becomes available?

If additional information becomes available during the course of the research, you will be told about it and you are free to discuss it with your researcher and decide accordingly.

14. What happens when the research study stops?

The study spans over a period of 3 days only. If at all the study is discontinued before the stipulated time due to unavoidable circumstances, the same would be communicated and discussed with you accordingly.

15. What if something goes wrong?

If any adverse event occurs or something goes wrong during the study, the complaints will be handled by the competent person and IEC. The cost will be beared by the person undertaking the study.

16. Will my taking part in this study be kept confidential?

Yes, it will be kept confidential. All information collected about you during the course of the research will be kept strictly confidential.

17. What will happen to the results of the research study?

The result of the study will be published in indexed journal. Your identity will be kept confidential in case of any publication/report.

18. Who is organizing the research?

This research study is organized by the candidate and Department of Oral and Maxillofacial Surgery of Babu Banarasi Das College of Dental Sciences, Lucknow.

19. Will the results of the study be made available after study is over?

Yes, only the data obtained will be published.

20. Who has reviewed the study?

The study has been reviewed by the Head of the Department and IEC of the institution.

Contact for further information

Dr. Yati Dube
Department of Oral and Maxillofacial Surgery
BBDCODS, Lucknow
yatidube01@gmail.com

Dr. Laxmi Bala
Secretary,
Ethics Committee
BBDCODS, Lucknow
bbdcods.iec@gmail.com

Signature of Principal Investigator…….

Name of Principal Investigator ……

Date……..

ANNEXURE – 7

बाबू बनारसी दास कॉलेज ऑफ डेंटल साइंसेज

(बाबू बनारसी दास यूनिवर्सिटी)

बीबीडी सिटी, फैजाबाद रोड, लखनऊ - 227105 (भारत)

प्रतिभागी सूचना दस्तावेज (पीआईडी)

1. अध्ययन शीर्षक

पोस्टऑपरेटिव दर्द के प्रबंधन में मौखिक डिक्लोफेनाक टैबलेट के साथ ट्रांसडर्मल डिक्लोफेनाक पैच की प्रभावकारिता की तुलना करना।

2. आमंत्रण पैराग्राफ

आपको एक शोध अध्ययन में भाग लेने के लिए आमंत्रित किया जा रहा है, इसलिए आपके लिए यह समझना महत्वपूर्ण है कि शोध क्यों किया जा रहा है और इसमें क्या शामिल होगा। कृपया निम्नलिखित जानकारी को ध्यान से पढ़ने के लिए समय निकालें। हमसे पूछें कि क्या कुछ ऐसा है जो स्पष्ट नहीं है या यदि आप अधिक जानकारी चाहते हैं। यह आपको तय करना है कि आप भाग लेना चाहते हैं या नहीं।

3. अध्ययन का उद्देश्य क्या है?

पोस्टऑपरेटिव दर्द के प्रबंधन में मौखिक डिक्लोफेनाक टैबलेट के साथ ट्रांसडर्मल डिक्लोफेनाक पैच की प्रभावकारिता की तुलना करना।

4. आपको क्यों चुना गया है?

अध्ययन में 100 प्रतिभागी शामिल हैं और आपको इस अध्ययन के लिए चुना गया है क्योंकि आपने वांछित समावेशन मानदंड को पूरा किया है।

5. आप क्यों भाग लेंगे?

शोध में आपकी भागीदारी पूरी तरह से स्वैच्छिक है। यदि आप ऐसा करते हैं, तो आपको यह सूचना पत्रक दिया जाएगा और सहमति प्रपत्र पर हस्ताक्षर करने के लिए कहा जाएगा। यदि आप भाग लेने का निर्णय लेते हैं तब भी आप बिना कारण बताए किसी भी समय वापस लेने के लिए स्वतंत्र हैं।

6. यदि आप भाग लेते हैं तो आपका क्या होगा?

आप लगातार 3 दिनों तक या दर्द से राहत मिलने तक (जो भी पहले हो) मेरे अध्ययन में शामिल रहेंगे। ऑपरेशन के बाद लगातार 3 दिनों तक हर 3 घंटे, 6 घंटे, 12 घंटे और 24 घंटे में दर्द की रिपोर्टिंग करनी होती है। आवश्यक प्रक्रिया के बाद, दाहिने हाथ पर एक ट्रांसडर्मल पैच लगाया जाएगा जिसे ट्रांसडर्मल पैच समूह के लिए 24 घंटे के बाद बदलना होगा और टैबलेट समूह में शामिल प्रतिभागियों के लिए केवल मौखिक रूप से दवा का सेवन करना होगा। दर्द की रिपोर्टिंग प्रत्येक समूह के प्रतिभागियों द्वारा की जानी है। ट्रांसडर्मल पैच या दवा के कारण किसी भी प्रतिकूल प्रभाव की तुरंत सूचना दी जानी चाहिए। बिना किसी अनुचित दुष्प्रभाव के ऑपरेशन के बाद दर्द से राहत पाने के लिए अध्ययन किया जा रहा है।

7. मुझे क्या करना होगा?

आप अपनी नियमित जीवन शैली रख सकते हैं और आपको ऑपरेशन के बाद दिए गए निर्देशों का पालन करना होगा जैसे कि थूकने से बचना, नरम भोजन करना, उचित मौखिक स्वच्छता बनाए रखना, मामूली प्रक्रिया के 24 घंटे बाद गर्म नमकीन कुल्ला, निर्धारित दवा का पालन करना, मामले में 24 घंटे के बाद पैच बदलने के लिए पैच आवेदन।

8. किस प्रक्रिया का परीक्षण किया जा रहा है?

यह ऑपरेशन के बाद दर्द को कम करने के लिए या तो दवा के सेवन या पैच के आवेदन (जिस समूह को रोगी को आवंटित किया गया है) के अनुसार किया जाता है।

9. अध्ययन के लिए क्या हस्तक्षेप हैं?

अध्ययन से संबंधित कोई हस्तक्षेप, जोखिम नहीं है। स्वयंसेवक को लाभ होता है क्योंकि वह बिना किसी अनुचित दुष्प्रभाव के प्रक्रिया के बाद दर्द से मुक्त हो जाएगा।

10. भाग लेने के दुष्प्रभाव क्या हैं?

साइड इफेक्ट दुर्लभ हैं यदि बिल्कुल (पैच समूह के लिए): आवेदन की साइट पर लालिमा, पित्ती

(टैबलेट समूह के लिए): गैस्ट्रिक जलन

यदि किसी भी प्रकार का अनुचित अनुभव होता है, तो तत्काल अधोहस्ताक्षरी को इसकी सूचना दें।

11. भाग लेने के संभावित नुकसान और जोखिम क्या हैं?

पैच या टैबलेट से जुड़े साइड इफेक्ट्स के अलावा अध्ययन के कोई नुकसान नहीं हैं जो दुर्लभ है और पहले ही ऊपर उल्लेख किया गया है।

12. भाग लेने के संभावित लाभ क्या हैं?

चूंकि दवा जो पोस्ट-ऑपरेटिव रूप से दी जाती है, गैस्ट्रिक जलन पैदा कर सकती है, पैच लगाने से इसे टालकर राहत मिल सकती है और गैर-घुसपैठ प्रकृति के कारण, विस्तारित अवधि की कार्रवाई के साथ दवा वितरण की दर्द रहित प्रणाली, आसान उपयोग, लगातार दर्द से राहत प्राप्त की जा सकती है।

13. क्या होगा यदि नई जानकारी उपलब्ध हो जाती है?

यदि शोध के दौरान अतिरिक्त जानकारी उपलब्ध हो जाती है, तो आपको इसके बारे में बताया जाएगा और आप अपने शोधकर्ता के साथ इस पर चर्चा करने और उसके अनुसार निर्णय लेने के लिए स्वतंत्र हैं।

14. जब शोध अध्ययन बंद हो जाता है तो क्या होता है?

अध्ययन केवल 3 दिनों की अवधि में फैला है। यदि अपरिहार्य परिस्थितियों के कारण निर्धारित समय से पहले अध्ययन बंद कर दिया जाता है, तो उसी के अनुसार आपको सूचित और चर्चा की जाएगी।

15. अगर कुछ गलत हो जाए तो क्या होगा?

यदि अध्ययन के दौरान कोई प्रतिकूल घटना होती है या कुछ गलत हो जाता है, तो शिकायतों को सक्षम व्यक्ति और आईईसी द्वारा नियंत्रित किया जाएगा। इसका खर्च अध्ययन करने वाले व्यक्ति द्वारा वहन किया जाएगा।

16. क्या इस अध्ययन में मेरे भाग लेने को गोपनीय रखा जाएगा?

हां, इसे गोपनीय रखा जाएगा। शोध के दौरान आपके बारे में एकत्र की गई सभी सूचनाओं को पूरी तरह गोपनीय रखा जाएगा।

17. शोध अध्ययन के परिणामों का क्या होगा?

अध्ययन का परिणाम अनुक्रमित जर्नल में प्रकाशित किया जाएगा। किसी प्रकाशन/रिपोर्ट के मामले में आपकी पहचान गोपनीय रखी जाएगी।

18. शोध का आयोजन कौन कर रहा है?

यह शोध अध्ययन बाबू बनारसी दास कॉलेज ऑफ डेंटल साइंसेज, लखनऊ के उम्मीदवार और मौखिक और मैक्सिलोफेशियल सर्जरी विभाग द्वारा आयोजित किया जाता है।

19. क्या अध्ययन समाप्त होने के बाद अध्ययन के परिणाम उपलब्ध कराए जाएंगे?

हां, केवल प्राप्त डेटा प्रकाशित किया जाएगा।

20. अध्ययन की समीक्षा किसने की है?

संस्थान के विभागाध्यक्ष और आईईसी द्वारा अध्ययन की समीक्षा की गई है।

अधिक जानकारी के लिए संपर्क करें

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प्रधान अन्वेषक के हस्ताक्षर ……

प्रधान अन्वेषक का नाम …….

तारीख ……..

CASE SHEET

OPD No. :
Date :

Name : Age :
Sex :

Occupation : Marital Status :

Address :

Contact No. :

Chief Complaint :

History of present illness :

Past Medical History :

Drug allergy :

Past Dental History :

Family History :

Personal History :

- Oral Hygiene habit
- Abusive habit
- Parafunctional habit
- Dietary habit

General Physical Examination :

- Gait, Built, Posture
- Nourishment, Mental state
- Pallor, Icterus, Cyanosis, Clubbing, Edema
- Menstruation

Vital Signs :

- Blood pressure
- Pulse
- Temperature
- Respiratory Rate

Extraoral Examination :

- Facial Symmetry
- Lymph Node
- TMJ
- Muscles of mastication
- Mouth opening
- Other findings

Intraoral Examination :

- Hard Tissue Examination
  - Missing, Filled, Fracture
  - Root stump
  - Superficial / Moderate / Deep decayed with pulpal involvement
  - Tender on Percussion
  - Mobility
  - Attrition, Abrasion, Erosion
  - Occlusion

- Soft Tissue Examination
  - Lips
  - Labial mucosa
  - Buccal mucosa
  - Vestibule
  - Tongue
  - Floor of the mouth
  - Hard and soft palate
  - Faucial pillars

  - Gingival and Periodontal status
- Colour, Contour, Consistency, Surface texture

- Recession, Bleeding on probing, Pocket

  - Salivary duct orifices

Local Examination :

Soft tissue - Hard tissue -

Provisional Diagnosis :

Differential Diagnosis :

Investigations and Reports :

- IOPA radiograph :
  - Crown, Root, Alveolar crest level, Lamina Dura, PDL space
  - Periapical changes, other pathological changes
  - Anatomical landmarks

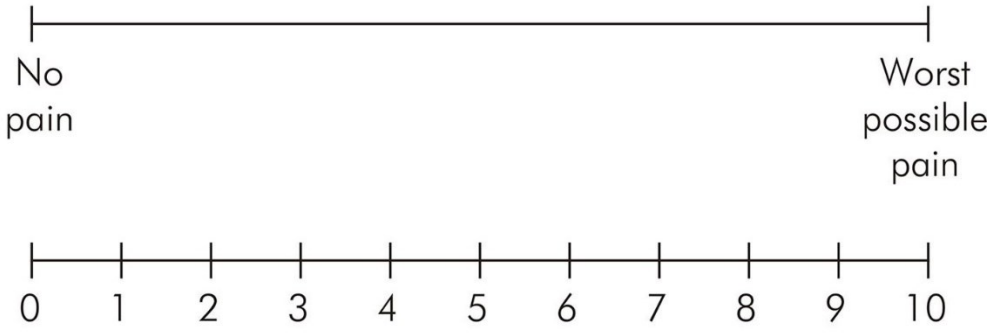
- OPG

Final Diagnosis :

Treatment Plan :

Post-operative pain evaluation :

- **VISUAL ANALOG SCALE**

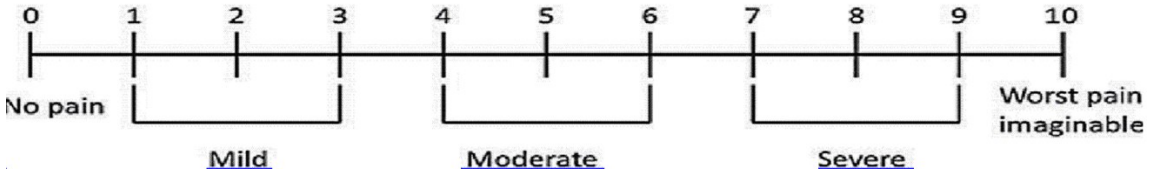


	3hrs	6hrs	12hrs	24hrs
Day 1				
Day 2				
Day 3				

- **VERBAL DESCRIPTIVE SCALE**

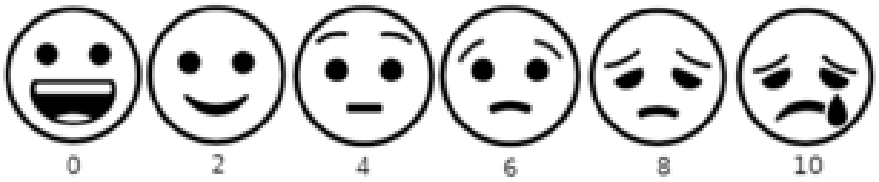
	3hrs	6hrs	12hrs	24hrs
Day 1				
Day 2				
Day 3				

- **NUMERICAL RATING PAIN SCALE**



	3hrs	6hrs	12hrs	24hrs
Day 1				
Day 2				
Day 3				

- **WONG BAKER FACES PAIN SCALE**

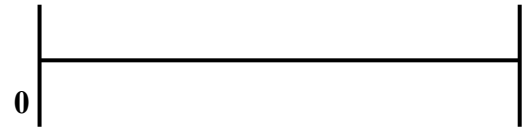


0-No Hurt 2-Hurts little 4-Hurts more 6-Hurts even more 8-Hurts whole lot 10-Hurts worst

❖ **PAIN QUESTIONNAIRE AND DRUG ADVERSE EFFECT QUESTIONNAIRE**

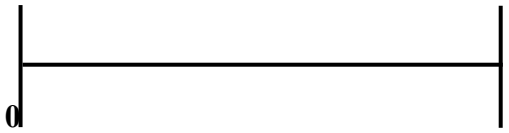
Pain questionnaire :

- At its worst, how would you rate your pain during the past 24hrs ?



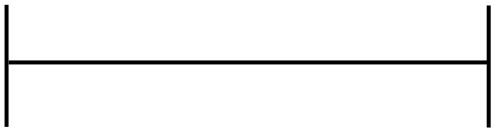
No pain Most intense pain imaginable

- On an average, how intense was your pain in the past 24hrs ?



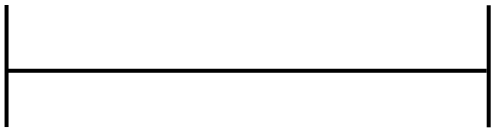
No pain Most intense pain imaginable

- How much did your pain interfere with your routine activities in the past 24hrs ?



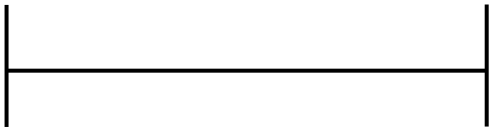
Not at all Unable to carry out daily activities

- Rate your dental status as of today ?



Worst dental health Best possible dental health

- Overall health status as of today ?



Worst possible health Best possible health

Drug adverse effect questionnaire :

- How would you say your health is ?
  Excellent☐ Very good☐ Good☐ Fair☐ Poor☐

- In the past 24 hours, have you felt like vomiting or have vomited ?
  Yes, I have vomited ☐ Yes, I felt like vomiting☐
  No, not at all ☐
- Have you felt like burning sensation in your stomach or uneasy feeling in your stomach in the past 24 hours ?
  Yes, a lot☐ Yes, a little☐ No, not at all☐

- Have you been feeling burning sensation / pain over chest for the past 24 hours ?
  All of the time ☐ Most of the time☐ Some time ☐
  None ☐

- In the past 24 hours have you felt any of the following symptoms ?
  Dizziness ☐ Headache ☐ Vertigo☐ Drowsiness ☐
  Impaired concentration ☐

- Are you having any of the following skin conditions around the region of the patch or anywhere else in your body, since past 24 hours ?

  Rash☐ Itching☐ Skin blisters☐ Reddish swelling☐ Redness ☐

Curiginal

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