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Efficacy Of Buprenorphine Transdermal Patch For Postoperative Analgesia In Arthroscopic Knee Surgeries

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Abstract

Background and Aims: Although no pain control following knee arthroscopic surgeries has attained gold standard, it is clear that patients should have optimum pain control post operatively after knee arthroscopy and arthroscopic surgeries for enhanced satisfaction and function. We conducted this study to evaluate the efficacy of buprenorphine transdermal patch on analgesic requirement in postoperative period after knee arthroscopic surgeries.

Material and Methods: Following institutional ethical committee approval and written informed consent, a prospective study was conducted in 60 patients of either gender belonging to ASA1 or ASA2 status, requiring knee arthroscopic surgeries. 60 patients were randomly divided into two groups of 30 each. Group A will receive transdermal buprenorphine patch and Group B will receive a placebo transdermal patch 12 hours before knee arthroscopic surgeries were done under spinal blockade. Intravenous opioid analgesics were avoided in postoperative period, and whenever required only i.m diclofenac 75mg was given. Outcome in terms of requirement of im rescue analgesic, visual analog pain score, any associated nausea vomiting, itching, and level of somnolence was noted in postoperative period at 1, 2, 4, 8, 12, 16, 24, 48 hr respectively.

Results: Mean doses of rescue analgesia were 1.33 in study group and 3.37 in the control group. Significantly lesser mean doses of rescue analgesia in study group with a P value of <0.0001.

Conclusion: Preoperative application of transdermal buprenorphine patch significantly reduces the requirement of rescue analgesia in postoperative period.

Keywords: Buprenorphine, knee arthroscopy, transdermal patch, Postoperative analgesia

Introduction

The International Association for the study of pain defines pain as **"**an unpleasant, sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage**".**[1]

Alleviating pain is one of the fundamental duties of an anaesthesiologist. Postoperative analgesia increases the patient's quality of life, with early mobilisation and faster recovery and decreases the duration of hospital stay, and may even adversely affect the outcome of surgery. [2]

Any approach pertaining to postoperative analgesia must be safe, effective and feasible. With the birth of effective anaesthesia in the 19th century, Postoperative Pain was recognized as a discipline worthy of attention in its own right. The goal for the postoperative pain management is to reduce an individual's pain to a tolerable level with minimal or no associated suffering or distress.

Knee arthroscopy is an approach to diagnose and to treat a wide variety of intra articular pathologies like anterior cruciate ligament, medial collateral ligament, posterior cruciate ligament repair or reconstruction and diagnostic arthroscopy to find out the exact cause

of pathology. Usually knee arthroscopy can be performed using spinal or epidural anaesthesia and peripheral nerve block.

Subarachnoid block with bupivacine is the most common mode of regional anesthesia used in lower limb surgeries like knee arthroscopy. Due to its limited duration of action, various adjuvants like morphine [3], fentanyl [4] and sufentanil [5] have therefore been added to bupivacaine to hasten the onset of block and prolong the duration of block.

However each drug has its own limitations and a need for alternative method or drug always exists. Like Standard local anaesthetic drugs such as bupivacaine and ropivacaine, lignocaine were unable to provide analgesia for longer-term surgeries or extended analgesia. For these reasons, Transdermal drug delivery systems (TDDSs) has been introduced. TDDSs are easy to use, non- invasive, simple, safe, reliable, compliant, and sustained methods of drug delivery.

"Buprenorphine, semi-synthetic is a highly lipophilic, alkaloid of morphine which is derivative of thebaine".[6] Transdermal patch Buprenorphine is incorporated into an adhesive polymer matrix (acrylate vinyl acetate), from which it is continuously released into the systemic circulation over a period of 7 days.[7]

Buprenorphine transdermal patches for postoperative analgesia are available in strengths 5, 10, and 20mg with rate of drug release of 5, 10, and 20 ug/h, respectively.

No literature is available about the use of transdermal buprenorphine patch for postoperative analgesia after total knee arthroplasty and knee arthroscopies. But literature supports use of transdermal buprenorphine patch for postoperative analgesia after abdominal surgical procedure.[8]

This study was designed to evaluate the effect of preoperative application of buprenorphine transdermal patch on analgesic requirement in postoperative period after knee arthroscopic surgeries.

Sample size and method of sample size calculation: with reference to the study "*Effect of preoperative application of buprenorphine transdermal patch on analgesic requirement in postoperative period in hip and knee replacement surgeries"* conducted by **Monu Yadav et al** [19] in 2019 Taking the mean duration of post operative analgesia as main outcome, the following inputs were used for sample size calculation. Alpha error 5%, beta 20% SD of 40 minutes in each group, effect size of 30 minutes. Using these parameters, the estimated sample size by statistical software WinPepi is 28 in each group. Rounding up propose to include 30 participants in study and control group.

Material and Methods:

Following approval from Institutional Ethical committee and written informed consent, a prospective, double blinded study was conducted in 60 patients of either gender belonging to ASA1 or ASA2 status, requiring arthroscopic knee surgery. Patients were selected randomly after applying stringent inclusion and exclusion criteria. Patients were divided into two groups of 30 patients each. Patients were assessed in preoperative period, and Buprenorphine patch of 5 mg (sustained release of 5µg/h) was applied on study group and placebo patch/ECG lead applied on clean, dry, hair free skin area 12 hours before surgery. From application of patch to 48 hours of post period the patients were monitored at set intervals T0, 1,2,4,8,12,24,48 hours for vitals PR, BP, SPO2, RR, VAS score and any side effects like skin irritation, respiratory depression, hypoxia, nausea, vomiting were monitored and noted. When the patient VAS score was 4 or more than 4 Inj. Diclofenac 75mg i.m. stat on demand for rescue analgesia was given and total requirement of rescue analgesia was noted.

VAS score: 0: no pain.

1-3: mild pain.

4-6: moderate pain.

7-10: severe pain.

Statistical Analysis: All cases were completed within the stipulated time. Data was collected, compiled and tabulated. The statistical analysis was done by using parametric test and final interpretation by using, Z test (standard normal variant) with 95% significance. Quantitative data was analyzed by student 't' test and qualitative data by Chi square test.

Observation and Results:

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Demographic profile and duration of surgery in both groups were comparable and non significant. Time to rescue analgesia was 349.17 minutes in study-group and 200.17 minutes in control and the difference was significant with a P value of <0.001.

There were 18 and 24 patients with ASA grade I in study and control groups and 12 and 6 with ASA grade II in study and control-group respectively. The difference was non-significant with P value of P=0.097.

Distribution of surgery:

Both PLACEBO and BTP groups had similar number of type of surgeries with total of Lt ACL and PCL reconstruction 15% , Lt ACL and PCL repair 6.6 %, Lt ACL reconstruction 6.6%, Lt ACL repair 15%,Lt knee arthroscopic menisectomy 1.6%, Rt ACL and MCL repair 11.6%, Rt ACL reconstruction 21.6 %, Rt ACL repair 18.3 %, Rt medical meniscus repair 3.3%.

The heart rate, SBP, DBP were measured at baseline, and post operatively at 1 HOUR, 2, 4, 8,12,24,48 hours. The baseline values were non-significant with a P value 0.91, 0.78. 0.29 Respectively. However at 4,8,12 hours of time intervals these were significantly low in the study group. It may be due to analgesic effect of buprenorphine transdermal patch in study group.

VAS scores were evaluated post operatively at 1 hour, 2 hour, 4 hour, 8 hour and 12 hour, 24 hours, 48 hours subsequent to the surgery. All the values were significantly lower in the study group at all time intervals. Mean doses of rescue analgesia were 1.33 in study group and 3.37 in the control group. Significantly lesser mean doses of rescue analgesia in study group with a P value of <0.0001as seen in **Table No 1 and Graph No 3**.

TABLE NO 1: Comparison of VAS score in Group I (PLACEBO) and Group II (BTP)

TIME INTERVAL	Group I (PLACEBO) (n=30)		Group II (BTP) (n=30)		**P Value**	
	Mean	**SD**	**Mean**	**SD**		**Inference**
To	2.1	1.61	2.4	1.15	0.40	Insignificant in both groups
1 hour	0	0	0	0	0	
2nd hr	1.3	1.2	0.3	0.47	0.0001	Significantly lower in Study group
4th hr	6.4	1.2	2.8	0.50	< 0.0001	Significantly lower in Study group
8th hr	5.3	1.49	3.2	0.48	< 0.0001	Significantly lower in Study group
12th hr	5	1.53	3.13	0.43	< 0.0001	Significantly lower in Study group
24 hr	5.3	1.29	3.46	0.77	< 0.0001	Significantly lower in Study group
48 hr	4.9	1.41	3.26	0.44	< 0.0001	Significantly lower in Study group

TABLE NO 2: mean doses of recue analgesia

Doses of rescue analgesia	Study group	Control group

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Mean doses	1.33	3.37
SD	0.48	0.56
P value	P<0.0001	
Inference	Significantly lesser mean doses of analgesic drugs in study group	

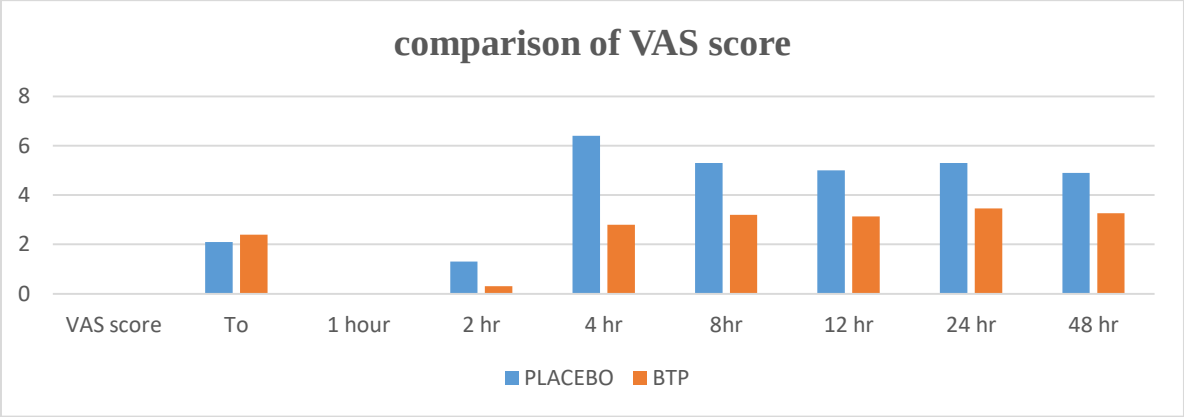
TABLE NO 3: Comparison of somnolence in both groups:

GROUP	Group I (PLACEBO) (n=30)		Group II (BTP) (n=30)		P value
	MEAN	**SD**	**MEAN**	**SD**	P value
	1	**0**	**1**	**0**	Insignificant

Table no 4: Comparison of complications in Group I (PLACEBO) and Group II (BTP)

Complications	**Group I (PLACEBO) (n=30)**		**Group II (BTP) (n=30)**	
	MEAN	**%**	**MEAN**	**%**
Headache	1	0.33	1	0.33
PONV	0	0	1	0.33
PRURITIS	0	0	0	
CONSTIPATION	0	0	0	0
RESPIRATORY DEPRESSION	0	0	0	0

Graph No 3: Bar diagram showing comparison of VAS score in both groups



TEST APPLIED: "independent student 't' test."

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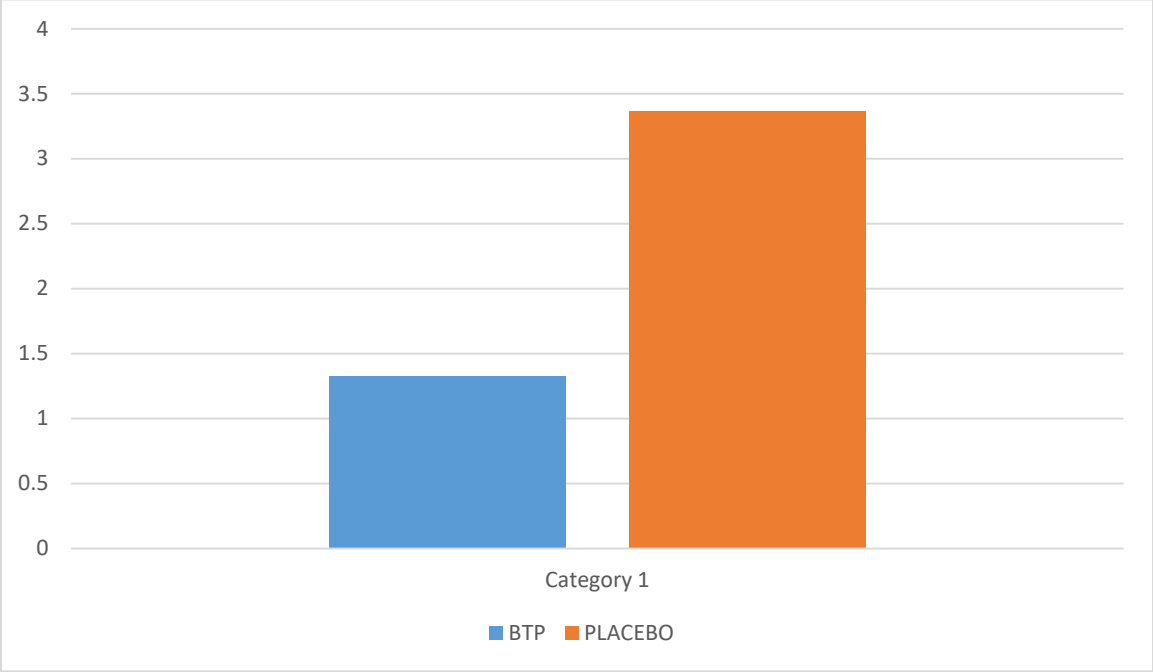
Results: Shows comparison of VAS score in the both groups from application of patches to 48 hours of post operative period. P values at intervals of 2, 4, 8,12,24,48 hours were statistically significant with < 0.05.

Graph no 4: showing mean doses of rescue analgesia



TEST APPLIED: "independent student 't' test."

Results: Shows comparison of mean doses of rescue analgesia in the both groups from application of patches to 48 hours of post operative period. P values shows statistically significant with < 0.05

Discussion:

Pain is an inevitable component of the postoperative period. Post-operative pain is associated with adverse outcomes such as patients discomfort, longer duration of hospital stay, exposure to analgesic drugs and their associated adverse events. Postoperative pain management aims at providing a subjective comfort to the patient by inhibiting pain.

Transdermal patch is a safe technique for post-operative pain relief and equivalent to traditional analgesic methods. With transdermal buprenorphine patch patient can be mobilized early and can resume activities quickly as compared to parenteral opioids.

Buprenorphine semi-synthetic derivative of thebaine [6] , a morphine alkaloid. Buprenorphine is incorporated into an adhesive polymer matrix (acrylate vinyl acetate), from which it is continuously released into the systemic circulation over a period of 7 days. Buprenorphine transdermal patch is available in different concentrations like 5, 10, 20 mg for post-operative analgesia. After transdermal application, it maintains an adequate concentration in blood for longtime, avoids first pass metabolism in liver and can be used in elderly patients suffering from dysphagia. Buprenorphine transdermal patch produces peak analgesic effect at 12 – 24 hours. Buprenorphine side effects include nausea, somnolence, pruritis they are rare and acceptable.

Various studies have evaluated the use transdermal buprenorphine patch for post-operative analgesia[40-53.]

The dosage of transdermal buprenorphine patch for post-operative analgesia in our study was decided after careful review of the various studies, which used different doses of buprenorphine transdermal patches like 5,10,20 mg in different types of surgeries, as mentioned in the review of literature.

Cardiovascular Parameters:

Our study was slightly different from other studies in context of non-significant differences in heart rate between the groups. This may be due to minimal hemodynamic effects of buprenorphine on heart rate leading to normalization of mean heart rate values.

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Similar to study "Efficacy of transdermal buprenorphine patch on post-operative pain relief after elective spinal instrumentation surgery" conducted by **Saikat Niyogi et al in 2017** [17]. The post-operative mean score of HR, SBP and DBP in buprenorphine group were lower than placebo group throughout the study with P value <0.05.

Respiratory Parameters:

The oxygen saturation and respiratory rates values were comparable in both the groups in preoperative as well as post operative period. There were no episodes of fall in saturation or, respiratory depression in both groups throughout the study. P values at intervals of 1, 2, 4, 8,12,24,48 hours were statistically insignificant with **> 0.05.**

None of the patients in both groups was excessively sedated in the study period. This is similar to study "Efficacy of transdermal buprenorphine patch on post-operative pain relief after elective spinal instrumentation surgery" conducted by **Saikat Niyogi et al in 2017**[17]**.**

Visual Analogue Scale:

In our study, time intervals for measuring VAS score was at T0 (at the time of patch application) and post operatively at 1st hour, 2nd hour, 4th hour, 12th, 24, 48 hours. All the P values were significantly lower in the study group as observed from **Table 1 and Graph 3**. There was gradual increase in the mean VAS scores from 2nd hour to 4th hour this may be due to weaning effect of the anaesthesia. Mean VAS score was observed in control group at 4 hours post operatively.

The lower values in the study group may be due to analgesic effect of BTP. Also, the peak action of buprenorphine transdermal patch comes at around 12- 24 hours explains the gradual decrease in the mean VAS scores in study group , and were higher in the control group. This is similar to study "Efficacy of transdermal buprenorphine patch on post-operative pain relief after elective spinal instrumentation surgery" conducted by **Saikat Niyogi et al in 2017** [17]**.**

The mean doses of rescue analgesia were 1.33 in study group and 3.37 in the control group. Significantly lesser mean doses of rescue analgesia in study group with a P value of <0.0001 as observed from **Table 2 and Graph 4**.

Post-operative analgesia corresponding to time point of first rescue analgesia was significantly longer in the group that received buprenorphine patch and total number of rescue analgesia was also less in BTP group. This was most probably due to the additional factor in the study group by use of buprenorphine patch which most probably would have worked to decrease total number of rescue analgesia and to increase time duration for rescue analgesia.

Various studies supported that buprenorphine transdermal patch is known to be effective in suppressing post operative pain leading to reduction in VAS scores.[9-22]

Our study matches with other studies in context of better VAS scores with use of buprenorphine transdermal patch due to its analgesic property.

Incidence Of Side Effects:

Unfortunately, opioids produce certain side effects such as respiratory depression, nausea, urinary retention, pruritus and patients may develop tolerance to their analgesic effects[23, 24, 25.] In our study postoperative sedation scores were insignificant in both groups at 1 HOUR, 2, 4, 8,12,24,48 hours. Of the total 420 observations for somnolence in 60 patients during period of observation of 48 hours, it was observed that none of our patients were somnolent. No serious or life threatening adverse events were noted in the study. There was one case of nausea and vomiting and 1 case of headache in study group, one case of headache in control group as seen in **Table No 5**. However these effects were transient and did not require any prompt intervention.

This is contrast to study conducted by **Yadav, Monu et a**l in 2019[19] where only 74% were fully awake, followed by 25 % were somnolent and 0.7% were no response to verbal stimulation. Our study didn't match with above study as observed in **Table 3**. Where use of buprenorphine patch was associated with higher sedation scores as patch used was of higher strength.

Conclusion: Based on the findings of the study, we can conclude that for arthroscopic knee surgeries, transdermal buprenorphine patch 5mg administered 12 hours prior to surgery, provides continuous, reliable and effective post operative analgesia. With overall decrease in frequency and total requirement of rescue analgesia without any major side effects.

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References:

1. Collins V.J, Philadelphia, Lea and Fabiger: Principles of anaesthesiology, general and regional anaesthesia, 3rdedition: 1993, Vol 2: 1232-1346, 1571-1605.
2. Joshi GP, Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. Anesthesiol Clin North America. 2005;23:21–36.
3. Kalso E. Effects of intrathecal morphine, injected with bupivacaine, on pain after orthopaedic surgery. British Journal of Anaesthesia. 1983; 55:415-22
4. Hunt CO, Naually JS, Bader Am et. Al. Perioperative analgesia with subarachnoid fentanyl-bupivacaine for cesearean delivery. Anesthesiology. 1989 Oct; 71 (4):535-40
5. Dahlgren G, Hultstrand C Jackobsson J et. Al. Intrathecal sufentanil, fentanyl or placebo added to bupivacaine for cesearean section. Anesth Analg. 1997 Dec;85(6):1288-93
6. Budd K. Buprenorphine. In: Bullingham RES, editor. Clinics in anaesthesiology. London: WB Saunders Company Ltd; 1983. p. 147 52.
7. Evans HC, Easthope SE. Transdermal buprenorphine. Drugs 2003;63:1999 2010.
8. Arshad Z, Prakash R, Gautam S, Kumar S. Comparison between transdermal buprenorphine and transdermal fentanyl for postoperative pain relief after major abdominal surgeries. J Clin Diagn Res 2015;9:UC01 4.
9. Sittl R, Nuijten M, Poulsen Nautrup B. Patterns of dosage changes with transdermal buprenorphine and transdermal fentanyl for the treatment of noncancer and cancer pain: a retrospective data analysis in Germany. Clin Ther. 2006 Aug;28(8):1144-1154. doi: 10.1016/j.clinthera.2006.08.002. PMID: 16982291.Regional Anesthesia & Pain Medicine 33.Suppl 1 (2008): e184-e184.
10. Privitera C, Guzzetta G et al in 2008 efficacy and safety of preoperative application of transdermal Buprinorphine patch for postoperative pain management of elderly patients with proximal femoral fractures; Regional Anesthesia & Pain Medicine 33.Suppl 1 (2008): e184-e184.
11. Karlsson M, Berggren AC. Efficacy and safety of low-dose transdermal buprenorphine patches (5, 10, and 20 microg/h) versus prolonged-release tramadol tablets (75, 100, 150, and 200 mg) in patients with chronic osteoarthritis pain: a 12-week, randomized, open-label, controlled, parallel-group noninferiority study. Clin Ther. 2009 Mar;31(3):503-13. doi: 10.1016/j.clinthera.2009.03.001. PMID: 19393841.J Opioid Manag. 2010 May-Jun; 6(3):193-202. doi: 10.5055/jom.2010.0017. PMID: 20642248.
12. Munera C, Drehobl M et al in 2010 Concluded that Compared with placebo, BTDS treatment was effective in treating patients with moderate to severe pain due to OA of the knee or hip. J Opioid Manag. 2010 May-Jun;6(3):193-202. doi: 10.5055/jom.2010.0017. PMID: 20642248
13. James IG, O'Brien CM, McDonald CJ. A randomized, double-blind, double-dummy comparison of the efficacy and tolerability of low-dose transdermal buprenorphine (BuTrans seven-day patches) with buprenorphine sublingual tablets (Temgesic) in patients with osteoarthritis pain. J Pain Symptom Manage. 2010 Aug;40(2):266-78. doi: 10.1016/j.jpainsymman.2010.01.013. Epub 2010 Jun 11. PMID: 20541900.doi: 10.1016/j.joca.2011.03.011. Epub 2011 Apr 6. PMID: 21477658.
14. Conaghan PG, O'Brien CM et al in 2011 transdermal buprenorphine patch and paracetamol with codeine and paracetamol in elderly patients with osteoarthritis of the hip or knee joints. doi: 10.1016/j.joca.2011.03.011. Epub 2011 Apr 6. PMID: 21477658.
15. Al-Tawil N, Odar-Cederlöf I, Berggren AC, Johnson HE, Persson J. Pharmacokinetics of transdermal buprenorphine patch in the elderly. Eur J Clin Pharmacol. 2013 Feb;69(2):143-9. doi: 10.1007/s00228-012-1320-8. Epub 2012 Jun 17. PMID: 22706617; PMCID: PMC3548110.Pergolizzi JV Jr, Raffa RB. Safety and Efficacy Of The Unique Opioid Buprenorphine For The Treatment Of Chronic Pain. J Pain Res. 2019; 12:3299-3317. Published 2019 Dec 13. doi:10.2147/JPR.S231948 doi:

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10.1185/03007995.2013.873714. Epub 2013 Dec 23. PMID: 24320787.

16. Karlsson J et al in 2014 no age-related dose adjustment of transdermal buprenorphine is needed. buprenorphine transdermal patch is equally safe and effective in younger and elderly patients with osteoarthritis-related pain; doi: 10.1185/03007995.2013.873714. Epub 2013 Dec 23. PMID: 24320787.
17. Niyogi S, Bhunia P, Nayak J, Santra S, Acharjee A, Chakraborty I. Efficacy of transdermal buprenorphine patch on post-operative pain relief after elective spinal instrumentation surgery. Indian J Anaesth. 2017;61(11):923-929. doi:10.4103/ija.IJA_118_17
18. Desai SN, Badiger SV, Tokur SB, Naik PA. Safety and efficacy of transdermal buprenorphine versus oral tramadol for the treatment of post-operative pain following surgery for fracture neck of femur: A prospective, randomised clinical study. Indian J Anaesth. 2017 Mar;61(3):225-229. doi: 10.4103/ija.IJA_208_16. PMID: 28405035; PMCID: PMC5372402.J Anaesthesiol Clin Pharmacol. 2019 Jan-Mar;35(1):124-128. doi: 10.4103/joacp.JOACP_13_17. PMID: 31057254; PMCID: PMC6495615.
19. Yadav M, Mohan CL, Srikanth I, Raj ER, Gopinath R, Chandrasekhar P. Effect of preoperative application of buprenorphine transdermal patch on analgesic requirement in postoperative period in hip and knee replacement surgeries. J Anaesthesiol Clin Pharmacol. 2019 Jan-Mar;35(1):124-128. doi: 10.4103/joacp.JOACP_13_17. PMID: 31057254; PMCID: PMC6495615.
20. Dr. Rakesh Kumar et al in 2020 Postoperative pain assessment using transdermal buprenorphine versus intramuscular diclofenac for analgesia: a randomized comparative trial ; European Journal of Molecular & Clinical Medicine (EJMCM) ISSN: 2515-8260 Volume 07, Issue 10, 2020
21. John J, Renny RA, Devassy C, Unnikrishnan MK, Venugopal V (2020) Postoperative Pain Management in Lower Limb Surgery Patients using Transdermal Buprenorphine and Diclofenac Formulation. J Anesth Clin Res. 11: 977.
22. Kishan Shetty et al in 2019 a comparative study of transdermal buprenorphine with transdermal fentanyl for postoperative analgesia in patients undergoing posterior stabilization of lumbar spine. Int. J. of Adv. Res. 7 (Oct). 327-349] http://dx.doi.org/10.21474/IJAR01/9836
23. Mukesh I Shukla, Ajay Rathod, Swathi N*, Jayesh Kamat, Pramod Sarwa, and Vishal Divecha: Evaluation of Epidural Clonidine for Postoperative Pain Relief. RRJMHS 2013;2:ISSN: 2319-9865.
24. Prasad R, Rao RR, Turai A, Prabha P, Shreyavathi R, Harsoor K. Effect of epidural clonidine on characteristics of spinal anaesthesia in patients undergoing gynaecological surgeries: A clinical study. Indian J Anaesth 2016;60:398-402.
25. Stoelting Robert, Hillier Simon: Pharmacology and physiology in anesthetic practice, 4th edition: 179-207, 340-344.

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