Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(1): 27-31
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6119.3

Evaluation of Postoperative Analgesic Requirement in Patients Undergoing Surgery with Buprenorphine Transdermal Patch

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Abstract

Introduction and Aims: Transdermal drug delivery is a simple non-invasive and compliant method. It provides a sustained drug release. The aims of this study was to assess the analgesic requirement of patients under General Anesthesia postoperatively after application of Buprenorphine Transdermal patch preoperatively, to assess added analgesic sparing effect, and to assess anxiety level and post extubation discomfort after surgery. *Methods and Materials:* In this prospective randomized controlled study sixty adult patients, undergoing elective open surgery under General Anesthesia were randomized into 2 groups: Group C (control group) receiving conventional intravenous analgesics, and Group B (study group) receiving transdermal Buprenorphine patch of 10 mcg/hr. All patients were monitored for vital parameters, VAS, MRSS, rescue analgesic requirement and adverse effects till fifth postoperative day. The data was analysed statistically using 't' test. *Results:* Number of patients requiring postoperative rescue analgesics was higher in group C. Total number of drug doses given in group C was also higher. Haemodynamic parameters were statistically insignificant in both groups at all time periods. VAS score was significantly less in group B till POD2, after which VAS was less in Group B, though not significant. MRSS scale was higher in Group B throughout postoperative period and at time of emergence. Number of patients having adverse effects was slightly high in group B but comparable in both groups. *Conclusion*: Transdermal buprenorphine patch is effective for postoperative analgesia for elective abdominal and head neck oral surgeries under General Anesthesia. It can reduce requirement of rescue post operative analgesics over atleast five days and maintain hemodynamic stability without serious complications.

Keywords: Buprenorphine; Transdermal patch; Rescue analgesia; Elective surgery.

How to cite this article:

Akanksha Agarwal, Pradip K Bhattacharya, G.N.Chavan et al. Evaluation of Postoperative Analgesic Requirement in Patients Undergoing Surgery with Buprenorphine Transdermal Patch. Indian J Anesth Analg. 2019;6(1):27-31.

Introduction

Effective control of post operative pain is a necessary component of perioperative patient management, which calls for a multidimensional approach. Transdermal drug delivery is a simple non-invasive and compliant method. It provides a steady and sustained drug release. It overcomes

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Received on 18.12.2018, **Accepted on** 03.01.2019

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the pharmacokinetic problems of oral and parentral methods [1].

Buprenorphine is a partial agonist opioid, acting at the mu receptors. It also has antagonistic activity at kappa opioid receptors, and a ceiling analgesic effect [2]. It has high lipid solubility, hence, highly effective through transdermal route.

Aims and Objectives

The aims of this study was to assess the analgesic requirement of patients postoperatively after application of Buprenorphine transdermal patch preoperatively in patients undergoing surgery under General Anesthesia, and to assess the analgesic sparing effect of the patch.

Methods and Materials

A prospective randomized controlled study was done in our institute between March 2015 to August 2016. After approval from Institutional Research Committee, a total of sixty ASA grade 1/2 physical status patients, of either sex, between ages of 18 to 60 years undergoing elective open surgery under General Anesthesia were included in the study. Informed written consent was obtained from all the patients. Patients exclusion criteria were ASA 3/4 physical status, opioid-dependent and sensitive patients, patients on antidepressants, or history of psychiatric illness, compromised cardiorespiratory function, pregnancy, skin allergy and refusal to consent.

Patients were randomized into 2 groups (1;1 randomization): Group C (control group), and Group B (study group), with thirty patients in each group.

Pre-anesthetic check up was done for all patients one day prior to surgery, during which they were explained about study and VAS (Visual Analogue Scale of 0 to 10, with 0 showing no pain and 10 showing extreme pain) score.

Buprenorphine transdermal patch of 10 mcg/h was applied 12 hours prior to surgery for every alternate patient, on hairless sites, most commonly upper outer arm, chest, upper back or side of chest.

On day of surgery, all baseline vital parameters (pulse rate, blood pressure, SpO_2) were recorded. VAS and MRSS (Modified Ramsay Sedation Score) scales were also noted. In OT, after securing intravenous line, and standard monitors, all patients were given anesthesia with uniform protocol. Inj. Fentanyl in dose of 0.5mcg/kg IV was supplemented when required. All group A patients were given Inj. Paracetamol 1 gm (in 100 ml NS) and Inj. Diclofenac 75 mg (in 100 ml NS) IV slowly as analgesics. At end of surgery, all patients were extubated after reversal of residual neuromuscular blockade with IV Inj Neostgmine 0.03-0.05 mg/kg and Inj. Glycopyrollate (0.4 mg), and after confirming adequate recovery of tone, power and consciousness. Patients were shifted to postoperative recovery area and monitored till shifted to ward.

Vital parameters and MRSS and VAS scores were recorded at time of emergence from anesthesia, then post-operatively at 1 hr, 4 hr, 8 hr, 12 hr, 24 hr, then on third, fourth and fifth day of surgery. In Control group, Inj. Paracetamol 1gm IV TDS was given till fifth day of surgery for routine analgesia. Rescue analgesic (inj Diclofenac 75 mgIV in 100 ml NS slowly) was administered when VAS>/=2 in both groups. Patients were also observed for any complication or side-effects due to drugs such as nausea, vomiting, application rash, constipation, headache, respiratory depression, till fifth day of surgery.

The analgesic efficacy of Buprenorphine transdermal patch (TDB) was evaluated by comparing total number of added analgesics in postoperative period till postoperative fifth day in both groups, apart from associated haemodynamic changes, and VAS. Safety of TDB was assessed by monitoring side effects such as nausea, vomiting, constipation, headache and serious complications such as respiratory depression. Level of sedation was assessed via MRSS (Modified Ramsay Sedation Scale, 1-awake, 2-lightly sedated, 3-moderately sedated, 4-deeply sedated, 5-responds only to painful stimuli, 6-unresponsive.). All the untoward side effects were managed accordingly.

The data was analysed statistically using 't' test.

Results

Total 60 patients were studied, (30 patients in each group), from the time of Preanesthetic Checkup and preoperative area till fifth postoperative day. In both groups, demographic characteristics such as age, sex, ASA status, duration of surgery were comparable.

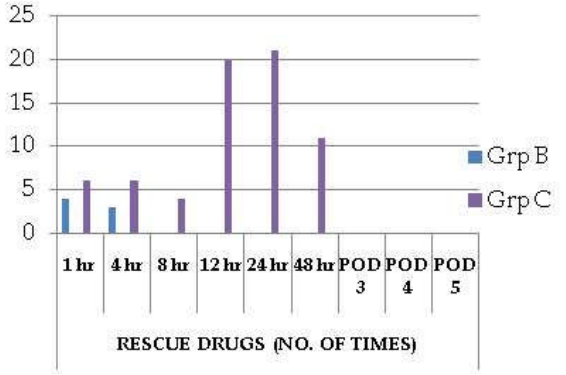
Table 1: Demographics

Demographics	Group B	Group C
No. of Males	11	12
No. of Females	19	18
Avg. Age (in years)	40.4	39.1
Avg. Duration of Surgery (Hours)	3	2.766

There was no significant difference in preoperative VAS score and vital parameters, that is, pulse rate, SBP, DBP and SpO_2, between the two groups ($p \leq 0.05$). Haemodynamic parameters were statistically insignificant in both groups at all time periods (emergence and postoperatively), though bit more stable in buprenorphine group. Number of patients requiring postoperative rescue analgesics was higher in group A (control) (n=27 vs n = 7 in group B). Total number of drug doses given in group C was also higher, as shown in Table 2 and Graph 1.

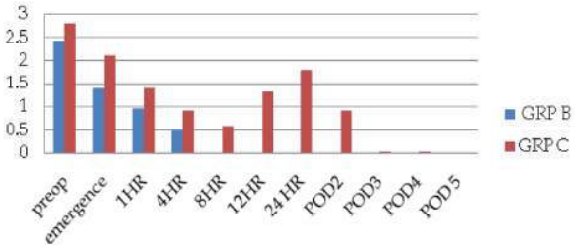
Table 2: Rescue Drugs (No. of Times).

Time	Group B	Group C
1 hr	4	6
4 hr	3	6
8 hr	0	4
12 hr	0	20
24 hr	0	21
48 hr	0	11
POD 3	0	0
POD 4	0	0
POD 5	0	0

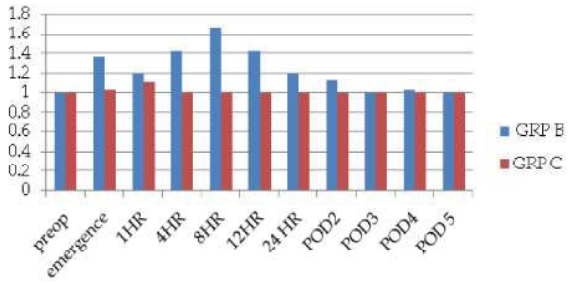


Graph 1:

VAS score was significantly less in group B at time of emergence and postoperatively after 4 hours till POD2, after which VAS was less in Group B, though not significant. (Graph 2).



Graph 2: VAS



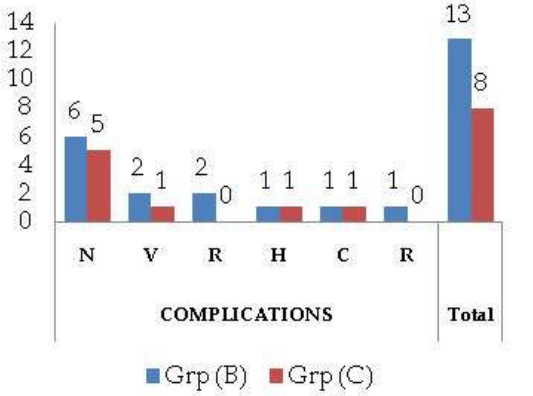
Graph 3: MRSS

MRSS scale was higher in Group B throughout postoperative period and at time of emergence (statistically significant), though it was always less than 3, not leading to excessive sedation. (Graph 3).

Number of patients having adverse effects was slightly high in group B, though comparable, most common effect being postoperative nausea. Two patients developed mild rash at site of patch application on POD3 and POD5. One patient had mild respiratory depression with fall in SpO_2 <95%, requiring oxygen through nasal prongs at 2L/ min on POD4 for a day, after which it was normal. (Table 3 and Graph 4)

Table 3: Complications.

Complications	Group B		Group C	
	No.	(%)	No.	(%)
Nausea	6	20	5	16.667
Vomiting	2	6.6667	1	3.3333
Rash	2	6.6667	0	0
Headache	1	3.3333	1	3.3333
Constipation	1	3.3333	1	3.3333
Resp Depr	1	3.3333	0	0
Total	13	43.33	8	26.66



Graph 4:

Discussion

Noxious stimuli like surgical incision produces

central sensitization and hyperexcitability, leading to amplification of the postoperative pain. It is postulated that if adequate analgesia is given intraoperatively, development of this sensitization is blocked, and hence, postoperative analgesia becomes more profound [2]. Transdermal Drug Delivery system provides safe, convenient and steady method of drug delivery as it bypass the first-pass metabolism and avoids peaks and troughs in plasma levels of the drug. It is more compliant as it is non-invasive and avoids multiple dosing. It also decreases incidence of drug related side effects [3] But some studies showed that gastrointestinal side effects associated with oral and transdermal opiods are comparable [2].

Buprenorphine is a partial agonist for mu-opioid receptors and has an antagonistic effect for kappa and delta receptors. It is 75 to 100 times more potent than morphine, and has good skin penetration [4]. But transdermal patches were not widely used for postoperative pain due to their slower onset (6-24 hrs), unpredictable absorption especially during hypothermia, interpatient variability, high cost, availability of limited number of drugs and physician's familiarity with injectable drugs [2].

In India, Buprenorphine patches are available in three different strength: 5, 10, 20 mcg/hr (over a period of 7 days). After removal of patch, buprenorphine concentration decline decreasing approximately 50% in 12 hrs (range 10-24 hrs).

In our study, we found that hemodynamic parameters were comparable in both groups, though slightly better controlled in group B. In a study by Niyogi et al. [3], intraoperative haemodynamic difference between transdermal buprenorphine and transdermal placebo groups was significant, with better controlled parameters inTDB group, for elective spinal instrumentation surgeries.

The efficacy of TDB has been established by many studies. Privitera, G. Gazzella et al. [5] used 35 mcg/ hr of TDB for shoulder and upper femur surgeries and concluded that transdermal buprenorphine can be safely used for effective postoperative analgesia with high patient satisfaction rates. Similarly, Tang et al. [4] found that analgesic effect of transdermal buprenorphine was better compared with conventional analgesic regimen of paracoxib intravenous injections and oral celecoxib, with significantly higher degree of patient satisfaction in transdermal buprenorphine group, but VAS score was not significantly higher. In our study too, VAS score was significantly low in group B at time of emergence and postoperatively after 4 hours till POD2, after which VAS was less in group B but not statistically significant. In immediate postoperative period at 1 and 2 hours VAS was comparable in both groups, may be due to effect of intraoperative analgesics administration along with delayed effect of transdermal patch. Similarly, requirement of rescue analgesics was higher in control group.

In our study patients of group B were more comfortable, though not highly sedated as observed by MRSS score. But one patient got mild respiratory depression in group B, with SpO_2 decreasing to 92% requiring 1-2 litres of oxygen for few hours. In a study by Santosh Kumar et al. [1] for postoperative pain control in abdominal surgeries, mean RSS was lowest in group A (placebo patch), followed by group B (transdermal buprenorphine patch 10 mg) and highest for group C (transdermal buprenorphine patch 20 mg).

Two patients in our study developed skin rash at site of patch application. Local skin allergy and pruritis were also found by Tang et al [4] and by Privitera at al. [5] in their studies. PONV was found in various studies as minor side effect of drug or surgery, but statistically significant difference was not observed between study and control groups [1,3,4]. In our study nausea was most common side effect in both groups, though incidence was comparable. Few patients had other side effects too, like headache, constipation. High incidence of PONV in our study was may be due to type of surgeries (abdominal, oral, head neck) or duration of operations (average 2.5 - 3 hrs).

Conclusion

Transdermal buprenorphine patch is effective for postoperative analgesia for elective abdominal and head neck oral surgeries under General Anesthesia, in which patch can be applied atleast 12 hours prior to surgery. It can reduce requirement of rescue post operative analgesics over atleast five days and maintain hemodynamic stability without serious complications. But further studies with greater sample size may be required to support this.

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