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ANALYSING THE EFFICIENCY OF TRANSDERMAL BUPRENORPHINE PATCH OF 10 MICROGM/HOUR IN PATIENTS RECEIVING GENERAL AND REGIONAL ANESTHESIA PRIOR SIX HOURS TO SURGERY

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Abstract

The present study was carried out in 60 Patients of age 20-50 years with ASA grade I & II of either sex. The following are the important observations done during the study: Patients receiving transdermal buprenorphine patch 10 microgm/hour 6 hours before surgery had shown the following outcome: The average age in Group A was 36.47±7.74 years, while in Group B, it was 37.00±6.41 years. Regarding gender distribution, the majority of participants were female (90.0%). Specifically, Group A consisted of 24 females (80.0%), whereas all 30 participants in Group B were female (100%). Further, a statistically significant change ($p<0.05$, ANOVA test) was observed in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and mean RPP (HR*MAP), all of which remained within clinically acceptable limits. Additionally, the average VAS score was low across participant groups. In Group A, the score decreased by the 6th hour, while in Group B, it reached 2.0 immediately after the postoperative period. Mean total post-operative analgesic requirements among the participants of group A and B were observed to be 660 and 595 mg respectively. Hence, the application of a transdermal buprenorphine patch at a dose of 10 mcg/hour, administered six hours before surgery, effectively provided analgesia for patients undergoing surgery under both general and regional Anesthesia. Pain scores remained below 3 after 30 hours postoperatively, and the need for rescue analgesics was reduced. Additionally, no significant adverse effects were reported, and there were no cases of bradycardia or hypotension throughout the study.

Key Word: Transdermal Buprenorphine, ASA grade I & II, General and Regional Anesthesia

INTRODUCTION

Opioid analgesics have been widely utilized for managing both acute and chronic pain due to their effectiveness. However, concerns about their safety, tolerability, and potential for abuse and dependence have limited their broader therapeutic use. While all opioids share common side effects, some exhibit a more favorable safety profile than others. Buprenorphine, a semi-synthetic opioid, acts as a μ-receptor agonist and a κ-receptor antagonist.[1] Over the past two decades, research has highlighted its complex and unique pharmacological properties, offering significant therapeutic advantages alongside a favorable safety profile. Previously underutilized, the introduction of a transdermal delivery system for buprenorphine has renewed interest in its clinical application. The transdermal formulation (developed by Gruenenthal GmbH, Aachen, Germany) provides a non-invasive, rate-controlled drug release mechanism, ensuring stable and predictable serum levels over

an extended period. This system has demonstrated benefits in long-term pain management, delivering consistent pain relief, minimal adverse effects, and high patient acceptance.[2]

Therefore, our objective is to evaluate the effectiveness of a transdermal buprenorphine patch (10 mcg/hour) in patients undergoing general or regional anesthesia when administered six hours before surgery.

MATERIAL AND METHODS

Study procedure

The study received approval from the Ethical Committee of Government Medical College & its affiliated hospitals in Kota for surgical procedures, Anesthesia, and research protocols. Written informed consent was obtained from all participants or their attendants. A total of 60 patients, aged between 20 and 50 years, classified as ASA grade I or II, of either gender, scheduled for abdominal surgeries under general or regional Anesthesia, and willing to participate, were included in the study. The study was conducted over a period from July 2021 to July 2022.

Study design, sample size and sampling procedure

A prospective, randomized, comparative study was conducted on 60 adult patients undergoing upper or lower abdominal surgeries under either general or regional anesthesia. Patients who met the inclusion criteria were randomly assigned to one of the following two groups:

- **Group A (General Anesthesia):** 30 patients received a transdermal buprenorphine patch (10 mcg/hour) applied to a hairless area six hours before surgery.
- **Group B (Regional Anesthesia):** 30 patients received a transdermal buprenorphine patch (10 mcg/hour) applied to a hairless area six hours before surgery.

Pre-procedure assessment

A comprehensive medical history was obtained, including an assessment of skin allergies to the drug, opioid intolerance, any cardiopulmonary or respiratory depression, and a history of opioid addiction.

Statistical analysis

Quantitative data, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), rate pressure product (RPP), respiratory rate (RR), oxygen saturation (SpO2), Visual Analog Scale (VAS) score, Ramsay Sedation Score, and the requirement for rescue analgesics, were recorded in an MS Excel sheet. The data were presented as Mean ± Standard Deviation (SD) in MS Word tables. The difference in mean values between the two groups was analyzed using Student's unpaired *t*-test. The need for rescue analgesia was summarized as proportions, and differences between proportions were assessed using the Chi-square test in SPSS software (version 22.0). A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: The mean age of the participants

AGE (Years)				
Groups	**N**	**Mean± SD**	**Median**	**Range**
Group A	30	36.47±7.74	37.00	27-54
Group B	30	37.00±6.41	39.00	20-44
Total	60			
	Sex			
	F		**M**	

Groups	N	%	N	%
Group A	24	80.0%	6	20.0%
Group B	30	100.0%	0	0.0%
Total	54		6	

In our study, participants were between 20 and 50 years old. The average age in Group A was 36.47±7.74 years, while in Group B, it was 37.00±6.41 years. Regarding gender distribution, the majority of participants were female (90.0%). Specifically, Group A consisted of 24 females (80.0%), whereas all 30 participants in Group B were female (100%).

Table 2: Clinical variables in participants

Perioperative Heart rate (BPM)		**Group A**	**Group B**	**Systolic blood pressure (mm of Hg)**		**Group A**	**Group B**
		Mean	**Mean**			**Mean**	**Mean**
6 h Before Surgery	**Baseline**	83.33	84.27	**6 h Before Surgery**	**Baseline**	119.33	121.33
After Surgery	**0 h**	87.47	84.27	**After Surgery**	**0 h**	120.00	121.33
	6 h	86.40	87.33		**6 h**	120.00	127.33
	12 h	84.80	86.13		**12 h**	119.33	126.67
	18 h	84.40	86.27		**18 h**	119.33	126.67
	24 h	84.40	86.27		**24 h**	119.33	124.67
	30 h	84.27	86.27		**30 h**	119.33	124.67
	36 h	84.13	85.20		**36 h**	119.33	124.67
	42 h	84.13	85.07		**42 h**	119.33	124.67
	48 h	83.87	85.07		**48 h**	119.33	123.33
	54 h	83.60	83.20		**54 h**	119.33	123.33
	60 h	83.60	81.33		**60 h**	119.33	122.67
	66 h	80.87	80.53		**66 h**	119.33	118.67
	72 h	81.33	80.80		**72 h**	118.67	119.33
Diastolic blood pressure (mm of Hg)		**Group A**	**Group B**	**Mean arterial pressure (mm of Hg)**		**Group A**	**Group B**
		Mean	**Mean**			**Mean**	**Mean**
6 h Before Surgery	**Baseline**	77.33	78.00	**6 h Before Surgery**	**Baseline**	91.33	92.44
After Surgery	**0 h**	77.33	78.00	**After Surgery**	**0 h**	91.55	92.44
	6 h	77.33	80.00		**6 h**	91.55	95.78
	12 h	76.67	80.00		**12 h**	90.89	95.56
	18 h	76.67	80.00		**18 h**	90.89	95.56
	24 h	77.33	80.00		**24 h**	91.33	94.89
	30 h	77.33	80.00		**30 h**	91.33	94.89
	36 h	76.67	80.00		**36 h**	90.89	94.89
	42 h	77.33	80.00		**42 h**	91.33	94.89
	48 h	74.67	80.00		**48 h**	89.56	94.44
	54 h	73.33	80.00		**54 h**	88.66	94.44

	60 h	73.33	80.00		**60 h**	88.66	94.22
	66 h	73.33	80.00		**66 h**	88.66	92.89
	72 h	73.33	80.00		**72 h**	88.44	93.11
Mean RPP(HR* MAP)		**Group A**	**Group B**	**Visual analogue scale**		**Group A**	**Group B**
6 h Before Surgery		**Mean**	**Mean**	**6 h Before Surgery**		**Mean**	**Mean**
	Baseline	7610.53	7790.20		**Baseline**	4.67	1.20
After Surgery	**0 h**	8008.17	7790.20	**After Surgery**	**0 h**	8.33	1.47
	6 h	7910.21	8364.18		**6 h**	7.87	8.60
	12 h	7707.47	8230.30		**12 h**	7.87	8.53
	18 h	7671.12	8243.67		**18 h**	7.60	8.60
	24 h	7708.25	8186.16		**24 h**	7.33	8.27
	30 h	7696.38	8186.16		**30 h**	6.47	7.20
	36 h	7646.58	8084.63		**36 h**	5.67	6.27
	42 h	7683.59	8072.29		**42 h**	4.67	5.60
	48 h	7511.12	8034.29		**48 h**	4.33	5.07
	54 h	7412.25	7857.69		**54 h**	4.00	4.60
	60 h	7412.25	7663.18		**60 h**	3.80	4.00
	66 h	7170.20	7480.43		**66 h**	3.40	2.67
	72 h	7193.10	7523.29		**72 h**	2.00	1.47
Ramsay Sedation Scale		**Group A**	**Group B**			**Group A**	**Group B**
6 h Before Surgery		**Mean**	**Mean**				
After Surgery	**Baseline**	2.00	1.87				
	0 h	1.10	1.00				
	6 h	1.10	1.00				
	12 h	1.10	2.00				
	18 h	2.00	2.00				
	24 h	2.00	2.00				
	30 h	2.00	2.00				
	36 h	2.00	2.00				
	42 h	2.00	2.00				
	48 h	2.00	2.00				
	54 h	2.00	2.00				
	60 h	2.00	2.00				
	66 h	2.00	2.00				
	72 h	2.00	2.00				

A statistically significant change ($p<0.05$, ANOVA test) was observed in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and mean RPP (HR*MAP), all of which remained within clinically acceptable limits. Additionally, the average VAS score was low across participant groups. In Group A, the score decreased by the 6th hour, while in Group B, it reached 2.0 immediately after the postoperative period.

Table 3: Comparison of frequency and total rescue analgesia (intravenous Inj. Diclofenac 75 mg) requirement among participants in the next 72 hours

Group		Frequency of use of rescue analgesic (postoperative)	Total rescue analgesic dose in mg
A	**Mean±SD**	8.80±1.90	660.00±142
B	**Mean±SD**	7.93±0.58	595.00±43.75

Mean total post-operative analgesic requirements among the participants of group A and B were observed to be 660 and 595 mg respectively.

DISCUSSION

Inadequate management of postoperative pain is associated with higher morbidity, delayed recovery, and extended hospital stays. To mitigate these issues and enhance pain relief, various approaches have been developed. One such method is the Transdermal Drug Delivery System (TDDS), which offers a non-invasive, user-friendly, and dependable means of administering medication.[3]By ensuring a gradual and continuous release of the drug, TDDS helps maintain stable plasma levels, preventing abrupt spikes and thereby minimizing the risk of adverse effects. Significant progress has been made in the development of transdermal drug delivery systems, with extensive research dedicated to this field.[4] Due to its non-invasive nature; this method presents a highly appealing and effective alternative to traditional drug delivery routes. It has been widely utilized in managing chronic pain in cancer and non-cancer patients also, demonstrating positive outcomes.[5]

The use of transdermal opioids for acute pain management has recently gained attention. Various opioids with both agonist and antagonist properties have been effectively used for chronic pain relief. While their administration through intravenous, neuraxial, and oral routes is well established for postoperative pain management, the application of long-acting transdermal opioids like buprenorphine remains limited.[6, 7] Additionally, research in this area is relatively scarce.

Research has demonstrated the effectiveness of transdermal buprenorphine in both general and regional Anesthesia individually.[8]However, no studies have directly compared its use between these two Anesthesia techniques. Therefore, this study was conducted to evaluate the efficacy and feasibility of a 10 microgram/hour transdermal buprenorphine patch in patients undergoing general or regional Anesthesia, applied six hours before surgery.

Demographic Variables

In the present study mean age were 36.27± 7.07 years, with age ranges from 20 to 50 years. The mean age of two groups of participants was comparable. The mean age in the present study was similar to the study conducted NiyogiS et al[9], while the mean ages were higher in the studies conducted by YadavM et al[10] (55.00±14.82) Anju Krishnan[11] (47.67±4.64) and Setti T et al[12](47.1±5.5)

In the present study majority participants were female (90.0%) with 24 (80.0%) in Group A and 30 (100%) in Group B. However, in similar studies by YadavMet al[10]and NiyogiSet al[9]the sex distribution was almost equal.

Perioperative Haemodynamic changes

Statistically significant change ($p < 0.05$, ANOVA test) in Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure and Mean RPP was found among the groups of participants, however observed changes were within clinically accepted ranges.

It was observed that the HR, SBP, DBP, MAP,RPP (HR*MAP) and Perioperative VAS changes were higher in group B (10 mcg/h) at most of the study points than group A.

Comparing the groups A and B (General Anesthesia and Regional Anesthesia)**,** it was observed that the scores were significantly higher in the group B at all points from 6 h to 72 h. Thus, Buprenorphine 10 mcg/ hr. patch had higher VAS scores in regional Anesthesia.

The effectiveness of the buprenorphine transdermal patch was found to be dose-dependent, with the greatest need for additional analgesia occurring during the first postoperative hour. The patch reached its peak effect between 12 to 24 hours, ensuring hemodynamic stability during intubation and beyond. Oifaet al[13] also observed that both buprenorphine infusion (BUP-i) and buprenorphine bolus (BUP-b) provided hemodynamic stability for patients undergoing abdominal surgery during both the intraoperative and postoperative periods. Systolic blood pressure was monitored, and if it dropped by more than 20% from baseline, a bolus dose of ephedrine (6 mg) was administered. Additionally, Setti et al. reported that the efficacy of the buprenorphine transdermal delivery system (BUP-TDS) was directly correlated with its dosage. Similarly, Arshadet al[14] found that buprenorphine TDS significantly reduced postoperative pain.

Frequency and total rescue analgesia requirement

The frequency and total doses of post-operative rescue analgesic requirement were statistically significantly higher in Group A and Group B ($p<0.001$, ANOVA test). Mean total post-operative analgesic requirements among the participants of group Aand Bwere observed to be 660 and 595mg respectively.Thus, the frequency of rescue analgesic requirement was higher in the Patients who received regional Anesthesia with 10 mcg/hr transdermal buprenorphine.

Our study's findings align with those of Setti et al[12], Böhme and Likar[15], who reported that the effectiveness of transdermal buprenorphine patches increases with dosage. However, they also noted the need for supplemental analgesia, especially during the first postoperative hour in gynecological procedures. Similarly, a prior study by Sittl et al[12] found that patients receiving transdermal buprenorphine required fewer additional analgesics.

Perioperative Ramsay Sedation Scale changes

In group A, the mean Ramsay sedation score reached to 2.0 by 18 h post-operatively and in group B by 12 h. However, we cound't get supporting studies that support our data.

CONCLUSION

The application of a transdermal buprenorphine patch at a dose of 10 mcg/hour, administered six hours before surgery, effectively provided analgesia for patients undergoing surgery under both general and regional Anesthesia. Pain scores remained below 3 after 30 hours postoperatively, and the need for rescue analgesics was reduced. Additionally, no significant adverse effects were reported, and there were no cases of bradycardia or hypotension throughout the study.

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