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TO EVALUATE THE EFFICACY AND HEMODYNAMIC EFFECTS OF TRANSDERMAL BUPRENORPHINE PATCH IN POSTOPERATIVE PAIN MANAGEMENT IN ABDOMINAL SURGERIES

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Abstract

The present study was carried out in 120 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 20 microgm/hour 6 hours before surgery had better haemodynamic stability. Among General anaesthesia groups, the HR and SBP were lower in group A (20 mcg/h) at most of the study points. However, the DBP and MAP were slightly higher in group A (20 mcg/h) at most of the study points. RPP (HR*MAP) was lower in group A (20 mcg/h) at most of the study points, except during the initial 6 hours and at 72 hours. In patients undergoing surgeries under Regional Anaesthesia, it was observed that the group B (20 mcg/h) had slightly lower HR. The SBP, DBP and MAP were similar in both the groups. Similarly RPP (HR*MAP) was lower in group B at most of the study points. VAS scores were significantly lower with transdermal buprenorphine patch 20 microgm/hour in both general anaesthesia and regional anaesthesia groups. With respect to General Anaesthesia, it was observed that the scores were significantly lower in the group A (20mcg/h) at all points from 6 h to 72 h. Among the regional anaesthesia, group B was observed that the scores were significantly lower in at all points from 6 h to 72 h. Thus, Buprenorphine 20 mcg/ hr patch had lower VAS scores in both general and regional anaesthesia. In patients done under general anaesthesia, the frequency of rescue analgesia was 5.40±1.16 (group A). In patients done under Regional anaesthesia the frequency of rescue analgesia was 5.13±0.63 in group B. In patients done under general anaesthesia, the total dose of rescue analgesic required was to group C, 405.00±87.20 mgs. In patients done under Regional anaesthesia the total dose of rescue analgesic required group B 385.00±47.16 mgs. All the patients were cooperative, oriented and tranquil by 18 hours of post-operative period. Sedation score of 2 was achieved earlier with 20 micrograms patch in both general and regional anaesthesia groups. No major adverse effects were observed in any of the study groups. Transdermal buprenorphine in a dose of 20 micrograms/hour applied 6 hours prior to surgery provides good analgesia in patients undergoing surgeries with both general and regional anaesthesia, with lower pain scores (less than 3, after 30 hours postoperative) and lesser requirement of rescue analgesics (group A, 405.00±87.20 mgs. And group B, 385.00±47.16 mgs), without significant adverse effects. No incidences of bradycardia or hypotension were observed during the study.

Keywords: Transdermal Buprenorphine Patch, Postoperative Pain Management, Abdominal Surgeries

INTRODUCTION

Postoperative pain management is a necessary component of patient undergoing major surgery. Pain in the initial days after surgery can lead to delayed ambulation leading to increase in cardiopulmonary and thrombotic morbidity as well as the

development of chronic pain. Pain can hamper the normal recovery process and extend the length of hospital stay, contribute towards patient dissatisfaction, cause a negative perception of hospital performance and increase the health care utilization costs.[1]

The present study was conducted to evaluate the pre-emptive application of 20 mcg/hr Buprenorphine transdermal patch. After surgery, patients were followed up for sedation and analgesia for next 3 days 6 hourly. The aim of this study was to evaluate the efficacy and haemodynamic effects of Buprenorphine patch in post-operative pain management in abdominal surgeries.

MATERIAL AND METHODS

Study procedure

Approval of the Ethical Committee of Government Medical College & Attached group of Hospitals, Kota was obtained for surgery, anaesthesia and this study. Written informed consent from all patients / their attendants was obtained. 120 patients of age 20-50 years with ASA grade I & II, of either sex, undergoing abdominal surgeries under general or regional anaesthesia and willing to participate in this study were enrolled in this study. Duration of study was from July 2021 to July 2022.

Study design, sample size and sampling procedure

A prospective randomized comparative study was done on 120 adult patient undergoing abdominal (Upper + Lower) surgeries under general or regional anaesthesia. In this study, patients fulfilling inclusion criteria were randomly allocated to the following four groups.

Group-A- General Anaesthesia- 30 patients receiving transdermal buprenorphine patch [20 microgm/hour] on hairless area, 6 hours before surgery.
Group-B- Regional Anaesthesia- 30 patients receiving transdermal buprenorphine patch [20 microgm/hour] on hairless area, 6 hours before surgery.

Pre-procedure assessment:

Complete medical history including skin allergy to drug, intolerance to opioid, any cardiopulmonary and respiratory depression and addiction to opioid was done.

Statistical analysis

The quantitative data (H.R., S.B.P., D.B.P, M.A.P., R.P.P., R.R., SPO_2, VAS Score, Ramsay Sedation Score, Requirement of rescue analgesic) were recorded in MS Excel sheet and arranged in the form of Mean ± Standard Deviation (SD) into MS Word tables. The difference between mean value of both groups were analysed using Student's unpaired 't' test. Requirement of Rescue analgesic was summarized in the form of proportions. The difference between proportions was analysed using Chi square test using SPSS version 22.0. P value of <0.05 was considered as significant.

RESULTS

Table 1: Demographic variables of the participants

Age (Years)					
Groups	**N**	**Mean±SD**		**Median**	**Range**
Group A	30	35.47±7.97		34.00	22-46
Group B	30	36.13±6.29		36.00	18-45
Total	120	36.27±7.07		37.00	18-54
Sex					
	F		**M**		
Groups	**N**	**%**	**N**	**%**	
Group A	26	86.7%	4	13.3%	
Group B	28	93.3%	2	6.7%	
Total	108	90.0%	12	10.0%	

In our study mean age was 36.27± 7.07 years. Age ranges from 18 to 54 years. The mean age of two groups of participants was comparable. Mean age of group C was 35.47±7.97 years and age ranges from 22 to 46 years, group D was 36.13±6.29 years and age ranges from 18 to 45 years. In our study majority participants were female (90.0%). Female participants in Group C were 26(86.7%) and 28(93.3%) in Group D.

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	86.27	84.93	6 h Before Surgery	Baseline	128.67	125.33
After Surgery	0 h	88.40	86.93	After Surgery	0 h	132.67	124.67
	6 h	88.00	**83.47**		6 h	125.33	**119.33**
	12 h	**80.13**	84.40		12 h	121.33	121.33
	18 h	82.93	**81.73**		18 h	120.67	123.33
	24 h	**81.33**	81.46		24 h	**115.33**	124.67
	30 h	**80.53**	82.27		30 h	**116.00**	123.33
	36 h	**81.33**	81.87		36 h	**119.33**	124.67
	42 h	**80.13**	82.00		42 h	120.00	124.00
	48 h	**80.40**	82.67		48 h	120.67	124.00
	54 h	**80.00**	82.13		54 h	**118.67**	121.33
	60 h	**80.13**	81.07		60 h	119.33	**117.33**
	66 h	**80.27**	82.13		66 h	**118.67**	124.00
	72 h	85.13	84.60		72 h	**116.00**	123.33
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	80.67	80.00	6 h Before Surgery	Baseline	96.67	95.11
After Surgery	0 h	82.00	80.00	After Surgery	0 h	98.89	94.89
	6 h	80.00	77.33		6 h	95.11	**91.33**
	12 h	80.00	78.00		12 h	93.78	92.44
	18 h	80.00	80.00		18 h	93.56	94.44
	24 h	**75.33**	80.00		24 h	**88.66**	94.89
	30 h	78.00	80.00		30 h	**90.67**	94.44
	36 h	80.00	80.00		36 h	93.11	94.89
	42 h	78.67	80.00		42 h	92.45	94.67
	48 h	79.33	80.00		48 h	93.11	94.67
	54 h	77.33	79.33		54 h	91.11	93.33
	60 h	78.67	80.00		60 h	92.22	92.44
	66 h	78.00	80.00		66 h	91.56	94.67
	72 h	77.33	80.00		72 h	90.22	94.44
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	8339.72	8077.69		Baseline	2.33	2.13
After Surgery	0 h	8741.88	8248.79	After Surgery	0 h	8.67	1.73
	6 h	8369.68	**7623.32**		6 h	7.80	8.27
	12 h	**7514.32**	7802.22		12 h	6.87	**7.27**
	18 h	7758.65	7718.85		18 h	**5.93**	6.27
	24 h	**7210.99**	7729.74		24 h	**4.87**	5.27
	30 h	**7301.39**	7769.85		30 h	**3.80**	4.27
	36 h	**7572.64**	7768.64		36 h	**2.53**	3.27
	42 h	**7407.75**	7762.67		42 h	**1.53**	2.27
	48 h	**7486.04**	7826.09		48 h	**.53**	1.27

	54 h	**7288.80**	7665.19		**54 h**	**.20**	.40
	60 h	**7389.86**	7494.38		**60 h**	**0.00**	**0.00**
	66 h	**7349.25**	7774.97		**66 h**	**0.00**	**0.00**
	72 h	7680.43	7989.91		**72 h**	**0.00**	**0.00**
Ramsay Sedation Scale		**Group A**	**Group B**			**Group A**	**Group B**
6 h Before Surgery		**Mean**	**Mean**				
After Surgery	**Baseline**	1.97	2.00				
	0 h	1.00	2.00				
	6 h	2.00	2.00				
	12 h	2.00	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				

Statistically significant change ($p<0.05$, ANOVA test) in heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure, Mean RPP (HR*MAP) were within clinically accepted ranges, the mean VAS score was found to be low, among the groups of participants. In group A by 6 h and in group B patients the score reached to 2.0 immediately in post-operative 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**	5.40±1.16	405.00±87.20
B	**Mean±SD**	5.13±0.63	385.00±47.16

Mean total post-operative analgesic requirements among the participants of group A and B were observed to be 405 and 385 mg respectively.

DISCUSSION

Demographic Variables

In the present study mean age was 36.27± 7.07 years, with age ranges from 18 to 54 years. The mean age of two Groups of participants was comparable. The mean age in the present study was similar to the study conducted **Niyogi S, Bhunia P, Nayak J et al (2017)[2]**, while the mean ages were higher in the studies conducted by **Monu Yadav, Mohan CL, Shrikanth I et al (2019)[3] (**55.00±14.82) **Anju Krishnan (2021)[4] (**47.67±4.64) and **SettiT, Sanfilippo F, Leykin Y et al (2012)[5]** (47.1±5.5)

In the present study majority participants were female (90.0%) with 26 (86.7%) in Group A and 28 (93.3%) in Group B. Thus both the groups were comparable. However, in similar studies by **MonuYadav, Mohan CL, Shrikanth I et al (2019)[3]** and **Niyogi S, Bhunia P, Nayak J et al (2017)[2]**, 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.

As can be seen from the tables 2, lower HR and SBP values were observed in group A at most of the study points. The RPP which represents the cumulative effect on haemodynamic was lower in the group A, indicating that better overall

haemodynamic is better maintained by transdermal buprenorphine patch [20 microgram/hour] applied 6 hours before surgery in patients undergoing surgeries under General Anaesthesia.

Thus, patients undergoing surgeries under General Anaesthesia (Group A), was observed that the HR and SBP were lower in group A (20 mcg/h) at most of the study points. However, the DBP and MAP were slightly higher in group A (20 mcg/h) at most of the study points. RPP (HR*MAP) was lower in group A (20 mcg/h) at most of the study points, except during the initial 6 hours and at 72 hours.

Comparing the two doses in patients undergoing surgeries under Regional Anaesthesia, it was observed that the group B (20 mcg/h) had slightly lower HR. The SBP, DBP and MAP were similar in both the groups. Similarly RPP (HR*MAP) was lower in group B at most of the study points.

The meta-analysis conducted by **Felipe, Chiodini, Machado et al (2020)[6]** showed that buprenorphine did improve pain management compared to placebo with evidence of increased nausea, somnolence and sedation scores, but no difference to placebo was reported in other common opioid-related side effects such as vomiting, pruritus , constipation, urinary retention and respiratory depression. In the present study 1 in group A failed to achieve sedation score at the end of surgery. However, at the 18th hour all had achieved a score of 2. In the present study no incidences of sleep apnea Mental / mood changes (agitation, confusion hallucination), difficulty in urinating, swelling / blister at the patch application site were observed. Signs of adrenal insufficiency (unusual tiredness, weight loss) or liver dysfunction were also not observed.

Perioperative VAS changes

Statistically significant change ($p<0.05$, ANOVA test) in Mean VAS was found among the groups of participants. Approximately Group A and B (who was applied Buprenorphine patch of 20 µg/h) had low VAS score.
As can be observed from the table 2, VAS scores were significantly lower in group B at baseline as the participants in this group had received regional anaesthesia. However, from 6 to 72 hours, group A had significantly lower VAS scores at all study points. *T*hus general anaesthesia with 20 mcg/h had lower VAS scores among the groups.

It was observed that the scores were significantly lower in the group A and B at all points from 6 h to 72 h. Thus, Buprenorphine 20 mcg/ hr patch had lower VAS scores in both general and regional anaesthesia.

In a study to compare the efficacy of transdermal Buprenorphine with Diclofenac for management of postoperative pain in patients undergoing surgeries under General Anaesthesia**, Narendra Kumar (2020)[7]** observed that the VAS scores were lower in the transdermal Buprenorphine group compared to Diclofenac group from 24 h to 72 h , though the difference failed to achieve statistical significance. They also observed that the VAS scores were significantly lower ($p<0.001$) from 6h to 72 h at all-time points compared to baseline, similar to the observation in the present study.

However, in a study by **Anju Krishnan (2021)[4]** comparing the efficacy of transdermal Buprenorphine with epidural Buprenorphine, the authors found that VAS scores were higher in the transdermal Buprenorphine group than epidural Buprenorphine group at all study points, indicating that the epidural route is better for postoperative analgesia.

Frequency and total rescue analgesia requirement

The frequency and total doses of post-operative rescue analgesic requirement were statistically significant in Group A and Group B ($p<0.001$, ANOVA test). Mean total post-operative analgesic requirements among the participants of group A and B were observed to be 405 and 385 mg respectively. Thus, 20 mcg/h was better in both general and regional anaesthesia with respect to both frequency and total dose of rescue analgesics requirements.

In a study to find out the optimum timing of application of the transdermal buprenorphine patch, **KadapamannilD, Rajan S, Tosh P et al (2018)[8]** observed that the frequency of rescue analgesic requirement were significantly lower when the patch was applied 72 hours prior to the surgery. In our study, the patch was applied 6 hours prior to the surgery .This could explain the frequent and higher analgesic requirements in our study.

Similarly**, Niyogi S, Bhunia P, Nayak J et al (2017)[2]** showed that the total dose of rescue analgesic required could be significantly reduced by the use of transdermal buprenorphine compared to placebo.

SettiT, Sanfilippo F, Leykin Y et al (2012)[9] used 17.5, 35, and 52.5 mg/h of TDB patches in patients undergoing open gynaecologic surgeries providing IV morphine and ketorolac as rescue analgesics. They found that the consumption of rescue analgesia was inversely correlated to the TDB dosage.

In another study by **Conaghan PG,O'Brien CM, Wilson M et al *(2011)*[10]** transdermal buprenorphine patch and paracetamol were compared with codeine and paracetamol in elderly patients with osteoarthritis of the hip or knee joints and there was significantly less requirement of rescue medication in buprenorphine patch and paracetamol group when compared with other group.

Desai SN et al., in an Randomised Control Trial (RCT) on patients undergoing hip fracture surgeries found that a 10 µg/h patch applied 24 hours before surgery resulted in lower pain scores and lower rescue analgesic requirement (68% patients) when compared to those receiving oral tramadol. [11]

The meta-analysis conducted by **Felipe ,Chiodini, Machado et al(2020)[6]** showed that in studies comparing transdermal buprenorphine with placebo, lower postoperative pain scores and lower postoperative analgesic consumption were observed in the buprenorphine groups.(104-106) Two studies showed increased sedation scores,18 nausea or somnolence 20 in the buprenorphine group, while one study showed no differences in drug-related side effects.

Perioperative Ramsay Sedation Scale changes

Table 2 depicts that all the patients were cooperative, oriented and tranquil by 18 hours of post-operative period. The mean Ramsay sedation score in group A by 6 h and in group B patients the score reached to 2.0 immediately in post-operative period.

Thus, with respect to general anaesthesia, sedation score of 2 was reached earlier (6h) in group C (20mcg/h). Similarly, with respect to regional anaesthesia, sedation score of 2 was reached earlier (immediate post-operative) in group D (20mcg/h).

Kadapamannil D, Rajan S, Tosh P et al (2018)[8] in their study for the optimum timing of application of the transdermal buprenorphine patch compared the scores in two groups with the application of the patch 48 hours or 72 hours prior to surgery. The authors observed that a score of 2 was achieved in both the groups by 6 hours after surgery.

The meta-analysis conducted by **Felipe ,Chiodini, Machado et al (2020)[6]** showed that buprenorphine did improve pain management compared to placebo with evidence of increased nausea, somnolence and sedation scores, but no difference to placebo was reported in other common opioid-related side effects such as vomiting, pruritus, constipation, urinary retention and respiratory depression. In the present study 1 in group C at the end of surgery failed to achieve sedation. However, at the 18th hour all had achieved a score of 2. In the present study no incidences of sleep apnoea, mental / mood changes (agitation, confusion hallucination), difficulty in urinating, swelling / blister at the patch application site were observed. Signs of adrenal insufficiency (unusual tiredness, weight loss) or liver dysfunction were also not observed.

CONCLUSION

Transdermal buprenorphine in a dose of 20 micrograms/hour applied 6 hours prior to surgery provides good analgesia in patients undergoing surgeries with both general and regional anaesthesia, with lower pain scores (less than 3, after 30 hours postoperative) and lesser requirement of rescue analgesics (group A, 405.00±87.20 mgs, and group B, 385.00±47.16 mgs), without significant adverse effects. No incidences of bradycardia or hypotension were observed during the study.

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