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Transdermal Buprenorphine Patch or Transdermal Fentanyl Patch in Lower Limb Surgeries: Hemodynamic Changes

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ABSTRACT
Fentanyl was first synthesized as an intravenous anaesthetic by Paul Janssen in 1960. It is a potent agonist of the μ-opioid receptor which is responsible for its analgesic and sedative properties. It is almost 100 times more potent than morphine and has a relatively wide therapeutic index, which makes it a very safe anaesthetic drug when monitored carefully. Drug patches were applied to patients 12 hours before proposed surgery in both groups after noting baseline hemodynamic parameter. Patients were premedicated with Antacids and Anxiolytics i.e., Tab Ranitidine 150mg po and Tab Alprazolam 0.5 mg PO HS under strict aseptic precautions 25g Quincke's Babcock spinal needle was inserted in L3-L4 and 0.5% (H) bupivacaine was injected. Adequate block was achieved. When SBP was compared between two groups at different time intervals, p value was >0.05 and so the results were statistically insignificant. When DBP was compared between two groups at different time intervals, p value was >0.05 and so the results were statistically insignificant.

INTRODUCTION

Transdermal drug delivery system refers to the administration of therapeutic agents through intact skin for systemic effect. It has emerged as one of the most rapidly advancing areas of novel drug delivery system by improving the therapeutic efficacy and safety. It maintains a steady state of the drugs in plasma by releasing the drug at a predetermined and controlled rate. It also overcomes significant drawbacks of the conventional oral dosage forms and parenteral preparations[1,2]. Transdermal delivery of lipophilic drugs like buprenorphine and fentanyl is facilitated by diffusion through blood, lymphatics and interstitial transport to deep tissues. The zero-order (constant rate of delivery) kinetics of transdermal delivery has been one of the cornerstones in the development of transdermal systems[3]. From a global perspective, advances in transdermal delivery systems can be categorized as undergoing three generations of development from the first generation of systems that produced many of today's patches by judicious selection of drugs that can cross the skin at therapeutic rates with little or no enhancement., through the second generation that has yielded additional advances for small molecule delivery by increasing skin permeability and driving forces for transdermal transport., to the third generation that will enable transdermal delivery of small molecule drugs macromolecules (including proteins and DNA) and virus-based/other vaccines through targeted permeabilization of the skin's stratum corneum[4,5]. Fentanyl was first synthesized as an intravenous anaesthetic by Paul Janssen in 1960. It is a potent agonist of the μ-opioid receptor which is responsible for its analgesic and sedative properties. It is almost 100 times more potent than morphine and has a relatively wide therapeutic index, which makes it a very safe anaesthetic drug when monitored carefully[6,7]. The transdermal patch containing fentanyl was introduced in the mid-1990s. Fentanyl is now on the WHO's list of essential medicines, the most effective and safe medicines needed in a health system. It bypasses first pass metabolism and hence has high bioavailability. Due to its highly lipophilic action, it achieves a large volume of distribution[8].

MATERIALS AND METHODS

It is a prospective, randomized single blind study in patients of age group 18-60 years and of American Society of Anesthesiologists (ASA) physical status I and physical status II posted for elective lower extremity surgery.

Study Design: Prospective, randomized single blind study.

Sample Size: 90 with each group having 45 patients.

Inclusion Criteria:

- Age - 18-60 years of either sex.
- Patients belonging to ASA -Grade I and II.
- Patients undergoing elective lower limb surgeries.

Exclusion Criteria:

- Patients with history of drug abuse or alcohol abuse
- Patients with known allergy to fentanyl and buprenorphine.
- Patients on antidepressants, antipsychotics, anxiolytics and anticonvulsants.
- Patients' refusal for the procedure.

We planned to conduct a prospective randomized single blind comparative study involving adult patients undergoing major lower limb surgery under spinal anaesthesia. Written and informed consent was taken from the patient, patients satisfying the inclusion and exclusion criteria were randomly allocated, using a computer- generated random number table and sealed envelope technique, to one of the following two groups of patients.

- **Group A:** This group received Buprenorphine patch (10mcg/hr).
- **Group B:** This group received Fentanyl patch of (25mcg/hr).

Drug patches were applied to patients 12 hours before proposed surgery in both groups after noting baseline hemodynamic parameter. Patients were premedicated with Antacids and Anxiolytics i.e., Tab Ranitidine 150 mg po and Tab Alprazolam 0.5mg PO HS under strict aseptic precautions 25 g Quincke's Babcock spinal needle was inserted in L3-L4 and 0.5% (H) bupivacaine was injected. Adequate block was achieved. Analgesia was assessed using visual analogue score, Ramsay Sedation Score (RSS) 40 and hemodynamic parameters respectively for next 3 days 12 hourly. Hemodynamic parameters and any adverse effects were also noted if any. Injection diclofenac (75mg IV) was used as a rescue analgesic in patient complaining of inadequate pain relief.

RESULTS AND DISCUSSIONS

Number of females in group B was 23 and in group F was 21 Number of males in Group B was 22 and in group F was 24. With a p- value of 0.673, the comparison between both groups is statistically insignificant (Table 1). Group B is 45 and Group F is 45 total ASA is 90 (Table 2). When SBP was compared between two groups at different time intervals, p value was >0.05 and so the results were statistically insignificant (Table 3). When DBP was compared between two groups at different time intervals, p value was >0.05 and so the results were statistically insignificant (Table 4). When HR was compared between two groups at different time intervals, p value was >0.05 and so the results were statistically insignificant (Table 5).

Table 1: Comparison of Gender Between Group B and Group F

		Group B		Group F				
		No. of cases	%Age	No. of cases	%Age	Total	Chi- square value	p-value
Gender	Female	23	51.1%	21	46.7%	44	0.178	0.673 (Not
	Male	22	48.9%	24	53.3%	46		significant,
Total	45	100.0%	45	100.0%	90			p>0.05)

Table 2: Comparison of ASA Between Group B and Group F

		Group B		Group F				
		Group B	Group B	Group F	Group F	Total	Chi- square value	p- value
ASA status	1	45	100.0%	45	100.0%	90		

Table 3: Comparison of SBP between Group B and Group F

	Group B		Group F			
	Mean	SD	Mean	SD	Z	p-value
SBP_POD 1 12 Hourly	114.98	1.32	114.93	1.39	-0.103	0.918
SBP_POD 1 24 Hourly	115.02	1.32	115.02	1.32	0.000	1.000
SBP_POD 2 12 Hourly	115.60	1.39	116.09	1.35	-1.612	0.107
SBP_POD 2 24 Hourly	116.18	1.40	115.56	1.47	-1.909	0.056
SBP_POD 3 12 Hourly	117.51	1.42	117.51	1.42	0.000	1.000
SBP_POD 3 24 Hourly	117.69	1.35	117.69	1.35	0.000	1.000

Table 4: Comparison of DBP between Group B and Group F

	Group B		Group F			
	Mean	SD	Mean	SD	Z	p-value
DBP_POD 1 12 Hourly	74.58	2.16	74.58	1.000	0.000	1.000
DBP_POD 1 24 Hourly	74.58	2.16	74.58	1.000	0.000	1.000
DBP_POD 2 12 Hourly	74.76	2.19	74.89	0.761	-0.304	0.761
DBP_POD 2 24 Hourly	75.29	2.34	74.89	0.501	-0.674	0.501
DBP_POD 3 12 Hourly	76.44	2.08	76.71	0.556	-0.589	0.556
DBP_POD 3 24 Hourly	76.44	2.08	76.71	0.556	-0.589	0.556

Table 5: Comparison of Gender Between Group B and Group F

	Group B		Group F			
	Mean	SD	Mean	SD	Z	p-value
HR_POD 1 12 Hourly	86.98	2.15	86.98	2.15	0.000	1.000
HR_POD 1 24 Hourly	87.02	2.17	87.02	2.17	0.000	1.000
HR_POD 2 12 Hourly	87.40	2.30	88.07	2.23	-1.371	0.170
HR_POD 2 24 Hourly	88.07	2.23	87.40	2.30	-1.371	0.170
HR_POD 3 12 Hourly	88.16	2.33	88.60	2.41	-0.986	0.324
HR_POD 3 24 Hourly	88.60	2.41	88.16	2.33	-0.986	0.324

Comparison of the Systolic blood pressure and Diastolic blood pressure showed no statistically significant difference between the two groups. This shows that transdermal patches as such had no significant impact on the blood pressure[9]. Comparison of the heart rate between two groups showed no statistically significant difference. This shows that transdermal patches as such had no significant impact on the heart rate. The incidence of nausea and vomiting was 20% patients in group Fentanyl and 17.8% patients in Group Buprenorphine but was not statistically significant. Inj Ondansetron 4mg was given to stop nausea and vomiting. No other adverse effects like erythema, rashes were seen. Our study was comparable to the study conducted by Wolff RF, Reid K, Di Nisio where they found that there were fewer side effects in patients who received Transdermal Buprenorphine compared to those who received Transdermal Fentanyl[10].

CONCLUSION

Post-operative hemodynamic variables were comparable and stable in both groups.

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