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Original Research Article

COMPARISON BETWEEN TRANSDERMAL BUPRENORPHINE AND TRANSDERMAL FENTANYL FOR POSTOPERATIVE PAIN RELIEF IN LUMBAR SPINE SURGERIES

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Abstract

Background: Buprenorphine and fentanyl patches have been used for pain management. But a direct comparison between them has been done rarely. Our goal primarily aimed to compare the efficacy of buprenorphine (10µg/h) patch and fentanyl (25µg/h) patch in the management of pain in lumbar spine surgeries. **Materials and Methods:** It is a prospective, double-blinded, randomized control trial study. Sixty patients, (30 in each arm) were included in this study between October 2021 and November 2022 at IMS & SUM Hospital in India. Both groups were compared for the duration of sedation, post-operative analgesia and the first need of rescue analgesia using Ramsay sedation scale and visual analogue score [VAS]. Data were entered in Microsoft Excel worksheet and analysed using SPSS version 20 (IBM Corp., Armonk, NY). To compare mean values across groups, one-way ANOVA was done. Chi-square test was used to compare proportions across the two groups. **Result:** Patients with Buprenorphine patch felt significantly more pain than with Fentanyl patch ($P<0.001$). Sedation effect in both groups were same after 36 hours. Fentanyl group needed less rescue analgesia than Buprenorphine group. **Conclusion:** Fentanyl transdermal patch is a safe and effective alternative to buprenorphine patch in pain management in lumbar spine surgeries.

INTRODUCTION

Postoperative pain must be managed in patients undergoing major surgery. It is challenging for pain physicians to effectively manage pain due to its psychological and physiological adverse effects. Hospitals tend to perform poorly and to charge more for health care when patients are suffering from pain. It is common for patients to feel dissatisfied with their hospital stay due to pain, which can make recovery process more challenging, increasing hospital stay length, and contribute to dissatisfaction.[1]

There has been a wide range of success in treating pain with drugs and multimodal approaches. In every technique or drug, there are advantages and disadvantages. Pharmacokinetic problems associated with oral and parenteral administration have been overcome using Transdermal Delivery Systems (TDS). 1 Drugs can be delivered through transdermal delivery systems which is a simple and compliant way. This device slowly releases drugs over time. It is homogenously incorporated into the skin with solid polymer matrix patches that contains the drug.[2]

Buprenorphine is a semi synthetic opioid. It is mu receptor agonist and kappa receptor antagonist. It is available in parenteral, transdermal and sublingual preparations. By using the non-invasive adhesive patch, buprenorphine is slowly and continuously released into the bloodstream. Postoperative pain following lower abdomen surgeries may be effectively managed with transdermal buprenorphine, based on its characteristics.[3]

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By 1960, Paul Janssen had synthesized the first fentanyl anesthetic. The drug is a potent opioid receptor agonist as well as an analgesic and sedative. With proper monitoring, it has a therapeutic index almost 100 times larger than morphine and is a very safe anesthetic. A transdermal patch containing fentanyl was introduced in the mid-1990s. Iontophoresis is used to deliver active transdermal fentanyl for the treatment of acute, moderate-to-severe postoperative pain. It is known that electro-repulsion of ionized drug molecules dramatically increases transdermal fentanyl delivery compared to passive diffusion of drugs in the fentanyl HCl iontophoretic transdermal system.[4]

Both buprenorphine and fentanyl patches have been used for pain management and many studies have reported their effectiveness.[5,6] But only one study has actually compared the efficacy of buprenorphine (10µg/h) patch and fentanyl (25µg/h) patch in arthroscopic lower limb surgeries.[7]

Our study primarily aims to measure the duration of sedation, post-operative analgesia and the first need of rescue analgesia using Ramsay sedation scale and visual analogue score [VAS].

Secondary aim is to measure heart rate, blood pressure, and look for side effects like nausea, vomiting, pruritus, respiratory depression in both the drugs.

MATERIALS AND METHODS

A randomized controlled study was carried out in a tertiary care hospital after obtaining approval from Institutional Ethical Committee (IEC REF NO/DMR/IMS.SH/SOA/2021/189). Written informed consent was taken from the subjects before enrolment. CONSORT guidelines were followed for reporting the trail.

Sixty patients, aged between 20 to 50 years, planned for elective lumbar spine surgeries, belonging to American Society of Anaesthesiologists (ASA) physical status I and II were included in this study between October 2021 and November 2022. Pregnant and breastfeeding females and patients with impaired pulmonary function were excluded. Further those patients with allergic to the drugs were also not included in the study. Double-blinding was followed to avoid bias. Both the physicians and the patients were not aware of the group allotment and intervention received. Drug administration was done by the nurses.

Patients were randomly allotted to two groups using computer-generated random numbers.

The patients were randomized in to two groups.

Group A: This group received transdermal Buprenorphine patch (10µg/h),on hair less area of chest, back, flank and upper arm.

Group B: This group received transdermal Fentanyl patch (25µg/h), on hair less area of chest, back, flank and upper arm.

After noting baseline hemodynamic parameters, both groups applied drug patches 6 hours prior to surgery. It was recommended that the patients be kept nil per oral for 8 hours (solids) and 2 hours (clear liquids). Intravenous line was secured with 18 G cannula as soon as the patient arrived in the operating room. At the time of surgery, patients were premedicated with inj. Midazolam 1mg IV, inj. Fentanyl 2 mcg/kg IV and inj. Ondansetron 4 mg IV. Patients were induced with inj. Propofol 2 mg/kg IV and intubated with inj. Vecuronium 0.1 mg/kg IV. Anesthesia was maintained with N2O and O2 (60:40), isoflurane and muscle relaxation was maintained with vecuronium. At the end of surgery, after reversing neuromuscular blockade with inj . glycopyrrolate (0.01 mg/kg), inj. Neostigmine (0.05 mg/kg), patients were extubated.

Using the Ramsay Sedation Score and Visual Analogue Scale, patients were assessed for sedation and analgesia every 12 hours for three days.[8,9]

Score	Clinical state or response to stimulation
1	Patient anxious and/or agitated and/or restless
2	Spontaneous eye openings
3	No spontaneous eye opening, response to vocal stimulus
4	No response to vocal stimulus, response to loud stimulus
5	No response to loud stimulus, response to tetanic (50 Hz, 40 mA, 0.25 s pulses, duration 4 s) stimulus
6	No response to tetanic stimulus

Figure 1: Ramsay Sedation Score

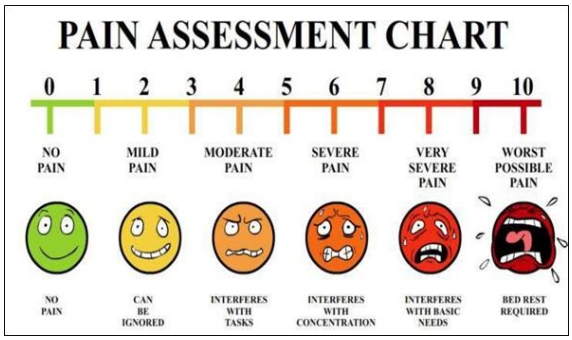

Figure 2: Pain Assessment Chart Using Visual Analogue Scale

We also assessed the hemodynamic parameters and noted any adverse effects. Inj. Diclofenac (75 mg IV) was used as rescue analgesia for patients complaining of inadequate pain relief.

Statistical Analysis: Patients (n=60) of age 20-50 years, undergoing lumbar spine surgeries under GA were included.

Based on previous study, for achieving a power of study equal to 80% with 0.05 level of significance sample size of 30 patients per group is required. 10

Data were entered in Microsoft Excel worksheet and analysed using SPSS version 20 (IBM Corp., Armonk, NY). To compare mean values across groups, one-way ANOVA was done. Chi-square test was used to compare proportions across the two

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groups. The P value < 0.001 was considered as statistically significant.

RESULTS

Thirty patients were enrolled in each group. Baseline characteristics of the patients in both the groups like age, gender and ASA grade were comparable. No significant difference was found among both the groups which showed that the groups are comparable. [Table 1]

Table 1: Baseline characteristics of patients

		Group A (n=30)	Group B (n=30)	*P* value
Age		40.07±7.45	36.90±8.25	0.124
Gender	Male	19 (63.3%)	19 (63.3%)	1.000
	Female	11 (66.7%)	11 (66.7%)	
ASA grade	I	17 (58.6%)	23 (66.7%)	0.138
	II	12 (41.4%)	7 (63.3%)	

Pain was more felt in Group A in comparison to Group B and the result was found to be statistically significant. [Table 2]

Table 2: Pain assessment using visual analogue scale

	Group A (n=30)	Group B (n=30)	*P* value
At 12hrs	4.50±1.14	3.27±0.69	<0.001
At 24hrs	3.53±0.63	2.60±0.56	<0.001
At 36hrs	3.27±0.45	2.17±0.65	<0.001
At 48hrs	3.27±0.45	1.10±0.66	<0.001
At 60hrs	3.03±0.41	0.63±0.67	<0.001
At 72hrs	2.77±0.57	0.50±0.57	<0.001

In Group A sedation was significantly better than Group B up to 36 hours. After 36 hours up to 72 hours, there was no significant difference in both groups. [Table 3]

Table 3: Ramsay sedation score

	Group A (n=30)	Group B (n=30)	*P* value
At 12hrs	2.00±0.53	1.37±0.49	<0.001
At 24hrs	2.27±0.69	1.40±0.56	<0.001
At 36hrs	1.90±0.61	1.33±0.48	<0.001
At 48hrs	2.03±0.67	1.87±0.68	0.343
At 60hrs	1.67±0.80	1.60±0.50	0.700
At 72hrs	1.23±0.43	1.27±0.45	0.770

Need for rescue analgesia was more in Group A but was not found to be statistically significant. [Table 4]

Table 4: Rescue Analgesia

		Group A (n=30)	Group B (n=30)	*P* value
Need of rescue analgesia	Yes	7 (23.3%)	0 (0.0%)	0.005
	No	23 (76.7%)	30 (100.0%)	

The occurrence of side effects was found to be identical in both the groups without any significant differences. [Table 5]

Table 5: Comparison of side effects

		Group A (n=30)	Group B (n=30)	*P* value
Side effects	Yes	9 (30.0%)	9 (30.0%)	1.000
	No	21 (70.0%)	21 (70.0%)	

No significant change in systolic blood pressure, diastolic blood pressure and heart rate was observed among both the groups. [Table 6]

Table 6: Comparison of Systolic Blood Pressure, Diastolic Blood Pressure & Heart Rate

		Group A (n=30)	Group B (n=30)	*P* value
Changes in Systolic Blood Pressure	At 12hrs	108.63±10.10	108.17±8.82	0.850
	At 24hrs	106.83±7.27	105.27±7.41	0.412
	At 36hrs	110.10±9.48	108.63±8.90	0.539
	At 48hrs	110.83±10.59	109.77±10.34	0.695
	At 60hrs	110.60±9.65	109.23±9.78	0.588
	At 72hrs	110.47±9.75	108.13±10.29	0.371
Changes in Diastolic Blood Pressure	At 12hrs	80.20±9.63	78.67±10.33	0.554
	At 24hrs	81.23±9.47	79.27±8.92	0.411
	At 36hrs	82.23±9.92	81.00±10.74	0.646
	At 48hrs	84.67±9.86	79.00±9.17	0.025
	At 60hrs	83.90±8.68	81.13±9.03	0.231
	At 72hrs	81.27±8.14	79.17±8.95	0.346
Changes in Heart Rate	At 12hrs	79.30±8.12	83.47±10.01	0.082
	At 24hrs	81.43±10.57	82.80±12.69	0.652
	At 36hrs	83.87±11.42	84.40±10.70	0.853
	At 48hrs	87.20±13.27	86.23±10.93	0.759
	At 60hrs	82.60±12.49	83.47±12.52	0.789
	At 72hrs	83.00±11.12	83.37±10.94	0.898

DISCUSSION

In this study, we compared the effect of transdermal buprenorphine and transdermal fentanyl for the post operative analgesic efficacy and adverse effects, in the patients undergoing lumbar spine surgeries. Various studies using different amounts of buprenorphine and fentanyl transdermal patches, as well as the effects of the drugs at different doses, were reviewed to determine the dosage for each drug. In this study, 60 patients who were undergoing elective posterior stabilization of the lumbar spine and provided informed consent were enrolled.

Since it was a double blinded study, only the data collector knew which group they belonged to because it was a sealed envelope technique that divided the patients into two groups. Depending on the envelope they picked, they were divided into either group A, which received transdermal buprenorphine, or group B, which received transdermal fentanyl.

We examined the safety, analgesic efficacy and side effects of two opioid TDS in postsurgical patients for three days, 12 hourly in our study. Both groups had similar haemodynamic variables, with no clinically significant deviations from baseline values. The use of fentanyl TDS has been associated with isolated cases of bradycardia in previous studies, but we did

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not find any adverse haemodynamic events in either group.

As a result of the demographic analysis, the mean age of patients in Group A was 40.07 years while that of patients in Group B was 36.90 years. A higher percentage of female individuals were found in our study than male individuals. ASA grading I was the most common ASA grade among both groups. Additionally, baseline vital parameters such as SBP, DBP, and Heart Rate did not differ significantly between the two groups.

A significant decrease in VAS score, which was used to quantify the pain, was observed in group B compared to group A from day one to day three. We found that in group A, there was no significant decrease in pain score compared to baseline values, suggesting that buprenorphine TDS is not as effective as fentanyl in reducing pain; however, we should remember that buprenorphine.

TDS did not increase VAS after surgery. Thus, we can say that buprenorphine TDS is effective in attenuating postsurgical pain.

Fentanyl TDS (Group B) was more effective in controlling postsurgical pain than Buprenorphine TDS (Group A) from day 1 to 3, as VAS decreased significantly from day 1 to 3, respectively. In conclusion, both TDS were effective at controlling postoperative pain, but fentanyl proved to be more effective.

Also, the Ramsay sedation score was determined at 12-hour intervals, which was found to be lower in Group B patients than Group A at 12 hours, 24 hours, and 36 hours. It was also found that the sedation score in Group A was 2.03 at 48 hours, but in Group B it was 1.87, which was not statistically significant (p-value 0.343). A similar result was also observed at 60 hours and 72 hours, when the sedation score did not differ among both groups of patients.

Liaquat Ali et al., found statistically significant difference ($p<0.050$) with respect to Ramsay sedation score at 15, 20, 25 and at 120 minutes after extubating the patients among the groups A (Control group), B (Fentanyl group) & C (dexmedetomidine group). Patients in group (C) and group (B) were little more sedated than group A.[11]

Our study results co-relate well with the findings of studies by Nishina et al, Recep Aksu et al, Wang BS et al, G. Turan et al, Barkha Bindu et al and D. Jain et al.[12-16]

In patients who received transdermal buprenorphine, of them 7(23.3%) patients required rescue analgesia, whereas in another group who received transdermal fentanyl none of them required rescue analgesia. This observation was found statistically significant with p-value 0. 005.The need for rescue analgesia, hence was higher in the buprenorphine group (7 out of 30) when compared to the fentanyl group (0 out of 30).

In both groups 9(30.0%) patients developed side effects and rest of them did not develop any side effects.

The results of our study are comparable to those reported by Wolff RF, Reid K, Di Nisio et al who found that patients receiving TDB experienced fewer side effects than those receiving TDF.[17]

During the study period, a 12-hour interval was kept between the measuring of systolic blood pressure (SBP). No significant difference was observed between the two groups at any time interval. Additionally, there was no statistically significant difference between the two groups in Diastolic blood pressure (DBP) and Heart rate (HR). Hemodynamic variables were compared in both groups and no clinically significant deviations were observed from baseline values. In our study, neither group suffered from any adverse hemodynamic events.

Patient satisfaction score is one of the important indicators in health care organization, which was recorded as Fair, Good and Excellent. None of the patients had excellent satisfaction among the first group, among Group B 10(33.3%) patients had excellent satisfaction. It was also found statistically significant with p-value <0.001. Both TDS were effective at controlling postoperative pain, so we can draw the following conclusion. As a result, fentanyl was superior. In light of this, we can conclude that fentanyl TDS is a more effective analgesic than buprenorphine TDS.

The effects of fentanyl TDS on postsurgical patients have not been extensively studied due to the possibility of respiratory depression. On the other hand, it has been used for chronic pain and in cancer pain. As a result of our study, we found that this is a much less serious problem than previously thought, and is safe and effective as other opioids. Hence Fentanyl TDS is safe and effective.

Fentanyl patch costs INR 1450 (Duragesic TM 25 mcg) and buprenorphine patch costs INR 890 (Buvlor TM 10 mcg). Fentanyl TDS, works for three days, while buprenorphine TDS works for seven days. In other words, buprenorphine TDS is cheaper than fentanyl TDS.

CONCLUSION

Thus, we can conclude that both transdermal fentanyl and transdermal buprenorphine were effective in controlling postsurgical pain and fentanyl is better in this regard as it has better analgesia and less sedation.

REFERENCES

1. Dunwoody CJ, Krenzischek DA, Pasero C, Rathmell JP, Polomano RC. Assessment, physiological monitoring, and consequences of inadequately treated acute pain. Pain Management Nursing. 2008 Mar 1; 9(1):11-21.
2. Dave S, Shriyan D, Gujjar P. Newer drug delivery systems in anaesthesia. J Anaesthesiol Clin Pharmacol 2017; 33:157 63.
3. Brannon-Peppas L. Polymers in controlled drug delivery. Medical Plastic and Biomaterials. 1997 Nov; 4:34-45.
4. Burns SM, Cunningham CW, Mercer SL. DARK classics in chemical neuroscience: fentanyl. ACS Chemical Neuroscience. 2018 Jun 12; 9(10):2428-37.
5. Wai EK, Roffey DM, Tricco AC, Don AS, Dagenais S. Fusion Surgery and Disc Arthroplasty. Evidence-Based Management of Low Back Pain-E-Book. 2011 Feb 11:422.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

6. Kimura H, Shikata J, Odate S, Soeda T, Yamamura S. Risk factors for cage retropulsion after posterior lumbar interbody fusion: analysis of 1070 cases. Spine. 2012 Jun 1;37(13):1164-9.
7. Khandelwal H, Negi A, Govil N, Singh A, Parag K, Bhardwaj BB. Comparative evaluation of analgesic efficacy of buprenorphine transdermal patch and fentanyl patch in management of postoperative pain after arthroscopic lower limb surgery: A randomized controlled trial. J Anaesthesiol Clin Pharmacol 2021; 37:272-8.
8. Sessler CN, Grap MJ, Ramsay MA. Evaluating and monitoring analgesia and sedation in the intensive care unit. Critical care. 2008 May; 12(3):1-3.
9. Dutheil F, Vilmant A, Boudet G, Mermillod M, Lesage FX, Jalenques I, Valet G, Schmidt J, Bouillon-Minois JB, Pereira B. Assessment of sick building syndrome using visual analog scales. Indoor air. 2022 Mar; 32(3):e13024.
10. Zia Arshad , Ravi Prakash , Shefali Gautam , Sanjeev Kumar. Comparison between Transdermal Buprenorphine and Transdermal Fentanyl for Postoperative Pain Relief after Major Abdominal Surgeries. Journal of Clinical and Diagnostic Research. 2015 Dec, Vol-9(12): UC01-UC04.
11. Ali L, Shrinivas TR. A study on comparison of extubation quality scale between fentanyl and dexmedetomidine. IJMA. 2020;3(1):154-8.
12. Turan M, Bagcivan I, Gursoy S, Sarac B, Duman M, Kaya T. In vitro effects of intravenous anesthetics on the sphincter of Oddi strips of sheep. Pancreatology. 2005 Jan 1;5(2-3):215-9.
13. Nishina K, Mikawa K, Maekawa N, Obara H. Fentanyl attenuates cardiovascular responses to tracheal extubation. Acta anaesthesiologica scandinavica. 1995 Jan;39(1):85-9.
14. Aksu R, Akin A, Biçer C, Esmaoğlu A, Tosun Z, Boyaci A. Comparison of the effects of dexmedetomidine versus fentanyl on airway reflexes and hemodynamic responses to tracheal extubation during rhinoplasty: A double-blind, randomized, controlled study. Current therapeutic research. 2009 Jun 1;70(3):209-20.
15. Wang C, Chakrabarti MK, Whitwam JG. Specific enhancement by fentanyl of the effects of intrathecal bupivacaine on nociceptive afferent but not on sympathetic efferent pathways in dogs. The Journal of the American Society of Anesthesiologists. 1993 Oct 1;79(4):766-73.
16. Jain K, Grover VK, Mahajan R, Batra YK. Effect of varying doses of fentanyl with low dose spinal bupivacaine for caesarean delivery in patients with pregnancy-induced hypertension. International journal of obstetric anesthesia. 2004 Oct 1;13(4):215-20.
17. Wolf RF, Reid K, di Nisio M, Aune D, Truyers C, Hernandez AV. Systematic review of adverse events of buprenorphine patch versus fentanyl patch in patients with chronic moderateto-severe pain. Pain Manag. 2012;2(4):351-62.

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