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Comparison of Pre-emptive Analgesic Effects of Transdermal Buprenorphine Versus Transdermal Fentanyl Patches in Patients with Carcinomas of the Maxillofacial Region: A Prospective Clinical Study

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ABSTRACT

Background and Objectives: Transdermal opioids have emerged as an effective and efficient analgesic modality to reduce post-operative pain effectively without the associated side effects of conventional iv opioids. This study aimed to assess the analgesic effectiveness of transdermal Buprenorphine 10 mcg/hr patches and transdermal Fentanyl 25 mcg/hr patches for alleviating postoperative pain oral cancer patients undergoing surgical resection with modified radicle neck dissection (MRND III) with reconstruction.

Materials and Methods: This prospective, double-blind, randomized study included adult patients diagnosed with squamous cell carcinoma in the maxillofacial region. Participants were randomly assigned to one of three groups: Group 1 (control) received 100 mg of intravenous tramadol in 100 ml of normal saline, Group 2 received a fentanyl patch (25 mcg/hr), and Group 3 received a transdermal buprenorphine patch (10 mcg/hr). All patients were provided with intravenous paracetamol (1g) as a rescue analgesic when necessary. The transdermal patches were applied immediately before surgery. The primary objective was to assess mean FLACC scores, while the secondary objective was to evaluate total rescue analgesic requirements.

Results: Group 3 demonstrated the lowest median FLACC scores, with a statistically significant difference ($P < 0.05$) at 2, 4, 8, 12, and 24 hours postoperatively (Kruskal-Wallis test). In addition, the total consumption of rescue analgesics was significantly lower in Group 3 compared to the other groups, without a corresponding increase in adverse events.

Conclusions: The study concluded that applying a 10 mcg/hr buprenorphine patch prior to surgery in patients undergoing oral cancer procedures provides effective postoperative pain relief with minimal adverse effects.

INTRODUCTION

Managing postoperative pain continues to be a significant challenge, affecting a large proportion of patients (57.7%). [1] Poorly controlled pain can lead to complications such as delayed recovery, hemodynamic instability, reduced respiratory effort, and potential psychological effects, all of which may contribute to the development of chronic postsurgical pain. Recent research shows that many patients still experience insufficient pain relief after surgery and highlights the importance of updated pain relief methods [2,3]

There has been a gradual increase in the number of studies highlighting inadequate post-operative analgesic cover after surgical resection of maxillofacial neoplasms, with a majority of patients complaining of severe post-operative pain and discomfort. [4] The use of a transdermal drug delivery system for the administration of opioid

analgesics helps reduce post-operative pain while simultaneously reducing the risk of respiratory depression, which is a common complication associated with intra-venous opioid administration. [5]

Although transdermal opioid patches are well-known for managing chronic pain, their use in treating acute postoperative pain has been growing. One advantage of transdermal drug systems (TDS) is that they avoid the pharmacokinetic issues linked to oral and parenteral administration, offering a simpler delivery method compared to intravenous and oral routes. [6] TDS eliminates the need for additional opioid dosing during the postoperative period by providing a controlled release of medication in small, steady amounts, ensuring consistent blood levels over time.

The efficacy of transdermal patches in reducing chronic pain has been well- researched before, with several studies proving its efficacy . [7] The primary goal of this study is to assess the efficacy of the fentanyl patch (25 mcg/hr) in comparison to buprenorphine patches (10 mcg/hr) for managing acute postoperative pain in maxillofacial carcinoma surgeries over a period of 24 hours.

METHODOLOGY:

This randomized, controlled, double-blind study was conducted following approval from the Institutional Ethical Committee of Saveetha Dental College. Over a 10-month period, patients who voluntarily participated provided written informed consent.

Patients aged 18–60 years, classified as American Society of Anesthesiologists (ASA) grade I–III, of any gender, diagnosed with squamous cell carcinoma, and scheduled for wide local excision, MRND III, and reconstruction under general anesthesia, were included in this study. Exclusion criteria involved patients undergoing minor surgeries with local anesthesia, those with known allergies to the study drugs, individuals with liver or kidney diseases, chronic alcoholics, and those experiencing chronic pain syndromes. Patients who had been using opioid analgesics or NSAIDs for over three months, as well as those on antiepileptic or antidepressant medications, were also excluded. Additionally, patients undergoing reconstructive surgery without primary tumour resection or undergoing surgical re-exploration were not included.

Participants were randomly assigned to one of three groups using RAS software version 3 with a random table allocation method before surgery. Allocation concealment and patch application were managed by a nurse not involved in the study to maintain blinding of both patients and evaluating physicians. Patients were enrolled one day prior to surgery, and any previous analgesics were discontinued. Paracetamol (1g intravenous) was administered as a rescue analgesic before surgery. Patients were informed about the study protocol and potential side effects of the patches.

Transdermal patches were applied one hour before surgery to a hairless area on the right upper arm. Patches were pressed firmly for 30 seconds, and patients were monitored for signs of local irritation as well as symptoms such as respiratory depression and hypoxia via pulse oximetry for one hour. The patches were concealed with gauze and micropore tape to ensure blinding for clinicians collecting data. Group 1 served as the control group with patients receiving no patch, only a gauze and micropore tape for blinding. Patients in Group 2 received transdermal fentanyl patches (25 mcg/hr), and patients in Group 3 received transdermal buprenorphine patches (10 mcg/hr).

Patients underwent wide local excision with MRND III and reconstruction under general anesthesia. Intraoperative and post-operative monitoring of vitals signs and fluid management were conducted according to ASA guidelines. Heart rate and mean arterial pressure was maintained within ± 20% of baseline values. Post-surgery, patients were transferred to the ICU while still intubated. Pain was assessed using the FLACC scale, with scores ranging from 0 to 10, at intervals of 2, 4, 8, 12, and 24 hours.

Patients with a FLACC score greater than 4 were given 1g intravenous paracetamol as rescue analgesia. If pain persisted or the VAS score exceeded 4 within six hours of the last paracetamol dose, 100 mg intravenous tramadol was administered. Intra-venous Ondansetron 4 mg was administered if the patient complained of nausea or vomiting. Primary outcomes included pain scores, while secondary outcomes focused on total rescue analgesic usage.

RESULTS:

A total of 50 participants were initially recruited for the study. Baseline characteristics, including age, weight, and sex, were similar across all three groups, with no significant differences noted in anesthesia or surgery

duration. Group 3 had significantly lower FLACC scores compared to Groups 1 and 2 during the first 24 hours postoperatively, with no substantial differences in scores observed between the groups after that period. It was observed that the patients in group 3 demanded the least amount of total rescue analgesics. This value was significantly lower in the third group as compared to the other two groups.

No significant changes in respiratory rate, breathing patterns, or any instances of respiratory depression were observed across the three groups, with oxygen saturation consistently remaining above 95% for all participants throughout the study.

More than fifty percents of the patients in Group 1 experienced nausea or vomiting. Pruritus was significantly more common in the fentanyl group (Group 2) than in the buprenorphine group (Group 3). A total of eight patients in Group 2 and four patients in Group 3 reporting this side effect. Although nausea and vomiting were reported more frequently in Group 3- and patients required increased frequency of administration of Injection Ondasetron - this difference was not statistically significant. Specifically, three patients in Group 2 and two in Group 3 reported these symptoms.

Table 1: Descriptive characteristics of the groups

CHARACTERISTICS	GROUP 1	GROUP 2	GROUP 3	P VALUE
Mean Age in years	36 +- 8.2	38+-7.5	39+- 7.3	0.18
Gender Distribution	21:19	25:15	27: 13	0.21
Mean Weight of the patient in Kgs	67+-7.5	59 +- 8.2	63+- 7.8	0.05
Duration of the surgery in minutes	112 +_ 18.9	118 +- 17.9	119 +- 30.6	0.19

Table 2: mean VAS score

TIME	GROUP 1	GROUP 2	GROUP 3	P VALUE
2 hrs	6.3 (2-8)	5.4 (3-8)	4.8 (2-7)	0.031
4 hrs	5.2 (3-8)	5.2(3-7)	4.7 (2-7)	0.042
8 hrs	5.1 (3-7)	4.8 (2-6)	3.9 (1-6)	0.028
12 hrs	4.8 (1-5)	4.7 (2-6)	3.6 (2-5)	0.023
24 hrs	2.8 (1-3)	2.7 (1-4)	2.4 (1-3)	0.038

Table 3: Mean consumption of rescue analgesic

	Group 1	Group 2	Group 3	P Value
Total Paracetamol Consumption (in mg)	2240 +- 200.80	1160+- 270.45	1080 +- 280.50	0.002

DISCUSSION:

Anesthesiologists use a range of methods to deliver analgesics for managing postoperative pain, each with distinct advantages and disadvantages. Although intravenous and oral routes are effective in the immediate postoperative phase, they are often associated with notable side effects. Transdermal patches have gained popularity for acute or postoperative pain management in various surgical fields. [8–10]. Transdermal patches of potent opioids such as buprenorphine and fentanyl offer ease of administration, a favourable safety profile, and less invasive drug delivery with sustained blood levels [11,12]. Fentanyl, a synthetic opioid, is ideal for transdermal application in managing acute pain due to its low molecular weight and increased lipid solubility. [11] Similarly, buprenorphine, which acts as a partial agonist at mu-opioid receptors, is characterized by its poor oral bioavailability, increased lipid solubility, and decreased molecular weight. It is available in transdermal patches with strengths of 5, 10, or 20 mcg/hr for extended analgesic effects. [12, 13]

While the existing literature proves the efficacy of both opioid patches in managing chronic and acute pain, a lack of comparative studies between them prevents clinicians from making informed clinical decisions. Additional randomized trials are needed to definitively establish optimal dosing and identify side effects. [14,15]

As postoperative pain severity is typically moderate to severe in the first 24 hours, the study focuses only on this period. Pain reduction during this period also reduces discomfort in intubated patients and improves patient compliance. Limiting the period of evaluation to 24 hours also helps to negate the effects of variation in the duration of action of Fentanyl and Buprenorphine, which is 3 days and 7 days respectively. [16,17]. Given the onset of action of opioid patches at 10 to 12 hours, and the duration of the surgery being 6- 8 hours, all patients received transdermal patches 1 hour before surgery. Non-opioid analgesics, specifically paracetamol, were used as rescue analgesics in the study to avoid exacerbating side effects associated with opioids [18].

Results indicate that the buprenorphine patch is more efficient in reducing acute postoperative pain, leading to reduced rescue analgesic requirements and minimal adverse events. Similar results were observed by Machado FC et al in a systematic review, which analyzed nine studies involving 615 patients. The review found that transdermal buprenorphine reduces the need for postoperative analgesics while maintaining similar pain scores, and most studies did not report a rise in adverse drug reactions. However, several of the studies had an unclear Risk of Bias (ROB) assessment, making the results of the systematic review questionable. [19]. In the present study, nausea/vomiting and pruritus were more common in the fentanyl group compared to the buprenorphine group, with no significant difference observed between the two buprenorphine. This aligns with observations by Walsh et al., who also noted a lesser degree of nausea/vomiting and pruritus in the buprenorphine group [20]. The study also found no hemodynamic instability in the fentanyl group, contrasting with a study by Oliashirazi et al., where some fentanyl patch users experienced hypotension and bradycardia [21].

Furthermore, while Tassinari et al. reported that the use of transdermal Buprenorphine patches were associated with increased incidence of nausea and vomiting. However, his studies used a higher dosage of Buprenorphine (40 mcg/hr). In this study, a 20 mcg/hr dose of buprenorphine was used and no significant increase in these symptoms were observed. The incidence of nausea and vomiting was lower compared to the fentanyl group while providing adequate pain relief. [22]

CONCLUSION

Transdermal Buprenorphine patches 10mcg/hr are found to be more effective than transdermal Fentanyl 25mcg/hr at reducing post-operative pain oral cancer surgeries. However, more conclusive studies and randomized control trials are required to draw conclusive evidence.

REFERENCES:

[1] Shen YC, Liao KL, Cheng KI, Tseng KY, Su MP. Persistent Postsurgical Pain in Oral Cancer Patients Reconstructed with Anterolateral Thigh Free Flap. Medicina (Kaunas). 2022 Mar 6;58(3):391. doi: 10.3390/medicina58030391. PMID: 35334567; PMCID: PMC8950433.

[2] Willingham M, Rangrass G, Curcuru C, Abdallah AB, Wildes TS, McKinnon S, Kronzer A, Sharma A, Helsten D, Hall B, Avidan MS. Association between postoperative complications and lingering post-surgical pain: an observational cohort study. British journal of anaesthesia. 2020 Feb 1;124(2):214-21.

[3] McNicol E, Horowicz-Mehler N, Fisk RA, Bennett K, Gialeli-Goudas M, Chew PW, Lau J, Carr D. Management of opioid side effects in cancer-related and chronic noncancer pain: a systematic review. The Journal of Pain. 2003 Jun 1;4(5):231-56.

[4]. Yekkirala AS, Roberson DP, Bean BP, Woolf CJ. Breaking barriersto novel analgesic drug development. Nat Rev Drug Discov 2017;16:545-64.

[5] Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol 2008;26:1261-8.

[6] Dave S, Shriyan D, Gujjar P. Newer drug delivery systems in anesthesia. J Anaesthesiol Clin Pharmacol 2017;33:157-63.

[7] . Schug SA, Ting S. Fentanyl formulations in the management of pain: An update. Drugs 2017;77:747-63.

[8] Desai SN, Badiger SV, Tokur SB, Naik PA. Safety and efficacy of transdermal buprenorphine versus oral tramadol for the treatment of post-operative pain following surgery for fracture neck of femur: A prospective, randomised clinical study. Indian J Anaesth 2017;61:225-9.

[9] Londhe S, Patwardhan M, Shah R, Oak M. Efficacy and safety of buprenorphine transdermal patch for immediate postoperative analgesia after total knee arthroplasty surgery. J Arthroplasty 2020;35:S178-81.

[10]. Kadapamannil D, Rajan S, Tosh P, Kumar L. Comparison of efficacy and safety of transdermal buprenorphine patch applied 48 versus 72 hours preoperatively in providing adequate postoperative analgesia

following major abdominal surgeries. Indian J Pain 2018;32:46-50.
[11]. Miyazaki T, Hanaoka K, Namiki A, Ogawa S, Kitajima T, Hosokawa T, et al. Efficacy, safety and pharmacokinetic study of a novel fentanyl-containing matrix transdermal patch system in japanese patients with cancer pain. Clin Drug Investig 2008;28:313-25.
[12]. Plosker GL, Lyseng-Williamson KA. Buprenorphine 5, 10 and 20 µg/h transdermal patch: A guide to its use in chronic non-malignant pain. CNS Drugs 2012;26:367-73.
[13]. Evans HC, Easthope SE. Transdermal buprenorphine. Drugs 2003;63:1999-2010.
[14]. Canneti A, Luzi M, Di Marco P, Cannata F, Pasqualitto F, Spinoglio A, et al. Safety and efficacy of transdermal buprenorphine and transdermal fentanyl in the treatment of neuropathic pain in AIDS patients. Minerva Anestesiol 2013;79:871-83.
[15]. Arshad Z, Prakash R, Gautam S, Kumar S. Comparison between transdermal buprenorphine and transdermal fentanyl for postoperative pain relief after major abdominal surgeries. J Clin Diagn Res 2015;9:UC01-4.
[16]. Summers S, Mohile N, McNamara C, Osman B, Gebhard R, Hernandez VH. Analgesia in total knee arthroplasty: Current pain control modalities and outcomes. J Bone Joint Surg Am 2020;102:719-27.
[17]. Pepper AM, Mercuri JJ, Behery OA, Vigdorchik JM. Total hip and knee arthroplasty perioperative pain management: What should be in the cocktail. JBJS Rev 2018;6:e5.
[18]. Oh CS, Jung E, Lee SJ, Kim SH. Effect of nefopam- versus fentanyl-based patient-controlled analgesia on postoperative nausea and vomiting in patients undergoing gynecological laparoscopic surgery: A prospective double-blind randomized controlled trial. Curr Med Res Opin 2015;31:1599–607.
[19]. Machado FC, Neto GC, Paiva LO, Soares TC, Nakamura RK, Nascimento LF, et al. Uso da buprenorfina transdérmica na dor aguda pós-operatória: Revisão sistemática [Transdermal buprenorphine for acute postoperative pain: A systematic review]. Rev Bras Anestesiol 2020;70:419-28.
[20]. Walsh SL, Preston KL, Stitzer ML, Cone EJ, Bigelow GE. Clinical pharmacology of buprenorphine: Ceiling effects at high doses. Clin Pharmacol Ther 1994;55:569-80.
[21]. OliashiraziA, Wilson-Byrne T, Shuler FD, Parvizi J. Patient-controlled fentanyl iontophoretic transdermal system improved postoperative mobility compared to intravenous patient-controlled analgesia morphine: A pooled analysis of randomized, controlled trials. Pain Pract 2017;17:197-207.
[22]. Tassinari D, Sartori S, Tamburini E, Scarpi E, Raffaeli W, Tombesi P, et al. Adverse effects of transdermal opiates treating moderate-severe cancer pain in comparison to long-acting morphine: A meta-analysis and systematic review of the literature. J Palliat Med 2008;11:492-501