EFFICACY OF TRANSDERMAL FENTANYL PATCH IN PAIN CONTROL DURING THIRD MOLAR SURGERY -A CLINICAL STUDY

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ABSTRACT

Aim: To assess the efficacy, safety, and feasibility of using transdermal fentanyl to treat pain following third molar extraction.

Methods: This prospective, parallel-group, comparative clinical study involved sixty healthy individuals aged 18 to 40 undergoing third molar extraction. Participants were divided into two groups: the FTS group (receiving a 50 µg/h fentanyl patch) and the control group (receiving a placebo patch along with NSAIDs and Tramadol). A minimally invasive surgical approach was used under local anesthesia. Pain levels were assessed using the Visual Analogue Scale (VAS) at various postoperative intervals (0, 2, 4, 8, 12, 24, 48, and 72 hours). Key outcomes included pain intensity, use of additional analgesics, occurrence of side effects, and patient satisfaction.

Results: The FTS group reported significantly lower pain scores compared to the Control group at both 24 hours ($p = 0.001^*$) and 72 hours ($p = 0.007^*$). Pain reduction in the FTS group was quicker and more pronounced, particularly between 48 and 72 hours ($p = 0.000^*$). Furthermore, 66.7% of patients in the FTS group did not require any rescue analgesics, whereas only 40% of the Control group managed without them ($p = 0.005^*$).

Conclusion: In contrast to traditional NSAID therapy, the transdermal fentanyl patch provides more efficient and longer-lasting postoperative pain relief following third molar surgery, resulting in a faster pain decrease and a decreased need for additional analgesics.

Keywords: Pain Management; Third Molar Surgery; Transdermal Fentanyl Patch; Opioid Analgesic.

INTRODUCTION

One of the most common procedures in oral and maxillofacial surgery is the surgical removal of impacted third molars. Managing pain after surgery remains a major challenge despite advances in surgical methods and pain management strategies. Widely recognized as a trustworthy clinical model for evaluating the analgesic efficacy of different drugs and delivery methods, this treatment is frequently linked to moderate to severe pain.[1] Following such procedures, traditional pain management often entails systemic administration of analgesics. However, individual variations in medication metabolism, patient compliance, and the incidence of side effects might affect their effectiveness.

Transdermal medication delivery has become a potential alternative, providing consistent systemic drug release and less fluctuation in plasma concentrations. First introduced in a transdermal form in 1984, fentanyl is a very potent synthetic opioid that has since been widely utilized in the treatment of persistent pain and specific postoperative disorders. [2] The Fentanyl Transdermal System (FTS) uses a rate-controlling membrane and a gel matrix reservoir to administer the drug consistently over 72 hours. Its favorable pharmacokinetics—including rapid absorption due to its high lipid solubility and low molecular weight—make it a strong candidate for postoperative pain control. [3,4]

However, its use in managing acute postoperative pain, particularly in third molar extractions, has not been extensively studied. It is necessary to assess the Transdermal Fentanyl Patch as a short-term pain management strategy in this setting in order to have a better understanding of its effectiveness, safety, and practical use.

METHODOLOGY

This prospective, parallel-group, comparative clinical study was carried out by the Department of Oral and Maxillofacial Surgery at the SIBAR Institute of Dental Sciences in Takkellapadu, Guntur, Andhra Pradesh, India, between December 2023 and June 2024. The primary objective was to compare the effectiveness of transdermal fentanyl with that of standard oral NSAID therapy in treating postoperative pain following third molar extraction. The study received ethical clearance from the SIBAR Institute of Dental Sciences' Institutional Ethics Committee (IEC Protocol No: Pr.298/IEC/SIBAR/2023), and all procedures followed the ethical principles outlined in the Declaration of Helsinki. All participants gave their informed permission before enrolling. The study included 60 systemically healthy people between the ages of 18 and 40 who required surgery to remove their impacted third molars. The sample size was calculated using an effect size of 0.8, $\alpha = 0.05$, and 80% power, based on data from a previous pilot study[6] on postoperative pain following mandibular third molar surgery. Using orthopantomographic imaging and Winter's[7] categorization of mesioangular, distoangular, vertical, or horizontal impactions, patients were classified. The study only included patients in ASA Class I or II and excluded those with a history of opioid use, liver or kidney problems, pregnancy, neurological conditions, or contraindications to local anesthesia. All subjects underwent routine blood testing in order to screen for undiagnosed systemic disorders. Patients were divided into two groups: the FTS group (group A) received a 50 g/hr transdermal fentanyl patch 30 minutes before surgery, which was left in place for 24–72 hours after the procedure. The control group (group B) received a placebo patch as well as oral ibuprofen 400 mg every 8 hours for three days, with tramadol 50 mg given as needed for breakthrough pain. To minimize selection bias, participants were alternately assigned to each group using a predetermined sequence, and the allocation was kept hidden by using sealed opaque envelopes. Postoperative assessments were performed by an independent, blinded

assessor. Participants were recruited for the six-month trial, and all patients had their condition watched over for 72 hours after their procedure. The CONSORT flow chart (Figure 1) shows the allocation process.

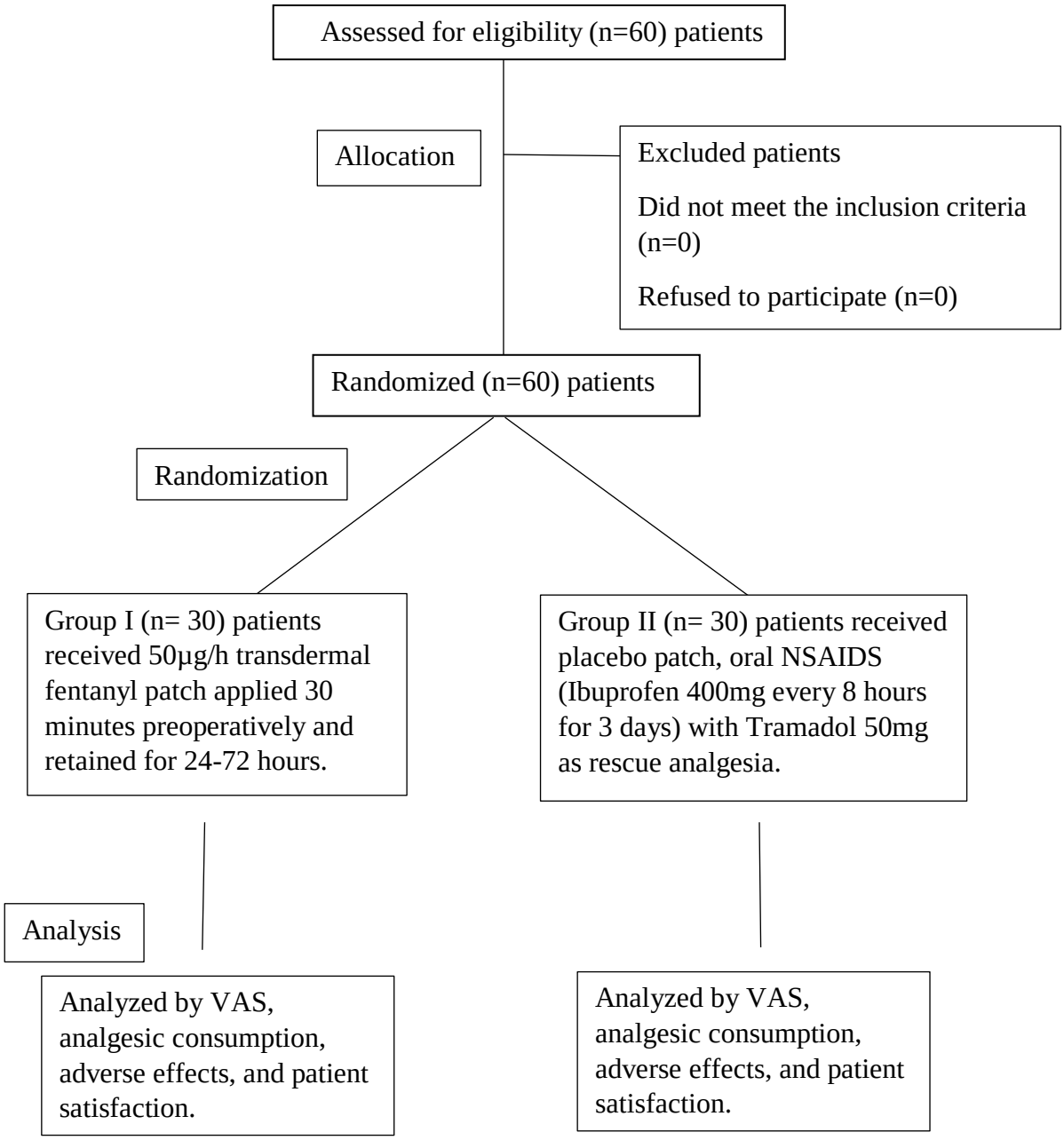

FIG. 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the study. VAS, Visual Analogue Scale.

Procedure: Using 2% lignocaine with 1:80,000 epinephrine (LIGNOX 2% A) under local anesthesia, one knowledgeable surgeon carried out a standardized, minimally invasive surgical operation. Using a No. 15 Bard-Parker blade with its handle and a Molt's No. 9 periosteal elevator, a mucoperiosteal flap was raised. A round bur was used to remove bone around the impacted third molar while it was constantly irrigated with 0.9% normal saline. To facilitate tooth extraction, root and/or crown sectioning was carried out as necessary. The wound was then treated with saline irrigation before being sutured shut using 3-0 or 4-0 black braided silk sutures. The length of the treatment was documented from the first incision to the last stitch. The recommended postoperative therapy included a 0.2% chlorhexidine mouthwash that should be used twice daily for a week to promote oral hygiene.

Pain levels were measured using a 10-point Visual Analog Scale (VAS) at several postoperative time points: 0, 2, 4, 8, 12, 24, 48, and 72 hours. The average VAS pain score was the main outcome measure, while secondary outcomes included total rescue analgesic use, the incidence of side effects (such nausea, vomiting, dizziness, pruritus, and respiratory depression), and overall patient satisfaction at the conclusion of 72 hours.

Statistical Analysis:

Statistical Analysis was performed using SPSS version 26.0**,** employing Mann–Whitney U test, Wilcoxon Signed-Rank test, for pain score comparisons, chi-square tests for categorical variables, and a significance threshold of $P < 0.05$**.**

Results:

Table 1 shows that among the 60 study participants, 30 (50%) were male and 30 (50%) were female. The average age of participants was 23.4 ± 3.2 years in Group 1 and 23.7 ± 3.5 years in Group 2.

Group	Total Subjects (n)	Male (n)	Female (n)	Mean Age (years) ± SD
FTS Group	30	15	15	23.4 ± 3.2
Control Group	30	15	15	23.7 ± 3.5

Table 1: Demographic Characteristics of Participants: Age and Gender Distribution in FTS and Control Groups.

Analysis using the **Mann–Whitney U test** revealed that the group receiving the transdermal fentanyl system (FTS) consistently reported significantly lower pain scores compared to the control group at all postoperative intervals. The most notable differences were observed at 24 hours ($p = 0.001$) and 72 hours ($p = 0.007$), indicating the superior analgesic effectiveness of the fentanyl patch. These findings highlight the ability of FTS to deliver continuous pain relief after third molar extraction, outperforming both the placebo patch and the standard oral NSAID regimen used in the control group (**Table 2**).

Time Interval (Hours)	FTS Group (Mean ± SD)	Control Group (Mean ± SD)	t-value	p-value
2	3.8 ± 1.2	5.2 ± 1.5	2.61	0.010*
4	4.5 ± 1.3	6.0 ± 1.7	2.87	0.004*
8	3.2 ± 1.1	5.1 ± 1.4	3.39	0.001*
12	2.8 ± 1.0	4.5 ± 1.3	3.11	0.002*
24	2.1 ± 0.8	3.7 ± 1.1	3.22	0.001*
48	1.5 ± 0.5	2.8 ± 0.9	2.93	0.003*
72	0.8 ± 0.4	1.5 ± 0.6	2.71	0.007*

*$p<0.05$ statistically significant, Mann–Whitney U test.

Table 2: Comparative analysis of Mean Postoperative Pain Scores (VAS) Between Groups.

Within-group comparisons using the **Wilcoxon Signed-Rank test** showed significant reductions in pain over time in the FTS group ($p < 0.05$), with the greatest improvement occurring between 48 and 72 hours ($p = 0.000$). These results reflect the long-acting nature of fentanyl, which offered consistent and early pain control, beginning as soon as 4 to 8 hours postoperatively ($p = 0.000$) (**Table 3**).

Time Interval (Hours)	Mean Pain Score (VAS) ± SD	Mean Difference ± SD	t-value	p-value
2 vs 4	3.7 ± 1.1 vs 4.4 ± 1.2	0.7 ± 0.5	2.84	0.005*
4 vs 8	4.4 ± 1.2 vs 3.3 ± 1.0	1.1 ± 0.7	4.05	0.000*
8 vs 12	3.3 ± 1.0 vs 2.7 ± 0.9	0.6 ± 0.4	2.10	0.038*
12 vs 24	2.7 ± 0.9 vs 2.2 ± 0.8	0.5 ± 0.5	3.12	0.002*
24 vs 48	2.2 ± 0.8 vs 1.6 ± 0.5	0.6 ± 0.4	3.65	0.000*
48 vs 72	1.6 ± 0.5 vs 0.9 ± 0.4	0.7 ± 0.3	5.27	0.000*

*p<0.05 statistically significant, Wilcoxon Signed-Rank test

Table 3: Pair wise comparison of Pain Reduction Within-the FTS Group.

The control group also demonstrated significant pain reduction over time, though the onset of relief was slower, particularly between 48 and 72 hours (p = 0.000). Despite these improvements, pain levels in the control group remained higher than in the FTS group at corresponding time points, indicating that while both groups benefited, the FTS group experienced more effective and sustained relief, reducing their need for supplementary analgesics (**Table 4**).

Time Interval (Hours)	Mean Pain Score (VAS) ± SD	Mean Difference ± SD	t-value	p-value
2 vs 4	5.1 ± 1.4 vs 6.1 ± 1.6	1.0 ± 0.6	2.70	0.007*
4 vs 8	6.1 ± 1.6 vs 5.0 ± 1.3	1.1 ± 0.7	3.50	0.000*
8 vs 12	5.0 ± 1.3 vs 4.4 ± 1.2	0.6 ± 0.5	2.85	0.005*
12 vs 24	4.4 ± 1.2 vs 3.6 ± 1.0	0.8 ± 0.6	3.07	0.002*
24 vs 48	3.6 ± 1.0 vs 2.7 ± 0.8	0.9 ± 0.5	4.15	0.000*
48 vs 72	2.7 ± 0.8 vs 1.4 ± 0.6	1.3 ± 0.5	5.68	0.000*

*p<0.05 statistically significant, Wilcoxon Signed-Rank test

Table 4: Pair wise comparison of Pain Reduction Within-the Control Group

Further supporting this, a **Chi-square test** showed that 66.7% of patients in the FTS group did not require any additional pain medication. In contrast, 40% of the control group needed rescue analgesics, with 33.3% requiring more than two doses. This difference was statistically significant ($p = 0.005$), emphasizing the enhanced and prolonged analgesic effect of the fentanyl patch (**Table 5**).

Variable	FTS Group (n=30)	Control Group (n=30)	χ^2-value	p-value
No Rescue Analgesic Needed	20 (66.7%)	8 (26.7%)	7.82	0.005*
1–2 Doses Taken	8 (26.7%)	12 (40.0%)		
>2 Doses Taken	2 (6.6%)	10 (33.3%)		

*p<0.05 statistically significant, Chi-square Test

Table 5: Comparative analysis of Rescue Analgesic Consumption between Groups.

In terms of safety, the FTS group reported fewer adverse effects. Nausea was seen in 6.6% of FTS patients versus 13.3% in the control group, vomiting occurred in 3.3% versus 10%, and dizziness was reported by 3.3% in the FTS group compared to 6.6% in the control group. Notably, no instances of pruritus or respiratory depression were observed in either group. These results suggest that transdermal fentanyl not only provides superior pain control but also has a lower incidence of common opioid-related side effects during the postoperative period **(Table 6).**

Adverse Effect	FTS Group (n=30)	Control Group (n=30)
Nausea	2 (6.6%)	4 (13.3%)
Vomiting	1 (3.3%)	3 (10.0%)
Dizziness	1 (3.3%)	2 (6.6%)

Pruritus	0 (0%)	0 (0%)
Respiratory Depression	0 (0%)	0 (0%)

Table 6: Incidence of Adverse Effects in FTS and Control Groups.

The **effect size (Cohen's d)** for the difference in mean VAS pain scores between the groups at 24 hours was 1.23 (95% CI: 0.55–1.91), representing a large clinical effect. Similar large effect sizes were noted at other time intervals as well, underscoring the significant analgesic benefit. Collectively, these findings suggest that transdermal fentanyl is a highly effective modality for managing postoperative pain following third molar surgery, offering both rapid and long-lasting relief, while minimizing the need for additional medication.

DISCUSSION

Following the extraction of the third molar, postoperative pain is typical, and it often peaks within the first few hours before gradually diminishing over the next several days. This discomfort is commonly treated with NSAIDs, but they can have adverse effects like gastrointestinal upset. Opioids, particularly fentanyl, have shown to be very effective at treating both acute and chronic pain conditions.

Fentanyl is an effective postoperative pain treatment since it is 50 to 100 times more potent than morphine. In contrast to conventional oral opioids, fentanyl may be administered through a transdermal patch, which allows the medication to be released at a controlled pace over a period of 48 to 72 hours. This method has been proven to help prevent several common opioid-related side effects, including nausea, vomiting, and addiction.[10]

Prior research has demonstrated the effectiveness of transdermal fentanyl patches in controlling postoperative pain, particularly after more invasive operations such third molar extractions.[8–9] As an illustration, Todorovic et al.[8] discovered that patients using fentanyl patches experienced significantly better pain relief 72 hours following surgery, along with a marked reduction in the need for rescue analgesics.

These findings are supported by the results of this study. On average, patients in the FTS group required 2.5 rescue analgesic tablets, compared to 3.8 tablets in the control group. Furthermore, the average time between the initial dosage of rescue medication was longer in the FTS group (6.5 hours) than in the control group (4.2 hours). The adverse effects were minimal; only two patients in the fentanyl group had mild nausea.

Viscusi et al.[9]'s research, which compared transdermal fentanyl to morphine and discovered comparable adverse effects, such as nausea and dizziness, albeit at a lower rate in the fentanyl group, is consistent with these findings.

Nonetheless, despite these positive findings, the study has certain drawbacks. It is not possible to assess the possibility for opioid tolerance or dependency because of the relatively small sample size and lack of prolonged follow-up. Additionally, the site of the patch application may influence fentanyl absorption because individual skin characteristics and temperature may differ. Additional research employing bigger sample numbers and exploring novel delivery methods, such the Fentanyl Iontophoretic Transdermal System (ITS), is necessary to ascertain its safety and long-term efficacy in treating severe postoperative pain.

Despite the fact that this experiment employed standardized procedures, evaluator blinding, and uniform group assignment to reduce bias, the short follow-up time and lack of double blinding may still have an impact on its internal validity. The findings are most applicable to

young, healthy individuals who have undergone similar third molar treatments, as they are unlikely to apply to older or more physically weak people.

CONCLUSION:

Present study concludes that Transdermal Fentanyl Patch offers superior and long-lasting postoperative pain relief in third molar surgeries, significantly lowering pain scores and reducing the need for additional analgesics when compared to NSAID therapy. While it demonstrates clear advantages such as extended analgesia and minimal adverse effects, further investigations involving larger sample sizes and exploring other delivery modalities are suggested to enhance its clinical applicability.

CONFLICT OF INTEREST:

The study received ethical clearance from the SIBAR Institute of Dental Sciences' Institutional Ethics Committee (IEC Protocol No: Pr.298/IEC/SIBAR/2023), and all procedures followed the ethical principles outlined in the Declaration of Helsinki. All participants gave their written informed consent was obtained from each participant before inclusion. Confidentiality of patient data was maintained throughout the study. No animals were used in this research. The authors have no conflicts of interest to declare.

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