VOLUME - 14, ISSUE - 08, AUGUST - 2025 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Anaesthesiology

COMPARISON OF TRANSDERMAL BUPRENORPHINE VERSUS TRANSDERMAL FENTANYL PATCHES IN CANCER PATIENTS FOR PAIN

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ABSTRACT **Background:** Chronic cancer pain remains a significant clinical challenge requiring long-term opioid administration. Transdermal systems offer consistent drug delivery, improved compliance, and reduced gastrointestinal side effects. This study compares the efficacy, safety, and patient satisfaction between transdermal buprenorphine and transdermal fentanyl patches in managing moderate to severe cancer pain. **Methods:** In this prospective, randomized, open-label study, 120 adult patients with moderate-to-severe cancer-related pain were randomly assigned to receive either transdermal buprenorphine (TD-BUP, 52.5 mcg/h) or transdermal fentanyl (TD-FEN, 25 mcg/h), titrated as per response. Pain scores, rescue analgesic requirements, adverse events, and quality of life were evaluated over four weeks. **Results:** Both groups showed significant reductions in pain scores (Numerical Rating Scale, NRS) from baseline. The TD-BUP group demonstrated a comparable analgesic effect to TD-FEN with fewer gastrointestinal side effects. Patient satisfaction scores and quality of life (EORTC QLQ-C15-PAL) were slightly higher in the TD-BUP group. **Conclusion:** Transdermal buprenorphine and fentanyl patches are both effective for cancer pain management. However, buprenorphine offers a better side-effect profile, making it a favorable option, especially in palliative settings.

KEYWORDS : Cancer pain, transdermal buprenorphine, transdermal fentanyl, opioids, analgesia, palliative care

INTRODUCTION

Cancer-related pain affects over 70% of patients with advanced malignancies and has a profound impact on quality of life [1,2]. Opioids remain the cornerstone for managing moderate-to-severe cancer pain, with increasing interest in alternative delivery systems such as transdermal patches [3].

Transdermal fentanyl, a potent μ-opioid receptor agonist, is widely used for chronic cancer pain [4,5]. Buprenorphine, a partial μ-agonist and κ-antagonist with high receptor affinity, is also available in a transdermal form [6,7]. Its ceiling effect on respiratory depression and favorable pharmacokinetics make it an attractive alternative [8].

However, direct head-to-head comparisons of these agents in cancer patients are limited [9]. This study aims to compare the efficacy, tolerability, and patient satisfaction of transdermal buprenorphine versus fentanyl patches in managing cancer pain.

METHODS

This prospective, open-label, randomized clinical trial was conducted at a tertiary care oncology center between January and December 2023. Ethical approval was obtained from the Institutional Review Board, and the study adhered to the Declaration of Helsinki guidelines. Informed consent was obtained from all participants [10].

Inclusion criteria included adults ≥18 years with histologically confirmed malignancy, moderate to severe cancer pain (NRS ≥ 4), and a life expectancy >1 month. Exclusion criteria included opioid hypersensitivity, severe hepatic/renal impairment, cognitive dysfunction, and concurrent trial participation [11].

Randomization And Interventions

Eligible patients were randomized (1:1) into:

- **Group A (TD-BUP):** Received buprenorphine transdermal patch 52.5 mcg/h (equivalent to ~10 mg oral morphine/day)
- **Group B (TD-FEN):** Received fentanyl transdermal patch 25 mcg/h (~60–90 mg oral morphine/day equivalent)

Patch application was every 72 hours for fentanyl and every 96 hours for buprenorphine. Doses were titrated based on pain scores and breakthrough pain needs, with oral morphine (immediate-release) allowed as rescue analgesia.

Outcome Measures

1. **Primary Outcome:**
   - Pain intensity using the Numerical Rating Scale (NRS) at baseline, day 3, 7, 14, and 28.
2. **Secondary Outcomes:**
   - Frequency of rescue medication use
   - Incidence of adverse effects (nausea, vomiting, constipation, sedation, respiratory depression)
   - Patient-reported satisfaction using a 5-point Likert scale
   - Quality of life using the EORTC QLQ-C15-PAL

questionnaire [12].

Statistical Analysis

Sample size was calculated based on an anticipated effect size of 0.5 for pain reduction, with 80% power and alpha = 0.05. Data were analyzed using SPSS v26. Continuous variables were expressed as mean ± SD, and categorical variables as frequencies/percentages. Independent t-tests and chi-square tests were used for group comparisons. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 120 patients were enrolled and completed the study, with 60 in each group. Demographic and clinical characteristics were comparable between groups (Table 1)

Table 1. Baseline Characteristics

Parameter	TD-BUP (n=60)	TD-FEN (n=60)	p-value
Mean age (years)	56.3 ± 12.7	58.1 ± 11.2	0.34
Gender (M/F)	38/22	40/20	0.69
Cancer type	Breast (25%), Head & Neck (20%), Lung (15%) etc.	Similar distribution	0.88
Baseline NRS score	7.1 ± 0.8	7.3 ± 0.7	0.21

Pain Relief

Both groups exhibited significant reductions in NRS scores over time ($p < 0.001$). By day 28:

- **TD-BUP group:** Mean NRS reduced to 2.4 ± 0.6
- **TD-FEN group:** Mean NRS reduced to 2.1 ± 0.7

The difference in final pain scores between groups was not statistically significant ($p = 0.12$), indicating comparable efficacy.

Rescue Analgesic Use

TD-FEN users required fewer doses of rescue morphine in the first week. However, by week 4, both groups had similar usage patterns.

Table 2. Adverse Events

Adverse Effect	TD-BUP (%)	TD-FEN (%)	p-value
Nausea	15	31	0.02
Constipation	18	35	0.01
Somnolence	12	10	0.72
Respiratory depression	0	2	0.31

Gastrointestinal adverse effects were significantly lower in the TD-BUP group [9].

Patient Satisfaction And Quality Of Life

- Higher satisfaction scores (Likert 4 or 5) were reported by 83% in TD-BUP vs. 75% in TD-FEN ($p = 0.18$).
- EORTC QLQ-C15-PAL showed greater improvements in physical and emotional functioning in TD-BUP, though not statistically significant

DISCUSSION

The current study demonstrates that both transdermal buprenorphine (TD-BUP) and transdermal fentanyl (TD-FEN) are effective in managing moderate-to-severe cancer pain, with comparable reductions in Numerical Rating Scale (NRS) scores over a four-week period. However, notable differences in the safety profile, tolerability, and patient-reported outcomes favor buprenorphine, suggesting it may be a superior option in selected patient populations.

Clinical Relevance Of Transdermal Opioids In Cancer Pain

Pain is among the most feared symptoms in cancer patients, particularly in those with advanced disease [1,2]. While oral morphine remains the standard first-line opioid for many settings, issues such as poor oral intake, dysphagia, and gastrointestinal toxicity necessitate alternative routes. Transdermal delivery systems offer several advantages: non-invasive administration, steady plasma drug levels, improved adherence, and lower peak-to-trough fluctuation compared to oral formulations [3].

Transdermal fentanyl has long been established as an effective agent in opioid-tolerant cancer patients [4]. Buprenorphine, once considered unsuitable for cancer pain due to its partial agonist profile, is now recognized as a viable and even preferable alternative in several settings [5,6].

Comparative Efficacy

Both groups in this study achieved statistically and clinically significant pain relief, with average NRS reductions exceeding 4 points. While the TD-FEN group exhibited slightly faster onset of pain control in the first week, this advantage diminished by the second week. By day 28, the pain scores in both groups were statistically indistinguishable, aligning with earlier randomized studies and meta-analyses [7,8].

Buprenorphine's analgesic ceiling effect has been a theoretical concern; however, our findings—as well as recent literature—suggest this is not clinically limiting in cancer patients when appropriately dosed [9,10].

Safety And Tolerability

One of the most critical findings in this study is the significantly lower incidence of gastrointestinal side effects in the TD-BUP group. Nausea and constipation—both highly distressing and quality-of-life-limiting symptoms—were significantly more common in the TD-FEN arm (nausea: 31% vs. 15%, constipation: 35% vs. 18%). These results are consistent with prior studies reporting buprenorphine's more favorable side effect profile [6,11].

Buprenorphine also has a ceiling effect on respiratory depression, attributed to its partial μ-opioid agonist activity, making it a safer option in frail or elderly populations, or in those with concurrent pulmonary compromise [7,12]. This pharmacologic characteristic is particularly relevant in palliative care settings, where minimizing adverse events is paramount.

Moreover, no significant respiratory depression was observed in either group in this study, which may reflect cautious opioid titration and use in opioid-naïve patients with preserved organ function.

Patient Satisfaction And Quality Of Life

Although not statistically significant, patients in the buprenorphine group reported higher satisfaction scores and greater improvement in physical and emotional well-being, as measured by the EORTC QLQ-C15-PAL. This may be attributed to lower side effect burden, simpler dosing schedule (96-hour patch for buprenorphine vs. 72-hour for fentanyl), and better functional tolerance.

Prior studies have highlighted the impact of symptom burden (especially constipation, sedation, and nausea) on adherence and overall satisfaction with opioid therapy [8]. This reinforces the importance of individualized therapy based not only on analgesic efficacy but also on tolerability and patient preference.

Pharmacokinetics And Practical Considerations

Buprenorphine's high receptor affinity and slow dissociation contribute to its long duration of action and ability to block other opioids at the receptor level. This can complicate rescue analgesic administration or opioid rotation, particularly in acute care settings [10,]. However, in stable cancer patients under regular follow-up, these properties are less problematic and may even reduce the need for dose escalation.

Fentanyl, by contrast, is a full μ-agonist with predictable linear pharmacokinetics, which some clinicians find easier to titrate, especially in opioid-tolerant patients. Nevertheless, in opioid-naïve or frail individuals, the risk of oversedation or

respiratory suppression—though low—remains a concern.

Another practical issue is patch adhesion. Buprenorphine patches are generally well tolerated, but humidity, sweating, and cachexia may impair transdermal absorption or lead to patch detachment. No significant differences in adherence were noted in this study, but clinicians should be vigilant in populations with poor skin integrity or extreme cachexia.

Comparison With Previous Literature

Our findings are consistent with studies such as those by Mystakidou et al. and Mercadante et al., which reported comparable analgesic efficacy between transdermal buprenorphine and fentanyl in cancer populations [4,]. However, many earlier studies focused on opioid-tolerant patients or employed different titration protocols, which limits direct comparison.

A recent systematic review by Fallon and Laird supported the use of transdermal opioids in cancer pain, while highlighting a relative paucity of high-quality head-to-head trials [5]. This study adds to the limited body of direct comparative data and supports the growing recognition of buprenorphine as a first-line agent in palliative opioid therapy [6,9].

Limitations

This study has several limitations. The open-label design introduces the possibility of observer and patient bias, although objective outcomes such as NRS scores and adverse event rates help mitigate this. The follow-up period of four weeks may be insufficient to capture long-term efficacy, tolerance, or issues like opioid-induced hyperalgesia or hormonal dysfunction.

Another limitation is the exclusion of opioid-tolerant patients and those with significant hepatic/renal dysfunction. Therefore, findings may not be generalizable to all cancer populations, particularly those undergoing complex opioid rotations or those with comorbid organ impairment.

Additionally, economic analysis was not performed. Although buprenorphine patches are often more expensive per unit than fentanyl, reduced side-effect management may offset this difference over time. Future studies should incorporate pharmacoeconomic evaluations.

Future Directions

Larger, multicenter trials with longer follow-up are warranted to assess long-term opioid requirements, patient-reported outcomes, and survival impact. Comparative studies evaluating cost-effectiveness, caregiver burden, and symptom clusters (e.g., pain-fatigue-depression triad) are also needed.

Pharmacogenomic research may further personalize opioid selection by identifying patients more likely to benefit from buprenorphine versus fentanyl, based on genetic variations in opioid metabolism and receptor polymorphisms.

CONCLUSION

Both transdermal buprenorphine and fentanyl patches are effective options for managing moderate to severe cancer pain. Buprenorphine demonstrated a better side-effect profile, potentially improving compliance and quality of life. It should be considered a first-line transdermal agent in appropriate cancer patients, particularly in palliative care settings.

Acknowledgements

We thank the patients and caregivers who participated in this study and the oncology and palliative care teams for their collaboration.

Conflicts Of Interest

None declared.

Funding

No external funding was received for this study.

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