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Research Article

Efficacy Comparison of Transdermal Fentanyl and IV Morphine PCA in Post-orthopedic Surgery Pain: A Randomized Clinical Trial

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Abstract

Aim: Effective postoperative pain management is crucial for early mobilization and recovery in orthopedic surgery patients. While intravenous patient-controlled analgesia (IV-PCA) with morphine is widely used, it has limitations including IV access dependency and mobility restrictions. Transdermal fentanyl (TDF) patches have emerged as an alternative due to their long-lasting analgesic effects. This study compares their efficacies in managing postoperative pain following orthopedic surgeries and evaluates patient satisfaction levels.

Material and Method: This prospective, randomized, controlled, comparative study included 40 patients aged 20-65 years undergoing orthopedic surgery under general anesthesia between July-December 2010. Patients were randomized into Group TDF (n=20) and Group IV-PCA (n=20). Postoperative pain intensity quantification was performed utilizing standardized VAS methodology, while concurrent sedation depth monitoring employed RSS parameters throughout the initial 24-hour postoperative period. Additionally, hemodynamic parameters, rescue analgesia requirements, side effects, and satisfaction levels were monitored.

Results: Post-surgical nociceptive metrics demonstrated significant temporal reduction across both cohorts ($p<.001$). Beyond the initial 90-minute phase, IV-PCA administration achieved superior analgesic efficacy compared to transcutaneous delivery ($p<.001$). Sedation parameters and adverse event profiles maintained statistical equivalence between modalities ($p>.05$). Patient-reported satisfaction metrics indicated significant preference for automated morphine administration protocols ($p<.001$).

Conclusion: Despite providing adequate initial pain relief, TDF patches demonstrated lower efficacy compared to IV-PCA with morphine in managing postoperative pain and achieving patient satisfaction following orthopedic surgery. These findings suggest the need for careful consideration when selecting postoperative pain management strategies.

Keywords: Pain, postoperative, patient-controlled analgesia, fentanyl/therapeutic use

INTRODUCTION

Postoperative pain, which is common following orthopedic surgical procedures, hinders early mobilization and rehabilitation, increases the risk of immobility-related complications, and prolongs hospital stays (1). Contemporary postoperative analgesia encompasses multiple therapeutic approaches, with intravenous patient-controlled analgesia (IV-PCA) systems, healthcare provider-initiated parenteral administration, and intermittent intravenous bolus protocols representing the primary interventional strategies (1,2). Contemporary evidence indicates IV-PCA morphine administration maintains predominance in acute surgical pain management, particularly for moderate to severe intensity cases requiring precise analgesic titration (3). However, it has been associated with significant limitations, including requiring IV access, specialized setup and supervision, risks of overdose, mobility restrictions, side effects, and system-related interruptions in pain control (1-3).

As an alternative, fentanyl offers several advantages in postoperative pain management, including high potency, a broad therapeutic window, and rapid onset of action. It is not only the mainstay of intraoperative analgesia during anesthesia induction. The pharmacological versatility of fentanyl manifests through diverse administration routes, encompassing transmembranous delivery platforms,

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sublingual applications, nasally-administered formulations, and transcutaneous drug delivery systems (1,4,5). Although transdermal fentanyl (TDF) patches are primarily used to manage cancer-related pain in patients who use chronic opioids, there is evidence that they are also effective in controlling chronic and acute postoperative pain (4).

Clinical investigations have established the therapeutic potential of transcutaneous fentanyl delivery systems in managing post-surgical nociception across multiple surgical disciplines, with documented efficacy in orthopedic interventions, abdominal procedures, and gynecological operations (1,6-10). However, most of the studies on the use of TDF patches conducted in Türkiye addressed its use in non-surgical conditions such as rib fractures and cancer pain (11,12).

In view of the foregoing, this study was conducted to address the said gap by comparatively evaluating the efficacies of TDF patches and IV-PCA with morphine in the management of postoperative pain after orthopedic surgeries and the satisfaction levels of patients with these analgesia methods.

MATERIAL AND METHOD

Study Design

We implemented a monocentric prospective clinical investigation utilizing a randomized controlled parallel-group methodology. Our research protocol received institutional ethics board authorization (Reference: 2, Authentication Date: 30.06.2010) and adhered to Declaration of Helsinki principles governing human subject research. All study participants provided documented voluntary informed consent prior to enrollment.

Population and Sample

The study population comprised consecutive patients aged 20 to 65 years who underwent orthopedic surgery under general anesthesia at the Operating Room of Pamukkale University Research and Training Hospital, Türkiye, between July and December 2010. The patients were evaluated for subjective pain severity one day before surgery using the visual analog scale (VAS) (13). The study's inclusion criteria were having a VAS score of ≥4 and grade I to III American Society of Anesthesiologists (ASA) physical status. Study exclusion encompassed: preoperative VAS<4, ASA classification IV-V, renal/hepatic dysfunction, ischemic myocardial pathology, decompensated cardiac dysfunction alongside advanced respiratory insufficiency, documented opioid/fentanyl hypersensitivity, pre-existing psychiatric/dermatologic diagnoses, weight parameters outside 50-100kg range, substance dependence history, alongside non-general anesthetic protocols. We calculated that our sample should consist of at least 38 people, 19 patients in each group, in order to obtain the α value of 0.05 and power (1-β) of 0.80 as stated in the literature (10). Considering that some patients may drop out of the study, we included 40 patients in the sample.

We randomized the 40 patients into two groups, Group TDF and Group IV-PCA, using sealed envelopes.

Preoperative Assessments and Interventions

Patients' demographic and clinical characteristics, including age, gender, weight, ASA physical status grades, and underlying orthopedic disease for surgery, were prospectively recorded. Double blinding was not possible. Pain-trained nurses performed all assessments for sedation and pain severity.

Patients' VAS and Ramsay sedation scale (RSS) scores were recorded before anesthesia induction preoperatively (10). In VAS, patients are asked to rate their pain severity on a scale from 0 (no pain) to 10 (worst possible pain). RSS evaluation utilized a 6-tier classification system (14): Level 1 indicates consciousness with psychomotor agitation; Level 2 signifies alert status with appropriate orientation and composure; Level 3 represents wakeful state with command-response capacity; Level 4 denotes somnolence with preserved quick arousal to glabellar/auditory stimulation; Level 5 indicates delayed arousal response; Level 6 represents complete absence of stimulus response.

For TDF cohort participants, transdermal fentanyl delivery systems (Durogesic® 50µg/hr, Janssen Pharmaceutica) were positioned on thoracic anterolateral surfaces or upper limb regions 10 hours pre-anesthetic induction. The system provided continuous fentanyl administration at 50µg hourly intervals. Protocol excluded supplementary pre-surgical medications. Clinical monitoring encompassed potential adverse effects: gastrointestinal manifestations, cardiovascular alterations, respiratory compromise, and cutaneous reactions.

The patients included in Group PCA were given paracetamol (Perfalgan, 10 mg/ml, 100 ml vial, Bristol-Myers Squibb Inc., İstanbul, Türkiye) and pethidine HCl (Aldolan, 100 mg/2 ml, G.L. Pharma GmbH, Lannach, Austria) as required before they arrived in the operating room.

Intraoperative Assessments and Interventions

Following mandated pre-surgical fasting, comprehensive physiological surveillance was initiated utilizing multi-parameter monitoring systems: cardiac electrical activity registration, peripheral oxygen saturation quantification, oscillometric arterial pressure evaluation, and end-tidal CO2 analysis. Propofol administration (1% solution, Fresenius Kabi) was quantitatively documented from anesthetic initiation through procedural completion. Airway management quality assessment employed the Cooper classification protocol (reference 15), stratifying intubation success into four categories: superior (8-9 points), adequate (6-7 points), suboptimal (3-5 points), and inadequate (0-2 points).

Emergence chronometry was calculated from anesthetic gas discontinuation to successful airway device removal. Extubation quality underwent standardized evaluation utilizing validated ordinal assessment methodology (15).

Postoperative Assessments and Interventions

Post-surgical transfer to acute recovery facilities was executed, with temporal documentation initiated upon patient arrival to establish reference baseline measurements.

Sedation quantification and pain assessment (both static and dynamic) utilizing RSS and VAS parameters were conducted at designated intervals: initial phase (30/60/90 minutes), intermediate phase (hours 2-8), and extended phase (hours 12-24). Concurrent adverse event documentation was maintained throughout these evaluation timepoints.

Among the patients in Group TDF, those with a VAS score of ≥4 at any of these time points were administered 1 g IV paracetamol (Perfalgan, 10 mg/ml, 100 ml vial). TDF patches were removed 24 hours after the surgery.

The patients in Group PCA were provided with a PCA device (Pain Management Provider, Abbott Laboratories, North Chicago, USA) with preset parameters for morphine administration (two mg of loading dose, basal infusion rate of 1 mg/hr, one mg with a 10-minute lockout, and a 4-hour maximum dosage of 25 mg) (Morphine HCl ampoule, 10 mg/ml, Galen, İstanbul, Türkiye). Patients with a VAS score of ≥4 at any of the said time points were administered additional rescue IV morphine HCl (1–2 mg). The total morphine dose received by each patient was recorded.

On the second postoperative day, a 4-point (excellent, good, moderate, and poor) Likert-type assessment tool was used to evaluate patients' satisfaction with the analgesia method (16).

Statistical Analysis

Primary endpoints comprised post-procedural RSS/VAS measurements, with patient satisfaction serving as secondary outcome parameter. Data underwent statistical evaluation utilizing contemporary analytical software (SPSS 17.0, Chicago). Quantitative variables received descriptive treatment through central tendency/dispersion metrics (mean±SD), supplemented by range values for specific parameters (e.g., opioid consumption profiles). Categorical data underwent frequency distribution analysis with proportional representation. Distribution normality underwent Kolmogorov-Smirnov verification. Inter-group comparisons for normally-distributed parameters (demographic characteristics, procedural duration, anesthetic agent utilization, airway management metrics) employed independent t-test methodology.

Paired t-test was used to conduct subgroup analyses. In comparing the differences in categorical variables (gender, ASA classification, operation type, patient comfort levels, side effects including nausea, vomiting, and pruritus) between the groups, Pearson's chi-square test was used for 2x2 tables with expected cells of 5 or more, Fisher's exact test for 2x2 tables with expected cells of less than 5, and Fisher-Freeman-Halton test for RxC tables with expected cells of less than 5.

Longitudinal sedation/pain score trajectories underwent repeated-measures compositional analysis with temporal decomposition. Post-hoc multiple comparison procedures (Bonferroni-adjusted) identified specific temporal coordinates driving observed variations in static/dynamic pain metrics. Statistical inference employed alpha threshold of 0.05 for significance determination.

RESULTS

Comparative analysis revealed statistically equivalent demographic/clinical parameter distributions between cohorts (p>0.05; demographic metrics detailed in Table 1). The distribution of underlying orthopedic conditions was similar between both groups, with no statistically significant differences observed (p=.999). The pre-induction RSS score was significantly higher than the preoperative RSS score in Group TDF (1.05±0.22 vs. 2.00±0.00, p<.001). The pre-induction RSS score was significantly lower than the preoperative RSS score in Group IV-PCA (1.50±0.51 vs. 1.20±0.41, p=.004). Inter-group RSS differentials achieved statistical significance at pre-induction and pre-surgical timepoints (p=.002; p<.001). Both cohorts demonstrated significant pre-induction VAS reductions compared to pre-surgical measurements (p=.024; p<.001). VAS metrics exhibited statistical equivalence between groups at both evaluation points (p>.05; comprehensive data presented in Table 2).

Anesthetic agent requirements demonstrated significant inter-group variation: IV-PCA cohort exhibited elevated propofol consumption (187.0±21.8 mg versus 125.0±28.9 mg; p<.001). Emergence characteristics revealed superior extubation metrics in IV-PCA recipients (2.60±1.19 versus 1.05±0.22; p<.001), while TDF group demonstrated enhanced Cooper intubation parameters (8.60±0.60 versus 7.05±1.93; p=.003). Remaining intraoperative anesthetic variables maintained statistical equivalence between groups (p>.05; detailed in Table 3).

There were no significant differences in RSS scores assessed during the 24 hours after surgery within or between the groups (p>.05). On the other hand, there were significant differences in both resting and ambulatory VAS scores assessed during the 24 hours after surgery within both groups (p<.001).

Additionally, initial resting VAS scores assessed at the 30th, 60th, and 90th minutes were significantly higher in Group IV-PCA than in Group TDF (6.15±1.23 vs. 4.70±0.574.65±1.39 vs. 3.55±0.51, and 3.55±0.89 vs. 3.10±0.31; p<.05 for all cases). While the ambulatory VAS score assessed at the 30th minute was significantly higher in Group IV-PCA than in Group TDF (p<.001), there was no significant difference between the groups in VAS score assessed at the 60th and 90th minutes (p>.05). Nociceptive assessment revealed temporal variations: while early post-surgical phase (<90 minutes) demonstrated comparable VAS metrics, subsequent evaluations (hours 2-24) consistently indicated superior analgesic efficacy in IV-PCA cohort for

both static/dynamic pain parameters (p<.05 universally; comprehensive data in Table 4).

Bonferroni posthoc analyses revealed that resting VAS values, which were initially significantly higher in Group IV-PCA than in Group TDF, significantly decreased in Group IV-PCA from the postoperative 30th minute onward (p<.001). Bonferroni posthoc analyses revealed that resting VAS values, which were initially significantly lower in Group TDF than in Group IV-PCA, minimally decreased in Group TDF after the postoperative 90th- minute and even slightly elevated from the postoperative 4th hour onward. Ambulatory VAS scores, which were initially significantly higher in Group IV-PCA than in Group TDF, rapidly declined from the postoperative 60th minute onward in Group IV-PCA (p<.001). Despite significantly lower initial ambulatory VAS scores in Group TDF than in Group IV-PCA, ambulatory VAS scores slowly declined in Group TDF over the course of postoperative 24 hours. The most pronounced declines in resting and ambulatory VAS scores occurred within the first 90 minutes postoperatively in both groups. However, while the resting and ambulatory VAS scores continued to decline in Group IV-PCA from the postoperative 2nd hour onward, they plateaued in Group TDF (Table 5).

Adverse event profiles maintained statistical equivalence across treatment modalities (p>.05).

Morphine consumption peaked at the postoperative 8th hour in Group IV-PCA (24.00±4.81 mg) and then gradually declined. In Group TDF, the rescue paracetamol requirement significantly decreased over the course of the postoperative 24 hours (from 100% in the postoperative 4th hour to 35% in the postoperative 24th hour) (Table 6).

There was a significant difference in patient satisfaction between the groups (p<.001). Of the 20 patients, 14 (70.0%) expressed excellent satisfaction in Group IV-PCA, compared to only 1 (5.0%) in Group TDF. Most patients in Group TDF expressed moderate (n=10, 50%) and good (n=8, 40.0%) satisfaction (Table 7).

Table 1. Demographic and clinical characteristics of the study groups

	Group TDF (n=20)	Group PCA (n=20)	p
Age (yearsl)†	45.0±13.9	41.4±13.4	.416*
Weight (kg)†	74.9±13.2	76.4±12.4	.713*
Sex‡			
Female	8 (40.0)	6 (30.0)	.507**
Male	12 (60.0)	14 (70.0)	
ASA physical status‡			
I	12 (60.0)	10 (50.0)	
II	7 (35.0)	9 (45.0)	.806**
III	1 (5.0)	1 (5.0)	
Operation time (min)†	179.5±68.3	174.0±85.7	.824*
Underlying disease‡			
Symptomatic hip osteoarthritis	6 (30.0)	7 (35.0)	.999**
Femur fracture	5 (25.0)	4 (20.0)	
Humerus fracture	3 (15.0)	3 (15.0)	
Tibia fracture	3 (15.0)	3 (15.0)	
Forearm fracture	2 (10.0)	2 (10.0)	
Rotator cuff tear	1 (5.0)	1 (5.0)	

†: mean±standard deviation, ‡: n (%); *: Independent Samples T-test, **: Pearson Chi-Square/Fisher Freeman Halton test; TDF: transdermal fentanyl, PCA: patient-controlled analgesia, ASA: American Society of Anesthesiologists

Table 2. Preoperative and preinduction RSS and VAS scores

	Group TDF (n=20)	Group PCA (n=20)	p *
RSS†			
Preoperative evaluation	1.05±0.22	1.50±0.51	**.002**
Pre-induction of anesthesia	2.00±0.00	1.20±0.41	**<.001**
p**	**p<.001**	**.004**	
VAS†			
Preoperative evaluation	5.10±0.97	4.85±0.93	.391
Pre-induction of anesthesia	3.85±0.99	4.15±1.09	.590
p**	**.024**	**<.001**	

†: mean±standard deviation, *: Independent Samples t test, **: Paired t test; RSS: Ramsay sedation score, VAS: visual analog scale, TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 3. Comparison of intraoperative anesthesia-related parameters between the groups

	Group TDF (n=20)	Group PCA (n=20)	p *
Propofol (mg)†	125.0±28.9	187.0±21.8	**<.001***
Cooper intubation score†	8.60±0.60	7.05±1.93	**.003***
Atropin use‡	1 (5)	0 (0)	.152**
Duration of extubation (min)†	5.60±2.98	5.50±2.44	.945*
Extubation quality†	1.05±0.22	2.60±1.19	**<.001***

†: mean±standard deviation, ‡: n (%), *: Independent Samples t test, **: Pearson Chi-Square/Fisher Freeman Halton test, TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 4. Intra- and inter-group comparisons of the RSS and VAS scores during the postoperative 24 hours between the groups

	Group TDF (n=20)	Group PCA (n=20)	p *
RSS†			
30th min	1.65±0.93	1.70±0.98	.914
60th min	1.85±0.88	1.65±0.81	.427
90th min	1.95±0.22	1.95±0.69	.653
2nd hour	2.00±0.00	1.95±0.22	.317
4th hour	2.00±0.00	2.00±0.32	.999
8th hour	2.10±0.31	2.05±0.39	.671
12th hour	2.10±0.45	2.10±0.45	.999
16th hour	2.15±0.37	2.00±0.32	.179
20th hour	2.10±0.31	2.00±0.32	.323
24th hour	2.05±0.22	2.05±0.39	.979
p**	.128	.837	
Resting VAS†			
30th min	4.70±0.57	6.15±1.23	**<.001**
60th min	3.55±0.51	4.65±1.39	**.004**
90th min	3.10±0.31	3.55±0.89	**.037**
2nd hour	3.05±0.22	2.65±0.67	**.011**
4th hour	3.70±0.87	2.45±0.69	**<.001**
8th hour	3.90±0.85	2.10±0.45	**<.001**
12th hour	3.55±0.51	1.90±0.45	**<.001**
16th hour	3.45±0.51	1.80±0.41	**<.001**
20th hour	3.25±0.44	1.55±0.51	**<.001**
24th hour	3.25±0.64	1.40±0.50	**<.001**
p**	**<.001**	**<.001**	
Ambulatory VAS†			
30th min	6.50±0.83	8.45±1.43	**<.001**
60th min	6.25±1.07	6.80±1.88	.257
90th min	5.40±0.88	5.75±1.83	.754
2nd hour	5.25±0.72	4.35±0.93	**.002**
4th hour	5.20±0.70	4.20±1.01	**.001**
8th hour	5.05±0.51	3.60±1.00	**<.001**
12th hour	4.80±0.77	3.00±0.56	**<.001**
16th hour	4.70±0.57	2.75±0.55	**<.001**
20th hour	4.45±0.69	2.75±0.55	**<.001**
24th hour	4.15±0.49	2.50±0.51	**<.001**
p**	**<.001**	**<.001**	

†: mean±standard deviation, *: Independent Samples t test, **: Paired t test; RSS: Ramsay sedation score, VAS: visual analog scale, TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 5. Bonferroni corrected post-hoc analysis of resting and ambulatory VAS scores during the postoperative 24 hours

		Resting VAS		Ambulatory VAS	
		Group TDF	Group PCA	Group TDF	Group PCA
Time 1	Time 2	p (Bonferroni)	p (Bonferroni)	p (Bonferroni)	p (Bonferroni))
30th min	60th min	.154	.053	.154	.004
30th min	90th min	**<.001**	**.002**	**<.001**	**.007**
30th min	2nd hour	**<.001**	**<.001**	**<.001**	**<.001**
30th min	4th hour	**<.001**	**<.001**	**<.001**	**<.001**
30th min	8th hour	**<.001**	**<.001**	**<.001**	**<.001**
30th min	12th hour	**<.001**	**<.001**	**<.001**	**<.001**
30th min	16th hour	**<.001**	**<.001**	**<.001**	**<.001**
30th min	20th hour	**<.001**	**<.001**	**<.001**	**<.001**
30th min	24th hour	**<.001**	**<.001**	**<.001**	**<.001**
60th min	90th min	.013	.126	.013	.126
60th min	2nd hour	**<.001**	**.005**	**<.001**	**.005**
60th min	4th hour	**<.001**	**<.001**	**<.001**	**<.001**
60th min	8th hour	**<.001**	**<.001**	**<.001**	**<.001**
60th min	12th hour	**<.001**	**<.001**	**<.001**	**<.001**
60th min	16th hour	**<.001**	**<.001**	**<.001**	**<.001**
60th min	20th hour	**<.001**	**<.001**	**<.001**	**<.001**
60th min	24th hour	**<.001**	**<.001**	**<.001**	**<.001**
90th min	2nd hour	.002	.231	.002	.231
90th min	4th hour	**<.001**	**<.001**	**<.001**	**<.001**
90th min	8th hour	**<.001**	**<.001**	**<.001**	**<.001**
90th min	12th hour	**<.001**	**<.001**	**<.001**	**<.001**
90th min	16th hour	**<.001**	**<.001**	**<.001**	**<.001**
90th min	20th hour	**<.001**	**<.001**	**<.001**	**<.001**
90th min	24th hour	**<.001**	**<.001**	**<.001**	**<.001**

VAS: visual analog scale, TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 6. Use of postoperative rescue morphine and paracetamol in Groups PCA and TDF

Time	Group PCA (n=20)		Group TDF (n=20)
	Morphine (mg)		Paracetamol
	Mean±SD	Min-max	n (%)
4th hour	20.25±5.27	10-28	20 (100.0)
8th hour	24.00±4.81	16-30	15 (75.0)
12th hour	20.10±5.86	6-30	11 (55.0)
16th hour	13.50±6.71	4-24	10 (50.0)
20th hour	8.40±6.31	4-28	5 (25.0)
24th hour	7.70±6.91	4-32	7 (35.0)

TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 7. Results of the questionnaire for patient satisfaction regarding analgesia methods

Patient satisfaction	Group TDF (n=20)	Group PCA (n=20)	p
Excellent	1 (5.0)	14 (70.0)	**<.001**
Good	8 (40.0)	5 (25.0)	
Moderate	10 (50.0)	1 (5.0)	
Poor	1 (5.0)	0 (0.0)	

‡: n (%); Fisher Freeman Halton test; TDF: transdermal fentanyl, PCA: patient-controlled analgesia

DISCUSSION

Our investigation revealed distinctive temporal efficacy patterns between transcutaneous fentanyl delivery and automated morphine administration systems. Initial post-surgical phase demonstrated superior nociceptive control with TDF implementation (static measurements through 90 minutes; dynamic assessments within 30 minutes). However, subsequent temporal analysis indicated sustained analgesic superiority in IV-PCA cohort, commencing at post-procedural hour 2 and maintaining throughout the observational period. This pharmacodynamic evolution suggests differential therapeutic profiles: TDF systems exhibit enhanced immediate post-surgical efficacy, while automated morphine delivery protocols demonstrate superior sustained analgesia throughout the critical 24-hour recovery phase in orthopedic interventions.

Findings in the literature regarding the comparison of TDF patches with IV-PCA are conflicting, particularly in the context of orthopedic surgeries. These discrepancies in the findings of relevant studies may be due to differences between the studies' methodologies, TDF doses, timing of application, and patient characteristics. In one of these studies, Ebrahimzadeh et al. (5) found no significant difference between TDF patches and IV-PCA with morphine in terms of pain severity and patient satisfaction scores after orthopedic surgeries, even though they applied a lower dose of TDF (25 µg/hour) compared to the 50 µg/hour dose we applied. Similarly, in a study where TDF doses (12.5-25 µg/h) were titrated according to patient age to minimize the side effects while maintaining efficacy, Hall et al. (1) found no significant difference between TDF patches and IV-PCA with morphine in terms of analgesic efficacy, patient discharge times, and side effects in patients undergoing total knee replacement.

Contrasting observations were reported by Minville and colleagues (10), who demonstrated superior analgesic outcomes with prophylactic transcutaneous fentanyl administration in total hip arthroplasty patients, evidenced by reduced nociceptive scores and diminished opioid requirements compared to morphine-based IV-PCA protocols. The fact that they did not use preventive analgesia or premedication before surgery in the IV-PCA group may have had an impact on their findings. In comparison, even though our timing of TDF patch application was consistent with that of Minville et al. (10), we did not observe the prolonged pain-reducing effects of TDF patches Minville et al. did. Although the surgical distributions of our study groups were similar, differences in the underlying diseases may have caused our results to differ from those of Minville et al.

Several other studies investigating the effect of TDF patches on pain relief and total rescue morphine consumption during the first 48 to 72 hours after total knee arthroplasty have reported that using TDF patches in combination with PCA reduced postoperative pain and adjunctive morphine consumption (9,13). On the other hand, other studies found no significant benefit of TDF patches over placebo patches in patients undergoing forefoot surgery or surgical repair of hip fractures (7,8). Inconsistent findings in the literature regarding the efficacy of TDF patches suggest that significant analgesic benefits from TDF patches may not be obtained in certain surgical contexts or patient groups, emphasizing the importance of tailoring analgesic strategies to specific surgical procedures and patient needs.

Findings in the literature on the efficacy of TDF patches in the context of abdominal surgeries are also inconsistent. Transcutaneous fentanyl delivery systems demonstrated enhanced nociceptive control following gynecologic procedures, however, analgesic efficacy data remains heterogeneous for general abdominal surgical interventions (6,17,18). In one study, although the pain scores of the TDF patch group at certain time points within 36 hours postoperatively were found to be slightly higher than those of the placebo group, it was concluded that TDF patch applications were safe and effective in analgesia after laparotomy, since the mean pain severity score of the TDF patch group was significantly lower than that of the placebo group (18,19). In contrast, Jang et al. (6) found that TDF patches had no advantage over IV fentanyl in reducing pain scores or rescue analgesic use after laparoscopic cholecystectomy. These findings underscore the need to address the heterogeneity in patient characteristics and variations in TDF doses and application protocols between studies. In sum, the findings of this study, together with literature findings, suggest that TDF patches may offer specific advantages in selected scenarios but do not provide consistent superiority over IV-PCA in orthopedic surgeries in particular.

Our findings should be interpreted in the context of contemporary multimodal analgesia approaches. In current clinical practice, postoperative pain management typically employs multiple analgesic modalities rather than relying on a single method. While TDF may not be as effective as IV-PCA, it could be considered as part of a multimodal approach that doesn't restrict patient mobility. However, when developing multimodal analgesia protocols, thorough understanding of the efficacy and safety profile of each component remains essential.

Prospective, large-scale studies that account for confounding factors are needed to understand better the efficacy and relative advantages of TDF patches versus IV-PCA for postoperative pain management. Future studies should explore the potential of individualized analgesic strategies, integrating patient-specific factors such as age, weight, comorbidities, and surgical context in

order to optimize the efficacy and safety of TDF patches. Comparative studies examining the cost-effectiveness, ease of use, and long-term outcomes of TDF patches versus IV-PCA could provide valuable insights into their relative advantages and limitations in postoperative pain management.

Limitations of the Study

A notable methodological constraint emerged from restricted participant numbers, potentially limiting comprehensive characterization of analgesic response variability, particularly within demographically or clinically-defined subpopulations. Secondly, the use of fixed-dose (50 µg/h) TDF patches did not allow for taking individual factors such as body weight, age, and comorbidities into account, and therefore, not all patients received the optimal dose. Additionally, the single-center design and limited sample size restrict the generalizability of our findings. Thirdly, long-term postoperative pain or patient-reported outcomes beyond the initial 24-hour period were not assessed. Future studies should employ individualized TDF dosing, larger patient populations, and multi-center designs.

CONCLUSION

In conclusion, despite enhanced initial analgesic efficacy, TDF systems demonstrated suboptimal pain control compared to IV-PCA morphine delivery in the management of post-orthopedic surgical pain. These findings suggest that the selection of analgesic methods for postoperative pain management should consider patient characteristics, surgical type, and pain severity, with emphasis on developing individualized treatment approaches. Future studies should be conducted in larger patient populations, with individualized dosing regimens, and multi-center designs.

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REFERENCES

1. Hall MJ, Dixon SM, Bracey M, et al. A randomized controlled trial of postoperative analgesia following total knee replacement: transdermal Fentanyl patches versus patient controlled analgesia (PCA). Eur J Orthop Surg Traumatol. 2015;25:1073-9.
2. Hartrick CT, Bourne MH, Gargiulo K, et al. Fentanyl iontophoretic transdermal system for acute-pain management after orthopedic surgery: a comparative study with morphine intravenous patient-controlled analgesia. Reg Anesth Pain Med. 2006;31:546-54.
3. Langford RM, Chang KY, Ding L, Abraham J. Comparison of fentanyl iontophoretic transdermal system and routine care with morphine intravenous patient-controlled analgesia in the management of early postoperative mobilisation: results from a randomised study. Br J Pain. 2016;10:198-208.
4. Kaye AD, Menard BL, Ehrhardt KP, et al. Consensus Perioperative Management Best Practices for Patients on Transdermal Fentanyl Patches Undergoing Surgery. Curr Pain Headache Rep. 2019;23:50.
5. Ebrahimzadeh MH, Mousavi SK, Ashraf H, et al. Transdermal fentanyl patches versus patient-controlled intravenous morphine analgesia for postoperative pain management. Iran Red Crescent Med J. 2014;16:e11502.
6. Jang JS, Hwang SM, Kwon Y, et al. Is the transdermal fentanyl patch an efficient way to achieve acute postoperative pain control? A randomized controlled trial. Medicine (United States). 2018;97:e13768.
7. Merivirta R, Pitkänen M, Alanen J, et al. Postoperative pain management with transdermal fentanyl after forefoot surgery: A randomized, placebo-controlled study. J Pain Res. 2015;8:39-45.
8. Labmayr V, Rief M, Reinbacher P, et al. Simplified pain management including fentanyl TTS in PACU patients with hip fracture surgery to improve patients' well-being: a double-blind randomized trial. J Perianesth Nurs. 2024;39:461-7.
9. Sathitkarnmanee T, Tribuddharat S, Noiphitak K, et al. Transdermal fentanyl patch for postoperative analgesia in total knee arthroplasty: A randomized double-blind controlled trial. J Pain Res. 2014;7:449-54.
10. Minville V, Lubrano V, Bounes V, et al. Postoperative analgesia after total hip arthroplasty: patient-controlled analgesia versus transdermal fentanyl patch. J Clin Anesth. 2008;20:280-3.
11. Solak O, Öz G, Kokulu S, et al. The effectiveness of transdermal opioid in the management multiple rib fractures: Randomized clinical trial. Balkan Med J. 2013;30:277-81.
12. Kömürcü Ş, Turhal S, Altundag K, et al. Safety and efficacy of transdermal fentanyl in patients with cancer pain: phase IV, Turkish oncology group trial. Eur J Cancer Care (Engl). 2007;16:67-73.
13. Abrisham SMJ, Ghahramani R, Heiranizadeh N, et al. Reduced morphine consumption and pain severity with transdermal fentanyl patches following total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2014;22:1580-4.
14. Ramsay MAE, Savege TM, Simpson BRJ, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J. 1974;2:656-9.
15. Cooper R, Mirakhur RK, Clarke RSJ, Boules Z. Comparison of intubating conditions after administration of org 9426 (rocuronium) and suxamethonium. Br J Anaesth. 1992;69:269-73.

16. Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. Anesth Analg. 2010;111:120-8.

17. Myles PS, Williams DL, Hendrata M, et al. Patient satisfaction after anaesthesia and surgery: results of a prospective survey of 10,811 patients. Br J Anaesth. 2000;84:6-10.

18. Broome IJ, Wright BM, Bower S, Reilly CS. Postoperative analgesia with transdermal fentanyl following lower abdominal surgery. Anaesthesia. 1995;50:300-3.

19. Hosseini H, Kargar S, Shiryazdi SM, et al. Fentanyl transdermal patch (Durogesic® D-TRANS) for post abdominal laparotomy analgesia: a double blind randomized study. Minerva Chir. 2015;70:401-8.