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Original Research Article

COMPARISON OF INTRAVENOUS AND NEBULIZED FENTANYL FOR POST OPERATIVE ANALGESIA IN PATIENTS UNDERGOING INFRA-UMBILICAL SURGERIES UNDER SPINAL ANAESTHESIA

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ABSTRACT

Background: Effective postoperative analgesia is essential for patient comfort and recovery. Fentanyl, a potent synthetic opioid, can be administered through intravenous (IV) or nebulized routes. This study compared the efficacy, onset, duration, and side effect profile of intravenous versus nebulized fentanyl in patients undergoing infra-umbilical surgeries under spinal anaesthesia.

Materials and Methods: A prospective, randomized comparative study was conducted on 66 patients (ASA I–II; age 18–45 years) undergoing infra-umbilical surgeries under spinal anaesthesia. Patients were randomly allocated into two groups: Group IV (n=33) received IV fentanyl 2 µg/kg, and Group N (n=33) received nebulized fentanyl 5 µg/kg. Postoperative pain was assessed using the Visual Analogue Scale (VAS). The primary outcomes were onset and duration of analgesia, while secondary outcomes included need for rescue analgesia and incidence of side effects.

Results: The onset of analgesia was significantly faster in Group IV (7.9 ± 1.6 min) compared to Group N (11.2 ± 2.1 min, $p<0.001$). The duration of analgesia was significantly longer in Group N (141.6 ± 24.1 min) than in Group IV (125.3 ± 22.7 min, $p=0.007$). Rescue analgesia was required more frequently in the IV group (30.3%) than in the nebulized group (12.1%), though the difference was not statistically significant ($p=0.07$). Side effects such as nausea, sedation, pruritus, and respiratory depression were more common in the IV group, but differences were not statistically significant.

Conclusion: Intravenous fentanyl provides faster onset of analgesia, while nebulized fentanyl offers longer duration with fewer side effects. Nebulized fentanyl may thus serve as a safe and effective non-invasive alternative for postoperative pain management following infra-umbilical surgeries under spinal anaesthesia.

Keywords: Fentanyl; Postoperative analgesia; Nebulization

INTRODUCTION

Postoperative pain remains a significant concern in surgical practice. Despite advances in anesthetic and analgesic techniques, pain following infra-umbilical surgeries contributes to increased patient discomfort, delayed mobilization, prolonged hospital stays, and higher risk of complications. Effective postoperative pain management is thus a cornerstone of perioperative care, with the dual goals of improving patient satisfaction and enhancing recovery.[1,2]

Traditionally, intravenous (IV) opioids have been the mainstay for managing moderate-to-severe postoperative pain. Fentanyl, a synthetic opioid, has been widely utilized because of its rapid onset, potent analgesic effect, and relatively short duration of action. However, systemic side effects such as respiratory depression, nausea, vomiting, and

sedation limit its widespread use, especially in settings requiring early mobilization.[3,4]

Nebulized opioid administration has emerged as a potential alternative to systemic opioid delivery. The pulmonary route offers a non-invasive method with rapid systemic absorption owing to the large alveolar surface area and rich vascular supply. Previous studies have demonstrated that nebulized fentanyl provides effective analgesia in various clinical settings, including trauma, emergency medicine, and postoperative pain. It combines the advantage of ease of administration with a reduced risk of systemic side effects compared to IV delivery.[5]

Aim

To compare the efficacy of intravenous versus nebulized fentanyl for postoperative analgesia in patients undergoing infra-umbilical surgeries under spinal anaesthesia.

Objectives

1. To compare the onset of analgesia between intravenous and nebulized fentanyl.
2. To compare the duration of analgesia provided by intravenous and nebulized fentanyl.
3. To assess and compare the side effect profile of both groups.

MATERIALS AND METHODS

Source of Data: Patients aged 18–45 years scheduled for infra-umbilical surgeries under spinal anaesthesia at tertiary care hospital.

Study Design: A prospective, randomized, comparative clinical study.

Study Location: The study was conducted at the Department of Anaesthesiology at tertiary care hospital.

Study Duration: The study was conducted over a period of one year.

Sample Size: A total of 66 patients were enrolled and randomly allocated into two groups:

Group IV (n = 33): Received intravenous fentanyl 2 µg/kg diluted in 5 ml normal saline, administered slowly.

Group N (n = 33): Received nebulized fentanyl 5 µg/kg diluted in 5 ml normal saline using a venti mask at a constant flow rate of 10 ml/min for 10 minutes.

Inclusion Criteria

- Patients aged 18–45 years.
- ASA physical status I and II.
- Scheduled for infra-umbilical surgeries under spinal anaesthesia.
- Patients able to comprehend the pain assessment scale (VAS) after due explanation.

Exclusion Criteria

- Patient refusal.
- Known hypersensitivity to fentanyl.
- Morbid obesity (BMI > 30).
- Respiratory, renal, or hepatic systemic complications.
- Coagulation disorders.
- Patients on chronic opioid therapy or drugs interfering with fentanyl metabolism (e.g., MAO inhibitors, sibutramine).

Procedure and Methodology: After obtaining informed consent, patients were randomly assigned into two groups using a computer-generated randomization table. Standard spinal anaesthesia was administered for infra-umbilical surgeries. Postoperatively, patients reporting pain with a Visual Analogue Scale (VAS) >4 in the Post Anaesthesia Care Unit (PACU) were given fentanyl via their allocated route (IV or nebulization). Group IV received IV fentanyl as described, while Group N received nebulized fentanyl. Pain intensity was recorded using VAS at baseline, 5-, 10-, and 15-minutes post-administration, then every 15 minutes up to 1 hour, and subsequently every 30 minutes up to 6 hours. Patients not relieved of pain within 15 minutes or those requiring additional analgesia were given IV paracetamol (15 mg/kg) and excluded from further analysis.

Sample Processing: Data on demographic details, type of surgery, ASA grade, fentanyl dose, onset and duration of analgesia, VAS scores at different intervals, need for rescue analgesia, Ramsay sedation score, hemodynamic parameters (HR, BP, SpO_2), and adverse effects (nausea, vomiting, pruritus, respiratory depression) were recorded.

Statistical Methods: Data were compiled and analyzed using SPSS software (version 27.0). Continuous variables (onset of analgesia, duration) were expressed as mean ± SD and compared using independent t-tests. Categorical variables (e.g., incidence of nausea, rescue analgesia requirement) were analyzed using Chi-square or Fisher's exact test. A p-value <0.05 was considered statistically significant.

Data Collection: All relevant perioperative and postoperative data were entered into a structured proforma, including demographic details, type of surgery, drug administration details, pain scores, and side effect profiles. Standard monitoring (pulse oximetry, ECG, non-invasive blood pressure) was maintained throughout.

RESULTS

[Table 1] shows that the baseline demographic and clinical characteristics between the two groups were comparable. The mean age was similar in both groups (34.2 ± 6.3 years in Group IV vs. 33.7 ± 6.8 years in Group N), with no significant difference (p=0.77). The gender distribution was also nearly identical, with males comprising 54.5% in Group IV and 51.5% in Group N (p=0.80). The mean body weight was 61.8 ± 7.4 kg in Group IV and 60.9 ± 7.1 kg in Group N, which was not statistically different (p=0.61). The ASA physical status classification revealed that most patients belonged to ASA Grade I in both groups (63.6% vs. 66.7%), while Grade II comprised the remainder, again showing no significant difference

(p=0.79). The distribution of surgical procedures (hernia, hysterectomy, and others) was also comparable between the groups (p=0.93).

Table 1: Baseline Demographic and Clinical Characteristics (N=66)

Variable	Group IV (n=33)	Group N (n=33)	Test of significance	95% CI of Difference	p-value
Age (yrs), Mean ± SD	34.2 ± 6.3	33.7 ± 6.8	t=0.29	−2.9 to 3.9	0.77
Sex (Male), n (%)	18 (54.5%)	17 (51.5%)	χ^2=0.06	—	0.80
Weight (kg), Mean ± SD	61.8 ± 7.4	60.9 ± 7.1	t=0.51	−2.9 to 4.7	0.61
ASA Grade I, n (%)	21 (63.6%)	22 (66.7%)	χ^2=0.07	—	0.79
ASA Grade II, n (%)	12 (36.4%)	11 (33.3%)			
Type of Surgery (Hernia/ Hysterectomy/ Others)	14/12/7	15/10/8	χ^2=0.14	—	0.93

Table 2: Onset of Analgesia (minutes) (N=66)

Variable	Group IV (n=33)	Group N (n=33)	Test of significance	95% CI of Difference	p-value
Onset of analgesia (min), Mean ± SD	7.9 ± 1.6	11.2 ± 2.1	t=6.96	−4.3 to −2.3	<0.001*
% achieving analgesia <10 min, n (%)	26 (78.8%)	11 (33.3%)	χ^2=13.7	—	<0.001*

[Table 2] demonstrates that the onset of analgesia was significantly faster in the intravenous group compared to the nebulized group. The mean onset time was 7.9 ± 1.6 minutes in Group IV, whereas it was 11.2 ± 2.1 minutes in Group N. This difference was statistically highly significant (t=6.96, 95% CI: −4.3 to −2.3, p<0.001). Furthermore, 78.8% of patients in Group IV achieved analgesia within 10 minutes compared to only 33.3% in Group N, which was also statistically significant (p<0.001).

Table 3: Duration of Analgesia (minutes) (N=66)

Variable	Group IV (n=33)	Group N (n=33)	Test of significance	95% CI of Difference	p-value
Duration of analgesia (min), Mean ± SD	125.3 ± 22.7	141.6 ± 24.1	t=2.78	−27.8 to −4.9	0.007*
% requiring rescue analgesia within 2h, n (%)	10 (30.3%)	4 (12.1%)	χ^2=3.19	—	0.07 (NS)

[Table 3] compares the duration of analgesia between the two groups. Patients receiving nebulized fentanyl experienced a significantly longer duration of analgesia (141.6 ± 24.1 minutes) compared to those in the intravenous group (125.3 ± 22.7 minutes), with the difference being statistically significant (t=2.78, 95% CI: −27.8 to −4.9, p=0.007). Additionally, a higher proportion of patients in the intravenous group required rescue analgesia within the first 2 hours (30.3%) as compared to the nebulized group (12.1%). Although this difference approached significance, it did not reach statistical significance (p=0.07).

Table 4: Side Effect Profile (N=66)

Side Effect	Group IV (n=33)	Group N (n=33)	Test of significance	95% CI of Difference	p-value
Nausea/Vomiting, n (%)	6 (18.2%)	3 (9.1%)	χ^2=1.04	−0.07 to 0.25	0.31
Sedation (Ramsay ≥3), n (%)	7 (21.2%)	2 (6.1%)	χ^2=3.28	−0.02 to 0.30	0.07
Pruritus, n (%)	4 (12.1%)	1 (3.0%)	χ^2=1.82	−0.03 to 0.21	0.17
Respiratory Depression, n (%)	2 (6.1%)	0 (0%)	Fisher's Exact	—	0.15
SpO_2 (%), Mean ± SD	97.3 ± 1.8	97.8 ± 1.6	t=1.16	−1.4 to 0.4	0.25

[Table 4] summarizes the incidence of side effects in both groups. Nausea and vomiting were observed in 18.2% of patients in Group IV and 9.1% in Group N, though the difference was not statistically significant (p=0.31). Sedation, defined as a Ramsay sedation score ≥3, was more frequent in the intravenous group (21.2%) compared to the nebulized group (6.1%), showing a trend toward significance (p=0.07). Similarly, pruritus was seen in 12.1% of patients in Group IV versus 3.0% in Group N (p=0.17). Respiratory depression was reported in 2 patients (6.1%) in the intravenous group, whereas none occurred in the nebulized group, though this difference was not statistically significant (p=0.15). Oxygen saturation (SpO_2) remained comparable between the groups (97.3 ± 1.8% vs. 97.8 ± 1.6%, p=0.25).

DISCUSSION

Baseline comparability [Table 1]: Baseline variables were well balanced between groups: age, sex, weight, ASA grade distribution, and surgical case-mix all showed non-significant differences (all p>0.60). This homogeneity minimizes confounding and supports attributing differences in analgesic outcomes to the intervention routes rather than baseline imbalances—consistent with design quality emphasized in prior randomized work comparing nebulized and IV fentanyl in postoperative or acute pain settings. Helmy KM et al (2024).[6]

Onset of analgesia [Table 2]: Intravenous fentanyl achieved a significantly faster onset (7.9±1.6 vs 11.2±2.1 min; t=6.96; p<0.001), and a markedly greater proportion attained relief within 10 minutes (78.8% vs 33.3%; p<0.001). This mirrors multiple trials in which the IV route—owing to immediate systemic availability—outperforms nebulization for time-to-effect, even when nebulized doses are higher to offset pulmonary deposition losses. Comparable patterns (faster onset IV, adequate but slower onset via inhalation) have been reported after orthopedic procedures and ACL reconstruction, as well as in emergency department cohorts. Kumar A et al,[7] (2019) Pharmacokinetic data reinforce this mechanism: inhaled fentanyl achieves rapid but less abrupt peaks than IV due to alveolar deposition and absorption kinetics, explaining the slower onset yet acceptable early analgesia. Gautam B et al (2019).[8]

Duration of analgesia and early rescue [Table 3]: Despite slower onset, nebulized fentanyl provided longer analgesia (141.6±24.1 vs 125.3±22.7 min; t=2.78; p=0.007), with a lower (though not statistically significant) early rescue requirement within 2 hours (12.1% vs 30.3%; p=0.07). Prior trials have noted a tendency toward more sustained effect with nebulized fentanyl—likely reflecting smoother concentration-time profiles and reduced early offset—while maintaining comparable global analgesic quality to IV dosing. These trends are aligned with early and contemporary PK/PD studies showing effective systemic delivery via the pulmonary route with moderated peaks and prolonged tail profiles. Wingert TE et al,[9] (2023) & Bourgeois C et al (2024).[10]

Adverse effects and safety (Table 4): Side-effect rates numerically favored nebulization: lower incidences of nausea/vomiting (9.1% vs 18.2%), sedation ≥3 on Ramsay (6.1% vs 21.2%), pruritus (3.0% vs 12.1%), and no respiratory depression events (0% vs 6.1%), though differences did not reach statistical significance in this sample. This safety tilt toward nebulization is consistent with prior clinical comparisons and PK findings: inhaled delivery yields lower peak concentrations, reducing dose-related adverse effects while preserving efficacy. Tang C et al,[11] (2017) & Prasad D et al (2022).[12]

CONCLUSION

The present study demonstrated that both intravenous and nebulized fentanyl are effective in providing postoperative analgesia in patients undergoing infra-umbilical surgeries under spinal anaesthesia. Intravenous fentanyl offered a significantly faster onset of analgesia, making it preferable when rapid pain relief is desired. Conversely, nebulized fentanyl provided a longer duration of analgesia with a trend toward fewer opioid-related adverse effects such as sedation, pruritus, and respiratory depression. Thus, nebulized fentanyl represents a safe, non-invasive, and effective alternative to intravenous administration, particularly in situations where prolonged analgesia and better tolerability are prioritized.

Limitations

1. The study was conducted in a single-center setting with a relatively small sample size (n=66), which may limit generalizability of the findings.
2. The study population was restricted to ASA I–II patients aged 18–45 years, excluding elderly and higher-risk surgical candidates, thus reducing external validity.
3. The assessment period was limited to the immediate 6-hour postoperative phase, without evaluation of long-term pain outcomes.
4. Subjective measures such as the Visual Analogue Scale (VAS) may introduce inter-individual variability in pain reporting.
5. Potential pharmacokinetic differences due to nebulization technique (mask fit, inspiratory effort) were not standardized beyond flow rate, which may influence drug delivery efficiency.

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