



EFFICACY OF NEBULISED FENTANYL IN TWO DIFFERENT DOSES FOR POST OPERATIVE PAIN IN LOWER LIMB ORTHOPAEDIC SURGERIES

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ABSTRACT

Background : I.V. opioids for post operative pain management are used extensively worldwide, but it is often attributable to the opioid induced systemic side effects . The aim of our study is to find The an alternative which can provide effective post operative analgesia with minimal side effects . fentanyl being a highly lipophilic drug makes it suitable for inhalational route of administration thus reducing the possibility of systemic side effects. **Aims of study:** This aim of our study was to compare the effect of two doses of nebulized fentanyl for postoperative analgesia after lower limb orthopaedic surgeries. **Methodology :** Total 80 patients who had undergone unilateral lower limb surgeries under subarachnoid block , after taking consent and thorough understanding of the nature of our study were enrolled . They are then divided into 2 groups Group NF I included forty patients who received 2 $\mu\text{g}/\text{kg}$ of fentanyl nebulization, and Group NF II included forty patients who received 4 $\mu\text{g}/\text{kg}$ of fentanyl nebulization using a standard venturi mask. In the postoperative period, whenever the Visual Analog Scale ≥ 4 , patients received the analgesic corresponding to their respective groups. **Statistical analysis:** The data obtained were statistically analyzed using IBM SPSS 20 software. **Results:** There was no significant difference in the demographic characteristics, duration of surgery, the number of patients who required rescue analgesia, the onset of analgesia in both the groups is a bit delayed. The duration of analgesia was slightly longer in Group NF II in comparison to Group NF I. The rise in Ramsay sedation score was faster and peaked at 5 min. In Group NF II, however, it was lesser than that of Group NF I. Side effects in Group NF I were significantly lesser compared to Group NF II. **Conclusion:** Both the groups have shown effective analgesia.

KEYWORDS : Nebulisation , Venture Mask , Rescue Analgesia

INTRODUCTION

Patients undergoing orthopaedic surgeries experience significant postoperative pain that may persist for several days after surgery. It often remains under-treated which leads to immediate complications: infectious, neurological, cardiovascular, and thrombo- embolic sequelae caused by immobility because of pain. This makes the use of i.v. opioids popular among physicians , but the systemic side effects associated with the use of i.v. opioids often becomes very uncomfortable for patients as well as treating physicians ^[1]. Transpulmonary (inhalational) administration of medication produces rapid, effective drug delivery as a result of the thin alveolar-blood barrier, high tissue perfusion, and enormous surface area of the lungs. ^[2] Fentanyl being a highly lipophilic drug can produce postoperative analgesia if administered as a nebulized aerosol. ^[3-5] In a subsequent study, Singh *et al* ^[6] found that nebulisation with 4 $\mu\text{g}/\text{kg}$ fentanyl may be used as an alternative to IV 2 $\mu\text{g}/\text{kg}$ fentanyl for adequate post-operative pain relief. But with delayed onset of action in nebulised group.

When administered via nebulisation route there was no clinically significant respiratory depression or evidence of respiratory tract irritation reported in the previous studied thus far, nor is there any significant difference in nausea and drowsiness relative to intravenous route. This study was aimed to compare the effect of nebulized fentanyl in two different doses of 4 $\mu\text{g}/\text{kg}$ & 2 $\mu\text{g}/\text{kg}$ for postoperative analgesia in patients after lower limb orthopaedic surgeries.

Subjects And Methods: This prospective , double-blinded , randomized comparative clinical study was conducted in Department of Anaesthesiology , Gandhi Medical College , Bhopal ,M.P. from July 2019 to July 2020. After institutional ethical committee clearance and informed consent were obtained, 80 patients with the ASA (American society of anaesthesiologists) Grade I and II , age group 20–50 years posted for elective unilateral lower limb orthopaedic surgeries

under central neuraxial block were enrolled . The eighty patients were divided by sealed enveloped method into two groups.

Exclusion criteria include those who refused to take part in the study, patients with renal, cardiac, and hepatic impairment and bleeding diathesis, pregnant and breastfeeding women , patients with hypersensitivity to opioids , patients taking drugs that have interactions with fentanyl , patients with body mass index >30 kg/m², patients with neuropsychiatric disorders, and patients who were receiving sedatives or any other narcotic drugs.

Group NF I included 40 patients who received 10 ml of normal saline with 2 $\mu\text{g}/\text{kg}$ of fentanyl in 5ml of normal saline, nebulized using a nebulizer through standard venturi mask at 8–10 L/min flow of oxygen for 10 min.

Group NF II included 40 patients who received 10 ml of normal saline with 4 $\mu\text{g}/\text{kg}$ of fentanyl in 5 ml of normal saline, nebulized using a nebulizer through standard venturi mask at 8–10 L/min flow of oxygen for 10 min.

The subarachnoid block was carried out with 0.5mg/kg bupivacaine (heavy) through a 25G spinal needle. The target block level was kept between T8 and T10. Standard ASA monitoring was applied. Patients were kept in the postanesthesia care unit for 24 h after the end of surgery for observation. The postoperative pain was observed via Visual Analog Scale (VAS) after surgery. Both the groups received the analgesic drug by a blinded observer through nebulization routes.

The following parameters were recorded: duration of surgery (time from skin incision to the removal of drapes), the onset of analgesia (time from the admission of the analgesic until the VAS score becomes ≤ 2), duration of analgesia (time from the

onset of analgesia until the VAS score becomes greater ≥ 4), level of sedation using Ramsay sedation scale (every 5 min up to 30 min and then at intervals of 15 min up to 2 h), number of patients with inadequate analgesia, and signs of opioid side effects.

The sample size was estimated based on a pilot study. The data obtained were statistically analyzed using IBM SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, version 25.0. Armonk, NY: IBM Corp.). Qualitative data were analyzed using the Chi-square test and Z-test. Quantitative data were analyzed using the Student's t-test. $P < 0.05$ was considered statistically significant.

Results: There was no significant difference in the demographic profile, duration of surgery, and the number of patients who required rescue analgesia, as displayed in Table 1. There was no significant delay in the onset of analgesia in Group NF I in comparison with Group NF II. The duration of analgesia was also comparable in both the groups. In GroupNF II, the Ramsay sedation [Table 2] score was faster and was on higher side at all time intervals. Side effects in Group NF I were lesser compared to Group NF II [Table 3].

TABLE 1: DEMOGRAPHIC CHARACTERISTICS, DURATION OF SURGERY AND ONSET OF ANALGESIA

TITLE	GROUP N I	GROUP N II	TEST	P VALUE
AGE	35.8 ± 9.2	38.6 ± 10	t = 1.30	0.38
WEIGHT	58.6 ± 6.4	57.3 ± 7.61	t = 0.8264	0.8166
ASA I	30	31	X ² = 0.04	0.792
ASA II	10	9		
DURATION OF SURGERY	99.8 ± 7.5	100.4 ± 8.61	t = 0.332	0.739
ONSET OF ANALGESIA	5.1 ± 1.4	4.8 ± 1.0	t = 1.10	0.54
DURATION OF ANALGESIA	79.8 ± 6.9	82.4 ± 8.22	t = 1.53	0.249
PATIENTS REQUIRING RESCUE ANALGESIA	8	6	Z = 0.6	0.556

TABLE 2: RAMSAY SEDATION SCORE

TIME INTERVAL (MIN.)	MEAN ± SD		t	P
	GROUP N I	GROUP N II		
0	1.38±0.43	1.40±0.51	0.187	0.851
5	2.00±0.54	2.40±0.38	3.56	<0.001
10	2.10±0.43	2.56±0.46	4.62	<0.001
15	2.13±0.67	2.42±0.51	2.92	0.006
30	2.01±0.28	2.30±0.40	3.75	0.003
45	1.99±0.44	2.25±0.36	2.89	0.007
60	1.68±0.48	1.98±0.43	2.94	0.006
75	1.57±0.55	1.72±0.42	1.37	0.34
90	1.36±0.38	1.44±0.28	1.07	0.56
10	1.28±0.49	1.42±0.26	1.59	0.22
120	1.25±0.38	1.40±0.54	1.43	0.30

TABLE 3: SIDE EFFECTS COMPARISON

	GROUP N I	GROUP N II	Z	P
PONV	1	3	1	0.29
BRADYCARDIA	0	0	-	-
RESPIRATORY DEPRESSION	0	0	-	-
HYPOTENSION	0	0	-	-
PRURITUS	0	2	1.4	0.15
BRONCHOSPASM	0	0	-	-

Discussion: This study of comparison of the effect of nebulized fentanyl (4 µg/kg) versus nebulised fentanyl (2

µg/kg) is an effort to understand whether the dose dependent sedation and side effects can be avoided by decreasing the dose without affecting the efficacy. In our previous study we compared the intravenous fentanyl with nebulised fentanyl^[12] the result of which was that nebulized fentanyl produced more extended analgesia than intravenous fentanyl with fewer side effects and lesser sedation.

Furthermore, previously, Farahmand et al. had compared the effectiveness of nebulized fentanyl with intravenous morphine in the management of acute limb pain and proposed that nebulized fentanyl is a rapid, safe, and effective method for temporary control of acute limb pain in emergency department patients.^[4-6]

In our study we found that the onset of analgesia, duration of analgesia are comparable in both the groups. whereas sedation is significantly lesser in the group receiving 2µg/kg. Our results are similar to the results found by Singh AP et al. They have concluded that Quality of analgesia evidenced by change in VAS was dose dependent and after nebulisation by 4 µg/kg fentanyl, it was equivalent to 2 µg/kg IV fentanyl. The duration of pain relief in nebulisation group was prolonged (90 min vs. 30 min). In this study, we found that there was no difference in the onset of analgesia in Group NF I in comparison with Group NF II. The duration of analgesia was also similar in both the groups.

Ramsay Sedation Score in both the groups reached peak after 10 min. This can be due to the slow rise in peak plasma concentration by transpulmonary route of administration of fentanyl. This correlates with the finding by previous studies that maximum serum concentration of fentanyl is reached at 13 min after intranasal administration as compared to IV administration (2-3 min). contrary to that Mather LE^[13] comments that inhaled fentanyl, reached to therapeutic level in the blood stream as quickly as intravenous (IV). They have used two different novel proprietary aerosol generators delivered a single dose of the opioid. The transpulmonary route of drug administration depends vastly on drug delivery device, as we are using using a nebulizer through standard venturi mask it can be the reason for delayed onset in both the groups.

In the present study the vitals at all times were stable and did not show any significant variation. No major side effects like respiratory depression; hypoxia or bronchospasm was observed in any of the groups. This correlates with the finding by Singh AP et al^[2] Worsely^[13] and Higgins.^[14] Side-effects such as pruritus, nausea and vomiting were observed in both the groups and were dose dependent (more in group NF II).

However, there are certain limitations of our study. The number of patients included in the study is small and warrants further investigation by increasing the sample size. The present study included only patients who underwent lower limb orthopaedic surgeries under sub arachnoid block. However, the usefulness of inhaled fentanyl is limitless in situations where iv access is difficult (Old, ICU patients, burn patients, trauma patients).

Conclusion: Nebulization with fentanyl is a good alternative to intravenous fentanyl for adequate postoperative pain relief with fewer side effects. Nebulised fentanyl at dose 2 µg/kg have similar pain relief ;lesser sedation and lesser side effects.

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