



# TO COMPARE EFFICACY AND SAFETY OF INTRAVENOUS INJECTION TRAMADOL AND INJECTION FENTANYL AFTER UPPER ABDOMINAL SURGERIES, A RANDOMISED, DOUBLE BLIND STUDY

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## Abstract

**BACKGROUND:** The effective pain relief is the utmost importance to anyone treating, patients undergoing surgery. Pain relief has significant physiological benefits; hence, monitoring of pain relief is increasingly becoming an important postoperative quality measure. The goal for postoperative pain management is to reduce or eliminate pain and discomfort with a minimum side effects.

**METHODS:** 120 patients undergoing upper abdominal surgeries were randomised into two groups, Group F (n=60) who were given injection Fentanyl (100 mcg) 1-2µg/kg/wt and GROUP T (n=60) patients received injection Tramadol 2ml (100mg) 3mg/kg/wt was given for 6 hours postoperatively. Both group received injection Diclofenac 75mg IM as a rescue drug if pain persists even after giving injection Tramadol or injection Fentanyl. The postoperative pain relief was evaluated by visual analog scale (VAS). The efficacy of drugs and incidence of post operative nausea, vomiting and hypoxia were also measured.

**RESULTS:** The mean VAS score of group F was 3.57±1.045 at first six hours and reduces to 3.46±2.53 at 24 hours vs in group T 4.97±1.04 at first six hours to 4.46±2.53 at 24 hours. More patients in group T 26(43.4%) vs 12(20%) in group F were given rescue drug. There was a significant difference in the incidence of PONV 5 8.33% in group F and hypoxia in both the groups

**Index Terms** - VAS, Fentanyl, Tramadol, Postoperative Pain

## I. INTRODUCTION

Pain has been considered as an unpleasant sensation that we feel as a reaction to the stimulus of our surroundings, and that unpleasant sensation acts as a defense mechanism of our body to react to the stimulus. However, adverse pain sensation reduces not only our quality of life but also our productivity at work.<sup>1</sup> Most patients who undergo surgery experience acute postoperative pain; however, evidence suggests that only half of the patients achieve adequate or satisfactory postoperative pain relief. Postoperative pain, especially when poorly managed, leads to harmful acute effects (i.e., adverse

physiological responses like physiological stress response that includes increased heart rate, breathing rate,<sup>2</sup> Pain control following surgery is a major priority for both patients as well as doctors. Several preoperative, intraoperative, and postoperative interventions and management strategies are available for reducing and managing postoperative pain.<sup>3</sup> Tramadol is a centrally-acting, atypical opioid agonist with a dual mechanism of action. The analgesic effect of Tramadol is believed to be due to both binding to  $\mu$ -opioid receptors and weak inhibition of re-uptake of norepinephrine and serotonin. It is an opioid agonist and inhibitor of norepinephrine and serotonin reuptake. Tramadol has a low risk of abuse compared to conventional opioids such as morphine.<sup>4</sup> Fentanyl is a potent synthetic opioid drug approved by the Food and Drug Administration for use as an analgesic (pain relief) and anaesthetic. It is approximately 100 times more potent than morphine and 50 times more potent than heroin as an analgesic.<sup>5</sup> Fentanyl is one of the most widely used opioids for intravenous patient-controlled analgesia (IV-PCA)<sup>6</sup>. The study by **Hojat Sheikh Motahar Vahedi et al., 2019**, conducted a comparison between intravenous fentanyl and morphine to treat pain in patients suffering from acute traumatic limb injuries (ATLI). The study found that fentanyl was more effective than morphine in decreasing pain more quickly and with fewer side effects in patients with opioid addiction.<sup>7</sup>

The study by **Javad Mozafari et al., 2019**, compared the analgesic effect of intravenous fentanyl with that of intranasal ketamine in renal colic patients. Ketamine was found to be less effective than fentanyl in controlling renal colic-induced pain and to be associated with a higher prevalence of side effects.<sup>8</sup>

## AIMS AND OBJECTIVES

The aim and objective of this study was to compare the efficacy and safety of intravenous injection tramadol and injection fentanyl after upper abdominal surgeries, a randomised, double blind study

## MATERIAL AND METHOD

The study was carried out on 120 patients at A K Tibbiya College and Hospital Aligarh Muslim University Aligarh for a period of 1 year (2022-2023). Ethical committee registration number was CTRI/2022/12/048459. A written consent were taken from all the patients. 60 patients in each group of ASA 1 and II between the age of 18-65 years and weight of 45-90 kgs were elected for upper abdominal surgeries under spinal anaesthesia. Exclusion criteria include patient with ASA 3, neurological disorders, cardiac problem, history of coagulopathy.

All the surgeries were done under spinal anaesthesia. On arrival of patient into operating room all patients were preloaded with 5-10 ml/kg of Ringer lactate before spinal anaesthesia. ECG, SpO<sub>2</sub>, non-invasive BP were monitored through out the operation. Patients were randomly divided into two groups. GROUP F (n=60) patients received intravenous injection Fentanyl (100 mcg) 1-2 $\mu$ g/kg/wt for 6 hours postoperatively. GROUPT (n=60) patients received Injection Tramadol 2ml (100mg) 3mg/kg/wt was given for 6 hours postoperatively. Continuous monitoring of hemodynamic factors was done throughout surgery and post-surgery. Pain was checked and assessed at every 6 hour through a visual analog scale. Vas score 1-3 is considered as mild, 4-6 is considered as moderate, 6-8 is considered as severe and vas score 8-10 is considered as worst. Patient with persistent score between 6-10 was given injection diclofenac 75mg intramuscularly as a rescue drug.

## STATISTICAL ANALYSIS

The Demographic data was expressed in percentages and mean  $\pm$  standard deviation. The VAS score in the groups was calculated using the Chi-square test ( $\chi^2$ ). The efficacy of drugs on VAS score was calculated using the Student's Paired t-test and Unpaired t-test for intragroup and intergroup comparison respectively.  $p < 0.05$  was considered significant.

## RESULTS

There was no stastically significant difference between the two groups in any of the demographic data. At different time intervals Injection Fentanyl has more significant effect on patients with a P value is  $< 0.05$  as there were lesser number of patients with VAS score between 6-10 in group F then in group T. There were lesser number of patients in group F who require rescue drug as compared to group T. Out of 120 patients 43 patients have mild pain with a VAS score (1-3), 15 have moderate pain with a VAS score (4-6) and 02 have severe pain with a VAS score (6-8) in group F in the first 6 hours. While in Group T, 22

patients have mild pain VAS score (1-3), 27 have moderate pain VAS score (4-6) and 11 have severe pain with VAS score (6-8) in 0- 6 hours. No patient has worst pain with a VAS score 8-10 P NO 69. At 6-12 hours, in Group F, 51 patients have mild pain. 8 patients have moderate pain with VAS score (4-6). 1 patient with severe pain with vas score (6-8). In Group T, 38 patients were of mild pain with VAS score (1-3), 12 patients were of moderate pain and 10 patients were of severe pain. Injection Fentanyl has a significant effect on patients with a P value is <0.05. At 12-18 hours, in Group F, 54 patients have mild pain with VAS score (1-3). 6 patients have moderate pain. In group T, 51 patients have of mild pain and 9 patients have moderate pain with VAS score (4-6). No patient with severe pain & worst pain is found in both the groups. Therefore, it is clear that injection fentanyl has more significant effect on the pain with  $P < 0.05$ . At 18-24 hours in Group F, 59 patients have mild pain with a VAS score (1-3) and 1 patient has moderate pain. In group T, 57 patients were in mild pain and 3 patients were in moderate pain, there were no patients with severe & worst pain found in the groups.as shown in table no

Out of 60 patients, 26(43.34%) were given rescue drug and only 12 (20%) patients out of 60 in group F were given injection diclofenal 75 mg IM as a rescue drug with significant  $p=0.012$  that means  $p<0.05$ .

When we compare efficacy of Tramadol on pain at different time intervals at 6, 12, 18, 24 hours was  $3.554\pm 1.058$ ,  $3.378\pm 1.424$ ,  $4.477\pm 2.349$  and  $3.409\pm 2.590$  respectively. There is decrement in vas score with a significant p value. When we compare efficacy of Fentanyl on pain at different time intervals at 6, 12, 18, 24 hours  $4.9\pm 1.045$ ,  $4.89\pm 1.381$ ,  $5.57\pm 2.1$ ,  $4.46\pm 2.539$  was respectively. There is decrement in vas score with a significant  $p < 0.05$ . Injection fentanyl was more efficient as compare to injection Tramadol as mean $\pm$ sd was more decreased in patients with group F.

Side effects of either drug was observed out of 60 patients in group T 54(90%) and 5(8.33%) patients in group F were having nausea and vomiting. 45(75%) patients in group F and 1(1.66%)patient were having hypoxia and required oxygenation.

	Age	Sex		Weight (Kgs)	Height (cm)	ASA		Socio economic status				
		M	F			I	II	I	II	III	IV	V
Group F (n=60)	25.56 $\pm$ 5.7	15	45	12.00 $\pm$ 8.48	10.00 $\pm$ 9.432	38	22	2	10	25	0	23
Group T (n=60)	21.78 $\pm$ 8.6	18	42	12.00 $\pm$ 7.906	10.00 $\pm$ 8.509	32	28	1	12	28	0	42

Table 1 Demographic profile of two groups with mean SD

	Nausea and Vomiting	Hypoxia
Group F (n=60)	05 (8.33%)	45 (75%)
Group T (n=60)	54 (90%)	01 (1.66%)

Table 2 Post operative side effects and complications in patients

	0-6 hrs				6-12 hrs				12-18 hrs				18-24 hrs			
	1-3	3-6	6-8	8-10	1-3	3-6	6-8	8-10	1-3	3-6	6-8	8-10	1-3	3-6	6-8	8-10
Group F (n=60)	43	15	02	0	51	08	01	0	54	06	0	0	59	01	0	0
Group T (n=60)	22	27	11	0	38	12	10	0	51	09	0	0	57	03	0	0

Table 3 distribution of patients according to VAS score

		0-6 hrs	6-12 hrs	12-18 hrs	18-24 hrs
Efficacy of Injection fentanyl	MEAN ±SD	3.554 ±1.058	3.378 ±1.424	4.477 ±2.349	3.409 ±2.590
	t & p value		t=0.3506, p = 0.0785	t = 6.016, p = 0.01	t = 0.8271 p =0.045
Efficacy of Injection Tramadol	MEAN ±SD	4.97 ±1.045	4.89 ±1.381	5.57 ±2.198	4.46 ±2.539
	t & p value		t =0.3360 p =0.036	t = 6.206 p =0.010	t = 0.4743, p =0.043
Inter group	t & p value	t=3.680 p = 0.0103	t=3.76 p=0.012	t=4.20 p=0.02	t=3.87 p=0.014

Table 4 Efficacy of both the drugs

## DISCUSSION

Pain was assessed postoperatively with VAS and injection Fentanyl 0.5-1.5 mcg/kg/hour was given to group F (n=60) and injection Tramadol 1-3 mg/kg through infusion was given to group T (n=60). In the first 6 hours, 2 patients out of 60 in group F and 11 patients in group T has severe pain with VAS score 6-8 with significant difference ( $p < 0.05$ ), so there is a lesser number of patients in group F with severe pain. At 6-12 hours, there is 1 patient in group F and 10 patients in group T who has severe pain. It shows that after the second dose of Fentanyl, results were improved and only 1 patient of group F had severe pain so there is a significant difference with p-value ( $p = 0.024$ ). When we compare group F to group T at 6–12 hours, injection Fentanyl shows a better effect. 6 patients in group F and 9 patients in group T have moderate pain with VAS scores 4-6 ( $p = 0.001$ ) which is statistically significant. After 12 hours, severe pain subsides in both the groups. It shows that Injection Fentanyl has more effective results on post-operative pain as compared to injection Tramadol which is similar to the studies of **Reza Shariat Moharari et al., 2021**<sup>9</sup> and **Tsung kun changet et al., 2020**<sup>10</sup> **Suhail Bandey and Vivek Singh et al., 2016**<sup>11</sup> whereas **Zehra Hatipoglu et al 2018**<sup>12</sup> are discord to our study

Opioid analgesics are one of the mainstays of postoperative pain treatment as postulated by **Serbulent Gokhan Beyaz et al**<sup>13</sup> These agents usually act upon  $\mu$ -receptors in central and peripheric nervous systems. Opioids may be used in many formulas and many different ways: subcutaneous, transcutaneous, transmucosal, intramuscular, intravenous, oral, intrathecal, epidural and intraarticular.

**F. O. Holley et al., 2018**<sup>14</sup> stated the use of constant-rate delivery of Fentanyl by intravenously and transdermal routes for the treatment of pain after major surgery. 45 males, ASA I-III, received in a double-blinded fashion either placebo (n = 6) or Fentanyl (n = 39) intravenously, at one of four dose rates (25, 50, 100 or 125mcg/hr). Stable serum concentrations of Fentanyl were produced by the end of surgery and were maintained for a total of 24 hours. Both the 100 mcg/hr and 125 mcg/hr dose rates produced significant analgesic efficacy as assessed by postoperative morphine requirements.

**D. J Duthie et al., 1986**<sup>15</sup> found that Fentanyl in an infusion rate of 100 mcg /hr intravenously, was effective and safe when given by prolonged constant rate infusion for the relief of pain after major surgery. In our study, we have given injection Fentanyl 100 mcg at every 6 hours.

**Harold Minkowitz et al., 2020<sup>16</sup>** stated from his study that IV Tramadol 50mg is highly effective in the management of mild to moderate postoperative pain, but in our study, we measured the vas score of group T patients at 6, 12, 18, 24 hours, it was found that 11 patients have severe pain at first 6 hours then the number reduced to 10 at 12 hours and 0 at 18 hours. Based on these results we can say that injection Tramadol along with Habbe shifa can manage severe post-operative pain.

**Fleur Meijer et al., 2020<sup>17</sup>** postulated that injection Fentanyl reduces stress hormone and induces sedation. After surgery which aligns with our study. There is a more sedative effect of Fentanyl in comparison to Tramadol as in our study 23 (38.4%) patients in Group F need oxygen and 1(1.66%) patient in Group T requires oxygen, but sedation does not last for long hours and no patient had developed hypercapnia as injection fentanyl has a shorter half-life i.e., of 2-4 hour. Fentanyl binds with stereospecific receptors at many sites within the CNS and increases pain threshold, alters pain reception, and inhibits ascending pain pathways.

When we compare the efficacy of injection Fentanyl at 6, 12, 18, 24 hours considering the baseline at 6 hours we found  $t=0.3360$   $p=0.007$ ,  $t=6.226$   $p=0.010$ ,  $t=0.977$   $p=0.038$  respectively which shows that it has a significant effect at every 6 hours as  $p < 0.05$  which is similar to the study of Carlos F Ramos et al,2023<sup>18</sup>

When we compare the efficacy of injection Tramadol at 6, 12, 18, and 24 hours considering the baseline at 6 hours we found  $t=0.3506$   $p=0.79$ ,  $t=6.016$   $p=0.010$ ,  $t=0.827$   $p=0.045$  respectively which shows that it has non-significant result at 12 hours  $p > 0.05$  and has significant results at 18 and 24 hours which shows that Injection Tramadol has delayed effect on postoperative pain. When we compare the efficacy of both drugs we found that the injection Fentanyl is more efficient than the injection Tramadol as post-operative analgesia. As mean SD of injection Fentanyl and Tramadol at 6 hours was  $4.97 \pm 1.04$  and  $3.54 \pm 1.05$  respectively and at 12 hours it was  $4.89 \pm 1.3$  and  $3.37 \pm 1.4$  respectively and 18 hours it was  $5.57 \pm 2.1$  and  $4.47 \pm 2.3$  respectively and at 24 hours it was  $4.46 \pm 2.5$  and  $3.40 \pm 2.4$  respectively.

In our study, those patients did not get relieved even after giving injections Fentanyl or Tramadol and had persistent pain with a VAS score of more than 8 has been given NSAIDs Injection Diclofenac 75mg IM as a rescue drug. In Group F 12 (20%) patients out of 60 needed rescue drugs while in Group T 26 (43.34%) patients out of 60 needed rescue drugs. It has been proven that a lesser number of patients in group F were given injection and hence Group F patients were more pain free with a significant p-value  $p < 0.05$  which is similar to the study of **Naina P Dalvi et al., 2016.**<sup>19</sup>

## CONCLUSION

Injection Fentanyl has a better effect on post-operative pain it increases patient satisfaction it can be a good choice as a post-operative analgesia with minimal side effect as compare to injection tramadol.

Injection fentanyl produces sedation and may also cause respiratory depression so it is to be cautious to always check the availability of oxygen beside the bed of patient, whereas injection Tramadol has adverse side effects of nausea and vomiting so an antiemetic should be given to patients.

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