Original Article

A Comparative Study of IV Fentanyl versus IV Paracetamol for Pain Relief in Postoperatively After Cardiac Surgery

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ABSTRACT

Objective: To compare the efficacy of IV acetaminophen and IV fentanyl for pain reduction after cardiac surgery.
Study Design: Randomized Controlled Trial study.
Place and Duration of Study: This study was conducted at the Department of Anesthesia, Nishtar Hospital Multan, and Shaikh Zaid Hospital Rahim Yar Khan, from March, 2019 to February, 2021.
Materials and Methods: Total 76 patients underwent cardiac surgery requiring general anesthesia. A Visual Analog Scale (VAS) on 0-10 scales was used for assessment of pain. The scores for pain assessment were given as 0 for no pain, 1-4 for mild, 5-7 for moderate and 8-10 for severe pain. Patient's pain score was recorded by the same author that recorded the intraoperative observations, after 5, 15, and 30 minutes after surgical procedure. If the score on the numerical rating score was greater than 3, rescue analgesia fentanyl 25 μg was administered in increments. Total dose of fentanyl used was also recorded. SPSS version 23 was used for data analysis. Numerical variables like age and VAS score were analyzed and presented as mean and SD. Categorical variables like age were presented as frequency and percentages. Tests of significance student's t-test and chi square test were applied to see association among variables. P value ≤ 0.05 was considered as significant.
Results: Mean pain score was 1.66 ± 0.74 and 2.16 ± 0.88 in fentanyl and paracetamol groups, respectively, and the difference was statistically significant (p =0.010). QoR score was 14.63 ± 1.34 and 15.34 ± 1.38 in fentanyl and paracetamol groups, respectively, and the difference was of statistical significance (p =0.026). Nausea was reported by 36.8 % patients of the fentanyl group and 26.3 % of the paracetamol group, however, the difference was not statistically significant (p = 0.324). Vomiting was reported by 34.2 % patients of the fentanyl group and 13.2 % of the paracetamol group, and the difference was statistically significant (p = 0.031). Complaint of dry mouth was present in 52.6 % patients of the fentanyl group and 28.9 % of the paracetamol group, and the observed difference was of statistical significance (p = 0.036).
Conclusion: It can be concluded from the results of our study that, IV paracetamol was not associated with significant pain reduction as compared to IV fentanyl however it was safer in terms of dry mouth and vomiting.
Key Words: Fentanyl, Paracetamol, Intravenous, Postoperative, Cardiac Surgery, Pain score, adverse effects, Efficacy

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INTRODUCTION

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One of the most common surgical procedures performed all over the world is cardiac surgical procedure. Persistent incisional pain in 10 to 50% patients were reported while one third of patients experienced moderate to severe intensity of persistent pain that lead to reduced quality of life [1,2]. Nerve injury along with tissue injury causes persistent incisional pain that is secondary to the surgical dissection and deleterious aspects in association to the healing process. Nociceptive pathway present in the central nervous system (CNS) is activated due to continuous pain signals that lead to incites and make of sensitization in central nervous system. [3,4]. Acetaminophen is a well-known justified non-opioid analgesic [5]. Since the approval of an intravenous (IV) formulation from Food and Drug Administration (FDA) the use of drug has been increased as a part of

perioperative multimodal analgesia. Evaluation of IV acetaminophen has been done in recent studies after large-scale analysis of randomized controlled trials. Patients, in which acetaminophen was administered, had better acute pain control which, in turn, was the strongest predictor for improved patient satisfaction. In some of the published studies, it was reported that after cardiac surgery use of acetaminophen showed reduction in acute postoperative pain scores and opioid consumption by 25-35% and 40-50%, respectively [6]. For persistent incisional pain, poorly controlled acute postoperative pain acts as a strong predictor. [7] However there are some other mechanisms by which acetaminophen reduce the development of persistent incisional pain. Mechanism of pain reduction of acetaminophen is very complex and number of central pathways also involve. Acetaminophen act by inhibiting the prostaglandins through the COX pathway, it also activates cannabinoid CB1 receptors and inhibits nitric oxide pathways [8,9]. Acetaminophen also acts peripherally by decreasing release of prostaglandin E2 release at surgical area [10]. Number of mechanisms involve to peripheral as well as central sensitization and origin of persistent pain. A useful medicine Acetaminophen is very active and efficacious in reduction of post-operative pain that hinders the many pathways involved in acute and chronic pain. Thus there are few evidences that lead to believe that administration of perioperative acetaminophen may reduce pain due to cardiac surgery incision. Our study is a comparative study, between efficacy of IV acetaminophen and IV fentanyl for pain reduction after cardiac surgery.

MATERIALS AND METHODS

The departmental research and hospital Ethical Review Committee Department of Anesthesia, Nishtar Hospital Multan, and Shaikh Zaid Hospital Rahim Yar Khan, from March 1, 2019 to February 28, 2021 approved the study and then written informed consent was taken from all the patients. Patients underwent cardiac surgery requiring general anesthesia, had age greater than 18 and ASA status I and II were included in the study. WHO sample size calculator was used for calculation of sample size and statistics were taken from the reference study by Turan et al. [11]. Patients hypersensitive to the study drugs, obese, airway difficulties, inadequate fasting, or liver problems were excluded from the study. Patients were informed the purpose of study and numerical rating scale by a senior surgeon of day care center. Sealed envelope technique, prepared by computer generated randomization table, was used for dividing the patients into two distinctive groups. The scores for pain assessment were given as 0 for no pain, 1-4 for mild, 5-7 for moderate and 8-10 for severe pain. Before 30 minutes of procedure oral midazolam 7.5 mg was administered to all the patients in the ward as premedication. Before the surgery, IV paracetamol (15 mg/kg) was administered in the preoperative area (before 15 min) Group P and Group F received IV fentanyl 2 μg/kg at induction of anesthesia while the method for general anesthesia was similar in both the groups. Patients were oxygenated for three minutes and monitored for vitals (non-invasive blood pressure), pulse oximetry and electrocardiogram. For induction of anesthesia the 2 mg/kg of IV propofol was used and was maintained by isoflurane 1.5% in oxygen and nitrous oxide (40:60). After unconsciousness endotracheal tube (ETT) was inserted. NIBP (including systolic and diastolic mean blood pressures, pulse oximetry, heart rate, end-tidal CO2) and respiratory rate were monitored and recorded. After every three minutes one of procedure the author of study observed these readings until the end of process. Increased heart rate, blood pressure and respiratory rate more than 20% of baseline indicated poor pain control during the surgery and was regarded as pre-induction time. Fentanyl was administered as rescue analgesia in the increments of 25 μg in intraoperative period for both groups. After completion of the surgery the patients were allowed to return to consciousness and on verbal command the ETT was removed and patients then were transferred to the recovery room. Patient's pain score was recorded by the same author that recorded the intraoperative observations, after 5, 15, and 30 minutes after surgical procedure. If the score on the numerical rating score was greater than 3, rescue analgesia fentanyl 25 μg was administered in increments. Total dose of fentanyl used was also recorded.

SPSS version 23 was used for data analysis. Numerical variables like age and VAS score were analyzed and presented as mean and SD. Categorical variables like age were presented as frequency and percentages. Tests of significance student's t-test and chi square test were applied to see association among variables. P value $\leq$ 0.05 was considered as significant.

RESULTS

Mean age of all the patients in fentanyl group was 34.89 ± 8.92 years while of those in paracetamol group was 37.89 ± 9.95 years, with no statistically significant difference (p = 0.171). Fentanyl group consisted of 18 males and 20 females, while paracetamol group consisted of 22 males and 16 females (p = 0.358). Table-I

Mean pain score was 1.66 ± 0.74 and 2.16 ± 0.88 in fentanyl and paracetamol group, respectively statistically significant difference was observed (p =0.010). QoR score was 14.63 ± 1.34 and 15.34 ± 1.38 in fentanyl and paracetamol groups, respectively, and the difference was of statistical significance (p =0.026). Nausea was reported by 36.8 % patients of the fentanyl group and 26.3 % of the paracetamol group, however, the difference was not statistically significant (p =

0.324). Vomiting was reported by 34.2 % patients of the fentanyl group and 13.2 % of the paracetamol group, this difference is also significant statistically (p = 0.031). Complaint of dry mouth was present in 52.6 % patients of the fentanyl group and 28.9 % of the paracetamol group, and the observed difference was of statistical significance (p = 0.036). Table-II.

Table No.1: Baseline data

Variable	Fentanyl (N = 38)	Paracetamol (N = 38)	p-value
Age, years	34.89 ± 8.92	37.89 ± 9.95	0.171
Gender, M / F	18/20	22/16	0.358

Data is entered as mean ± standard deviation or number

Table No.2: Outcome Data

Variable	Fentanyl (N = 38)	Paracetamol (N = 38)	p-value
Pain score	1.66 ± 0.74	2.16 ± 0.88	0.010
QoR score	14.63 ± 1.34	15.34 ± 1.38	0.026
Nausea	14 (36.8 %)	10 (26.3 %)	0.324
Vomiting	13 (34.2 %)	05 (13.2 %)	0.031
Dry mouth	20 (52.6 %)	11 (28.9 %)	0.036

Data is entered as mean ± standard deviation or number (percentage)

DISCUSSION

The most commonly used drugs for resolution of postoperative pain are short acting narcotic agents as these drugs are very potent analgesics but are associated with certain side effects which beg the need for the use of safer and equally potent analgesics such as IV paracetamol [12,13]. The results of our study suggest that even though use of IV paracetamol was associated with significantly lower incidence side effects such as dry mouth and vomiting, overall efficacy of this analgesic in cardiac surgery patients is statistically lower as compared to IV fentanyl. In the past very few studies have been done to compare IV paracetamol with IV fentanyl after cardiac surgery. In a study by Turan et al. they compared IV paracetamol with placebo and the results they reported are in contrast to the results of our study. They reported that IV paracetamol was of similar efficacy to the opioid consumption and but was not superior at 30 and 90 days follow up [11]. Choiniere et al [14] however reported high incidence and prevalence of pain in patients who underwent cardiac surgery. Koyuncu et al [15] reported in their study that in women who underwent abdominal hysterectomies IV paracetamol was associated with reduced pain postoperatively as compared to the placebo. The main difference between the studies of Koyuncu et al. and the current study is that the abdominal hysterectomies are less invasive, involving no bone and therefore heal better as compared to cardiac surgeries which can account for the contrasting results of the both studies.

Studies in the past have demonstrated that postoperative pain is most commonly associated with incisional pain but progression of this acute pain to chronic pain is blocked by administration of optimum analgesia. In recent study the authors demonstrated that even though IV paracetamol does influence acute post-operative pain, it is not sufficient and potent enough to block the progression of acute pain to chronic pain [11]. In a previous randomized controlled trial which was a double blind study, the authors studied the comparison of IV morphine with IV paracetamol in United Kingdom in patients with acute limb trauma presenting to the emergency department. The results showed no significant difference between the two treatment modalities in terms of pain relief, however they did report higher incidence of side effects among patients who were given IV morphine [16].

In another randomized controlled trial IV paracetamol was compared with IV morphine in 84 patients of knee arthroscopy [17]. The results showed that two treatment modalities had no significant difference in terms of the outcome variables i.e. pain score and patient satisfaction however the adverse effects such as vomiting, nausea and dizziness were reported more in morphine group patients.

In a study by Sinatra et al. [18] IV paracetamol was compared with the placebo in patients who underwent major orthopedic surgery and the results showed IV paracetamol to be an effective, tolerable and potent analgesic when administered over the period of 24 hours. Similarly, many studies compared IV paracetamol to oral ibuprofen [19] as well as its role as opioid sparing agent [20] after different surgeries and found that it can prove to be an effective agent for pain relief in major surgeries. However, our study gave different results to the most of the past studies and thus in order to establish IV paracetamol as an effective replacement to opioids, further studies with larger sample size is required.

CONCLUSION

It can be concluded from the results of our study that, IV paracetamol was not associated with significant pain reduction as compared to IV fentanyl however it was safer in terms of dry mouth and vomiting.

Author's Contribution:

Concept & Design of Study:	Nadeem Ahmad Khan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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