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ORIGINAL ARTICLE

Comparison of Continuous Infusion of Intravenous Tramadol and Fentanyl on Postoperative Analgesia in Cardiac Surgery

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ABSTRACT

Objective: To compare the efficacy between the fentanyl and tramadol infusion on post-operative cure of pain after a valvular heart surgery.

Methods: Total of 40 patients were included in the study who underwent valvular heart surgery. Patients were divided into two groups, 20 patients were included in Tramadol group while 20 patients were assigned the Fentanyl group. After getting off from cardiopulmonary bypass pump (CPB), drug infusions were started. The drugs were continued for a duration of 48 hours after the surgery. The dose of Fentanyl was 0.5-1ug.kg-1.h-1 through continuous infusion for about 48 hours whereas Tramadol was given at a dose of 0.1-0.2 mg.kg- 1.h-1. Additionally, both the groups were also given intravenous paracetamol 1gm every 8 hours. Verbal rating scale comprising of 11 points was used to assess the efficacy of analgesia. The interval of data collection was 6h, 12h, 24h, 36h and 48h after surgery.

Results: The mean cross clamping time, CPB time, mechanical ventilation, ICU stay and hospital stay of group F was 90.51±5.18 minutes, 120.65±5.58 minutes, 589.45±3.64 minutes, 4.01±0.45 days and 8.11±1.97 days, respectively. While, the mean cross clamping time, CPB time, mechanical ventilation time, ICU day and hospital days of group T was 86.91±4.11 minutes, 111.31±2.84 minutes, 507.45±5.54 minutes, 3.15±0.67 days and 7.4±1.14 days, respectively. The differences were statistically significant except hospital days (p=0.1777).

Conclusion: It is evident from the given study that tramadol infusion is having equally analgesic characteristics as compared to fentanyl infusion after valvular heart surgery.

Keywords: Cardiopulmonary bypass (CPB), Postoperative analgesia, Pain relief, assessment, Tramadol infusion.

INTRODUCTION

Adequate post-operative analgesia decreases sympathetic discharge and provides hemodynamic stability after cardiac surgeries and is required to decrease the patient's distress and reduce hospital stay. There is well known association between post-operative pain and enhanced anxiety, decreased mobility, and higher rates of hospital related infections[1]. Proper post-operative analgesia leads to reduce the patient's anxiety and morbidity, as well as the stay in ICU and hospital and in turn reduce the total cost of related to surgery.

It is necessary for patients undergoing cardiac surgery to get admitted in the critical care unit for a duration of 2-3 days after the surgery. During this time, the patients have to go through a number of procedures such as ETT(endotracheal tube) care, physiotherapy, passive exercises, all of these increase intensity of pain[2]. If the pain is not relieved adequately, it can cause complications including pneumonia, atelectasis, DVT (Deep Vein thrombosis) due to incapability of coughing and mobilizing sputum effectively[3]. Hence, it is necessary that patients undergoing cardiac surgery must be subjected to adequate pain relief methods.

The structure of Fentanyl, N-(1-phenethyl-4-piperidinyl-N-Phenyl-propanamide is closely related to meperidine[4]. Fentanyl in the form of continuous infusion has been administered as post-operative analgesia in a number of surgeries including abdominal surgery, major spinal surgery, peripheral orthopedic surgery, cesarean section, normal vaginal delivery and thoracotomy[5]. Another drug used for post-operative pain relief is Tramadol hydrochloride. It has structural similarity to morphine and codeine[6,7]. It has been observed that 12mg/h infusion of tramadol after abdominal surgery provides enhanced pain relief than intermittent IV bolus of tramadol in a dose of 50mg[8,9]. There are some studies showing that when tramadol is given as continuous infusion and titrated with respect to patient's need, it is able to relief the post-operative patient's anxiety after cardiac surgery that is comparable to the effects of morphine or alfentanil infusion[10].

This study was designed to compare the effect of tramadol and fentanyl infusion on post-operative pain relief after valvular surgery. There are limited number of studies available that compare the effects of fentanyl with tramadol in terms of efficacious post-operative analgesia. The following study was performed to compare the efficacy of fentanyl infusion with that of tramadol for relieving post-operative pain after a cardiac surgery.

METHODS

The study was initiated after obtaining the approval from ethical committee. Informed consent from the patients was taken. 40 patients, scheduled for valve replacement cardiac surgery were included in the study.[11] The type of cardiac surgery also included valve repair surgery. Children (age<14) and older patients(age>65),patients having renal or hepatic impairment, patients having neurological disorders and patients who already had cardiac surgery were excluded from the study.

Patients were given oral bromazepam 3mg 60-90 minutes before surgery as premedication. After reaching Operation Theater, IV midazolam 2-3mg and fentanyl 25-50 ug was given for facilitation of arterial and venous lines under local anesthesia. The agent used for the induction of anesthesia was propofol at a dose of 1-2mg/kg and fentanyl 2-5 µ/kg. In order to aid the tracheal intubation, atracurium 0.5 mg kg-1 was administered. Maintenance of anesthesia was done by continuous infusion of fentanyl in a dose of 1-2ug.kg-1.h-1 and isoflurane in oxygen/air at a concentration of 0.5-1.0%. Central venous line was placed under general anesthesia.

The monitoring of all the patients was done with ECG, pulse oximetry, direct arterial BP, urinary output and capnography during the surgery.The temperature was determined by the use of nasopharyngeal probe. The CPB (Cardiopulmonary Bypass) was established by using a membrane oxygenator and roller pump having arterial line filter. Antegrade cold crystalloid cardioplegic agent was given to every patient intermittently.

Post-operative ventilation was done by following the protocols in post-operative cardiac unit. Patients were ventilated mechanically and FIO2 of 50% was used. Respiratory frequency was adjusted to keep PaCO2 and blood PH within normal limits, and the tidal volume was set to 6-8 ml/Kg. After the surgery was completed, patients were randomly divided among two groups:

Tramadol group having 20 patients and Fentanyl group having 20 patients. 2ug.kg-1 fentanyl was given on start of CPB, on start of rewarming and at time of shifting the patient to ICU.

Group F was given Fentanyl infusion for the purpose of postoperative pain relief 0.5 -1ug.kg-1.h-1 in a continuous infusion for 48 hours while group T was given Tramadol continuous infusion 0.1-0.2 mg.kg -1 .h-1immediately after the patients were separated from the CPB for a duration of 48 hours , in post-operative period. The evaluation of pain was performed using the 11-point verbal rating scale (VRS), having 0= no pain to 10= worst pain imaginable at the following intervals: 6 hours, 12 hours, 24 hours, 36 hours, and 48 hours.

If further analgesia was required by a patient, he was given a bolus dose of 25-50ug of fentanyl in fentanyl group while 25-50mg of tramadol to the tramadol group, when the verbal rating scale was more than 3. Additionally, both the groups were also given intravenous paracetamol 1gm every 8 hours.

Data was entered and analyzed by using SPSS Version 25.0. All the quantitative variables were presented as, mean±SD and qualitative variables with frequency and percentages. Both groups outcome variables were compared by independent sample t test. P-value <0.05 was considered as significant.

RESULTS

Forty patients were included in this study, both gender. The patients were divided into two groups as Group F n=20 and Group T n=20. The mean age, weight and ejection fraction of the patients of group F was 25.83±2.48 years, 57.52±6.56 kg and 64.41±4.16, respectively. There were n=14 (70%) males and n=6 (30%) females. While, the mean age, weight and ejection fraction of the patients of group T was 26.21±3.38 years, 57.95±5.22 kg and 56.75±1.92, respectively. There were n=15 (75%) males and n=5 (25%) females. Types of operation have been shown in table I. The difference were statistically insignificant except ejection fraction (p=0.000). (Table. I).

The mean cross clamping time, CPB time, mechanical ventilation time, ICU days and hospital days of group F was 90.51±5.18 minutes, 120.65±5.58 minutes, 589.45±3.64 minutes, 4.01±0.45 days and 8.11±1.97 days, respectively. While, the mean cross clamping time, CPB time, mechanical ventilation time, ICU days and hospital days of group T was 86.91±4.11 minutes, 111.31±2.84 minutes, 507.45±5.54 minutes, 3.15±0.67 days and 7.4±1.14 days, respectively. The differences were statistically significant except hospital days (p=0.1777). (Table. II).

The mean arterial carbon dioxide, respiratory rate, heart rate, central venous pressure and arterial pressure of both the groups are shown in table III. After applying the independent samples t test, it was seen that all the differences were statistically significant at (p<0.005). (Table. III). There was no significant difference in pain scores in two groups.

Table I: Demographic characteristics of both groups

Variable	Group F n=20	Group T n=20	P-value
Age (years)	25.83±2.48	26.21±3.38	0.700
Weight (kg)	57.52±6.56	57.95±5.22	0.711
Ejection fraction	64.41±4.16	56.75±1.92	0.000
Gender			
Male	n=14 (70%)	n=15 (75%)	0.723
Female	n=6 (30%)	n=5 (25%)	
Type of operation			
Mitral valve replacement(MVR)	12	13	0.675
Mitral valve replacement and tricuspid valve repair(TVR)	3	2	0.871
Aortic valve replacement(AVR)	1	1	1
MVR and AVR	3	3	1
MVR, TVR and AVR	1	1	1

Table II: Intraoperative and postoperative variables of both groups

Variable	Group F n=20	Group T n=20	P-value
Cross clamping time (minutes)	90.51±5.18	86.91±4.11	0.020
CPB time (minutes)	120.65±5.58	111.31±2.84	0.000
Mechanical ventilation (minutes)	589.45±3.64	507.45±5.54	0.000
ICU day	4.01±0.45	3.15±0.67	0.000
Hospital days	8.11±1.97	7.4±1.14	0.177
VRS score	1.6-5±0.2	1.2±0.1	0.04*

Table III: Arterial carbon dioxide, respiratory rate, heart rate, central venous pressure and arterial pressure of both the groups

	Group F n=20					Group T n=20				
	PaCO2 (mmHg)	RR (cycle/min)	HR (beats/min)	CVP (mmHg)	MAP (mmHg)	PaCO2 (mmHg)	RR (cycle/ min)	HR (beats/ min)	CVP (mmHg)	MAP (mmHg)
0 hour	33.73±3.22	11.23±0.91	97.11±2.12	10.11±2.46	80.87±5.73	35.55±4.33	11.19±1.01	93.14±11.87	10.54±2.12	78.75±7.90
6 hours	36.41±4.33	27.11±4.21	97.15±9.09	11.21±2.65	81.20±8.06	36.54±2.01	29.11±3.33	94.22±5.21	12.20±3.21	84.10±4.54
12 hours	35.33±2.19	25.55±4.32	94.21±12.1	11.20±2.09	78.12±6.76	35.36±3.60	29.10±3.46	90.17±12.21	14.21±4.65	83.21±5.87
24 hours	33.12±5.44	25.10±4.32	94.31±1.24	13.20±1.12	85.12±10.43	34.21±2.1	30.29±4.56	89.10±11.25	14.01±5.43	85.43±12.3
36 hours	38.65±5.67	24.32±3.21	94.20±9.87	14.10±1.98	83.28±3.45	38.45±8.9	28.98±3.84	93.27±5.67	14.23±4.32	84.54±11.32
48 hours	38.10±3.21	26.32±2.12	96.43±4.32	14.28±1.21	82.35±6.76	38.19±4.20	30.29±3.33	97.23±7.54	14.32±2.35	80.54±21.2

DISCUSSION

A matter of consideration for the patients undergoing surgery is the management of pain that occurs postoperatively[12]. The early relief reduces the hospital stay and cost and increases the quality of life of patient by bringing about early mobilization. It is recommended to apply “individual approach” in spite of specified doses and drugs. Other factors that affect the pain intensity include age, psychological, medical and physical condition of the patient, level of anxiety, the type of surgical procedure performed, type of analgesia and anesthesia. The goal of management of postoperative pain is to minimize the dosage of medication in order to reduce the side effects while giving appropriate analgesia. However, a multidisciplinary approach is required for proper planning of the treatment.

“Cardiac surgery is unique” says Chaney MA[13] and due to this fact, the risks it involves are also unique. It is seen that patients coming for cardiac surgery keep on getting older and sicker. There are various factors during perioperative period that affect the post-operative outcome. Hence the type of postoperative analgesia is often difficult to determine as the patients undergoing cardiac surgery are fragile in health and older in age and have less tolerance. Multiple factors are present in adults that are likely to affect the outcome of analgesia, that are, renal dysfunction, myocardial dysfunction, calcified aorta etc. It is therefore necessary to carefully assess the type of analgesia given postoperatively.

The results of current study indicate that themean cross clamping time, CPB time, mechanical ventilation, ICU day and hospital days of group F was 90.51±5.18 minutes, 120.65±5.58 minutes, 589.45±3.64 minutes, 4.01±0.45 days and 8.11±1.97 days, respectively. While, the mean cross clamping time, CPB time, mechanical ventilation, ICU day and hospital days of group T was 86.91±4.11 minutes, 111.31±2.84 minutes, 507.45±5.54 minutes, 3.15±0.67 days and 7.4±1.14 days, respectively. The differences were statistically significant except hospital days (p=0.1777). (Table. II).

When Kumar KP et al[14] compared the analgesic effects of tramadol and pregabalin in postoperative patients, he found out that tramadol group provided better analgesic effects and there was decreased requirement of rescue analgesia in this group. However, the tramadol effects included greater amount of sedation and side effects such as nausea, vomiting, drowsiness in comparison to pregabalin. The study demonstrated that tramadol patients showed lesser pain score and it was evident that tramadol had superior analgesic efficacy as compared to pregabalin.

There are various benefits offered by Tramadol when compared with conventional opioids[15]. These include least potential for tolerance, addiction and respiratory depression. Even in healthy individuals, it has minor effects on respiratory patterns and breathing.

In current study there was significant difference in VRS score among both groups these findings were comparable with a prospective, randomized double blinded study compared the analgesic efficacy of remifentanil, morphine and fentanyl, done by Gubert A et al[16]. The study used visual analogue scale for the assessment of pain and Ramsay sedation score to assess the degree of sedation. It was observed that pain and sedation was equivalent in all three groups whereas side effects such as vomiting and nausea were greater in Morphine group and itching was found to be more in Fentanyl group. The visual analogue scale showed 2.9, 2.4 and 2.0 for morphine, fentanyl and remifentanil groups respectively. It was concluded that fentanyl and morphine had equivalent analgesic efficacy as remifentanil however remifentanil was found to be superior in terms of showing lesser side effects.

Edward et al[17] performed a metanalysis in order to determine the efficacy of combination of oral tramadol plus acetaminophen in reducing the postoperative pain crises, he discovered that the combination had more efficacy as compared to the components alone. The "number-needed-to-treat" was better for the combination as compared to the drugs alone. Nonetheless, the adverse effects of the both the groups; combination and drugs alone were similar. It was concluded that when tramadol was used in combination with acetaminophen, its analgesic activity was enhanced as compared to tramadol alone along with lesser adverse effects.

Moore RA et al[18] compared the safety and analgesic efficacy of oral tramadol with that of other analgesics with the help of meta-analysis in randomized controlled trials among patients with severe or moderate pain after dental extraction or surgery. The study was done upon 3453 patients and used the categorical pain relief scale. Tramadol was found to be more analgesic as compared to other analgesics and placebo. It demonstrated a dose-response for analgesic efficacy in dental and postoperative pain. The response was greater at greater doses. The side effects were similar to other analgesics. The analgesic efficacy of tramadol was found to be equivalent to combination of aspirin plus codeine and acetaminophen plus propoxyphene.

Sandler AN et al[19] tested the efficacy of fentanyl in different modes of administration. The effect of epidural and intravenous fentanyl was compared upon patients undergoing thoracotomy. The amount of fentanyl given by epidural infusion given was greater than the amount of fentanyl given by intravenous route to achieve the same analgesic effects. It was seen that plasma concentration at any time period was not different among the two groups. There was similar degree of respiratory depression. The side effects and the remaining efficacy by either route was of similar degree and the mode of absorption of fentanyl analgesia was through the systemic route.

A study[20] was done to determine the difference between the analgesic efficacy of tramadol and fentanyl infusion upon patients undergoing ambulatory knee arthroscopy. No significant difference could be concluded among the patients of two groups in terms of supplemental analgesic requirement, pain score, or side effects. It was established that tramadol provides little relief of pain in comparison to fentanyl when used for induction of anesthesia.

Similarly, when Kwok FJ et al[21] compared the efficacy between patient-controlled analgesia by tramadol or fentanyl, it was seen that fentanyl PCA or tramadol have similar cognitive effects on day one and two. Nonetheless, the patients receiving tramadol PCA had better analgesia on postoperative day 1.

In the study we performed, we used continuous infusion of fentanyl and tramadol. Our patient population included patients with valvular heart disease that belong to ASA class III or IV. Due to chronic illness these patients have slightly higher level of anxiety, which influences the management. In this study, we have not considered the literacy level of patients that must have influence on demonstration of level of severity of pain.

CONCLUSION

It is evident from the given study that tramadol infusion is having equally analgesic characteristics as compared to fentanyl infusion for postoperative analgesia after valvular heart surgery.

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