Comparative Study of Postoperative Analgesia in Coronary Artery Bypass Grafting: Thoracic Epidural Nalbuphine versus Fentanyl - A Randomized Controlled Study

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ABSTRACT

BACKGROUND

Epidural analgesia provides superior analgesia, stable haemodynamics, decreased respiratory system complications, earlier extubation, and superior left ventricular function. When opioids are used as adjuvants to local anesthetics, they act synergistically, resulting in superior and prolonged analgesia. This also results in reduced adverse effects of both classes of the drugs. The present study was carried out to compare the efficacy of epidurally administered Nalbuphine and Fentanyl in the post-operative pain management.

METHODS

This randomized controlled trial involved 60 participants undergoing coronary artery bypass grafting. They were randomly allotted to two groups, each consisting of 30 participants. During the post-operative period, thoracic epidural was activated after extubation. One group received 10 mL of 0.25% Bupivacaine and 10 mg Nalbuphine through epidural catheter, and other group received 10 mL of 0.25% bupivacaine with Fentanyl 2 mcg/mL. The haemodynamic parameters and visual analog score (for pain assessment) were recorded throughout the study period and compared between the two groups.

RESULTS

Hypotension occurred in 16.7% in both the groups, bradycardia occurred in 10% of the participants in the Fentanyl group only. The need for rescue analgesia was similar in both the groups (6.7%). The mean duration of analgesia was 381 minutes in the Nalbuphine group compared to 285 minutes in the Fentanyl group. There was a statistically significant difference in the VAS score and duration of analgesia between the two groups ($p<0.05$).

CONCLUSIONS

Opioid analgesics are highly effective as adjuvants in post-operative pain management. In this study involving patients undergoing coronary artery bypass grafting, Nalbuphine was found to be effective in achieving adequate and prolonged post-operative analgesia, in comparison to Fentanyl.

KEYWORDS

Coronary Artery Bypass Graft, Epidural Opioids, Nalbuphine, Fentanyl, Visual Analog Score

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BACKGROUND

Coronary Artery Bypass Grafting (CABG) is one of the commonly performed surgical procedures worldwide. About two-thirds of the patients undergoing CABG report moderate to severe pain. Achieving optimal pain relief after cardiac surgery can be challenging.[1] A wide variety of techniques are available for post-operative pain relief, of which epidural analgesia is a well-established technique. Pain management in the postoperative period is one of the most important components of post-operative care. Inadequate pain control and uncontrolled surgical stress response could initiate pathophysiological alterations in all major organs that may lead to considerable postoperative morbidity. Insufficient analgesia in cardiac surgical patients can lead to haemodynamic instability (Hypertension, Tachycardia, Vasoconstriction), immunological disturbances (impaired immune response), metabolic derangement (extensive catabolism) and platelet activation which are detrimental to patient undergoing CABG.[2]

Epidural analgesia results in superior pain management, better haemodynamics, decreased respiratory complications, earlier extubation and superior left ventricular function. Opioids as adjuvants to local anaesthetics are synergistic in action, provide superior and prolonged analgesia, thereby resulting in reduced adverse effects in both the classes of the drugs. Among the opioids, Nalbuphine is a kappa-opioid receptor agonist and mediates its actions also through its partial mu-opioid receptor antagonism.[3] However, Fentanyl acts on G-protein coupled receptors which results in decreased cAMP production, thereby inhibiting the ascending central nervous system pathways of pain.[4] However, the efficacy of Nalbuphine for post-operative analgesia, occurrence of any adverse effects, influence on haemodynamic parameters and the need for rescue analgesia, when used as adjuvant with Bupivacaine is seldom assessed.

Objectives

This study was designed to compare the effectiveness of post-operative pain relief, quality of analgesia, haemodynamic variations, side effects of epidurally administered bupivacaine with nalbuphine and bupivacaine with fentanyl, need for rescue analgesia in patients undergoing CABG surgery.

METHODS

Study Setting and Participants

The randomized control trial was carried out in the Department of Anaesthesiology of our tertiary teaching institution for a period of one year between October 2018 and September 2019. All the patients who were electively posted for CABG during the study period were recruited for the study. Patients with infection at site of epidural catheter insertion or any other contraindication for thoracic epidural, left main coronary artery disease, left ventricular dysfunction, arrhythmias, haemodynamic instability, patients who underwent CABG along with valve surgery or emergency surgery were excluded from the study.

Study Groups

The present study comprised of two groups, each group consisting of 30 participants. The participants were randomly allotted into either group, of which group A participants received 10 mL of 0.25% Bupivacaine and 10 mg Nalbuphine through epidural catheter and the group B participants received 10 mL of 0.25% Bupivacaine and Fentanyl 2 mcg/mL.

Ethical Approval and Informed Consent

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study. Each participant was explained in detail about the study and written informed consent was obtained prior to enrolling in the study and the data collection.

Data Collection

Epidural catheter was placed one day prior to the surgery, after securing intravenous access, under standard monitoring and supplemental oxygen through a mask. Under strict aseptic precautions, epidural catheter was placed at the level of T2 - T3 or T3-T4 interspace using loss of resistance technique using Tuohy's needle. During the surgery, intravenous Injection of Fentanyl was used for analgesia in the dose of three to four µg/Kg during induction of anaesthesia and 1.5 µg/Kg/hour till the end of surgery. After the surgery, upon arrival at the post-operative recovery room, patients in both the groups received 20 mg/Kg of Paracetamol as analgesic. Patients received Paracetamol three times a day in the above-mentioned dose. After extubation, patient's pain was assessed using Visual Analogue Scale (VAS) Score and epidural analgesia was activated. When the patient complained of pain and VAS score was greater than three, a bolus of the study drug was administered through epidural catheter, over a period of 15 minutes. Hemodynamic parameters like Heart rate, Blood pressure, oxygen saturation (SpO_2), Respiratory rate, VAS Score and Ramsay sedation score were recorded at an interval of 0, 3, 6, 9, 12, 15, 30 minutes and 1 hour, 2, 3, 4, 5, 6, 7 hours duration. Postoperative analgesia was assessed from the time of first epidural injection. After 30 min of epidural injection, if analgesia was found to be inadequate or when VAS score was 4 or more, patient received intramuscular injection of Diclofenac 75 mg as rescue analgesia. Hypotension was treated with fluids (normal saline or Ringer's Lactate) in a dose of 10 to 20 mL/Kg and/or vasopressors (Injection Phenylephrine 1 µg/Kg; bradycardia was treated with Atropine (Injection atropine 1.2 mg). Occurrence of nausea, vomiting, pruritus, sedation, respiratory depression were recorded and addressed ac.

Data Analysis

Data was entered and analyzed using SPSS ver. 20 software. The comparison of haemodynamic response and duration of analgesia was evaluated using Independent Samples t test. A p value <0.05 was considered statistically significant.

RESULTS

This present study was carried out among 60 participants, of which 30 participants belonged to Group A (Nalbuphine) and 30 participants belonged to Group B (Fentanyl). Majority of the participants in Group a belonged to the age group of 45-60 years (53.3%) while in group B, majority of the participants were above 60 years (60%). Majority of the participants in both the groups were males (83.3%) and were overweight (53.3% in Group A and 60% in Group B). Left ventricular ejection fraction values of both the groups were comparable. (Table 1) Baseline haemodynamic parameters prior do epidural drug injection, like mean heart rate, blood pressure and SpO_2 in both the groups were comparable. (Table 2).

The mean VAS score was lower (2.5) among the group A (Nalbuphine) participants compared to 3.1 in the Group B (Fentanyl) participants. (Table 2).

The mean SpO_2 between the groups were analysed and it was observed that Fentanyl group had lower SpO_2 compared to the Nalbuphine group. At 12 minutes the SpO_2 in the Fentanyl group was 96.7%, compared to 98% in Nalbuphine group. Further at 30 minutes the SpO_2 dipped to 96.1% in the Fentanyl group as against 97.4% in the Nalbuphine group. (Figure 1)

The mean VAS scores between the two groups shows that Nalbuphine group had lower pain scores compared to Fentanyl group. Although there was a dip in the VAS scores in both the groups at 60 minutes, the gradual rise in the VAS scores was higher in the Fentanyl group compared to Nalbuphine group. (Figure 2)

With regards to the post-operative haemodynamic parameters, hypotension was present in 16.7% in both the groups, while bradycardia did not occur in the Nalbuphine group as against 10% in the Fentanyl group. The need for rescue analgesia was similar in both the groups (6.7%). The mean duration of analgesia was 381.6 minutes in the Nalbuphine group compared to 285.2 minutes in the fentanyl group (Table 3).

Independent sample t test was used to evaluate differences in various parameters between the groups. There was a statistically significant difference in the VAS score and duration of analgesia between the two groups ($p<0.05$). (Table 4)

Sl. No.	Characteristic	Nalbuphine N (%)	Fentanyl N (%)
		Age (in years)	
1.	30-45	1 (3.3)	0 (0)
	45-60	16 (53.3)	12 (40)
	>60	13 (43.3)	18 (60)
		Sex	
2.	Males	25 (83.3)	25 (83.3)
	Females	5 (16.7)	5 (16.7)
		Body Mass Index (kg/m²)	
	<18.5	1 (3.3)	1 (3.3)
3.	18-23	6 (20)	4 (13.3)
	23-27.5	16 (53.3)	18 (60)
	>27.5	7 (23.3)	7 (23.3)
4.	Ejection fraction	55.5 ± 3.4	56.2 ± 2.7

Table 1. Background Characteristics

Sl. No.	Characteristic	Nalbuphine (Mean ± S.D)	Fentanyl (Mean ± S.D)
1.	Heart rate	80.1 ± 8.5	79.7 ± 9.01
2.	Systolic blood pressure	117.5 ± 17.2	117.4 ± 9.5
3.	Diastolic blood pressure	67.6 ± 8.3	67.2 ± 6.2
4.	Respiratory rate	13.7 ± 0.8	13.8 ± 0.7
5.	SpO_2	98.1 ± 0.6	97.7 ± 0.9
6.	Visual Analog Score	2.5 ± 0.9	3.1 ± 0.9

Table 2. Haemodynamic Parameters and Visual Analog Score of the Study Participants

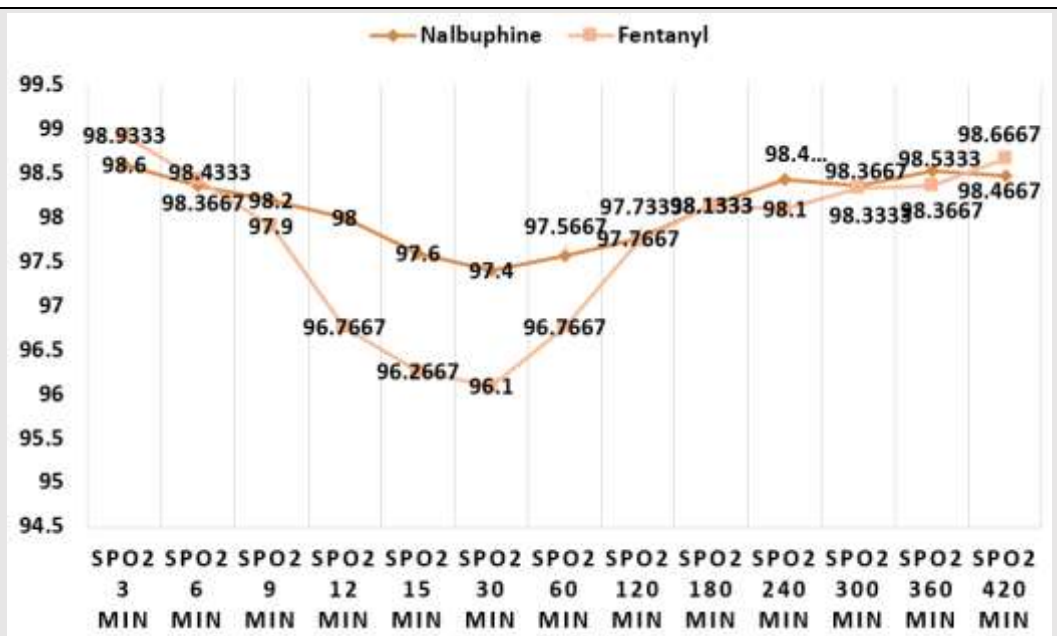

Figure 1. Mean SpO_2

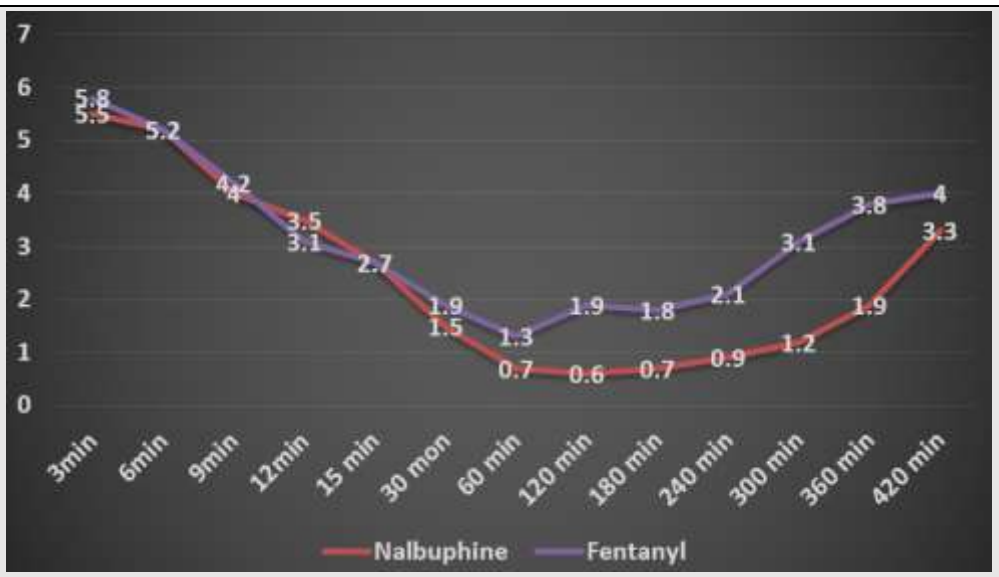

Figure 2. Mean VAS Score (Pain Score) between the Study Groups

Sl. No.	Characteristics		Nalbuphine N (%)	Fentanyl N (%)
1.	Hypotension	Present Absent	5 (16.7) 25 (83.3)	5 (16.7) 25 (83.3)
2.	Fluid (volume infusion)	Present Absent	5 (16.7) 25 (83.3)	3 (10) 27 (90)
3.	Bradycardia & Injection Atropine administration	Present/ Administered Absent/ Not Administered	0(0) 30 (100)	3 (10) 27 (90)
4.	Nausea/Vomiting	Present Absent	1 (3.3) 29 (96.7)	4 (13.3) 26 (86.7)
5.	Pruritus	Present Absent	0(0) 30 (100)	0(0) 30 (100)
6.	Rescue analgesia	Present Absent	2 (6.7) 28 (93.3)	2 (6.7) 28 (93.3)
7.	Duration of analgesia (minutes)	Mean Std. Deviation	381.6 29.6	285.2 44.01

Table 3. Postoperative Observations or Events

Sl. No.	Parameter	Mean Difference	S.E of Mean	t Value	p Value
1.	Baseline Ejection fraction	-0.7	0.8	-0.8	0.405
2.	Heart rate	0.4	2.3	0.2	0.87
3.	Systolic Blood Pressure	0.04	3.6	0.01	0.992
4.	Diastolic Blood Pressure	0.4	1.9	0.2	0.823
5.	Respiratory Rate	-0.04	0.2	-0.2	0.824
6.	SpO_2	0.4	0.2	1.8	0.081
7.	Visual Analog Score	-0.7	0.2	-3.0	0.004*
8.	Duration of analgesia	96.4	9.7	9.9	0.0001*
9.	Age	-3.1	1.9	-1.6	0.11

Table 4. Comparison of Nalbuphine and Fentanyl Groups

*statistically significant

DISCUSSION

The need for post-operative analgesia has been extensively analysed and it has been universally accepted that acute perioperative pain alters the pain pathways resulting in hyperalgesia and central sensitization.[5] Further, persistence of postoperative pain increases the connective tissue stress and impedes wound healing. Acute postoperative pain triggers neuroendocrine, immune and inflammatory response and as a consequence, results in elevation of stress hormones, immunosuppression and increased myocardial oxygen consumption. This impairs cardiovascular and respiratory functions, and increases morbidity and mortality.[6] Opioid analgesics have been traditionally used as adjuvant analgesia in post-operative pain management, and the present study compared the effect of epidurally administered Nalbuphine and Fentanyl in the post-operative pain management in patients who underwent Coronary Artery Bypass Grafting.

Majority of the study participants in both the groups were above 45 years of age and were males. Both the groups were similar with respect to the baseline haemodynamic parameters. The present study observed a significant difference in the visual analog score (VAS) between the two groups. The mean scores were lower in the Nalbuphine group (2.5±0.9) compared to the Fentanyl group (3.1±0.9) and the observed difference was statistically significant ($p<0.05$). Similarly, Nalbuphine provided longer duration of analgesia (381.6 minutes) compared to Fentanyl (285.4 minutes) and this difference was statistically significant ($p<0.0001$). Similar study findings were seen in a study done by Chatrath V et al, wherein the duration of analgesia among those who received Nalbuphine was 380 minutes.[7] Similarly, in another study done by Verma D et al, the duration of analgesia was longer with Nalbuphine, lasting for 378 minutes, similar to our study findings.[8] the Nalbuphine group also had lesser incidence of bradycardia and nausea and vomiting in comparison to the fentanyl group.

Nalbuphine, a mixed agonist-antagonist opioid is highly effective when used as an adjuvant with bupivacaine. As a sole analgesic, it is very effective in controlling mild to moderate pain and causes minimal adverse effects.[9] Bupivacaine, as a local anaesthetic is extensively used for local infiltration, peripheral nerve blocks, epidural and spinal anaesthesia. However, for major procedures like CABG, use of Nalbuphine as an adjuvant helps in increasing the efficacy, in addition to achieving haemodynamic stability.[10] The present study has also documented minimal complications like hypotension and bradycardia.

CONCLUSIONS

Opioid analgesics are highly effective adjuvants to local anaesthetic agents in post-operative pain management for epidural administration. In this study, Nalbuphine was found to be effective in achieving adequate and prolonged post-operative analgesia, in comparison to Fentanyl in patients undergoing coronary artery bypass grafting.

REFERENCES

[1] Zubrzycki M, Liebold A, Skrabal C, et al. Assessment and pathophysiology of pain in cardiac surgery. J Pain Res 2018;11:1599-1611.
[2] Ziyaeifard M, Azarfarin R, Golzari SEJ. A review of current analgesic techniques in cardiac surgery. Is epidural worth it? J Cardiovasc Thoracic Res 2014;6(3):133-140.
[3] Larsen D, Maani CV. Nalbuphine. Treasure Island (FL): StatPearls Publishing February 9, 2020. https: //www.ncbi.nlm.nih.gov/books/NBK534283/
[4] Pathan H, Williams J. Basic opioid pharmacology: An update. Br J Pain 2012;6(1):11-16.
[5] Pogatzki-Zahn EM, Segelcke D, Schug SA. Postoperative pain – from mechanisms to treatment. Pain Rep 2017;2(2):e588.
[6] Finnerty CC, Mabvuure NT, Ali A, et al. The surgically induced stress response. JPEN J Parenter Enteral Nutr 2013;37(Suppl 5):21S-29S.
[7] Chatrath V, Attri JP, Bala A, et al. Epidural nalbuphine for postoperative analgesia in orthopedic surgery. Anesth Essays Res 2015;9(3):326-330.
[8] Verma D, Naithani U, Jain DC, et al. Postoperative analgesic efficacy of intrathecal tramadol versus nalbuphine added to bupivacaine in spinal anesthesia for lower limb orthopedic surgery. J Evolution of Medical and Dental Sciences 2013;2(33):6196-6206.
[9] Khan FA, Hameedullah. Comparison of fentanyl and nalbuphine in total intravenous anesthesia (TIVA). J Pak Med Assoc 2002;52(10):459-465.
[10] Mukherjee A, Pal A, Agrawal J, et al. Intrathecal nalbuphine as an adjuvant to subarachnoid block: What is the most effective dose? Anesth Essays Res 2011;5(2):171-175.