ISSN: 2515-8260, Volume 09, Issue 07, 2022

Comparison between dexmedetomidine and fentanyl for sedation efficacy during mechanical ventilation and time taken for in post-operative adult cardiac surgical patients

Anita Behera[1], Prasanta Kumar Brahma[2], Jayanti Singh[1]

[1]Department of Anesthesia, IMS and SUM Hospital, Siksha 'O' Anusandhan Deemed to be University, K8, Kalinga Nagar, Bhubaneswar-751003, Odisha, INDIA

[2]Department of Community Medicine, IMS and SUM Hospital, Siksha 'O' Anusandhan Deemed to be University, K8, Kalinga Nagar, Bhubaneswar-751003, Odisha, INDIA

Corresponding Author*
Dr. Anita Behera, MD
Associate Professor, Department of Anesthesia,
IMS and SUM Hospital, Bhubaneswar, Odisha
Email ID: anitabehera@soa.ac.in, +919439725351

Abstract

Aims and Objectives: To compare the efficacy of sedation and time taken for extubation using dexmedetomidine and fentanyl sedation in post-operative adult cardiac surgical patients.

Methods: A prospective randomized double-blind study involving 60 patients undergoing open heart surgery was conducted. The patients were divided into two groups, each involving 30 patients. One group received fentanyl at 1 µg/kg/h (Group A) and the other received dexmedetomidine at 0.5 µg/kg/h (Group B) for post-operative sedation with intermittent rescue dose of fentanyl 0.5 µg/kg bolus in either group as per requirement. The efficacy of sedation was assessed using the Ramsay sedation score. The time taken for extubation from the stoppage of infusion was noted.

An open heart surgery prospective randomized double-blind trial including 60 patients was carried out. Two groups of 30 patients each were formed from the patients. With occasional rescue doses of fentanyl 0.5 g/kg bolus in either group as needed, one group (Group A) received fentanyl at 1 g/kg/h and the other (Group B) received dexmedetomidine at 0.5 g/kg/h for post-operative sedation. The Ramsay sedation score was used to evaluate the effectiveness of the sedation. It was noticed how long it took to extubate once the infusion was stopped.

Results: Haemodynamic parameters between the two groups were comparable. Sedation scores between fentanyl and dexmedetomidine groups were comparable. Average time (in minutes) required for extubation was 140.04 (±43.6 SD) in the dexmedetomidine group compared with 359.4 (±93.3 SD) in the fentanyl group. The difference in mean time for extubation was statistically significant.

Conclusions: As compare to fentanyl Dexmedetomidine facilitates adequate sedation for mechanical ventilation and also early extubation.
Keywords: Dexmedetomidine, fentanyl, mechanical ventilation, sedation

Introduction

Adequate sedation and analgesia are necessary in postoperative cardiac surgery patients to keep mechanical ventilation in sync, reduce the stress response, minimise unintentional extubation, and prevent the dislodging of intravascular devices. Commonly Opioids and benzodiazepines, which are frequently used for post-operative sedation, are linked to severe respiratory depression and a protracted recovery period after the infusion is stopped.

Dexmedetomidine acts on the locus coeruleus' a2 receptor to induce sedation and analgesia [2,3]. Patients receiving a dexmedetomidine infusion are easily awakened, able to follow instructions, and cooperative when receiving mechanical ventilation. Dexmedetomidine has no effect on arterial oxynation-to-carbon dioxide ratio or respiration rate in postoperative patients. With the loading dose, hypotension and bradycardia were seen. This study evaluated the effectiveness of dexmedetomidine sedation to fentanyl in terms of sedation, analgesia, and the time needed for extubation.

Methods

After the approval of the institutional ethical committee, this randomized prospective double-blind study was conducted involving 60 patients; informed consent was taken from their parents. The patients were randomly allocated into two groups of 30 each (randomization done by lottery method).

Inclusion criteria:

Age more than 18 years to 80 years posted for open cardiac surgery.

Exclusion criteria were patients undergoing re-operation, patients with severe liver dysfunction, second and third degree heart block, patients potentially requiring ventilation for more than 24 h, Patients with IABP, with severe congestive heart failure, neurological disorder and hypersensitivity to opiods. All the patients after fasting for 6 to 8 hours prior to surgery were pre medicated with Tablet Ranitidin 150mg Tab Metochlopramide 10mg and Tab Lorazepam 2mg at previous night and 4 hours before operation in morning with sips of water. On table a large bore intravenous canula was put under local anesthesia. Patient was monitored with ECG oxygen saturation, temperature invasive monitoring of blood pressure end tidal carbon dioxide and central venous pressure.

This 60-patient, randomised, prospective, double-blind trial was carried out with the parents' informed agreement following institutional ethical committee approval. The patients were divided into two groups of 30 each at random (randomization done by lottery method).

inclusion standards:

For open heart surgery, ages between 18 and 80 are posted.

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Patients undergoing re-operation, those with severe liver dysfunction, second- and third-degree heart blocks, those who might need ventilation for longer than 24 hours, those with IABP, those with severe congestive heart failure, those with neurological disorders, and those with opiate hypersensitivity were excluded from the study. Prior to surgery, all patients were pre-medicated with tablets containing Ranitidin 150 mg, Metochlopramide 10 mg, and Lorazepam 2 mg after fasting for 6 to 8 hours.

With the help of intravenous (IV) Midazolam at 0.1 mg/kg, anaesthesia was induced. 2 to 3 mg/kg each of propofol and fentanyl And Vecuronium was. Endotracheal intubation was made easier by the administration of vecuronium 0.15 mg/kg. With the help of intermittent vecuronium and isoflurane in O2, anaesthesia was kept going. Fentanyl 1 g/kg and midazolam 0.05 mg/kg were administered again during sternal closure. Either a dexmedetomidine infusion at the dose of 0.5 gm/kg/h or a fentanyl infusion at the dose of 1 gm/kg/h was started as soon as the patient was transferred to the post-operative intensive care unit [10]. In the post-operative intensive care unit, sedative infusions of either fentanyl or dexmedetomidine were given at random using a lottery approach by a different anesthesiologist (who was not engaged in the study). The name of the medicine being given to the patient was a secret to the study's observer.

The Ramsay Sedation Score (RSS) and hemodynamic parameters were tracked hourly in Table 1. For agitated and upset patients in both groups, 0.5 g/kg of fentanyl was administered as rescue sedative, and the frequency of this need was observed. The next morning at six in the morning, sedation was stopped to facilitate an early extubation trial. The period from the start of the dexmedetomidine or fentanyl infusion to its termination the next morning at 6 am was the overall amount of sedation. After stopping the sedative medication, the time until extubation was also documented.

When patients fulfilled our extubation requirements, which included the following: they were deemed ready to be weaned from the ventilator. waking up, stable hemodynamics, normothermia, and a PaO2/FiO2 of greater than 200 torr following corrective surgery (e) normocapnic with a support pressure of less than 10 cm H2O, and (f) spontaneously breathing at a rate under 25. The patient was extubated, and more oxygen was given through a nasal cannula. The degree of hemodynamic compromise was categorised into three categories: mild, moderate, and severe. Sedation had to be stopped, pharmacological intervention, or temporary pacing was required for severe haemodynamic compromise. The amount of inotrope eaten by each group was compared using the inotrope score. [13]. Both the fentanyl and dexmedetomidine groups' demographic information was comparable. The type and length of operation did not differ statistically significantly.

Table 1: Clinical Sedation Scale used for the study

Ramsey Sedation Score (RSS)

1. Anxious, agitated, restless
2. Eyes open, co-operative, oriented, tranquil
3. Responds (opens eyes) only to command, light touch, normal tone of voice
4. Brisk response to light glabellar tap or loud noise/voice
5. Sluggish response to light glabellar tap or loud noise/voice
6. No response to light glabellar tap or loud noise/voice

Results:

Both the fentanyl and dexmedetomidine groups' demographic information was comparable. The type and length of operation did not differ statistically significantly. Both groups had sedation for an average of 13.2 hours. According to Table 2 and Figure 1, there was no statistically significant difference in the need for rescue sedation between the two groups.

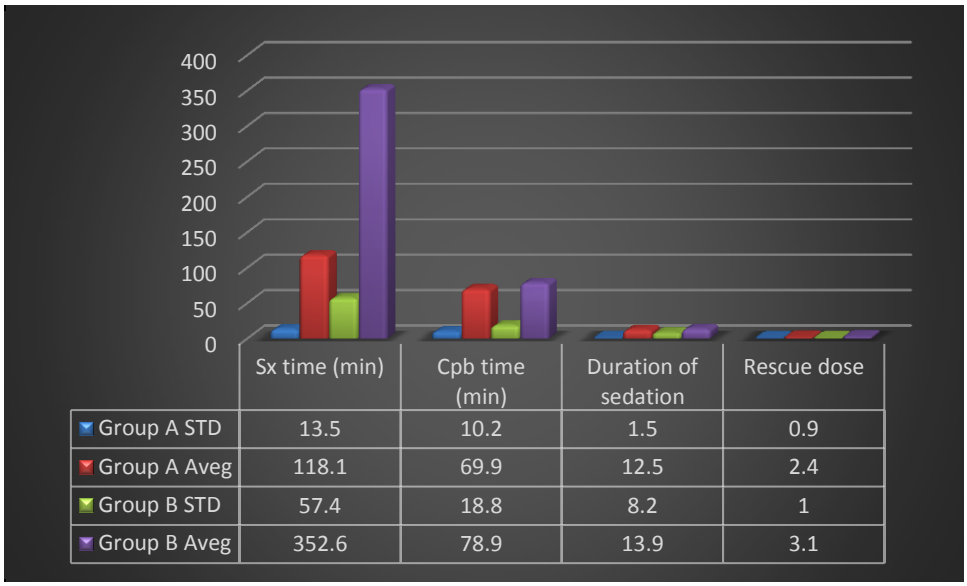
Table 2 Demographic Data

	Fentanyl	Dexmedetomidine	*P* value
Age (years)	57±10.63	54.3±62.8	0.32
Weight (kg)	64.4±10.0	10.25±11.07	0.55
Gender (M/F)	20/10	19/11	-
Surgery time (min)	118.1±13.5	352.6±57.4	0.02
CPB time in min (range)	69.9±10.2	78.9±18.8	0.34
Duration of sedation (h)	12.5±1.5	13.9±8.2	0.34
Rescue sedation doses	2.4±0.9	3.1±1.0	0.002
Diagnosis			
CABG CABG+MVR MVR DVR	24 2 3 1	24 1 3 2	-

ISSN: 2515-8260, Volume 09, Issue 07, 2022

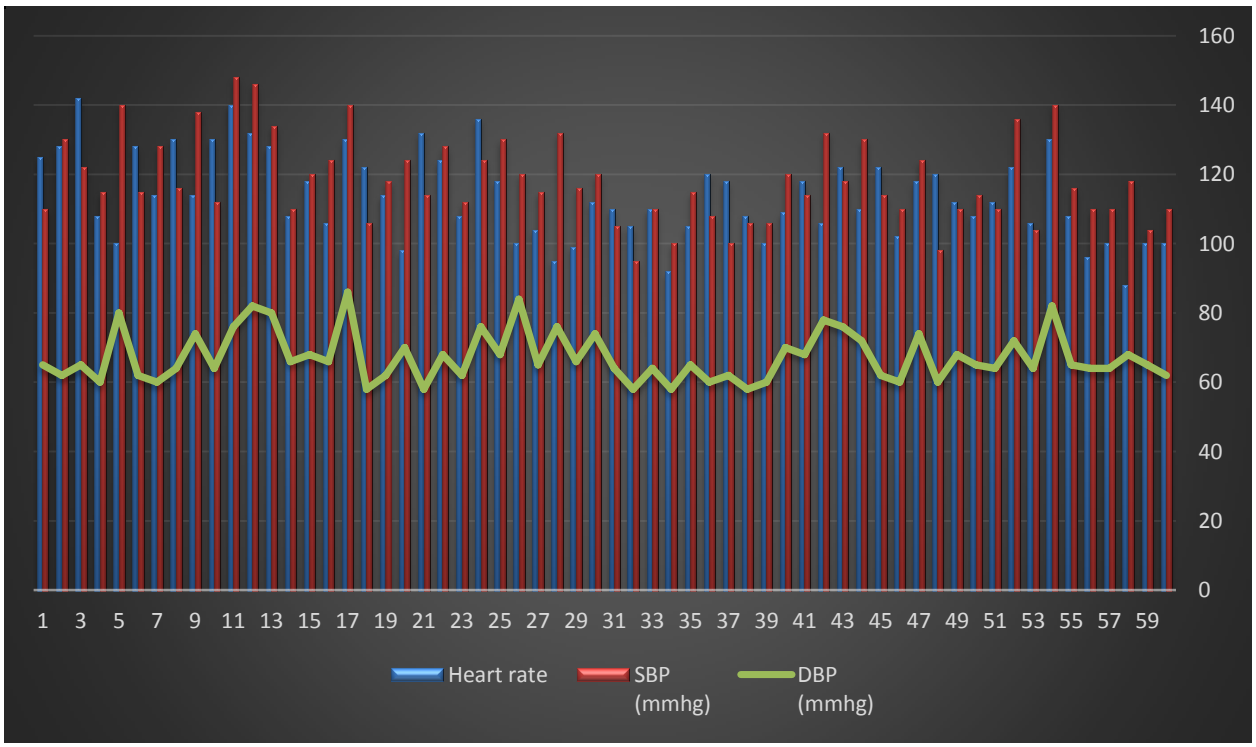
There was no statistical as well as clinically significant difference in the haemodynamic parameters, i.e. the pulse, systolic blood pressure and diastolic blood pressure, between the two groups, as seen in Figure 2.

The haemodynamic measures, including the pulse, systolic blood pressure, and diastolic blood pressure, did not differ statistically or clinically between the two groups, as shown in Figure 2.



	Sx time (min)	Cpb time (min)	Duration of sedation	Rescue dose
Group A STD	13.5	10.2	1.5	0.9
Group A Aveg	118.1	69.9	12.5	2.4
Group B STD	57.4	18.8	8.2	1
Group B Aveg	352.6	78.9	13.9	3.1

Figure 1: The haemodynamic measures, including the pulse, systolic blood pressure, and diastolic blood pressure, did not differ statistically or clinically between the two groups.



With a 6.321.72 in the fentanyl group and a 7.012.19 in the dexmedetomidine group, respectively, the average inotropic score in the first 24 hours was comparable between the two

groups (P value = 0.137). In the fentanyl group, bradycardia occurred far less frequently. Even though the heart rate dropped in the first few hours in the dexmedetomidine group, it was still 10 to 15% below baseline and did not need treatment. In neither group was there any substantial hypotension.

The average time for extubation from the cessation of sedative infusion was 140.04±43.6 min in the dexmedetomidine group as compared with 359.4±93.3 min in the fentanyl group, with a *P* value of 0.001 (statistically significant) [Table 3].

Sedation score between the two groups were comparable with no accidental extubation because of insufficient sedation and no patient was re intubated. The median with interquartile range of RSS sedation score in the fentanyl and dexmedetomidine groups were comparable, as shown in Figure 2.

With a P value of 0.001 (statistically significant), the average time for extubation following the end of sedative infusion was 140.0443.6 min in the dexmedetomidine group and 359.493.3 min in the fentanyl group [Table 3].

No patient was accidentally extubated due to insufficient sedation, and the sedation scores between the two groups were equal. As demonstrated in Figure 2, the median and interquartile range of the RSS sedation scores in the fentanyl and dexmedetomidine groups were similar.

Table: 3 Descriptive analysis of extubation time between the two groups

	Fentanyl	Dexmedetomidine
Time for extubation (min) minimum–maximum	200-620	75-240
Median time for extubation (min)	359	136
Mean time for extubation (min)	93.3	43.6
Std. deviation	359.4	140.4

*P<0.001, highly significant

Statistical analysis

The demographic data of the two groups (Fentanyl and dexmedetomidine) were comparable. A total60 no of cases were included in our study, and we divided 30 patients into each group. The mean ± SD in age and weight of group A (57.0±10.62 and 64.4 ± 9.9) and group B (54.3±10.24 and 62.8±11.0). Baseline characteristics of both the groups (Table 1).The two-tailed P value equals 0.3209 in group A by conventional criteria, and this difference was considered not statistically significant. The group B two-tailed P value equals 0.5515; this difference is considered insignificant. The average and STDEV duration of sedation to extubation (Min) were around fentanyl (359.4 ± 93.3) and dexmedetomidine (140.4 ± 43.6). Our study also monitored

each patient's heart rate, SBP, and DBP, such as the mean and STVD of group A (118.1 ± 13.5, 123.6±11.1, and 68.9±8.8) and group B (109.2±9.8, 112.9±10.9 and 65.7±6.1) .

Discussion

Most patients in the post-surgical ICU need sedation and analgesia to help with mechanical ventilation, calm anxiety, ease pain, promote sleep, prevent a sudden rise in systemic or pulmonary vascular resistance due to agitation, and to avoid accidentally dislodging indwelling catheters or drainage tubes by frequent movement.

Dexmedetomidine has been shown to have both sedative and analgesic effects, reduced delirium and agitation, low respiratory depression, and predictable and desired cardiovascular effects when compared to traditional sedatives and opiates [2,9]. Sedation and anxiolysis are greatly aided by the central nervous system's stimulation of parasympathetic outflow and suppression of sympathetic outflow from the locus coeruleus in the brainstem [4]. Increased firing of inhibitory neurons is made possible by decreased locus coeruleus noradrenergic output (GABA). Heart rate and blood pressure are reduced as a result of centrally active a2adrenergic agonists' activation of central sympatholytic effects [3,9]. The activation of the a2 adrenergic receptor in the dorsal horn of the spinal cord and inhibition of substance P release cause the primary analgesic effects and potentiation of opioid-induced analgesics Chrysostosmou *et al*.[14] retrospectively reviewed their experience with post-operative dexmedetomidine infusion in paediatric patients undergoing cardiac surgery. Dexmedetomidine was administered in the post-operative unit at a dose of 0.1–0.5 µg/kg/h for3–26 h, and they reported successful post-operative sedation in 93% of the patients with absent or minimal pain scores. They also reported that 87% of the patients on dexmedetomidine infusion were easily weaned and extubated.

In our study, there was a highly significant delay in extubation in the fentanyl group, the average time being 359.4±93.3 min as compared with dexmedetomidine (140.4±43.6 min). Dexmedetomidine has minimal effects on respiration and, therefore, facilitates early extubation,[9,12,14-16] whereas fentanyl, being an opioid, the respiratory depressant action is the most serious adverse effect causing delay in the extubation.[17-23].

Park et al.[24] compared hypnotic-based sedation (propofol and/or midazolam) with analgesia-based sedation (remifentanil) in a general intensive care unit,and found that analgesia-based sedation provided more satisfactory sedation during mechanical ventilation and also allowed early extubation ascompared with hypnotic-based sedation. Muellejans*et al*.[25] compared remifentanil versus fentanyl foranalgesia-based sedation in the intensive care unit and concluded that analgesia-based sedation with fentanyl or remifentanil was comparable and helped in early extubation of the patients.

In our study, we compared the analgesic fentanyl based sedation (most common agent used in the postoperative cardiac intensive care unit because of its haemodynamic stability) with the central a2 agonist dexmedetomidine; the RSS was comparable between the two groups as shown in Figure 2.

Tobias *et al*.[12] in a prospective randomized study showed that dexmedetomidine at 0.5 µg/kg/h provided more effective sedation and decreased the rescuedoses of morphine. In our study, the sedation levels in the dexmedetomidine group were adequate and comparable with the fentanyl group; the rescue doses offentanyl required were comparable in both the groups.

Venn *et al*.[26] in a prospective randomized study showed that dexmedetomidine at an initial loading dose of 1 µg/kg/h over 10 min followed by maintenance dose of 0.7 µg/kg/h provided optimal sedation, but 18 of 66 patients had adverse haemodynamic effects of either hypotension or bradycardia, in 11 of 18 patients the haemodynamic effects were during bolus infusion. Bloor *et al*[27]. The magnitude of decrease in heart rate and blood pressure increasewas proportional to the dose of dexmedetomidine increased. At lower doses, the decrease were of modest clinical interest and did not warrant corrective action.

In our study, the haemodynamic effects were minimal and did not require any intervention. This was probably due to the avoidance of an initial loadingdose and also a low infusion dose of 0.5 µg/kg/h.[7**].**

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