Role of dexmedetomidine in early extubation of the intensive care unit patients

Shikha Gupta, Dupinder Singh, Dinesh Sood, Suneet Kathuria
Department of Anaesthesiology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India

Abstract

Background and Aims: Patients on ventilatory support in intensive care unit (ICU) require sedation and analgesia to facilitate mechanical ventilation and endotracheal tube tolerance. The selection of the agent should be such that it does not interfere with the early extubation of the patients. We compared the efficacy of dexmedetomidine with midazolam to facilitate extubation of patients from mechanical ventilation in terms of the sedative properties, cardiovascular responses, ventilation, and extubation characteristics and safety profile.

Materials and Methods: A total of 40 adult, mechanically ventilated patients of either sex, aged 18-60 years, meeting the standard criteria for weaning, randomized into 2 groups of 20 patients each, received intravenous infusion of dexmedetomidine (0.2-0.7 mcg/kg/h) or midazolam (0.04-0.2 mg/kg/h) as needed for Ramsay sedation scale 2-4. Extubation following standard extubation protocol was done. Time for extubation and vital parameters were regularly recorded.

Results: The time to extubation in the dexmedetomidine group was significantly lower than in the midazolam group. Heart rate and blood pressure was significantly lower in dexmedetomidine group than the midazolam group at most of the times.

Conclusions: Dexmedetomidine has clinically relevant benefits compared with midazolam in facilitating extubation due to its shorter time to extubation, more hemodynamic stability, easy arousability, and lack of respiratory depression.

Key words: Dexmedetomidine, extubation, intensive care unit, midazolam, sedation

Introduction

The process of weaning from mechanical ventilation is central to the management of critically ill patients. It is a very complex and difficult task. Attention should be paid to wean off the ventilator as quickly as possible after the conditions that warranted placing the patient on the ventilator begin to resolve and stabilize.[1] Delayed or unnecessarily prolonged weaning increases length of intensive care unit (ICU) stay, health-care cost, decreases the ICU bed availability and adversely affects patient outcome.[2,3] Aggressiveness in weaning off the ventilator, however, must be balanced against the possibility that premature discontinuation may occur. Premature discontinuation carries its own set of problems, including difficulty in reestablishing artificial airways and compromised gas exchange, etc.

Majority of ICU patients who are on ventilatory support require intravenous (i.v.) sedative and analgesic medications to facilitate mechanical ventilation, improve tolerance to the endotracheal tube, the invasive procedures, physiotherapy, tracheal suctioning, turning postures, changing of dressings, allays anxiety, blunts excessive hemodynamic, and metabolic responses.[4-6]

Two major classes of medications used for this purpose in ICU are the sedative hypnotic agents and opioid analgesics. Benzodiazepines are the agents most commonly used to provide sedation in ICU.[7,8] Lorazepam given by intermittent boluses or continuous i.v. infusion was recommended in the Society of Critical Care Medicine, 2002 consensus guidelines, as the preferred sedative drug for ICU patients.
who require prolonged mechanical ventilation. Whereas, midazolam was recommended only for short term (<48 h) sedation because of concerns for unpredictable awakening observed after prolonged infusion. Midazolam causes a fall in systemic vascular resistance that is more evident when vascular resistance is raised, such as in hypertensive patients. It produces some respiratory depression and also apnea when given along with opioids. Its elimination is prolonged in critically ill patients resulting in prolongation of its actions and extubation failure.

The $\alpha_2$ agonist dexmedetomidine is a newer sedative and analgesic agent used for ICU sedation for up to 24 h after surgery. It provides a hemodynamic stability and appears to have no clinically important adverse effects on respiration. Its sedative properties are unique in that it produces only mild cognitive impairment, allowing easy communication between health-care provider and patient in the ICU. It does not affect the respiratory drive and therefore, it should not interfere with weaning from mechanical ventilation.

In this study, we compared the efficacy of dexmedetomidine with midazolam to facilitate extubation of patients from mechanical ventilation in terms of the sedative properties, cardiovascular responses, ventilation, and extubation characteristics and safety profile.

**Materials and Methods**

This study was conducted in a randomized, open labeled manner on 40 adults, aged 18-60 years. All these patients were postabdominal surgery patients, being mechanically ventilated for <96 h prior to start of study drug infusion, and were anticipated to be weaned-off mechanical ventilation in next 24 h. A written informed consent was taken from legally acceptable relatives of all patients. Patients with significant liver (Childs Pugh class-C) or kidney disease, severe neurological disorders, acute myocardial infarction, heart block, heart rate <50 beats/min, systolic blood pressure <90 mm Hg despite continuous infusions of vasopressors, receiving other sedatives and anticonvulsant drugs, pregnant/lactating females, and patients allergic to midazolam or dexmedetomidine were excluded from the study.

As institutional protocol, these patients were receiving morphine or fentanyl for analgesia and midazolam or lorazepam, for sedation as per choice of treating intensivist. Readiness for weaning trial was considered on the basis of following criteria: awake, adequate cough on suctioning, $\text{PaO}_2$ >60 mm Hg, oxygen saturation $\geq$90%, fraction of inspired oxygen $\leq$0.4, positive end expiratory pressure $\leq$10 cm H$_2$O, respiratory rate (RR) $\leq$35/min, ventilation $\leq$15 L/min, no inotropic or vasopressor infusions, mean arterial pressure $>60$ mm Hg, and no evidence of acute myocardial ischemia (i.e., chest pain, consistent electrocardiogram findings, elevated biomarker levels, or new arrhythmia). To check the readiness for weaning all these patients were subjected to daily sedation interruptions and were assessed hourly for wakefulness, defined as Ramsay sedation scale (RSS) score 1-4 and ability to perform at least 3 of the following on request: Eye opening, tracking, hand squeezing, and toe movement. Patients were subjected to a spontaneous breathing trial (SBT). Patients who successfully completed a 2 h trial of spontaneous breathing were further tried for discontinuation of mechanical ventilation and possible extubation depending upon their ability to maintain and protect airway and their ability to cough and clear secretions. On the other hand, SBT was discontinued if there was tachypnea (RR $>35$/min for 5 min), hypoxia ($\text{SpO}_2$ < 90%), sustained changes in heart rate and blood pressure of more than ±20% or increased anxiety and diaphoresis. The patients who failed SBT were randomized into two groups of 20 patients each to receive either of the study drug infusion protocol using computer-generated random numbers.

**Group I:** Patients received i.v. infusion of dexmedetomidine at a rate of 0.2-0.7 mcg/kg/h (adjusted as needed for the desired level of sedation i.e., RSS 2-4).

**Group II:** Patient received i.v. infusion of midazolam at the rate of 0.04-0.2 mg/kg/h (adjusted as needed for the desired level of sedation i.e., RSS 2-4).

Sedation was categorized into three levels according to RSS as:

1. **Insufficient:** If sedation level was Grade 1 on the RSS.
2. **Adequate (desired):** If sedation level was Grade 2-4 on the RSS.
3. **Excessive:** If sedation level was Grade 5-6 on the RSS.

After starting weaning, the analgesia was provided with regular paracetamol infusion to all patients. The study drug infusion was given up to a maximum period of 24 h. Hemodynamic parameters were recorded every 4 hourly during study drug infusion and then every 2 hourly after discontinuation of study drug. The patients were regularly accessed for possible extubation. After meeting the criteria for extubation, the extubation was done following standard extubation protocol and the time for extubation (from start of the study drug infusion until extubation) and duration of study drug infusion given was recorded.
Patients who maintained effective spontaneous breathing without any mechanical assistance for 24 h after extubation were considered as successfully weaned and those who did not, were excluded from the study and were considered as extubation failure. The arterial blood gas sample was taken at the beginning of weaning, just before extubation and 1 h after extubation.

**Statistical analysis**
Quantitative data were described in mean ± standard deviation and were compared using Students’s t test or Mann-Whitney test. Categorical data were described by absolute and percentage frequencies and were compared using Chi-square test. Differences were considered significant when $P \leq 0.05$.

**Results**
Patients in the two groups were comparable demographically in terms of age, sex, body mass index, indication for putting on the ventilator, and duration of ventilation prior to start of study drug infusion [Table 1].

![Table 1: Demographic profile](https://example.com/table1.png)

| Group       | Group I          | Group II         | P value |
|-------------|------------------|------------------|---------|
|             | Demedetomidine   | Midazolam        |         |
| Age (years)| 43.35±11.595     | 39.00±14.127     | 0.294   |
| Sex         | 12/8             | 13/7             | 0.744   |
| BMI (kg/m²)| 25.778±3.725     | 25.911±3.082     | 0.665   |
| Ventilator indication | Poly-trauma | 8 (40%) | 7 (35%) |
|              | Sepsis          | 6 (30%)          | 8 (40%) |
|              | Prolonged abdominal surgery | 6 (30%) | 5 (25%) |
| Period of ventilation prior to starting study drug infusion | 92 h, 36 min | 94 h, 15 min |         |

BMI = Body mass index

The level of sedation as assessed by RSS among patients in two groups was comparable at various time intervals [Table 2]. Most of patients in both groups remained adequately sedated throughout the study period. Excessive sedation was seen only in midazolam group (two patients at 12 h, two patients at 16 h and one patient at 20 h). No case of excessive sedation was seen in demedetomidine group.

The time to extubation was found to be significantly lesser in the demedetomidine group (24.210 ± 1.6651 h) than in the midazolam group (31.350 ± 3.3447 h) [Table 3].

Patients in both groups remained hemodynamically stable throughout the study period. The difference in heart rates in the two groups was comparable and was statistically insignificant at 0-12 h. Whereas, the heart rates in the demedetomidine group were significantly lower than in the midazolam group at 16, 20, and 24 h after the drug infusion. In the intragroup comparison, the mean fall in heart rates from the baseline values was significant in demedetomidine group at 16, 20, and 24 h, whereas it was insignificant in midazolam group. After extubation the heart rate in the demedetomidine group was found to be significantly lower than in the midazolam group, when the two groups were compared with each other from the time of extubation until 12 h postextubation [Table 4 and Figure 1].

The baseline values of systolic blood pressure in the demedetomidine group and midazolam group were statistically insignificant. The change in mean systolic blood pressure from baseline value until 16 h of starting the study drug infusion was statistically insignificant in both groups. However, a significant fall from baseline was observed at 20 h in demedetomidine group alone and at 24 h in both demedetomidine and midazolam groups. On intergroup comparison, the fall in systolic blood pressure was comparable in both groups except at 24 h where a statistically significant fall in systolic blood pressure was observed in demedetomidine group as compared with midazolam group. Significantly lower systolic blood pressure values in demedetomidine group were observed as compared to midazolam group at various time intervals after extubation.

![Table 2: Adequacy of sedation](https://example.com/table2.png)

| Time (h) | Group I | Group II | P value |
|---------|---------|----------|---------|
|         | Demedetomidine | Midazolam |         |
|         | Inadequate sedation | Adequate sedation | Excessive sedation |
|         | 20 | 0 | 0 | |
|        4 | 2 | 18 | 0 | |
|        8 | 1 | 19 | 0 | |
|       12 | 0 | 20 | 0 | |
|       16 | 0 | 20 | 0 | |
|       20 | 1 | 19 | 0 | |
|       24 | 0 | 20 | 0 | |

| Time (h) | Group I | Group II | P value |
|---------|---------|----------|---------|
|         | Midazolam |         |         |
|         | Inadequate sedation | Adequate sedation | Excessive sedation |
|         | 20 | 0 | 0 | 1.000 |
|        4 | 4 | 16 | 0 | 0.382 |
|        8 | 3 | 17 | 0 | 0.298 |
|       12 | 2 | 16 | 2 | 1.000 |
|       16 | 0 | 18 | 2 | 0.152 |
|       20 | 1 | 18 | 1 | 0.799 |
|       24 | 0 | 20 | 0 | 1.000 |
extubation also. The comparative diastolic blood pressure trends at various time intervals before and after extubation were almost similar as that of systolic blood pressure in both dexmedetomidine and midazolam groups [Figure 1].

The baseline values of oxygen saturation (SpO₂) in the dexmedetomidine group and midazolam group were statistically insignificant. On intergroup comparison, the oxygen saturation values were comparable in both groups except at 24 h after starting the study drug infusion, where significantly lower value of SpO₂ was observed in midazolam group as compared to dexmedetomidine group. After extubation, the oxygen saturation in the dexmedetomidine group was found to be significantly higher than in the midazolam group at all-time intervals, when the two groups were compared with each other statistically [Figure 2].

Discussion

The ideal drug for sedation in the ICU is one with a rapid onset of action, a short duration of action and which produces sedation without affecting the cardiovascular or respiratory system. It should have a short elimination half-life with no accumulation on repeated or continuous administration, and should be metabolized by pathway not dependent on renal, hepatic, or pulmonary functions. Etomidate, opioids, benzodiazepines, thiopentone, and ketamine are few examples which individually lacked some of these desirable properties and hence failed to become the drug of choice.

In daily practice of intensive care, the trend has been to use a combination of opioids and benzodiazepines. Opioids in the usual dose are excellent sedatives, analgesics, producing euphoria, and drowsiness with little effect on arterial blood pressure. However, opiates by themselves are not appropriate for prolonged, continuous sedation because of the number of side-effects such as decreased intestinal motility, tolerance, withdrawal after discontinuation of drug, and possible influence on immune status.

Benzodiazepines such as diazepam or lorazepam act rapidly, but the presence of active metabolites prolongs recovery.

| Table 3: Time to extubation (in h) |
|-----------------------------------|
| **Group**                      | **Mean ± SD** | **P value** |
| ---------------------------------|---------------|-------------|
| Dexmedetomidine                  | 24.21±1.6651  | 0.0260      |
| Midazolam                        | 31.35±3.3447  |             |

SD = Standard deviation

| Table 4: Heart rate trends before and after extubation |
|--------------------------------------------------------|
| **Time** | **Dexmedetomidine** | **Midazolam** | **P value** |
|-----------|---------------------|---------------|-------------|
| Before extubation |
| 0 h       | 117.44±11.703       | 117.00±6.440  | 0.683       |
| 4 h       | 112.44±9.954        | 113.70±6.199  | 0.497       |
| 8 h       | 110.50±12.557       | 110.95±6.048  | 0.796       |
| 12 h      | 103.83±11.719       | 111.50±5.568  | 0.113       |
| 16 h      | 95.33±13.408        | 109.50±5.568  | 0.012       |
| 20 h      | 91.22±12.670        | 110.7±5.992   | 0.020       |
| 24 h      | 86.60±12.331        | 109.05±6.452  | 0.024       |
| After extubation |
| 0 h       | 105.15±14.295       | 118.25±6.290  | 0.020       |
| 2 h       | 95.70±12.503        | 114.60±7.315  | 0.017       |
| 4 h       | 91.65±12.368        | 110.60±7.432  | 0.041       |
| 6 h       | 88.30±11.970        | 107.00±4.377  | 0.031       |
| 8 h       | 86.25±11.652        | 107.70±6.097  | 0.020       |
| 10 h      | 85.40±11.348        | 108.00±5.026  | 0.036       |
| 12 h      | 84.85±9.949         | 108.95±5.671  | 0.024       |

n = 20, values are given as mean heart rate (beats/min) ±SD. SD = Standard deviation

Figure 1: Hemodynamic trends
Midazolam, a water-soluble benzodiazepine with sedative, anxiolytic, anticonvulsant and muscle relaxant properties, with low toxicity, has been used as a sedative in ICU, but it produces respiratory depression, delayed recovery and hypotension. A “midazolam infusion syndrome” resulting from high doses, is characterized by delayed arousal after discontinuation, leading to an increase in the length of ventilatory support.

Dexmedetomidine, a new, potent alpha-2 agonist acting in the locus ceruleus, inhibits sympathetic stimulation, and provides analgesia and sedation without respiratory depression and hemodynamic instability. It produces only mild cognitive impairment allowing easy communication between health-care provider and the patient in ICU.

In the present study, we compared the efficacy of dexmedetomidine and midazolam in facilitating extubation in patients on mechanical ventilatory support. Following the start of dexmedetomidine infusion, there was no difference in the percentage of time within the target RSS range (96.6% in dexmedetomidine group vs. 87.6% in midazolam group \(P > 0.05\)). There were 3.3% and 8.3% patients who were inadequately sedated in dexmedetomidine and midazolam group respectively. There were 4.2% patients over-sedated midazolam group and none in dexmedetomidine. Our study is in accordance with that of Riker et al., who reported that there was no difference in the primary efficacy outcome in terms of percentage of time within the target Richmond agitation sedation scale (RASS) range (77.3% for dexmedetomidine - treated patients and 75.1% for midazolam - treated patients; difference, 2.2% [95% confidence interval (CI); −3.2-7.5%]; \(P = 0.18\)). The MIDEX trial comparing midazolam with dexmedetomidine with respect to the proportion of time at target sedation level (measured by RASS) in ICUs of 44 centers in nine European countries concluded that dexmedetomidine/midazolam ratio in time at target sedation was 1.07 (95% CI, 0.97-1.18).

In our study, the time to extubation in the dexmedetomidine group (24.21 ± 1.6651 h) was found to be significantly lower (7.14 h) than in the midazolam group (31.35 ± 3.3447 h). Venn et al. in 2000 compared dexmedetomidine with propofol for sedation in the ICU. They showed that the extubation times were similar and rapid with the use of both sedative agents (median [range] 28 [20-50] and 29 [15-50] min \(P = 0.63\)) for the propofol and dexmedetomidine groups, respectively. Shehabi et al. in 2004 showed that mean time to extubation was shorter in dexmedetomidine group (24.21 h [22-28 h]) than midazolam group (31.35 h [26-38 h] \(P < 0.05\)).

Despite the similar levels of target sedation achieved by patients treated with dexmedetomidine and midazolam, several important differences were noted. Mean systolic blood pressure decreased by 17% in dexmedetomidine group and 5% in midazolam group \(P < 0.05\), whereas the mean diastolic blood pressure was reduced by 13.97% in dexmedetomidine group and 9.26% in midazolam group \(P < 0.05\). In preextubation period, the mean heart rate remained lower in dexmedetomidine group than midazolam group at all times, but it was statistically significant at 16th, 20th, and 24th h of starting the infusion. In postextubation period, the heart rate was significantly lower in dexmedetomidine group as compared with midazolam group. A 28% reduction in heart rate from baseline was seen in dexmedetomidine group, whereas it was 7% reduction midazolam group \(P < 0.05\).

Venn et al. also reported significantly lower heart rate in the dexmedetomidine group (mean [standard deviation] 75 [6]
vs. 90 [4] beats/min) however, no significant differences were found in arterial pressures between the groups. Shehabi et al. in 2004 also reported a 16% reduction in mean systolic blood pressure and 21% reduction in heart rate over the first 4 h followed by minimal (±10%) changes throughout the infusion.[31] In 2008, Arpino et al.[32] also found that the heart rate trended down after dexmedetomidine initiation in most patients, but did not result in the discontinuation of dexmedetomidine in any patient. The addition of dexmedetomidine was associated with minimal changes in mean arterial pressure.

In our study, the mean SpO2 levels in postextubation period remained significantly higher in dexmedetomidine group (98.7%) as compared with midazolam group (97.7%). Patients sedated with dexmedetomidine were easily arousable and cooperative with the procedures such as physiotherapy, radiology, suctioning, positioning, etc., without showing irritation. Dexmedetomidine treated patients showed rapid recovery in the level of consciousness after discontinuation of drug infusion as compared to midazolam where 10% of patients were over-sedated. All patients were successfully extubated without any weaning failure.

Though the baseline sedation score following daily sedation interruption in both groups were comparable, but still the midazolam infusion given prior to start of study drug infusion could also have resulted in delayed time to extubation in midazolam group. Other limitations of study are a small sample size and we also did not compare the severity of sickness and types, duration and severity of surgery in two groups. Future studies of ICU sedation must look beyond the quality of sedation to focus on additional important clinical outcomes like delirium and long-term cognitive functions, etc.

We hereby conclude that dexmedetomidine has clinically relevant benefits compared to midazolam in facilitating extubation because of its shorter time to extubation, more hemodynamic stability, easy arousability and lack of respiratory depression; hence, it can be used as an effective, and safe sedative agent to facilitate extubation in ICUs.

References

1. MacIntyre NR, Cook DJ, Ely EW Jr, Epstein SK, Fink JB, Heffner JE, et al. Evidence-based guidelines for weaning and discontinuing ventilatory support: A collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. Chest 2001;120 6 Suppl:375S-95.

2. Kress JE Pohlman AS, O’Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000;342:1471-7.

3. Kollef MH, Levy NT, Ahrens TS, Schaffir R, Prentice D, Sherman G. The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. Chest 1998;114:541-8.

4. Arroliga A, Frutos-Vivar F, Hall J, Esteban A, Apezteguía C, Soto L, et al. Use of sedatives and neuromuscular blockers in a cohort of patients receiving mechanical ventilation. Chest 2005;128:496-506.

5. Bion JF, Ledingham IM. Sedation in intensive care — A postal survey. Intensive Care Med 1987;13:215-6.

6. Eckenhoff je, Kneale DH, Dripps RD. The incidence and etiology of postanesthetic excitement. A clinical survey. Anesthesiology 1961;22:667-73.

7. Soliman HM, Molot C, Vincent JL. Sedative and analgesic practice in the intensive care unit: The results of a European survey. Br J Anaesth 2001;87:186-92.

8. Mehta S, Burry L, Fischer S, Martinez-Motta JC, Hallett D, Bowman D, et al. Canadian survey of the use of sedatives, analgesics, and neuromuscular blocking agents in critically ill patients. Crit Care Med 2006;34:374-80.

9. Carson SS, Kress JP, Rodgers JE, Vinayak A, Campbell-Bright S, Levitt J, et al. A randomized trial of intermittent lorazepam versus propofol with daily interruption in mechanically ventilated patients. Crit Care Med 2006;34:1326-32.

10. Müller H, Schleussner E, Stoyanov M, Kling D, Hempelmann G. Haemodynamic effects and characteristics of midazolam during induction of anaesthesia (author’s transl). Arzneimittelforschung 1981;31:2227-32.

11. Dundee JW, Johnston HM, Gray RC. Lorazepam as a sedative-ansesic in an intensive care unit. Curr Med Res Opin 1976;4:290-5.

12. Dundee JW, Samuel IO, Toner W, Howard PJ. Midazolam: A water-soluble benzodiazepine. Studies in volunteers. Anaesthesia 1980;35:454-8.

13. Dundee JW, Wilson DB. Amnesic action of midazolam. Anaesthesia 1980;35:459-61.

14. Venn RM, Bradshaw CJ, Spencer R, Brealey C, Caudwell E, Naughton C, et al. Preliminary UK experience of dexmedetomidine, a novel agent for postoperative sedation in the intensive care unit. Anaesthesia 1999;54:1136-42.

15. Martin E, Ramsay G, Mantz J, Sum-Ping ST. The role of the alpha2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. J Intensive Care Med 2003;18:29-41.

16. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology 1992;77:1134-42.

17. Belleville JP, Ward DS, Bloor BC, Maze M. Effects of intravenous dexmedetomidine in humans. I. Sedation, ventilation, and metabolic rate. Anesthesiology 1992;77:1125-33.

18. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care 2000;4:302-8.

19. Gerlach AT, Dasta JF. Dexmedetomidine: An updated review. Ann Pharmacother 2001;35:454-8.

20. Sudheesh K, Harsoor S. Dexmedetomidine in anaesthesia practice: A wonder drug? Indian J Anaesth 2011;55:323-4.

21. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnesic, and analgesic properties of small-dose dexmedetomidine infusions. Anesthesiol 2000;90:699-705.

22. Gómez-Vázquez ME, Hernández-Salazar E, Hernández-Jiménez A, Pérez-Sánchez A, Zepeda-López VA, Salazar-Páramo M. Clinical analgesic efficacy and side effects of dexmedetomidine in the early postoperative period after arthroscopic knee surgery. J Clin Anesth 2007;19:576-82.
23. Botha J, Le Blanc V. The state of sedation in the nation: Results of an Australian survey. Crit Care Resusc 2005;7:92-6.
24. Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. Crit Care Med 2002;30:119-41.
25. Ogawa K, Tanaka S, Murray PA. Inhibitory effects of etomidate and ketamine on endothelium-dependent relaxation in canine pulmonary artery. Anesthesiology 2001;94:668-77.
26. Sanders KD, McArule P, Lang JD Jr. Pain in the intensive care unit: Recognition, measurement, management. Semin Respir Crit Care Med 2001;22:127-36.
27. Stapleton JV, Austin KL, Mather LE. A pharmacokinetic approach to postoperative pain: Continuous infusion of pethidine. Anaesth Intensive Care 1979;7:25-32.
28. Mencía SB, López-Herce JC, Freddi N. Analgesia and sedation in children: Practical approach for the most frequent situations. J Pediatr (Rio J) 2007;83(Suppl):S71-82.
29. Riker RR, Shehabi Y, Bokesch PM, Cersso D, Wisemandle W, Koura F, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: A randomized trial. JAMA 2009;301:489-99.
30. Jakob SM, Ruokonen E, Grounds RM, Sarasola T, Garratt C, Pocock SJ, et al. Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: Two randomized controlled trials. JAMA 2012;307:1151-60.
31. Shehabi Y, Ruettimann U, Adamson H, Innes R, Ickeringill M. Dexmedetomidine infusion for more than 24 hours in critically ill patients: Sedative and cardiovascular effects. Intensive Care Med 2004;30:2188-96.
32. Arpino PA, Kalafatas K, Thompson BT. Feasibility of dexmedetomidine in facilitating extubation in the intensive care unit. J Clin Pharm Ther 2008;33:25-30.

How to cite this article: Gupta S, Singh D, Sood D, Kathura S. Role of dexmedetomidine in early extubation of the intensive care unit patients. J Anaesthesiol Clin Pharmacol 2015;31:92-8.

Source of Support: Nil, Conflict of Interest: None declared.