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A comparative study to evaluate efficacy of IV infusion of dexmedetomidine versus IV infusion of propofol for post-operative ICU sedation

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Abstract---Aim: The purpose of the present study is to evaluate the efficacy of dexmedetomidine and propofol as an IV infusion for post-operative ICU sedation. Methodology: This study was performed on Dr. Moopen's Medical College, Wayanad, Kerala, India and duration was from January 2022 to September 2022. Thirty patients who were ambulatory and who required the post-operative mechanical ventilation or post-operative sedation were enrolled, in which 15 patients received Dexmedetomidine and remaining 15 patients received propofol. All these patients were treated for the period of 8 to 24 h. Data were analyzed using Student's t-test and Chi-square test. The value of $P < 0.05$ was considered as statistically significant. Results: Demographic data were comparable. Pulse rate, respiratory rate and blood pressure were comparable. Depth of sedation and extubation time were similar. To maintain analgesia throughout the study period, patients receiving propofol infusions required significantly more analgesics than patients receiving Dexmedetomidine. Conclusion: Dexmedetomidine appears to be a safe and acceptable ICU sedative agent when both the clinician's and patient's perspectives are considered.

Keywords---dexmedetomidine, intensive care unit sedation, propofol.

Introduction

The optimum intraoperative anaesthetic agent for cardiac surgery should allow the patients to recover rapidly and prevent undesirable outcomes such as pulmonary complications, prolonged mechanical lung ventilation, and prolonged stay in the intensive care unit (ICU). Prolonged mechanical ventilation and ICU stay are associated with high morbidity and mortality rates following cardiac surgery.^{1,2} Anaesthetic techniques and agents used during surgery to accelerate weaning from mechanical lung ventilation and patient's recovery are essential for fast-track cardiac anaesthesia and are increasingly being adopted. Dexmedetomidine (DEX) is a highly selective short-acting α_2 -adrenoceptor agonist with properties including sedative, analgesic, anxiolytic, opioid and anaesthetic sparing effects.³ DEX has minimal impact on respiratory depression, improves oxygenation and lung compliance, and reduces postoperative pulmonary complications.^{4,5} DEX also alleviates perioperative stress, inflammatory and immune response leading to an excellent postoperative recovery.⁶ Perioperative use of DEX as an anaesthetic adjunct and postoperative sedation was reported to reduce the time spent on mechanical ventilation, improve 30days mortality, shorten ICU and hospital stay, and decrease postoperative complications, including the incidence of pulmonary complications and delirium and acute kidney injury.^{7,8} Propofol is an intravenous anesthetic agent that is used for induction and maintenance of anesthesia. The use of propofol for induction of anesthesia in patients undergoing cardiac surgery is well described.⁹ In these studies, doses of propofol of 1.0–2.5 mg/kg were associated with significant hypotension. Inappropriate sedative use in the intensive-care unit (ICU) is associated with adverse outcomes, including patient discomfort, excessive sedation, longer ICU and hospital stays, an increased incidence of ventilator-associated pneumonia, and greater hospital costs. The use of propofol or midazolam is recommended. As pain is often the culprit in agitation, an opioid analgesic is recommended, in addition to the previously mentioned agents, to provide adequate analgesia. However, propofol lacks analgesic properties, and its usage is often limited by hypotension and respiratory depression.¹⁰ Benzodiazepine is also associated with respiratory depression and the potential for the drug to accumulate, leading to a prolonged recovery period. DEX sedates via interaction with the locus ceruleus, and has less effect on arousability and patient interaction.^{11,12} In post-surgical patients, dexmedetomidine does not interfere with respiration rate, or arterial oxygenation and carbon dioxide pressure.¹³ The objective of this study was to investigate and evaluate the efficacy and safety of dexmedetomidine in comparison to propofol in the management of sedation for post-operative intensive care unit (ICU) patients, as a sedative agent. Sedatives are used in most patients undergoing various surgeries during the post-operative period to reduce anxiety during rewarming and to reduce cardiovascular instability. Articles show that using protocols to guide sedation in various groups of critically ill patients decreases the duration of both mechanical ventilation and ICU stay.¹⁰

Aim of the present study

The purpose of the present study is to evaluate the efficacy of dexmedetomidine and propofol as an IV infusion for post-operative ICU sedation.

Methodology

This study was performed on Dr. Moopen's Medical College, Wayanad, Kerala, India and duration was from January 2022 to September 2022. Thirty patients were enrolled, who required the post-operative mechanical ventilation or post-operative sedation, in which 15 patients received Dexmedetomidine and remaining 15 patients received propofol. All patients were treated for the period of 8-24 hours. Data presented here is of only 30 patients done at our centre. Patients undergoing surgery on an inpatient basis, with age from 18 to 70 years of both gender and willing to give the consent were included in the study. Patients currently being treated or were treated within the last 30 days with alpha-2 agonist and blockers, with central nervous system (CNS), cardio vascular system (CVS), liver, renal problems, history of obstructive sleep apnea, pregnant or lactating females, in whom, propofol would be given for anesthesia were excluded from the study. After Institutional Ethics Committee approval and a written informed consent from patient or relatives, the patients were enrolled in the study. As per randomization, when each patient had VAS ≥ 4 and Ramsay sedation score ≤ 2 , they received either dexmedetomidine or propofol and were treated for the period of 24 h. Dexmedetomidine was administered by a loading dose of injection with 1 mcg/kg over 10 min, followed by a maintenance infusion of 0.2-0.7 mcg/kg/h. The rate of the maintenance infusion was adjusted to achieve the desired level of sedation. Propofol was started at 5 mcg/kg/min (0.3 mg/kg/h). The infusion rate was increased by increments of 5-10 mcg/kg/min (0.3-0.6 mg/kg/h) until the desired level of sedation was achieved. A minimum period of 5 min between adjustments was allowed for the onset of peak drug effect. The primary efficacy parameter was to evaluate cardio-respiratory end points at equi-sedative doses of Dexmedetomidine and propofol in the ICU. Patient's global assessment of pain intensity (0-10 VAS), global assessments of the treatment efficacy by the patient and by the investigator were also noted. If VAS > 4 , analgesia (fentanyl) was given. Data were analyzed using Student's t-test and Chi-square test. The value of $P < 0.05$ was considered as statistically significant.

Results

All the 30 patients completed the study. In Dexmedetomidine group, 6 out of 15 were male. In propofol group, 10 out of 15 were male. The mean pulse-rate, respiratory rate, blood pressure between the groups was not statistically significant ($P > 0.05$). Over the whole study period, the mean VAS score was maintained between 2-3.5 and 2-3 for dexmedetomidine and propofol groups respectively. However, patients receiving propofol infusions required additional analgesics than patients receiving dexmedetomidine. Fentanyl required in patients receiving propofol infusion was 125 (100-150) mcg. No adverse event was observed in this study. With respect to patient assessment for efficacy, nine patients (i.e., 60%) out of 15 in dexmedetomidine group had shown excellent

rating whereas none of the patients in propofol group has shown excellent rating, in addition to excellent rating 6 (40%) and 10 (66.67%) patients had given "Good" rating and 0 and 5 (33.33%) patients had given "Poor" rating on treatment with dexmedetomidine and propofol therapy, respectively. (Table 1) According to investigators, assessment for efficacy represented in ten patients (66.67%) out of 15 in dexmedetomidine group had shown excellent rating as compared to 2 (13.33%) patients in propofol group, whereas 5 (33.33%) and 9 (60%) patients had given "Good" rating and 0 and 4 (26.67%) patients had given "Poor" rating on treatment with dexmedetomidine and propofol therapy, respectively. According to investigators, assessment for safety, 9 (60%) and 3 (20%) patients had given "Excellent" rating, whereas 6 (40%) and 8 (53.33%) patients had given "Good" rating and 0 (0%) and 4 (26.67%) patients had given "Poor" rating upon treatment with dexmedetomidine and propofol, respectively. (Table 2)

Discussion

Critically ill patients requiring mechanical ventilation frequently need sedatives and analgesics to facilitate their care. There is an increasing body of evidence showing that protocol-based strategies do not only reduce variation and cost of intensive care medicine, but also improve morbidity and mortality of critically ill patients.¹⁴ Analgesia and sedation are among these areas where considerable variations exist among practitioners.^{15,16} The concepts of analgesia and sedation in intensive care medicine have changed considerably over the last decade. Deep sedation is no longer the standard practice for most patients as it prolongs weaning from mechanical ventilation and the length of ICU stay and potentially increases morbidity.^{17,18} On the other hand, inadequate sedation can result in anxiety, agitation and in recall of stressful experience in the post-ICU phase.¹⁹ Therefore, analgesics and sedatives must be carefully titrated to the individual needs.²⁰ The present randomized, open study demonstrated that both infusions of dexmedetomidine and propofol produced sedation, and significant analgesia. Cardiovascular stability and respiratory function were both well maintained. There is a growing interest in the use of α_2 -adrenoceptor agonists like dexmedetomidine as it has a shorter half-life and has additional analgesic properties and maintains cardio respiratory function. Finally, antagonists to the effects of α_2 -adrenoceptor agonists have been described that make quick reversal of sedation an option.²¹ These properties may prove useful for post-operative or intensive care unit sedation. A rise in blood pressure may occur 1 min after the bolus and is attributed to the direct effects of α_2 -adrenoceptor stimulation of vascular smooth muscle. Dexmedetomidine does not appear to have any direct effects on the heart. The application of a single high dose of dexmedetomidine reduced norepinephrine release by as much as 92% in young healthy volunteers. The release of epinephrine is also reduced by the same amount. This seems to be more important than either central α_2 -adrenoceptor agonism or non- α adrenaline imidazole- preferring receptors in effecting the change. Dexmedetomidine is associated with little respiratory depression. This study confirmed a lack of a clinically significant respiratory effect. Belleville et al. reported that dexmedetomidine could be associated with episodes of obstructive apnea, and this was increasingly common at doses of 1 and 2 mg/kg that were given for 2 minutes and presumably associated with a rapid increase in sedation.²² Obstructive apnea was not evident in our study. An obstruction resulting in

apnea is more likely related to the deep sedation and oral/pharyngeal anatomic events that are common to deep sleep. These properties might prove to be useful in a post-operative setting or in the intensive care unit. Previous studies have reported attenuation of hypertension and tachycardia in response to laryngoscopy and intubation by dexmedetomidine and clonidine. Dexmedetomidine has an alpha-2 to alpha-1 receptor selectivity ratio that is 10 times greater than that of clonidine and has a significantly shorter elimination half-life.

Conclusion

In the present study, dexmedetomidine appears to be a safe and acceptable ICU sedative agent when both the clinician's and patient's perspectives are considered. Depth of sedation is similar to that given by propofol and the extubation time is equally rapid, despite the longer elimination half-life of dexmedetomidine.

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Tables

Table 1- Overall assessment of efficacy by investigators

Efficacy	Dexmedetomidine		Propofol	
	No	%	No	%
<i>Excellent</i>	10	66.67	02	13.33
<i>Good</i>	05	33.33	09	60.00
<i>Poor</i>	00	00	04	26.67
<i>Total</i>	15	100	15	100

Table 2- Overall assessment of safety by investigators

Safety by investigator	Dexmedetomidine		Propofol	
	<i>No</i>	<i>%</i>	<i>No</i>	<i>%</i>
<i>Excellent</i>	09	60	03	20.00
<i>Good</i>	06	40	08	53.33
<i>Poor</i>	00	00	04	26.67
<i>Total</i>	15	100	15	100