Original Research Article

Effectiveness of dexmedetomidine over propofol on extubation

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Abstract

In major surgeries like cardiovascular and neurosurgeries, sedation qualities and recovery after extubation are the important characteristics required for an ideal sedative drug. Dexmedetomidine and propofol are two commonly used sedative agents and have distinct pharmacologic characteristics that make them appealing in this patient population. Propofol is commonly used in the ICU for short term (less than 24 hours) sedation in ventilated patients postoperatively.In this study , we compared these two drugs in a set of 200 patients , who underwent major surgeries, by retrospectively collection of the data over a period of one year. The outcome of the two drugs is measured mainly in terms of the time of extubation, and post sedation effects like delirium and the length of stay in the ICUs and hospitalis considered and compared. Results revealed that Dexmedetomidine is superior to propofol in terms of the time required for extubation and the post sedative effects and finally influencing the length of stay in the hospital.

Keywords: Dexmedetomidine, open heart, propofol.

Introduction

The recovery process from major surgeries involves weaning from the assisted mechanical ventilation ,by extubation.The process of assisted mechanical ventilation decreases the work of breathing for patients by inhaling oxygen and exhaling carbon dioxide via a ventilator or breathing machine.In patients who are mechanically ventilated , the main goals are to maintain a level of comfort without agitation, lower anxiety levels and minimize pain[1,2].Sedative agents and analgesics are commonly used in postoperative cardiac surgery patients to achieve these goals. Proper sedation and analgesia can adequately provide comfort, which in turn can facilitate sufficient mechanical ventilation. There are several sedative agents that are available for use, but each class of drug has distinct pharmacokinetic and pharmacodynamic properties that elicit different side effects[1].Propofol and dexmedetomidine are the two common sedatives with different pharmacological properties used to provide effective target and minimize the hemodynamic complications during this recovery phase. Selecting a better sedative drug is determined by its mechanism of action, onset of action, duration of action and termination of action of the drug along with other properties which may be unique to that drug.

Dexmedetomidine and propofol are two commonly used sedative agents and have distinct pharmacologic characteristics that make them appealing in this patient population. Propofol is commonly used in the ICU for short term (less than 24 hours) sedation in ventilated patients postoperatively [3].Propofol is an intravenous phospholipid emulsion that has anesthetic, sedative and hypnotic properties and was approved in 1993 by the United States FDA for use as a sedative in mechanically ventilated patients.It has been used as a standard for sedation because of its properties of rapid onset, short duration of action and relatively low cost; however, the adverse effects of propofol are concerning, especially in cardiovascular patients[4,5]. These adverse effects include but are not limited to bradycardia, hypotension and respiratory depression[6].Although propofol may produce hemodynamic instability, it still has ideal pharmacokinetic properties for patients requiring short-term sedation.

Dexmedetomidine is a potent a2-adrenoreceptor agonist with anxiolytic, sedative, analgesic and sympatholytic (reduces tachycardia and hypertension) properties,making it attractive for perioperative uses. Approved in 1999 in the United States as a continuous infusion for sedation and analgesia in the ICU, dexmedetomidine has been used to provide sedation for cardiac surgery patients transitioning from the operating room to the ICU before extubation[7,8].Continuous infusion of dexmedetomidine produces a sedative/hypnotic state that resembles natural sleep but does not interfere with the normal course of ventilator weaning and extubation because it does not suppress the respiratory drive or decrease the arterial oxygen saturation[9,10].Subsequently, sedation with dexmedetomidine could promote early extubation.The most concerning side effects of dexmedetomidine are bradycardia and hypotension due to its sympatholytic properties, thus necessitating its careful use in vulnerable patient populations for whom these effects would not be tolerated[8].Choice of drug may have an impact on length of mechanical ventilation, length of stay and mortality. Prolonged mechanical ventilation is associated with complications, such as pneumonia and lung injury, increased cost and increases the risk of morbidity and mortality in long term stay (more than seven days). As patients recover and their independent ventilatory capability and the demand for mechanical ventilation decrease, it is

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advantageous to withdraw these patients from mechanical ventilation as early as possible. Early extubation is a key component to reducing complications relating to longterm mechanical ventilation, and development of early extubation protocols may be of value to practitioners as it may help reduce the patient's length of stay (LOS) in the ICU and in the hospital, resulting in decreased hospital costs and ultimately improved patient outcomes[11].Extended LOS in the ICU increases the risk for development of delirium with subsequent adverse events,5 and ICUs have a higher overall risk of infection when compared with the general floors[12].Total hospital LOS itself is associated with more costly care and increased incidence of postoperative complications[13].The use of dexmedetomidine or propofol may also affect hospital mortality rate due to the hemodynamic implications attributed to their pharmacodynamics. Dexmedetomidine, although fairly new, has been accepted and expanded for use in postoperative cardiac surgery patients. The unique properties of dexmedetomidine make it desirable in postoperative cardiac surgery patients because it lacks the effects of respiratory depression, has potential for decreased opioid use and functions as a sympatholytic. These favorable characteristics could lead to patients having decreased times to extubation, decreased ICU Length of stay and overall decreased hospital Length of stay. Although propofol is still widely used as a postoperative sedative, recent randomized controlled trials and retrospective studies comparing the effects of dexmedetomidine compared to propofol on times to extubation in postoperative adult cardiac surgery patients support dexmedetomidine as an effective alternative drug choice for short-term postoperative sedation for mechanical ventilation [8,14,15].However, studies comparing the drugs' effects on ICU Length of stay, total hospital Length of stay and and mortality rates have showed conflicting results. Major risk factors that contribute to lung injury are due to high tidal volumes and barotrauma. Most cardiovascular and respiratory surgery patients remain on the ventilator postoperatively due to the high dose opioid-based anesthesia and the initial vulnerable hemodynamic state. An important component of postoperative management following surgeries is the use of sedation to reduce the stress response, facilitate assisted ventilation, and provide anxiolysis.

A retrospective study was done to assess the effectiveness of dexmedetomidine over propofol on extubation.

Objective: To determine the effectiveness of dexmedetomidine over propofol on extubation time in intensive care unit (ICU) admitted patients.

Methods: This study was a retrospective observational study looking at the time to extubation postoperatively, when comparing patients who received dexmedetomidine versus propofol as primary sedative agent.This analysis was conducted following approval by the institutional ethical board.

The institutions medical records and pharmacy billing system were reviewed to identify patients who had received propofol or dexmedetomidine in the cardiovascular intensive care unit.

Inclusion criteria: The inclusion criteria were adult patients, 18 years of age or older, located in the cardiovascular ICU, requiring mechanical ventilation on arrival to the ICU, and who received either a dexmedetomidine or propofol infusion intraoperatively and postoperatively in addition to general anesthesia medications. Patients who underwent valve repair or replacement, coronary artery bypass grafting (CABG), or CABG plus valve repair or replacement surgery were included.. The patients were all open-heart surgery patients.

Exclusion criteria: Patients were excluded if they were pregnant or lactating, incarcerated, or received both dexmedetomidine and propofol concurrently intraoperatively or postoperatively, with the exception of an induction dose of propofol at the start of the case. All variations of dosages and duration of both sedative agents were included.

Outcomes of interest were:

Primary and Secondary Outcomes

The primary end point was time to extubation postoperatively, when comparing patients who received dexmedetomidine versus propofol as the primary sedative agent. The time was measured in minutes, from when the patient left the operating room, as recorded in the anesthetic record, to the time of extubation in the CVICU documented by the respiratory care team. The primary end point of time to extubation postoperatively was only assessed on the initial extubation attempt. Secondary outcomes included ICU and hospital length of stay from the index cardiac procedure and incidence of delirium identified by the presence of 1 confusion assessment method for the ICU (CAM-ICU) positive score[16]

Number of deaths were included as a secondary outcome between both treatment groups. The primary and secondary outcomes were defined a priori.

Assesment of effectiveness of sedation – RASS score.

During cardiac surgery, the patient's goal RASS - The Richmond agitation sedation scale, an instrument to assess sedation and agitation of adult ICU patients,is -5 for full general anesthesia. A RASS of -5 is defined as the patient having no response to voice or physical stimulation.

Typically,general anesthesia is maintained with a volatile anesthetic agent, either with a vaporizer attached to the ventilator, or through direct administration into the cardiopulmonary bypass circuit. Addition of an intravenous sedative such as propofol or dexmedetomidine may be used to supplement this. We do not have a protocol in place that guides the practice of administration of these agents; rather, it is left up to the discretion of the attending anesthesiologist. They may choose to administer these intraoperatively, especially when they plan to continue them postoperatively. Intraoperative paralytics, sedation, analgesia, inotropes, vasopressors, and blood products were collected. Postoperatively, sedation and mechanical ventilation were weaned per unit protocols based on hemodynamic parameters, surgical bleeding, and temperature normalization. If the patient was not having any clinically significant bleeding or hemodynamic instability, ventilator settings were weaned to target extubation within 6 hours of presentation to the cardiovascular ICU. The RASS goal postoperatively would be -2 to -1 on arrival to the cardiovascular ICU and a goal of 0 once the patient is warmed and stable. Patients are passively and actively warmed to achieve normothermia, at which point reversal of neuromuscular blockage is ensured, with administration of glycopyrrolate and neostigmine.The RASS goal of -2 to -1 is maintained with either propofol or dexmedetomidine with the addition of opioids to supplement for analgesia[17].

Statistical Analysis

Patient demographics, medical history, intraoperative clinical data, and outcomes were summarized with the mean(SD) and median (25th,75th percentiles) for continuous variables, and with percentages for categorical variables.Unadjusted comparisons between patients who received dexmedetomidine versus propofol were performed using the Wilcoxon rank sum test for continuous variables and the Pearson $\chi 2$ test for categorical variables.All analyses were performed using the SPSS Software version 16.0. Results were considered statistical significant at the p value of 0.05 significance level.

Results

There were 80 patients who received Dexmedetomidine and 120 with Propofol for the sedation in those who underwent cardiac surgeries , out of the 200 study group patients.

Mainly the surgeries were Coronary artery bypassgraft (VABG) and Valve repair surgeries and both types , in the department of Cardiology and cardiovascular ICUs requiring mechanical ventilation support (Intubation). In the group of CABG , 65% patients received Dexmedetomidine and 65% Propofol and 25% received Dexmedetomidine and 18.3% received Propofol in Valve surgery

patients . In the patients who were admitted to ICUs undergoing both CABG and Valve surgeries ,10% received Dexmedetomidine and 16.7% received Propofol.

Table 1: Intraoperative Clinical Variables.

	Dexmedetomidine, n= 80	Propofol, n= 120	P value
Procedure			0.028
CABG	52(65.0%)	78(65.0%)	
Valve Surgery	20(25.0%)	22(18.3%)	
Both	8(10.0%)	20(16.7%)	
1. Operating Room duration, minutes	310	280	
2. Intraoperative medications:			
Dexmedetomidine, total (mg)	0.11(0.095±0.066)	0	<0.01
Propofol, mg	0	208(247±180)	<0.01

Around 310 minutes was the duration of operative procedure and 280 minutes in the group of Dexmedetomidine and Propofol groups respectively.The dosage of Dexmedetomidine was around 0.11 mg in total for all the days and around 208 mg for propofol for all the days.

Procedures

Mainly the time to extubation was considered as the primary outcome assessment and other variables like total length of stays in days for ICU and Hospital , and the percentage of patients with delirium symptoms post sedation and the number of deaths occurred, were considered as the secondary outcomes of the two drugs in comparison , while the extubation.

Table 2: Clinical Outcomes by Treatment.

Clinical Outcomes by Treatment.	**Dexmedetomidine, n= 80**	**Propofol,n= 120**	**P value**
Primary outcome:Time to extubation, minutes	360 (330±1220)	420(390±2200)	<0.001
Secondary outcomes			
ICU LOS, days	4(4.1±2.2)	4(4.2±2.1)	0.88
Hospital LOS days	7(7.9±3.3)	7(8.5±4.3)	0.55
Delirium, n (%)	7(9)	28(18)	0.21
Delirium, days	0(0.11±0.78)	0(0.31±0.58)	0.22
Death, n	1	1	0.44

Discussion

When compared with patients who received propofol based sedation, patients who received dexmedetomidine-based sedation regimens intraoperatively and postoperatively had an association with a decreased time to extubation, with no difference in the incidence of delirium or ICU and hospital length of stay. Our findings add additional insight into the published literature that currently only focuses on postoperative sedation plans to decrease the morbidity with prolonged intubation times.A study by Chuich et al ,[18] revealed similar results as that of the current study comparing the two drugs, retrospectively,where a similar outcome measures were analysed. The primary outcome being the time for extubation was found to be 425 minutes for Propofol and 357 minutes for dexmedetomidine. The secondary outcomes were ICU and Hospital Length of stay of about average 4 days and 7 days respectively in both the drug groups . The group which received dexmedetomidine had less delirium symptoms than the propofol group.

A study by Tsai et al [19]that looked at patients and surgery related factors that affect time to recovery of consciousness in elective cardiac surgery found similar results because their retrospective study demonstrated that older age and longer bypass duration were significant independent risk factors for delayed emergence. Their study also found lower body mass index, male gender, and higher preoperative blood urea nitrogen to be additional risk factors. The study though did not focus on anesthetic agents utilized, andtiming of recovery of consciousness was questionable because this data point depended on nursing staff.There is no consensus in regard to decreased time to extubation in patients given dexmedetomidine versus alternative sedation regimens. Chorney et al[20]showed that there was no difference in the time to extubation when dexmedetomidine was compared with no routine postoperative sedation (4.7 vs 3.9 hours, $P = 0.16$) in post–cardiac surgical patients.

In contrast, a larger retrospective analysis by Curtis et al[2]evaluated nearly 2 years of data comparing patients who received propofol-based or dexmedetomidine based sedation after cardiac valve or CABG surgery and who did not undergo prolonged surgery.

A total of 582 patients were included in the study, which showed a decreased time to extubation (8.8 vs 12.8 hours, $P = 0.026$), decreased hospital LOS (181.9 vs 221.3 hours, $P = 0.001$),and early extubation (200 vs 169 patients, $P = 0.008$), defined as postoperative extubation of less than or equal to 6 hours in patients who received dexmedetomidine.

Finally,a retrospective cohort study by Wanat et al[1],examined 352 patients admitted to the ICU after cardiac surgery who received either dexmedetomidine or propofol infusions postoperatively. The study showed a decreased duration of mechanical ventilation (7.37±4.30vs12.88±15.42
hours, $P = 0.042$) with no difference in hospital or ICU length of stay in the dexmedetomidine group.

Instead of looking at postoperative sedation only, our aim was to look at the total perioperative (intraoperative and postoperative) treatment of the cardiac surgery patients.

The patients in both groups received very similar agents intraoperatively, with no difference noted in cumulative doses of fentanyl, succinylcholine, rocuronium, or etomidate. In the dexmedetomidine group, the patients did receive induction with propofol but were never placed on a continuous infusion of propofol.

In addition, the dexmedetomidine group received statistically more ketamine and less midazolam than the propofol group, although the dose variations are not clinically significant. As a potential marker for the hemodynamic stability between both sedation groups, the vasopressor and inotrope requirement did not differ based on weight-based dosing schemes. Our study did not directly look at vital signs and adverse effects given multiple confounders intraoperatively. Our

study did include tobacco use as a prespecified covariate in the analysis of time to extubation, ICU discharge, hospital discharge, and delirium, and its effect was not statistically significant. Although the authors recognize this limitation in the imbalance in the baseline characteristics, accounting for tobacco use as a covariate with no effect on our primary and secondary outcomes makes the chance of this changing our primary outcome result unlikely.

Limitations

1. The limitations include the retrospective single-center analysis completed at an academic medical center. The decision to use either dexmedetomidine or propofol was made solely at the discretion of the intraoperative anesthesiologist and, as such, may be subject to additional unmeasured confounders. In addition, we did not collect data regarding volatile inhaled anesthetics.

2.The ICU length of stay was determined based on when the patient was transferred from the ICU to the cardiac surgery stepdown floor. There is limited bed availability given a large patient volume, so regardless of whether step-down orders were placed,if the patient remained in the ICU,those days w ere factored into ICU length of stay.

3.Given multiple confounding factors, our study did not look at the safety of dexmedetomidine from an adverse effect profile.

4. Although the time of day of surgery completion could affect the time to extubation, our staffing model includes 24-hour ICU physician and respiratory therapy coverage and no restrictions on timing of extubation, which should mitigate this effect.

5. An additional limitation would be our inability to classify the patients as elective or emergent surgical patients to clarify the severity of illness of the patient population studied.

6. Finally, although the time to extubation was decreased by 1 hour a cost analysis was not performed to determine the economic impact of using intraoperative and postoperative dexmedetomidine.

Conclusion

In this single-center retrospective analysis, intraoperative and postoperative dexmedetomidine was associated with earlier extubation in the cardiac surgery patient population, with no effect on ICU or hospital length of stay. Additional factors, including operating room duration, older age, the receipt of blood products, and presence of delirium, contributed to prolonged ventilation times.

Application of the data might allow for strategies to modify patient's risk factors to decrease their time to extubation. Dexmedetomidine-based regimens could serve as a suitable alternative to propofol-based regimens for fast track extubation.

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