

Comparison of Intensive Care Unit Sedation Using Dexmedetomidine, Propofol, and Midazolam

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Abstract

Introduction: This study compares the effectiveness of dexmedetomidine for the sedation of patients admitted to our intensive care unit (ICU) with propofol and midazolam in respect to tracheal extubation and length of stay in ICU and to study changes in heart rate (HR), mean arterial pressure, SpO₂ during and after sedation.

Materials and Methods: A total of 90 patients randomized into three groups of 30 to receive either dexmedetomidine, propofol, or midazolam drug. The dexmedetomidine group loading dose was 0.5-1 µg/kg per 10 min, followed by maintenance infusion at 0.1-1 µg/kg/h. The propofol group received a loading dose of 0.5-1 mg/kg followed by an infusion of 25-75 mcg/kg/min. The midazolam group received an infusion of 0.012-0.024 mg/kg/h. Respiratory rate, HR, blood pressure, Ramsay sedation score, tramadol need, saturation, time to extubation, duration in ICU were monitored and recorded all through the ICU stay.

Results: Hypotension occurred in 6.4% patients in dexmedetomidine group, 14.22% in propofol group, and 5% in midazolam group. Bradycardia occurred in 7.5% patients receiving dexmedetomidine at the time of loading of drug. During sedation mean pulse rate in dexmedetomidine group was 77.54 ± 9.34, in propofol group 89.34 ± 10.1 and for midazolam group 90.23 ± 10.7. Reduced time to tracheal extubation for dexmedetomidine group (7.4 ± 1.85) h, for propofol (5.6 ± 1.56) h compared to midazolam (16.9 ± 15.62) h.

Conclusion: Dexmedetomidine is a satisfactory agent for sedation in ICU. Dexmedetomidine provides hemodynamic stability and has no clinically important adverse effects on respiration. The mean time from cessation of sedation to tracheal extubation was shorter for dexmedetomidine and propofol treated patients than from midazolam treated patients.

Key words: Anaesthesia, Dexmedetomidine, Diastolic blood pressure, Heart rate, Midazolam, Propofol, Respiratory rate, SpO₂, Systolic blood pressure, Time to tracheal extubation

INTRODUCTION

Patients in an intensive care unit (ICU) are exposed to a variety of noxious stimuli including pain after surgery, frequent venipuncture, and discomfort from the presence of an endotracheal tube. Sedation is frequently required as a component of compassionate care in these patients. Promotion of rest and sleep in critically ill patients facilitates healing. Multisystem adverse effects of sleep deprivation have been reported. Physical activity also plays a pivotal role in recovery and long-term outcomes.

Other goals of adequate sedation include optimizing safety for patients and caregivers, facilitating mechanical ventilation, reducing anxiety and delirium, inducing sleep, and, ultimately, providing comfort and safety.

The sedatives used most often include propofol and midazolam. These medications provide adequate sedation but also can cause oversedation. Oversedation can lead to prolonged duration of mechanical ventilation, longer ICU and hospital stays, increased incidence of ventilator-associated pneumonia, and inability of patients to communicate with health-care providers or family members.

Undersedation is also harmful and can lead to anxiety, ventilator dyssynchrony, dislodged equipment, delirium, increased oxygen consumption, and hyperactivity. Making the distinction between too much sedation and not enough sedation can sometimes be difficult when propofol and midazolam is used.

Access this article online



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Month of Submission : 11-2016
Month of Peer Review : 12-2016
Month of Acceptance : 12-2016
Month of Publishing : 01-2017

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For decades, gamma-aminobutyric acid (GABA) receptor agonists (including propofol and benzodiazepines such as midazolam) have been the most commonly administered sedative drugs for ICU patients worldwide. Despite the well-known hazards associated with prolonged use of GABA agonists, few investigations of ICU sedation have compared these agents to other drug classes. Instead, the recent focus in the practice of critical care sedation has been on nurse-implemented algorithms and drug-interruption protocols to optimize drug delivery, regardless of class. These protocols and algorithms are promising but not uniformly beneficial, and their adoption into routine practice has been slow.

Inadequate sedative techniques may adversely affect morbidity and even mortality in the ICU, and the search for the ideal sedative agent continues. The ideal agent should satisfy the physician's desire for an effective, safe, titratable, cheap, and rapidly acting drug that has both sedative and analgesic properties and should also prevent anxieties and unpleasant memories for the patient. The published accounts of patients' recollections of the ICU are on the whole reassuring, but adverse experiences, such as physical discomfort from procedures, inability to communicate and lack of sleep, continue to feature prominently. Thus, when a new sedative agent is compared with the currently used sedative drugs in the ICU, its pharmacokinetic and pharmacodynamic properties will, of course, be contrasted. More importantly, both the physician's and the patient's perceptions of its efficacy require investigation.

The alpha-2 agonist dexmedetomidine is a new sedative and analgesic agent which has been licensed recently in the USA as ICU sedation for up to 24 h after surgery. Dexmedetomidine provides 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. We therefore compared the sedative and analgesic properties, safety profile, cardiovascular responses, ventilation and extubation characteristics, and patient perceptions of dexmedetomidine with those of the commonly used agents propofol and midazolam in the ICU.

MATERIALS AND METHODS

Trial Design

After approval from Ethical Committee and written informed consent of the patient, 90 patients of both gender were recruited for the study. This study was randomized. Open label trial conducted in the ICU in Basaveshwar Teaching and General Hospital, Kalaburagi. ICU has

24 h coverage by resident house staff. Assessment as to whether patients would require sedation for short term (<24 h), medium term (>24-<72 h) or long term >72 h) mechanical ventilation on admission to ICU was done. Patients stratified by predicted sedation time while receiving mechanical ventilation were randomized and were entered into trial.

Eligibility Criteria

Inclusion criteria

- Patients of either gender
- Patients >18 years of age
- Patients who require immediate sedation as to permit the initiation and tolerance of mechanical ventilation.

Exclusion criteria

- Known or suspected allergy or intolerance to dexmedetomidine, propofol or midazolam
- Pregnancy
- Head injury
- Patient currently treated with or been treated with alpha-2 agonist and blockers
- Status epilepticus
- Coma due to cerebrovascular accidents or unknown etiology
- Acute unstable angina
- Acute myocardial infarction.

Material used

- i. Injection dexmedetomidine
- ii. Injection propofol
- iii. Injection midazolam.

Method

Patient enrolled in the study divided into three groups. There are 30 patients allocated for each group.

Group 1: Patient randomized in dexmedetomidine group received a loading dose of dexmedetomidine 0.5-1 mcg/kg over 10 min followed by a maintenance infusion of 0.1 to 1 mcg/kg/h. The rate of the maintenance was subsequently titrated to achieve a target Ramsay sedation score that was specified for each for each patient response to therapy.

Group 2: Patients randomized to the propofol group received a loading dose of 0.5-1 mg/kg then an infusion of 25-75 mcg/kg/min was adjusted to achieve the target Ramsay sedation score. As for the propofol group in situations in which rapid control of sedation was required an infusion bolus could be administered.

Group 3: Patients randomized in midazolam group received an infusion of 0.012-0.024 mg/kg/h adjusted to achieve

the target Ramsay sedation score. Situations in which rapid control of sedation was required an infusion bolus could be administered.

Only tramadol 1 mg/kg was given to patients of all the three groups as analgesic agent.

Measurement Scales

The Ramsay sedation score was used to quantitate the desired degree of sedation, specified at the regular intervals and adjusted as the patient's condition (i.e., recovery or deterioration) dictated. Patients were maintained at Ramsay sedation score of >2 by adjustments to the sedative regimens. Patients receiving muscle relaxants and sedation were given a Ramsay sedation score of 6.

Measurements

The Ramsay sedation score (target and actual) was recorded hourly for the first 72 h or up to the time of discharge from ICU if this occurred before 72 h. After 72 h, it was recorded as the patient's condition or infusion rate was altered. Time to tracheal extubation, time to ICU discharge and requirements of reintubation were recorded. A record of vital signs was maintained every 20 min for 40 min, then every 6 h for 48 h following extubation or until ICU discharge, whichever comes first. Decisions as to when a patient was ready for a trial of extubation or for discharge from the ICU were left to the attending intensivists.

Ramsay described Ramsay sedation scale to judge sedation level in critically ill patients.

Ramsay Sedation Score

Awake

1. Anxious and/or agitated
2. Cooperative, oriented and tranquil
3. Response to command.

Asleep

1. Quiescent with brisk response to light glabellar tap or loud auditory stimulus
2. Sluggish response to light glabellar tap or loud auditory stimulus
3. No response.

Complications which occurred as a result of patient's conditions, mechanical ventilation or infusion of sedative agent were recorded in all the three groups.

Primary Outcome Measures

The time from withdrawal of sedation until tracheal extubation and ICU discharge for each stratum was taken as the primary outcome measures. The situations in

which patients required multiple independent periods of sedation or reintubation due to alterations in their disease processes, the first period of sedation accompanied by tracheal extubation was utilized for data collection surrounding this event. Data were collected for the duration of the patient ICU stay. ICU length of stay was recorded as the time from admission to ICU until the patient was discharged.

Statistical Analysis

All statistical analyses were performed using INSTAT for windows. Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Data were expressed as either mean and standard deviation or numbers and percentages. All the data were compared with one-way analysis of variance (ANOVA).

RESULTS

These Table 1 and Figure 1 show distribution of patients according to age in all groups. The mean and standard deviation of age in all groups have been demonstrated. There was no statistically significant difference in age distribution in any group ($P > 0.05$).

M:F ratio for dexmedetomidine = 1.3:1

M:F ratio for propofol = 1.5:1

M:F ratio for midazolam = 1.4:1

Male = 51 female = 39 Total = 90 (Table 2 and Figure 2).

Table 1: Age distribution

Age (years)	n (%)		
	Dexmedetomidine	Propofol	Midazolam
18-30	8 (26)	12 (40)	9 (30)
31-45	12 (40)	9 (30)	10 (34)
46-60	10 (34)	9 (30)	11 (36)
Mean	37.03	36.7	37.9
Standard deviation	12.75	12.18	12.48

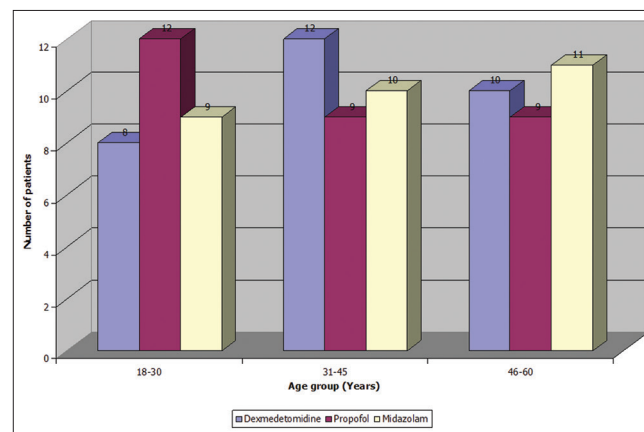


Figure 1: Age distribution

These Table 3 and Figure 3 show distribution of patients according to weight in all age groups.

- The mean and standard deviation of weight in all age groups have been demonstrated.
- There was no significant difference in weight distribution in any age group ($P > 0.05$).

P value is calculated by one-way ANOVA. Baseline pulse rate in all three groups is not statistically significant ($P > 0.05$).

During Sedation

P value during sedation is <0.001 means statistically significant difference is present among the groups.

From Stoppage of Sedation of Extubation

$P < 0.001$ means statistically significant difference is present among the groups.

At Extubation

$P < 0.001$ means statistically significant difference is present among the groups.

From Extubation to ICU Discharge

$P > 0.05$ means there is no significant difference present among the groups (Table 4 and Figure 4).

This Table 5 shows the mean changes in respiratory rate in all groups. The difference in respiratory rate was not significant at baseline, during sedation, from stoppage of sedation to extubation and extubation to ICU discharge. Difference among the groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

These Table 6 and Figure 5 show the mean changes in systolic blood pressure (SBP) in Dexmedetomidine, propofol, and midazolam group.

Table 2: Sex distribution

Sex	n (%)		
	Dexmedetomidine	Propofol	Midazolam
Male	17 (56)	18 (60)	16 (54)
Female	13 (44)	12 (40)	14 (46)
Total	30	30	30

Table 3: Weight distribution

Weight (kg)	n (%)		
	Dexmedetomidine	Propofol	Midazolam
35-54	8 (26)	9 (30)	12 (40)
55-74	13 (44)	12 (40)	9 (30)
75-95	9 (30)	9 (30)	9 (30)
Mean	64.56	64.3	62.2
Standard deviation	13.02	15.7	14.11
Total	30	30	30

At all times, the difference is SBP among all the three groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

These Table 7 and Figure 6 show mean changes in diastolic BP in dexmedetomidine, propofol, and midazolam group. At all times, the difference is SBP among all the three groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

These Table 8 and Figure 7 show mean changes in mean BP in all the three groups. At all times difference in mean BP among all the three groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

This Table 9 shows mean changes in SPO_2 dexmedetomidine, propofol, and midazolam group. At all times the difference in SPO_2 , BP among all the three groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

This Figure 8 shows the mean time (h) from cessation of sedation to extubation for dexmedetomidine is 7.4 h, for propofol is 5.6 h and for midazolam is 16.9 h.

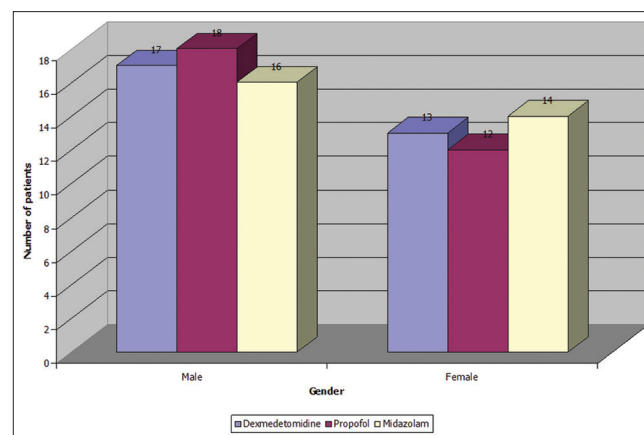


Figure 2: Sex distribution

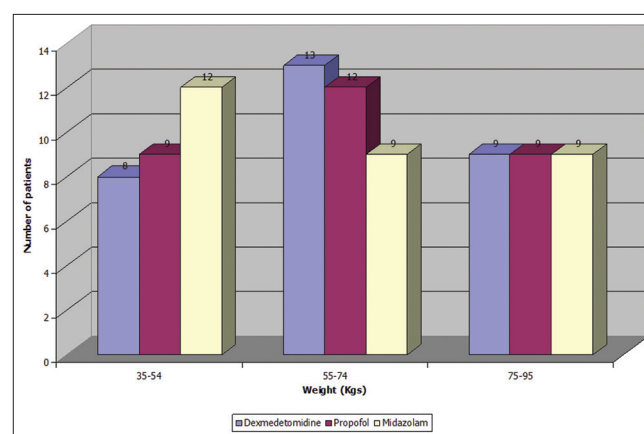


Figure 3: Weight distribution

Table 4: Mean changes in pulse rate

Sedative used/ SD of PR	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	92.00	78.26	83	84.7	89.21
Standard deviation	3.7	4.97	2.56	2.27	0.75
Propofol	92.26	85.66	92.33	94.23	92.49
Standard deviation	3.55	3.02	1.74	1.47	0.84
Midazolam	92.6	84.93	93.86	94.4	92.45
Standard deviation	3.64	2.21	1.814	1.32	0.85
P value	>0.05	<0.0001	<0.0001	<0.0001	>0.05

ICU: Intensive care unit, SD: Standard deviation

Table 5: Mean changes in systolic blood pressure

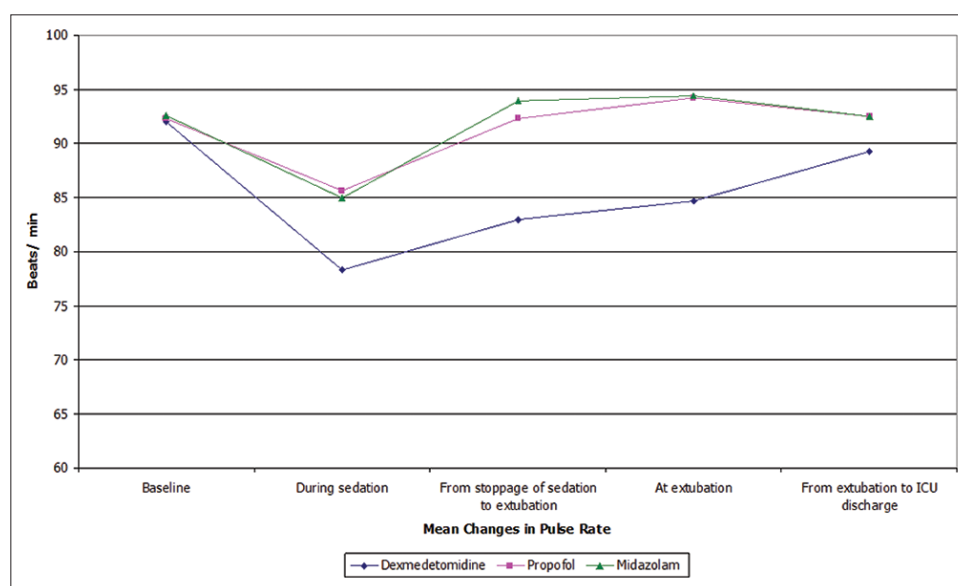
Sedative used/ SD of SBP	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	132.7	121.6	125.8	126.9	119.8
Standard deviation	11.1	8.61	8.88	9.47	9.5
Propofol	134.8	118.8	127.4	128.2	121.4
Standard deviation	11.5	10.1	10.09	10.10	9.26
Midazolam	134.3	123.6	126.9	128.4	122.9
Standard deviation	15.2	8.79	9.74	8.78	9.17
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

Table 6: Mean changes in respiratory rate

Sedative used/ SD of RR	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	18.83	13.93	14.5	14.46	14.6
Standard deviation	1.36	0.78	0.5	0.5	0.56
Propofol	18.46	14	14.56	14.5	14.5
Standard deviation	2.36	0.83	0.5	0.5	0.50
Midazolam	18.56	13.93	14.53	14.56	14.53
Standard deviation	1.04	0.78	0.5	0.5	0.50
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

**Figure 4: Mean changes in pulse rate**

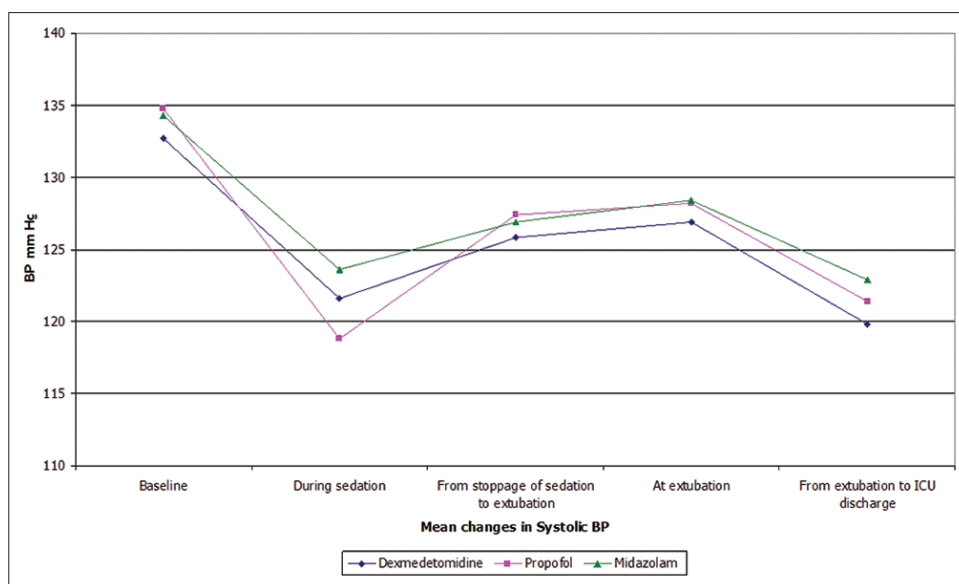


Figure 5: Mean changes in systolic blood pressure

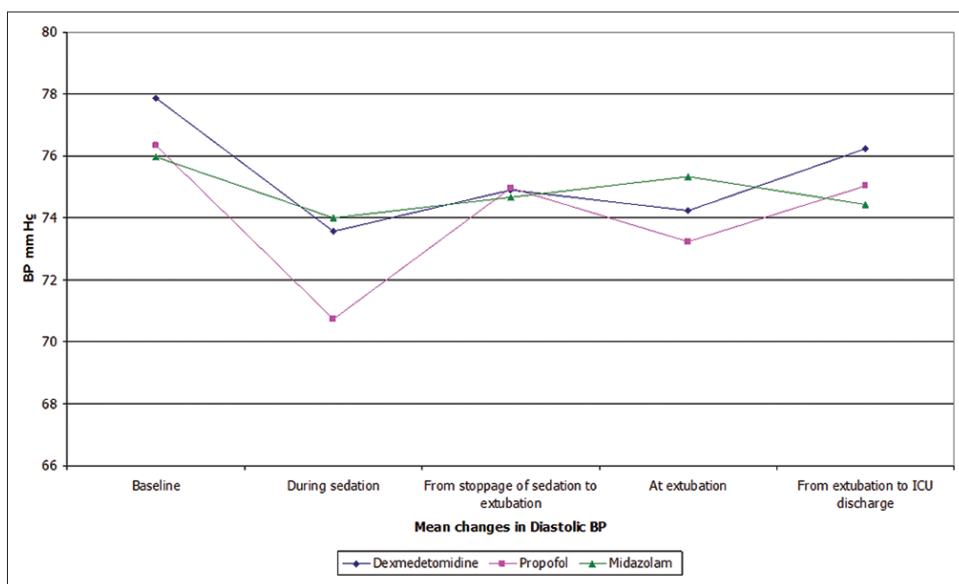


Figure 6: Mean changes in diastolic blood pressure

P value of dexmedetomidine, propofol, and midazolam group is <0.001 , which is statistically significant.

This Figure 9 shows cessation of sedation to ICU discharge for dexmedetomidine its 83 h for propofol is 92 h and for midazolam it is 78 h.

P value calculated by ANOVA test among all the three groups is >0.05 which is statistically not significant.

DISCUSSION

This study was considered to assess the efficacy of a new drug dexmedetomidine with propofol and midazolam,

established i.v., sedative agent regularly used in ICU in terms of changes in vitals, duration of extubation ICU discharge and complications.

The alpha-2 agonist dexmedetomidine is a new sedative and analgesic agent which has been licensed recently in the USA as ICU sedation for up to 24 h after surgery. Dexmedetomidine provides 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. We therefore compared the sedative and analgesic properties, safety profile, cardiovascular

Table 7: Mean changes in diastolic blood pressure

Sedative used/ SD of DBP	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	77.87	73.56	74.89	74.23	76.22
Standard deviation	8.40	7.40	7.26	6.96	6.01
Propofol	76.32	70.75	74.98	73.23	75.04
Standard deviation	7.56	7.56	6.47	7.14	6.90
Midazolam	75.98	73.99	74.67	75.33	74.44
Standard deviation	8.03	7.48	6.95	7.36	6.09
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

Table 8: Mean changes in mean blood pressure

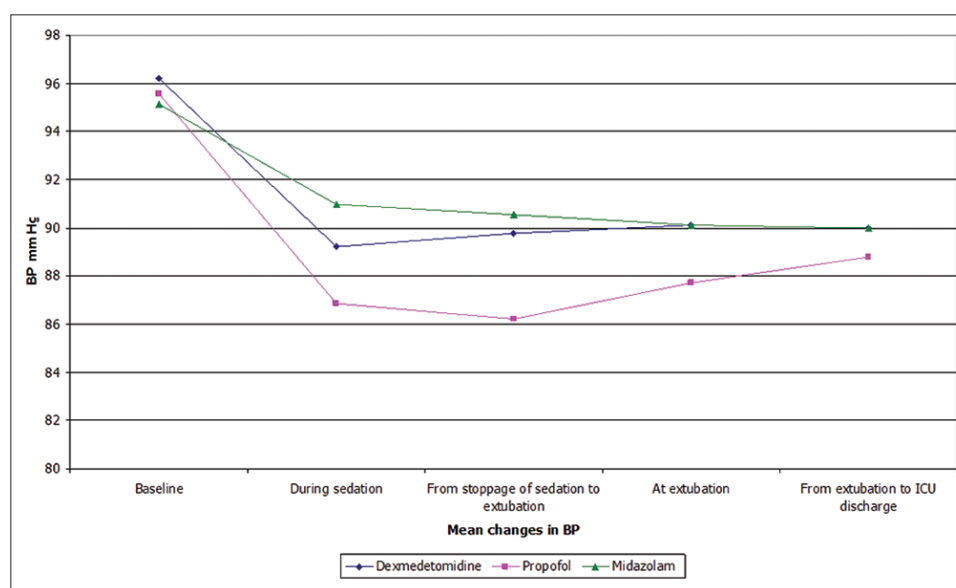
Sedative used/ SD of MBP	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	96.21	89.23	89.78	90.11	89.98
Standard deviation	5.98	6.11	6.07	7.46	4.69
Propofol	95.56	86.86	86.21	87.73	88.78
Standard deviation	6.85	5.48	4.38	5.27	5.69
Midazolam	95.11	90.99	90.54	90.11	89.99
Standard deviation	7.91	6.49	6.17	6.11	5.42
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

Table 9: Mean changes in SpO₂

Sedative used/ SD of SpO ₂	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	98.33	98.78	98.21	98.99	98.11
Standard deviation	0.95	0.68	0.71	0.64	0.63
Propofol	97.6	98.21	98.34	98.22	98.1
Standard deviation	1.08	0.58	0.66	0.63	0.63
Midazolam	96.99	97.1	98.34	98.21	98.85
Standard deviation	0.93	0.62	0.63	0.60	0.66
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

**Figure 7: Mean changes in mean blood pressure**

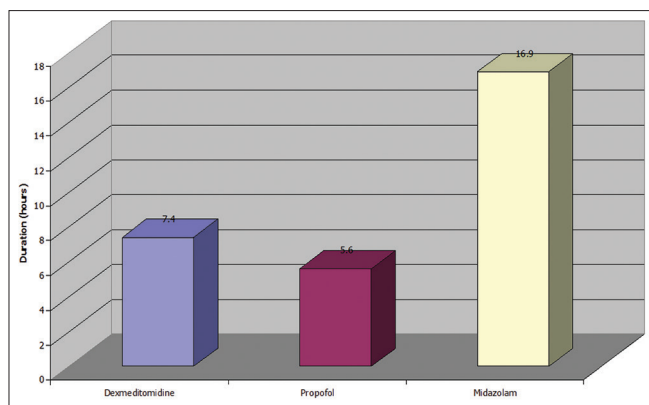


Figure 8: Duration from cessation of sedation to extubation

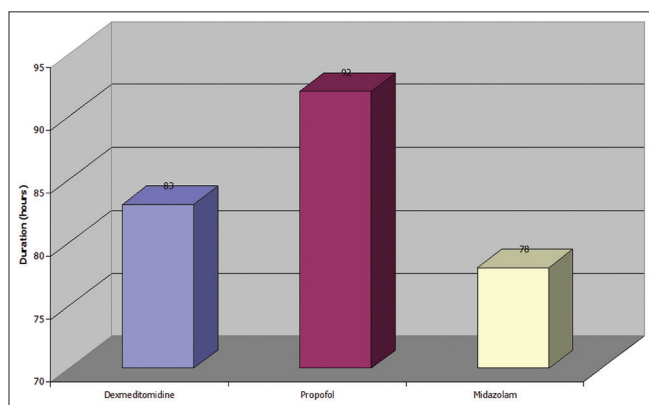


Figure 9: Duration from cessation of sedation to intensive care unit discharge

responses, ventilation and extubation characteristics, and patient perceptions of dexmedetomidine with those of the commonly used i.v. sedative agent propofol and midazolam in the ICU.

On analyzing the demographic data, the three groups were statistically comparable with respect to age, sex, and weight.

The patients in this study were of gynecological and obstetrical cases, emergency laparotomy cases, trauma cases, post-operative routine cases, aspiration pneumonia cases, and COPD cases.

The groups were studied and compared with respect to:

- Duration of sedation ICU length of stay
- Changes in cardiovascular and respiratory status
- Any complications.

In this trail, the use of dexmedetomidine propofol and midazolam for sedation in patients in the ICU was associated with reduced time to tracheal extubation for dexmedetomidine (7.4 ± 1.85) h, for propofol (5.6 ± 1.56) h compared to midazolam (16.9 ± 15.62) h.

P value between dexmedetomidine and propofol group is >0.05 which is statistically not significant.

P value between dexmedetomidine and midazolam group is <0.001 which is highly significant. *P* value between propofol and midazolam group is <0.001 which is patients on dexmedetomidine and propofol having shorter extubation times than with the midazolam. Study done by Anger *et al.*¹ concluded that management of pain and sedation therapy is a vital component of optimizing patient outcomes; we sought to evaluate efficacy and safety outcomes between post-operative mechanically ventilated cardiac surgery patients receiving dexmedetomidine versus propofol therapy on arrival to the ICU. No differences in the ICU length of stay and duration of mechanical ventilation were seen between the propofol and dexmedetomidine groups, respectively. Reichert *et al.*² concluded that no statistically significant differences were noted between the propofol and dexmedetomidine groups when assessing the outcomes of opioid requirements and the time to extubation, above-mentioned both studies shows that no significant difference in the time to extubation after stoppage of sedation as this is also the finding of our study that there was no significant difference in the time to extubation. Aitkenhead *et al.*³ concluded that desired level of sedation was achieved easily in most patients in both groups. There were slight falls in arterial pressure, but there were no significant differences between the groups. Heart rate (HR) was lower in patients who received propofol. When the infusion was discontinued, there was less variability, in recovery of consciousness in patients who had received propofol. In a subgroup of patients, weaning from mechanical ventilation was achieved significantly faster after discontinuation of propofol than of midazolam. Grounds *et al.*⁴ concluded that propofol infusion allowed rapid and accurate control of the level of sedation which was satisfactory for longer than with midazolam, patients given propofol recovered significantly more rapidly from their sedation once they had fulfilled the criteria for weaning from artificial ventilation and as a result spent a significantly shorter time attached to a ventilator. There were no serious complications in either group. This study is in accordance to our study in which we found that significant difference is present in weaning the patient from mechanical ventilator after stoppage of sedation. Midazolam took longer time in weaning.

In our study, we found that patients receiving dexmedetomidine have significantly lower HR compare to propofol and midazolam, during sedation mean pulse rate in dexmedetomidine group was 77.54 ± 9.34 , in propofol group 89.34 ± 10.1 and for midazolam group 90.23 ± 10.7 .

During sedation with dexmedetomidine, propofol and midazolam $P < 0.001$ which is highly significant.

Hence, it clearly showed in our study that dexmedetomidine infusion leads to reduction in HR during sedation as it is statistically significant when compared with propofol and midazolam. Hoy and Keating⁵ concluded that intravenous dexmedetomidine is generally well tolerated when utilized in mechanically ventilated patients in an intensive care setting and for procedural sedation in non-intubated patients. While dexmedetomidine is associated with hypotension and bradycardia, both usually resolve without intervention. Eren and Cukurova⁶ concluded that dexmedetomidine was as effective as higher doses of midazolam in sedation. The hemodynamic and respiratory effects were minimal. Although dexmedetomidine caused significant decrease in the BP and HR, it probably just normalized increased levels caused by preoperative stress. Venn *et al.*⁷ who demonstrated statistically significant reduction in pulse rate in patients receiving dexmedetomidine infusion in the ICU. After discontinuation of sedation HR was initially lower in patients receiving dexmedetomidine, but after a return to baseline in these patients, there was no difference among the groups ($P \sim 0.15$).

All of the above studies showing that dexmedetomidine infusion leads to reduction in HR which is in accordance to our study which also shows that patients receiving dexmedetomidine infusion having lower HR.

In our study during the sedation with dexmedetomidine, propofol and midazolam there was no significant effect on respiratory rate was noted ($P > 0.05$). Hoy and Keating⁵ concluded that intravenous dexmedetomidine is generally well tolerated when utilized in mechanically ventilated patients in an intensive care setting and for procedural sedation in non-intubated patients. It is not associated with respiratory depression.

Arain and Ebert⁸ concluded that during sedation with dexmedetomidine and propofol; there was hemodynamic variables (HR and mean arterial BP), sedation, bispectral index score of sedation, ventilation (respiratory rate, O_2 sat, and $ETCO_2$) were determined during surgery and up to 95 min after surgery. Intraoperative sedation levels were targeted to achieve a bispectral index score of 70-80; patient baseline cardiorespiratory variables were similar between groups. There were no differences between groups in psychomotor performance and respiratory rate during recovery. Hence, this study also supports our outcome that dexmedetomidine and propofol not significantly affect respiratory rate during and after sedation in the period of recovery. Hsu and Cortinet (2004) concluded that dexmedetomidine infusions (1) did not result in clinically significant respiratory depression, (2) decreased rather than increased the apnea/hypopnea index, and (3) exhibited some similarity with natural sleep.

Arterial pressures were reduced in dexmedetomidine, propofol, and midazolam sedation. The difference in arterial pressure between all the three groups during sedation was found to be statistically not significant ($P > 0.05$). Stephan and Sountag propofol alone decreased mean arterial pressure and cardiac index; HR was increased. Myocardial blood flow and myocardial oxygen consumption were decreased by 26% and 31%, respectively. This result is in accordance of our study where arterial pressure reduced during propofol sedation. Ebert *et al.*⁹ propofol infusions significantly lowered sympathetic nerve activity and BP and increased HR. Cardiac baroreceptor sensitivity determined during nitroprusside was reduced 60% during propofol infusions. The above-mentioned studies show that there is reduction in arterial pressure after propofol sedation which our study also showed. Hence, our study is in accordance to the studies above. Sunzel and Paalzow concluded that a maximal reduction of BP and $PaCO_2$ was produced after sedative doses of midazolam and diazepam. A possible acute tolerance development toward the BP reduction was found after the repeated administration of diazepam but not after the midazolam administration. The plasma concentrations producing half the maximal effects after administration of midazolam was 50-60 ng/ml, indicating that the influence on BP and $PaCO_2$ after drug administration is evoked at lower plasma concentrations than sedation. Lebowltz *et al.*, midazolam was associated with more gradual and less pronounced hemodynamic alteration; the only significant changes from baseline were decreases in mean arterial pressure 5 and 10 min after injection. In our study, we found that there was reduction in arterial pressure during midazolam sedation this finding is in accordance of both the studies mentioned above where the investigator found that there was reduction in arterial pressure so his findings support our observation. Ebert *et al.*⁹ concluded that dexmedetomidine decreased catecholamines 45-76% and eliminated the norepinephrine increase. Catecholamine suppression persisted in subsequent infusions. The first two doses of dexmedetomidine increased sedation 38 and 65%, and lowered mean arterial pressure by 13%, but did not change central venous pressure or pulmonary artery pressure. Rogue *et al.* (2002) concluded that plasma norepinephrine concentrations, BP, HR, and some HR variability measures were lower after 1 h infusion of dexmedetomidine. Thus, the above-mentioned studies show that there is fall in BP with dexmedetomidine, propofol, and midazolam which is in accordance to our study in which fall of BP was present with all the three drugs.

The mean SpO_2 in all the three groups during sedation, from cessation of sedation to extubation at extubation and from extubation to ICU discharge, were comparable

in dexmedetomidine, propofol, and midazolam groups and there was statistically significant difference found ($P > 0.05$).

Complications

In this study, chest complications (nosocomial pneumonia, barotraumas) were the most common complication noted. 18% patients in dexmedetomidine groups, 25.4% patients in propofol group, 21% patients in midazolam group had chest complications. These findings were in accordance to Goodman *et al.*¹⁰ who studied the ventilatory effects of propofol infusion and concluded that it leads to more chest complications.

Ventricular tachycardia (6.89%) occurred only in propofol group. This finding was in accordance with King *et al.* who showed that propofol infusion leads to acute cardiac failure, cardiomyopathy, and other cardiac complications.

Bradycardia occurred in 7.5% patients receiving dexmedetomidine and the time of loading of the drug. This finding was in accordance with Eren and Cukurova⁶ who showed that dexmedetomidine cause bradycardia.

Intravenous line sepsis occurs more frequently with propofol 11.2% as compared to midazolam 8.9% and dexmedetomidine 7.3%.

Prolonged sedation after cessation of sedation occurred most frequently with midazolam 11.34% than with propofol 3.11% and not seen in dexmedetomidine group. This finding in accordance with study done by Slark *et al.*, in which he found that patients receiving midazolam lead to prolonged sedation.

Hypotension occurred 14.22% in propofol group, 6.4% in dexmedetomidine group, and 5% in midazolam group. More hypotension in propofol group is in accordance to study done by Larsen *et al.*

None of the complications were statistically significant.

CONCLUSION

Dexmedetomidine a new sedative-analgesic agent is safe to be used in the ICU. Dexmedetomidine provides hemodynamic stability and has no clinically important adverse effects on respiration. Tracheal extubation was earlier in patients receiving, dexmedetomidine and propofol than from midazolam.

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How to cite this article: Singh G, Srinivas K. Comparison of Intensive Care Unit Sedation Using Dexmedetomidine, Propofol, and Midazolam. *Int J Sci Stud* 2017;4(10):115-124.

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