

## ORIGINAL ARTICLE

### A COMPARITIVE STUDY TO EVALUATE EFICACY OF IV INFUSION OF DEXMEDETOMIDINE VERSUS IV INFUSION OF PROPOFOL FOR POST-OPERATIVE ICU SEDATION

K. Vindhya<sup>1</sup>, Krishna Prasad<sup>2</sup>, Soubhagya Lakshmi<sup>3</sup>, K. V. P. Brahmajee Rao<sup>4</sup>, V. Sirisha<sup>5</sup>

#### HOW TO CITE THIS ARTICLE:

K. Vindhya, Krishna Prasad, Soubhagya Lakshmi, K. V. P. Brahmajee Rao, V. Sirisha. "A Comparitive Study To Evaluate Efficacy of IV Infusion of Dexmedetomidine Versus IV Infusion of Propofol for Post-Operative ICU Sedation". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 01, January 01; Page: 17-22, DOI: 10.14260/jemds/2015/4

**ABSTRACT:** Patients requiring mechanical ventilation usually needs adequate sedation and analgesia to facilitate their care. Dexmedetomidine, a short-acting  $\alpha_2$ -agonist, possesses anxiolytic, anesthetic, hypnotic, and analgesic properties. **AIM:** The objective of this study is to evaluate and compare the safety and efficacy of iv infusion of Dexmedetomidine with iv infusion of propofol for sedation in post-operative ICU patients. **MATERIALS AND METHODS:** Fifty patients who were ambulatory and who required the post-operative mechanical ventilation or post-operative sedation were enrolled, in which 25 patients received Dexmedetomidine and remaining 25 patients received propofol. All these patients were treated for the period of 8 to 24 h. **STATISTICAL ANALYSIS USED:** 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 is similar. To maintain analgesia throughout the study period, patients receiving propofol infusions required significantly more analgesics than patients receiving Dexmedetomidine. **CONCLUSIONS:** Dexmedetomidine appears to be a safe and acceptable ICU sedative agent.

**KEYWORDS:** Dexmedetomidine, intensive care unit, sedation, propofol.

**INTRODUCTION:** Patients requiring mechanical ventilation usually needs adequate sedation and analgesia to facilitate their care. Deep sedation is no longer the standard practice for most patients as it prolongs weaning from mechanical ventilation and length of ICU stay and potentially increasing morbidity. Dexmedetomidine is a more selective  $\alpha_2$  agonist with a 1600 times greater selectivity for the  $\alpha_2$  receptor compared with the  $\alpha_1$  receptor. It belongs to the imidazole subclass of  $\alpha_2$  receptor agonists especially for the 2A subtype which causes it to be a much more effective sedative and analgesic. It sedates via interaction with locus ceruleus, and has less effect on arousability. It is metabolised by hydroxylation through direct glucuronidation and cytochrome P450 metabolism in liver. It's elimination half-life is 2 to 3 hours. Propofol is a short-acting, lipophilic sedative and hypnotic, causes global CNS depression, presumably through agonist actions on GABA<sub>A</sub> receptor.

In post-surgical patients, dexmedetomidine does not interfere with respiration rate, or arterial oxygenation and carbon dioxide pressure. The objective of this study is 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. This trial was designed in the Indian population to evaluate the efficacy and tolerability of Dexmedetomidine versus propofol alone in the management of sedation for the period after any major surgery.

## ORIGINAL ARTICLE

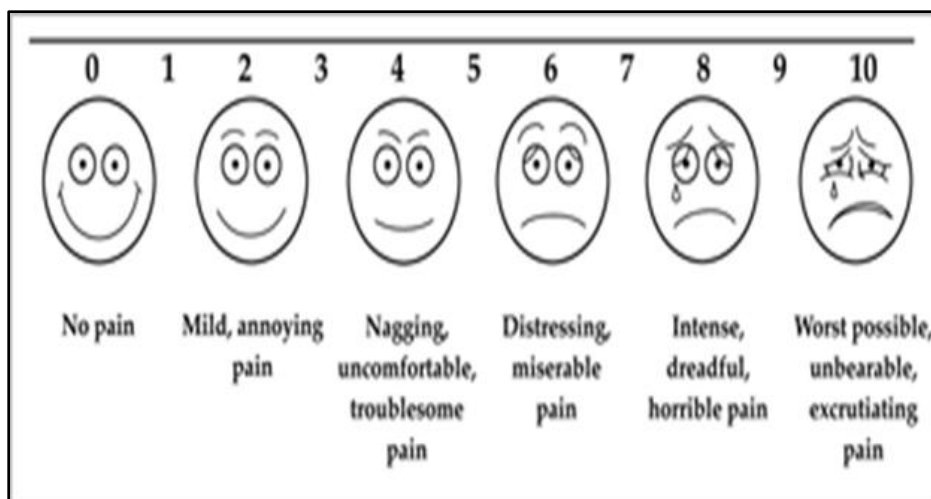
**MATERIALS AND METHODS:** The study was conducted in the RICU, Government general hospital attached to Rangaraya medical college, Kakinada between May 2014 to August 2014. After obtaining institutional ethical committee's approval & informed consent from the patients' attendants, 50 patients belonging to ASA grades I & II of both sexes, aged between 20-60 yrs were taken up for study. They were randomly divided into 2 groups - Group D & Group P each comprising of 25 Patients. GROUP D patients received DEXMEDETOMIDINE loading dose of 1mcg/kg over 10 min followed by maintenance dose of 0.2-0.7mcg/kg/hr. GROUP P patients received PROPOFOL 5mcg/kg/min and infusion rate was increased by increments of 5-10mcg/kg/min until desired level of sedation was achieved. Base line parameters like heart rate, NIBP, respiratory rate were recorded in both the groups.

In all patients HR, SBP, DBP, MAP, RR, RAMSAY SEDATION SCORE, VISUAL ANALOGUE SCALE were monitored for 30min, 1hr, 1.5 hr, 2.5hr, 4hr, 6hr, 10hr.

**Table 1 - Ramsay scale for the assessment of the level of sedation**

LEVEL OF ACTIVITY	POINTS
Patient anxious, agitated or restless	1
Patient cooperative, orientated and tranquil	2
Patient responding only to verbal commands	3
Patient with brisk response to light glabella tap or loud auditory stimulus	4
Patient with sluggish response to light glabella tap or loud auditory stimulus	5
Patient with no response to light glabella tap or loud auditory stimulus	6

### VISUAL ANALOGUE SCALE:



## ORIGINAL ARTICLE

**Statistical Analysis:** Data analysis was performed by unpaired student's t-test and chi-square test.  $p < 0.05$  was considered statistically significant and a  $p$  value  $< 0.0001$  was considered statistically very significant.

**RESULTS:** The demographic profiles of the patients in both the groups were comparable with regards to age, sex, weight.

Pulse rate, respiratory rate and blood pressures between the groups was not statistically significant. RSS was between 2-3 for both DEXMEDETOMIDINE and PROPOFOL groups. There was no statistical significant difference between the 2 groups throughout the study period with respect to sedation. 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.

	Group D (n=25)	Group P (n=25)
AGE (YEARS)	42+12.13	41.09+13.17
SEX (M:F)	15:10	13:12
WEIGHT	63.4+4.36	62.4+9.02

### HAEMODYNAMIC PARAMETERS

	1/2 H		1H		4H		6H		P-VALUE
	D	P	D	P	D	P	D	P	
Pulse rate	84.67 ±10.35	86.33 ±9.7	91.46 ±14.1	92.7 ±10.3	92.26 ±12.1	93.7 ±8.3	94.6 ±10.1	95.6 ±33.3	>0.05
Respiratory rate	14.33 ±1.29	18.07 ±4.37	16.43 ±0.10	20.04 ±4.20	16.46 ±0.28	18.04 ±1.20	18.43 ±0.2	20.04 ±1.20	>0.05
Systolic blood pressure	119.57 ±5.84	116 ±5.017	116.37 ±5.79	113.97 ±4.99	114.37 ±2.89	112.67 ±2.99	118.37 ±2.49	116.37 ±3.8	>0.05

# ORIGINAL ARTICLE

## HAEMODYNAMIC PARAMETERS

	1/2 H		1H		4H		6H		P-VALUE
	D	P	D	P	D	P	D	P	
Diastolic blood pressure	74.47 ±7.403	73.203 ±5.92	76.40 ±7.49	77.94 ±6.06	77.4 ±3.2	77.4 0±6.49	76.34 ±3.06	75.3 ±1.92	>0.05
Mean arterial pressure	80.91 ±5.66	81.19 ±19	85.37 ±6.1	84.91 ±4.6	93.19 ±2.0	92.65 ±4.1	90.1 ±8.6	91.34 ±6.3	>0.05

## RAMSAY SEDATION SCALE

Timepoint	Group D(n=25)	Group P(n=25)	P value		
30 min	2.36 ± 1.07	2.16 ± 0.23	0.365	> 0.05	Notsig
1 h	2.40 ± 1.00	2.44 ± 0.583	0.863	> 0.05	Notsig
1.5 h	2.72 ± 0.936	2.44 ± 0.651	0.225	> 0.05	Notsig
2.5 h	2.92 ± 0.759	2.16 ± 0.746	0.008	< 0.05	Significant
4 h	2.80 ± 0.816	2.76 ± 0.473	0.833	> 0.05	Notsig
6 h	2.84 ± 0.746	2.63 ± 0.66	0.297	> 0.05	Notsig
10 h	2.88 ± 0.6	2.64 ± 0.735	0.206	> 0.05	Notsig

## VISUAL ANALOGUE SCALE

Time point	Group D(n=25)	Group P(n=25)	Pvalue		
30 min	2.12 ± 1.36	3.64 ± 1.89	0.022	< 0.05	Significant
1 h	2.28 ± 1.17	3.27 ± 1.38	0.008	< 0.05	Significant
1.5 h	2.04 ± 1.62	2.72 ± 1.69	0.152	> 0.05	Not sig
2.5 h	2.08 ± 1.11	2.52 ± 1.32	0.208	> 0.05	Not sig
4 h	2.06 ± 1.49	2.72 ± 0.61	0.04	< 0.05	Significant
6 h	1.60 ± 1.11	2.60 ± 0.645	0.000	< 0.05	Significant
10 h	2.04 ± 1.58	2.72 ± 0.60	0.049	< 0.05	Significant

## ORIGINAL ARTICLE

**DISCUSSION:** Dexmedetomidine is as effective as propofol for producing and maintaining adequate short time sedation in mechanically ventilated patients.<sup>1</sup> The benefits of dexmedetomidine over currently available sedative agents include its lack of respiratory depression and ability to decrease the need for opioid analgesics<sup>1</sup>. 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 increase in use of  $\alpha_2$ -adrenoreceptor agonist like dexmedetomidine as it has a shorter half-life and has additional analgesic properties and maintains cardiorespiratory function.<sup>1</sup>

Finally, antagonists to the effects of  $\alpha_2$ -adrenoreceptor agonists have been described that make quick reversal of sedation an option.<sup>2</sup> A rise in blood pressure may occur 1 min after bolus and is attributed to direct effects of  $\alpha_2$ -receptor stimulation of vascular smooth muscles. Dexmedetomidine does not appear to have any direct effects on the heart.<sup>3</sup> A biphasic cardiovascular response has been described after the infusion of dexmedetomidine.<sup>4-6</sup> The administration of a bolus of 1 mcg/kg dexmedetomidine initially results in a transient increase of the blood pressure and a reflex decrease in heart rate, especially in younger, healthy patients.<sup>5</sup> The initial reaction can be explained by the peripheral  $\alpha_2B$ -adrenoreceptor stimulation of vascular smooth muscle and can be attenuated by a slow infusion over 10 or more minutes.

The initial response lasts for 5 to 10 minutes and is followed by a decrease in blood pressure of approximately 10% to 20% below baseline and a stabilization of the heart rate, also below baseline values; both of these effects are caused by the inhibition of the central sympathetic outflow overriding the direct stimulating effects.<sup>7</sup> Another possible explanation for the subsequent heart rate decrease is the stimulation of the presynaptic  $\alpha_2$ -adrenoreceptor, leading to a decreased norepinephrine release.<sup>8</sup> The application of a single high dose of dexmedetomidine reduced norepinephrine release by as much as 92% in young healthy volunteers.<sup>9</sup> The release of epinephrine is also reduced by the same amount.<sup>10</sup> 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.<sup>11</sup>

**CONCLUSION:** In the present study dexmedetomidine appears to be a safe and acceptable ICU sedation agent. Depth of sedation is similar to that given by propofol the cardiovascular respiratory variables of patient sedated with dexmedetomidine are similar to that of patients sedated with propofol. In conclusion, dexmedetomidine could be used safely and effectively, in post-operative ICU as sedative and analgesic agent.

### REFERENCES:

1. Coursin DB, Coursin DB, Maccioli GA. Dexmedetomidine. *Curr Opin Crit Car.*2001; 7: 221-6.
2. Scheinin H, Aantaa R, Anttila M, Hakola P, Helminen A, Karhuvaara S. Reversal of the sedative and sympatholytic effects of dexmedetomidine with a specific  $\alpha_2$ -adrenoreceptor antagonist atipamezole: A pharmacodynamic and kinetic study in healthy volunteers. *Anesthesiology*1998; 89: 574-84.
3. Housmans PR. Effects of dexmedetomidine on contractility, relaxation, and intracellular calcium transients of isolated ventricular myocardium. *Anesthesiology.*1990; 73: 919-922.

## ORIGINAL ARTICLE

4. Dyck JB, Maze M, Haack C, Vuorilehto L, Shafer SL. The pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers. *Anesthesiology* 1993; 78: 813-820.
5. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. *Anesthesiology* 1992; 77: 1134-1142.
6. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. *Anesth Analg* 2000; 90: 699-705.
7. Xu H, Aibiki M, Seki K, Ogura S, Ogli K. Effects of dexmedetomidine, an alpha 2-adrenoceptor agonist, on renal sympathetic nerve activity, blood pressure, heart rate and central venous pressure in urethane-anesthetized rabbits. *J Auton Nerv Syst.* 1998; 71: 48-54.
8. Aantaa R, Kanto J, Scheinin M, Kallio A, Scheinin H. Dexmedetomidine, an alpha 2-adrenoceptor agonist, reduces anesthetic requirements for patients undergoing minor gynecologic surgery. *Anesthesiology* 1990; 73: 230-235.
9. Kallio A, Scheinin M, Koulu M, Ponkilainen R, Ruskoaho H, Viinamaki O, Scheinin H. Effects of dexmedetomidine, a selective alpha 2-adrenoceptor agonist, on hemodynamic control mechanisms. *Clin Pharmacol Ther* 1989; 46: 33-42.
10. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and perioperative fentanyl. *Br J Anaesth* 1992; 68:126-131.
11. Hindmarch I. Psychomotor function psychoactive drugs. *Br J Clin Pharmacol* 1980; 10: 89-209.

### AUTHORS:

1. K. Vindhya
2. Krishna Prasad
3. Soubhagya Lakshmi
4. K. V. P. Brahmajee Rao
5. V. Sirisha

### PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Anaesthesia, Rangaraya Medical College.
2. Associate Professor, Department of Anaesthesia, Rangaraya Medical College.
3. Professor, Department of Anaesthesia, Rangaraya Medical College.
4. Post Graduate, Department of Anaesthesia, Rangaraya Medical College.

5. Post Graduate, Department of Anaesthesia, Rangaraya Medical College.

### NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. K. Vindhya,  
H. No. 2-60A/9,  
Venkat Nagar,  
Kakinada.  
E-mail: drvindhya.rmc@gmail.com

Date of Submission: 15/12/2014.  
Date of Peer Review: 16/12/2014.  
Date of Acceptance: 22/12/2014.  
Date of Publishing: 30/12/2014.