IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 10 Ser.4 (October. 2019), PP 51-59
www.iosrjournals.org

Comparison of Sedation and Analgesia Produced By Dexmedetomidine and Butorphanol in Critically Ill Patients on Mechanical Ventilation: A Prospective Observational Study

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Abstract: *BACKGROUND: Sedation in the intensive care unit for critically ill patients on mechanical ventilation is a complex clinical problem, and the current therapeutic approaches have potential side effects. This study aimed at comparing inj. Dexmedetomidine with inj.Butorphanol as sedative and analgesia.*
METHODS: 60 Patients of both sexes in the age group of 18-60 yrs requiring mechanical ventilation are included in the study. Once the patient on mechanical ventilation, the infusion of the specified drug was started using a syringe pump. Dexmedetomidine started at the rate of 1mcg/kg/hr loading dose over 15 minutes followed by 0.25 mcg/kg/hr, and Butorphanol was started at the rate of 5mcg/kg/hr depending upon the parameters of assessment and requirement of the patient. The infusion continued for 24hrs. Vital parameters, Ramsay Sedation score, Behavioural pain score were compared.
RESULTS: The patients receiving Dexmedetomidine infusion were hemodynamically more stable and were easily arousable when compared to patients receiving Butorphanol infusion
CONCLUSION: Dexmedetomidine is a suitable alternative to the commonly used sedatives in ICU, but its high cost may limit its use in the initial phase.
Keywords: *Butorphanol, Dexmedetomidine, ICU, mechanical ventilation, sedation*

Date of Submission: 21-09-2019 Date of Acceptance: 10-10-2019

I. Introduction

Sedation in ICU for critically ill patients on mechanical ventilation is a complex clinical challenge, and current therapeutic approaches have (1) potential side effects. Improper or inadequate sedation and analgesia in such patients causes agitation. Significant causes of agitation in ICU patients are fear, loss of control, confusion, sleep deprivation, pain, (2) chemical imbalances, medication, and mechanical ventilation. Hence to reduce agitation, it is essential that the used therapeutic approach should provide sufficient analgesia and sedation for such patients. Critically ill patients experience pain more readily than healthy subjects (hyper nociception), and the most painful experiences are endotracheal suctioning and frequent position change on the bed.(3) Hence to reduce agitation, it is essential that the used therapeutic approach should provide sufficient analgesia and sedation for such patients. The sequelae of severe pain can be long lasting psychological effects on the patient, together with hemodynamic changes like tachycardia, hypertension, and increase in SVR, causing an increase in myocardial oxygen consumption and demand that will result in myocardial ischemia(4)

II. Methodology

A prospective observational study conducted in Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinaoutapalli after approval from the hospital ethics committee, and obtaining written informed consent from the patient's attenders during the period between November 2016 and November 2018. A total of 60 patients who are intubated in medical ICU are selected for the study.

Study medication:
Group "A": Dexmedetomidine Group will receive a Loading dose-1.0mcg/kg over 15 min followed by a maintenance infusion of 0.25 mcg/kg/hr for proper sedation and analgesia assessed by using Ramsay sedation score and behavioral pain scale.
Group "B": Butorphanol group will receive the drug at a rate of 5mcg/kg/hr maintaining proper sedation and analgesia assessed by using Ramsay sedation score and behavioral pain scale.

III. Observation And Results

The patients who took part in this study, the majority were males are 43 in number (72 %) and females were 17 (28%).

The mean age of the patients in the dexmedetomidine group was 44.23 ± 11.84, and the mean age of the patients in the butorphanol group was 42.50 ± 14.37

On statistical comparison, the two groups were comparable with P = 0.612

Graph 1: Age distribution of patients

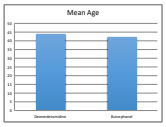


Table 1: Bar diagram showing age distribution of patients

VARIABLE	DEXMEDETOMIDINE		BUTORPHANOL		p-value
	Mean	SD	Mean	SD	
MEAN AGE	44.23	11.84	42.50	14.37	0.612

Graph 2: pie diagram showing sex distribution in patients of 2 groups

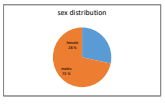
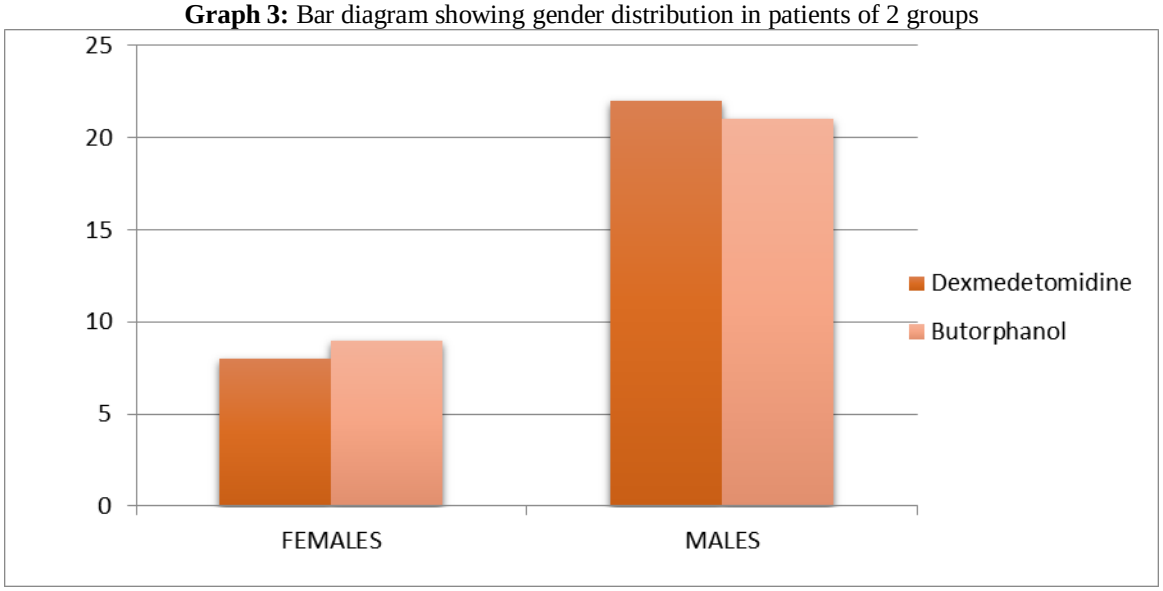


Table 2: Gender distribution in patients of 2 groups

SEX	DEXMEDETOMIDINE		BUTORPHANOL	
	COUNT	%	COUNT	%
FEMALE	8	26.67%	9	30%
MALE	22	73.33%	21	70%
TOTAL	30	100%	30	100%

Graph 3: Bar diagram showing gender distribution in patients of 2 groups



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Heart rate in the two groups was studied, and statistically significant values obtained between dexmedetomidine and butorphanol at 6 hr, 12 hr, 18 hr, and 24 hrs.

Table 3: Comparison of Heart rate in 2 groups

HEART RATE	DEXMEDETOMIDINE (Mean ± SD)	BUTORPHANOL (Mean ± SD)	P value
0 HRS	106.13 ± 12.33	106.90 ± 11.38	0.8033
6 HRS	96.40 ± 12.06	105.77 ± 10.38	0.0021*
12 HRS	93.33 ± 12.31	102.67 ± 11.36	0.0034*
18 HRS	87.63 ± 12.90	98.30 ± 8.34	0.0003**
24 HRS	83.90 ± 13.27	97.63 ± 12.89	0.0001**

* - statistically significant

** - extremely statistically significant

Graph 4: Line diagram showing comparison of Heart rate in 2 groups

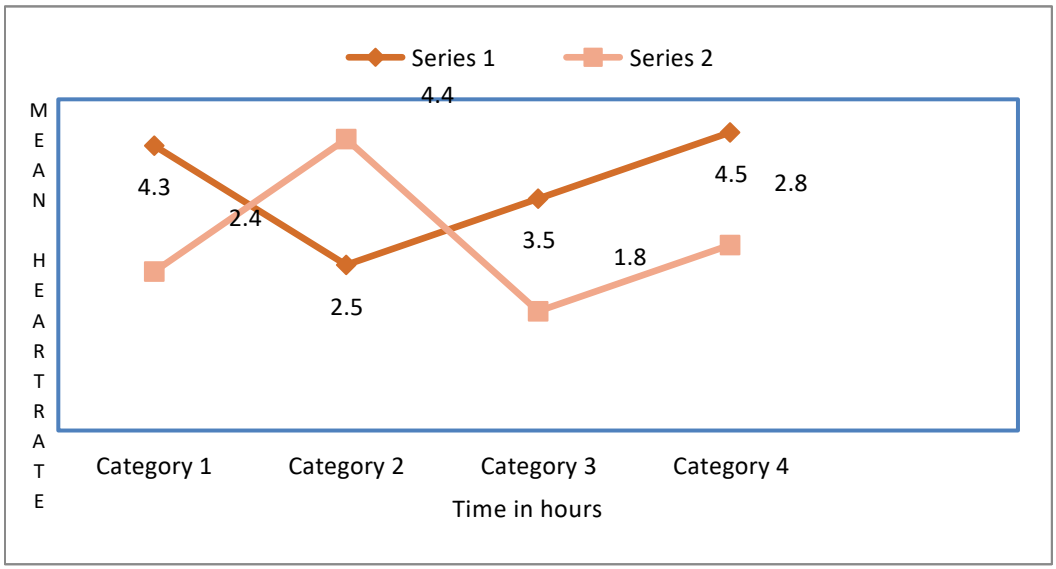


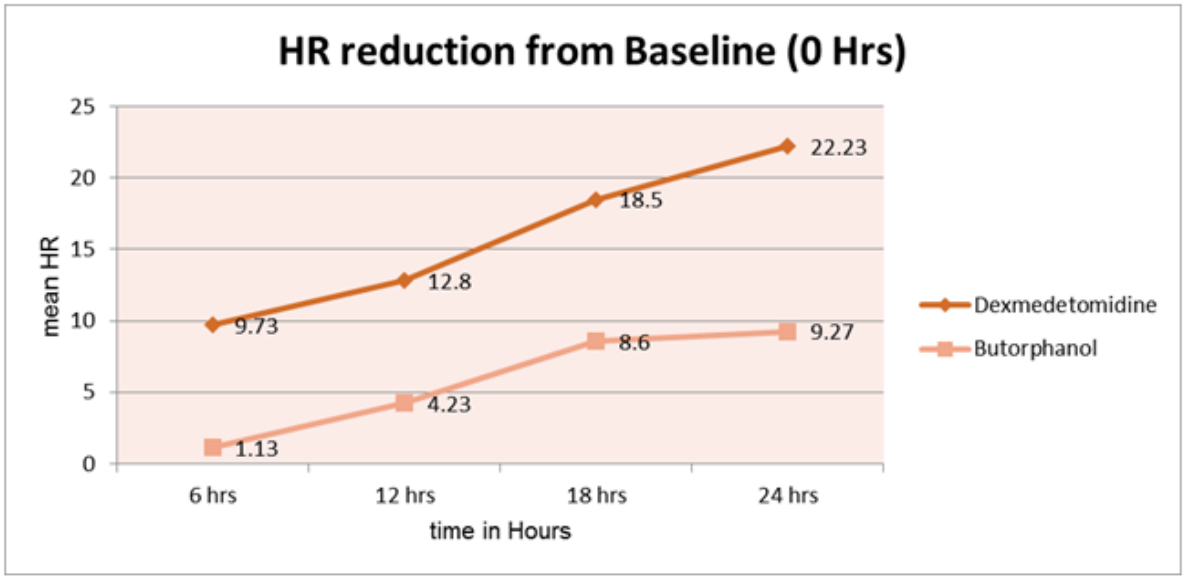
Table 4: HR reduction within each group

STUDY GROUP	HR reduction from (0 HRS) to	Mean difference	SE of Difference	P - value
DEXMEDETOMIDINE	6 HRS	9.73	1.507	<0.0001*
	12 HRS	12.80	2.160	<0.0001*
	18 HRS	18.50	2.264	<0.0001*
	24 HRS	22.23	2.465	<0.0001*
BUTORPHANOL	6 HRS	1.13	2.103	0.5941
	12 HRS	4.23	2.408	0.0893
	18 HRS	8.60	2.357	0.0010**
	24 HRS	9.27	3.164	0.0066**

* - very statistically significant
** - extremely statistically significant

On using Paired-t-test, we observed that there was a significant difference in HR reduction from baseline to 24 hrs within each group. However, the mean reduction of HR from baseline was extremely significant statistically for dexmedetomidine with p-value <0.0001. These observations tabulated in Table 4

Graph 5: Line diagram showingHR reduction within each group from baseline



The mean of MAP has been statistically compared, and also there was not a quite significant difference observed statistically between the groups on independent – t-test at 6hr and 12 hrs, but statistically, significant values obtained at 18 hr and 24 hrs.

Table 5: Comparison of MAP in 2 group

MAP	DEXMEDETOMIDINE (Mean ± SD)	BUTORPHANOL (Mean ± SD)	P value
0 HRS	113.13 ± 14.57	101.80 ± 18.31	0.0103*
6 HRS	101.60 ± 15.49	99.97 ± 16.90	0.6978
12 HRS	91.90 ± 14.19	94.37 ± 13.54	0.4937
18 HRS	86.10 ± 12.71	94.67 ± 11.84	0.0090*
24 HRS	82.43 ± 11.60	91.57 ± 13.22	0.0061*

Graph 6: Line diagram showing comparison of MAP in 2 groups

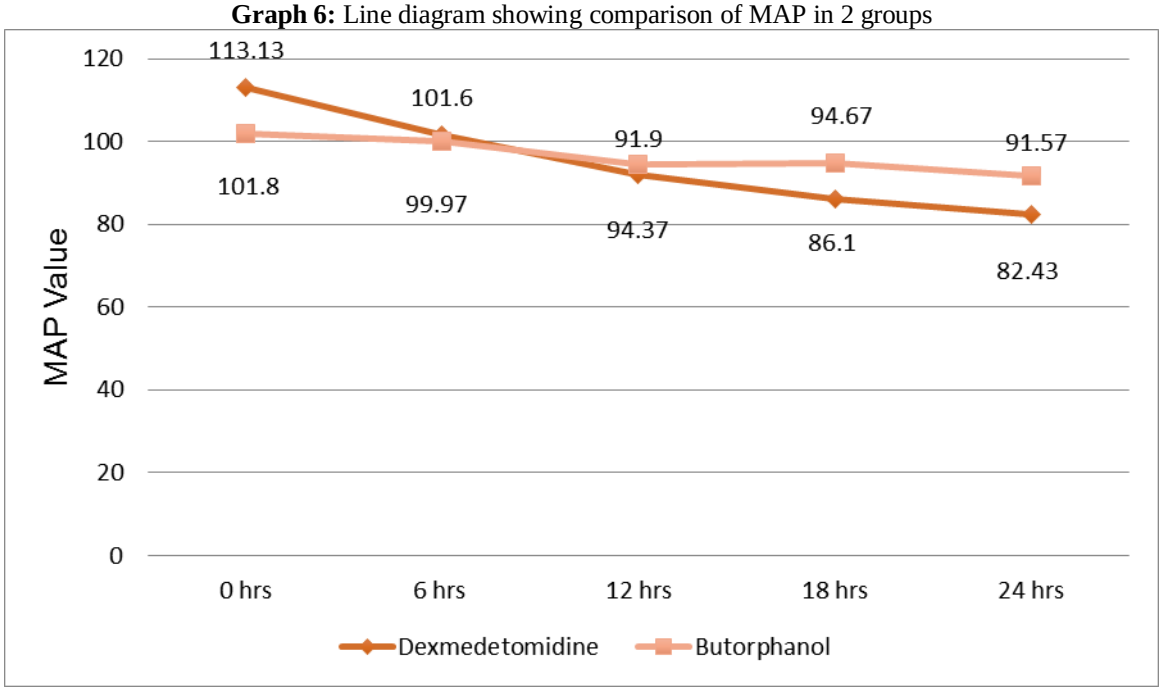


Table 6: MAP reduction within each group from baseline

STUDY GROUP	MAP reduction from (0 HRS) to	Mean difference	SE of Difference	P - value
DEXMEDETOMIDINE	6 HRS	11.53	1.837	<0.0001**
	12 HRS	21.23	2.145	<0.0001**
	18 HRS	27.03	2.094	<0.0001**
	24 HRS	30.70	2.475	<0.0001**
BUTORPHANOL	6 HRS	1.83	2.373	0.4460
	12 HRS	7.43	2.726	0.0107*
	18 HRS	7.13	2.595	0.0102*
	24 HRS	10.23	2.806	0.0010*

On using Paired-t-test, we observed that there was a significant difference in MAP reduction from baseline to 24 hrs within each group, But the mean reduction of MAP from baseline was extremely significant statistically for dexmedetomidine with p-value <0.0001

Graph 7: Line diagram showing MAP reduction within each group from baseline

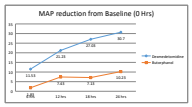
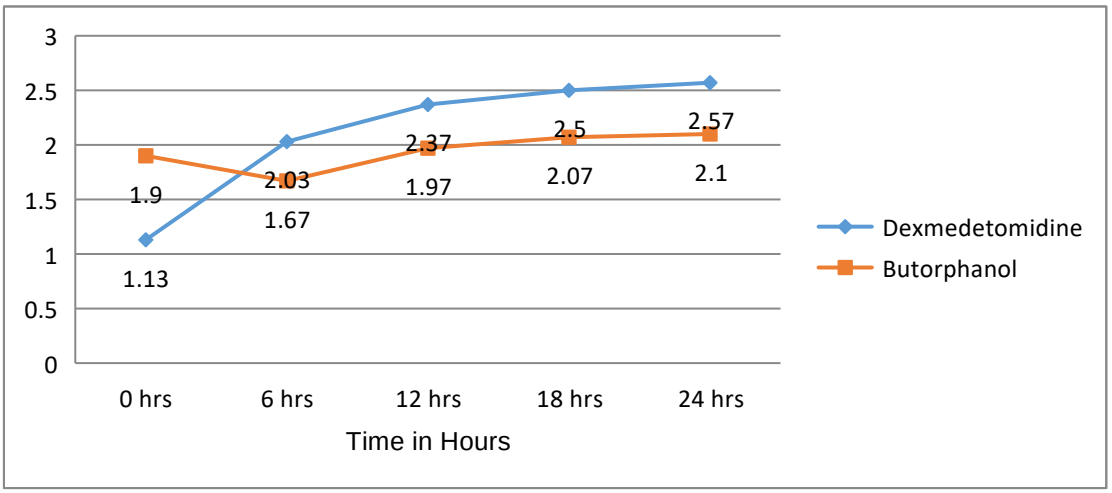


Table 7: Comparison of RSS in 2 groups

RSS	DEXMEDETOMIDINE (Mean ± SD)	BUTORPHANOL (Mean ± SD)	P value
0 HRS	1.13 ± 0.57	1.90 ± 1.97	0.0453
6 HRS	2.03 ± 1.00	1.67 ± 1.15	0.1937
12 HRS	2.37 ± 1.27	1.97 ± 1.19	0.2134
18 HRS	2.50 ± 1.17	2.07 ± 1.05	0.1357
24 HRS	2.57 ± 1.28	2.10 ± 1.03	0.1247

Graph 8: Line diagram showing comparison of RSS in 2 groups

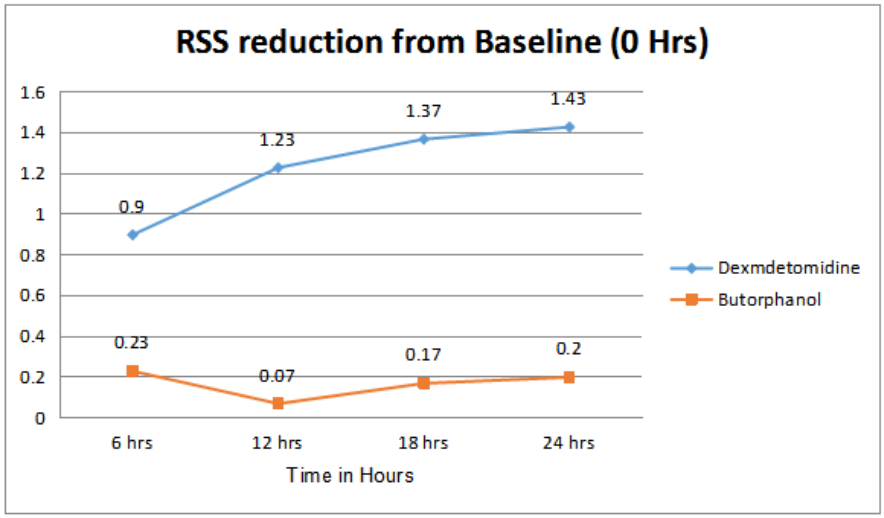


There is a variation in RSS between 2 groups. There is no significant difference between dexmedetomidine and butorphanol groups. However, on using Paired-t-test, it was observed that there was a significant difference in RSS reduction from baseline to 24 hrs for the dexmedetomidine group, which was extremely significant statistically for dexmedetomidine with p-value <0.0001. These observations tabulated in Table 7 and 8.

Table 8: RSS reduction within each group from baseline

STUDY GROUP	**RSS reduction from (0 HRS) to**	**Mean difference**	**SE of Difference**	**P - value**
DEXMEDETOMIDINE	6 HRS	0.90	0.175	<0.0001**
	12 HRS	1.23	0.238	<0.0001**
	18 HRS	1.37	0.222	<0.0001**
	24 HRS	1.43	0.228	<0.0001**
BUTORPHANOL	6 HRS	0.23	0.380	0.5436
	12 HRS	0.07	0.383	0.8632
	18 HRS	0.17	0.372	0.6572
	24 HRS	0.20	0.354	0.5760

Graph 9: Line diagram showingRSS reduction within each group from baseline

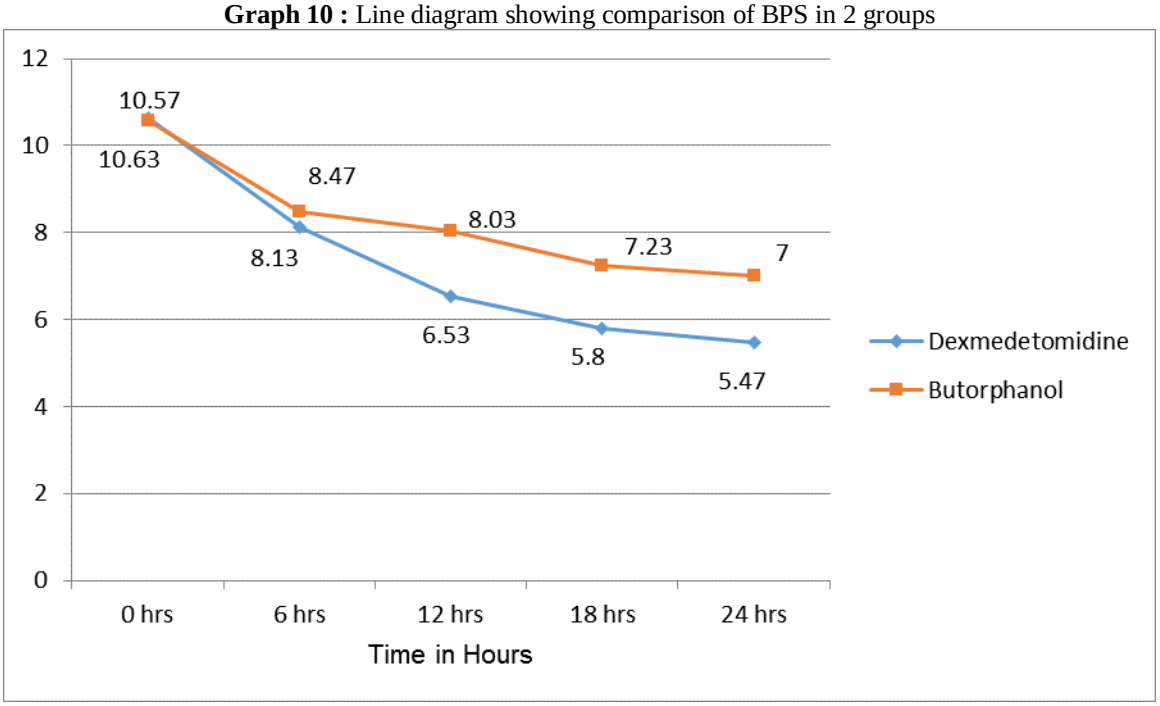


There is a little variation in BPS between 2 groups. There is a Significant difference between dexmedetomidine and butorphanol groups at 12 hr, 18 hr, and 24 hrs. These observations tabulated in Table 9.

Table 9: Comparison of BPS in 2 groups

BPS	DEXMEDETOMIDINE (Mean ± SD)	BUTORPHANOL (Mean ± SD)	P value
0 HRS	10.63 ± 2.04	10.57 2.08	0.9003
6 HRS	8.13 ± 2.15	8.47 2.00	0.5356
12 HRS	6.53 ± 1.85	8.03 1.94	0.0033*
18 HRS	5.80 ± 1.49	7.23 1.87	0.0018*
24 HRS	5.47 ± 1.31	7.00 1.86	0.0005**

Graph 10 : Line diagram showing comparison of BPS in 2 groups

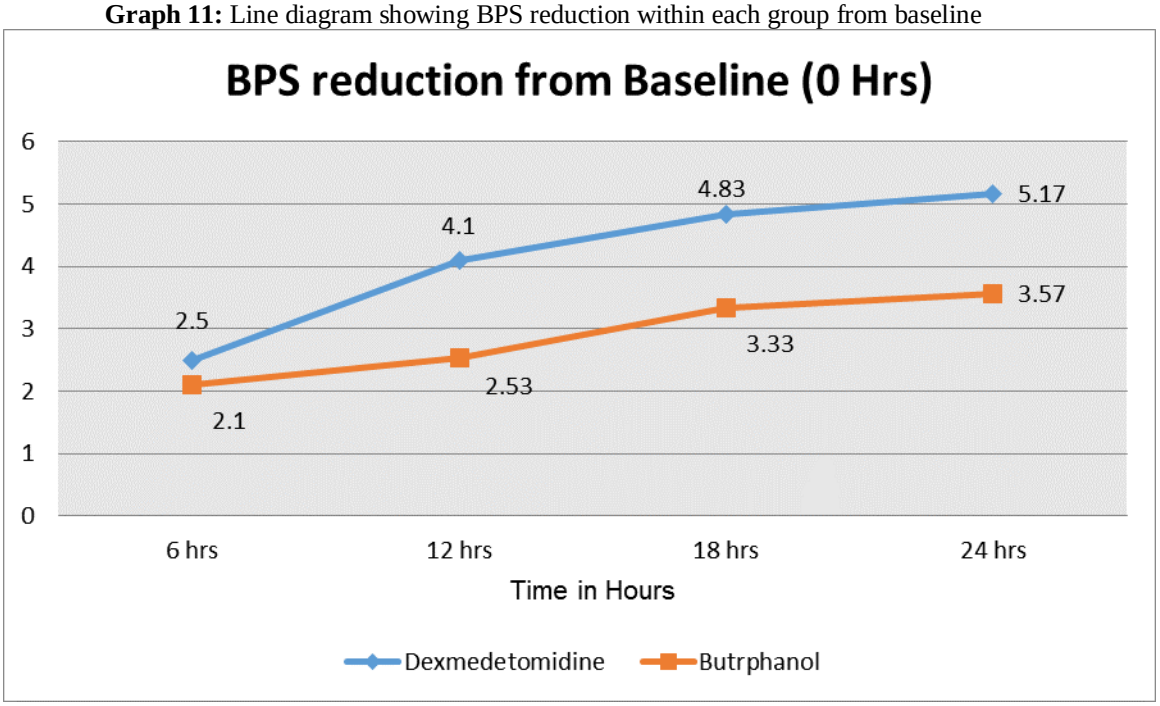


On using Paired-t-test, we observed that there was a significant difference in BPS reduction from baseline to 24 hrs within each group, and the mean reduction of BPS from baseline was extremely significant statistically for both dexmedetomidine group and butorphanol group with p-value <0.0001

Table 10: BPS reduction within each group from baseline

STUDY GROUP	BPS reduction from (0 HRS) to	Mean difference	SE of Difference	P - value
DEXMEDETOMIDINE	6 HRS	2.50	0.279	<0.0001**
	12 HRS	4.10	0.372	<0.0001**
	18 HRS	4.83	0.399	<0.0001**
	24 HRS	5.17	0.399	<0.0001**
BUTORPHANOL	6 HRS	2.10	0.289	<0.0001**
	12 HRS	2.53	0.266	<0.0001**
	18 HRS	3.33	0.330	<0.0001**
	24 HRS	3.57	0.358	<0.0001**

Graph 11: Line diagram showing BPS reduction within each group from baseline



IV. Discussion

Most of the patients admitted to an intensive care unit (ICU) for mechanical ventilation receive sedative and analgesic medications. (5) Inadequate sedative techniques may adversely affect morbidity and mortality in intensive care unit (6). Agitation and anxiety are known to occur at least once in about 70% of patients in ICUs (7). A shift from deep sedation, often enhanced by muscle relaxants that completely detaches the patient from their environment, to light sedation rendering the patient sleepy but easily arousable has been widely accepted (8)Regular assessment of the level of sedation should be routine in all ICU patients. It aims to prevent the hazards of over or under sedation which is associated with increased morbidity and even mortality (8)

ZHANG ET AL. Compared effects of different doses of dexmedetomidine on Heart rate and blood pressure in ICU patients. IN Group A Dexmedetomidine was infused at a rate of 1mcg/kg for 10 min followed by 0.4mcg/kg/hr.in group b dexmedetomidine was infused at a rate of 0.5mcg/kg for 10 min followed by 0.4mcg/kg/hr.in group c dexmedetomidine was infused at a rate of 0.4mcg/kg for 10 min followed by 0.4mcg/kg/hr.an ideal state of sedation may be achieved by using the maintenance dose of dex (0.4 µg/kg/h). However, this effect is induced slowly to obtain, more rapid sedative effect; we suggest using a loading dose of 0.5µg/kg/10 min (9)

R. ADAMS ET AL. Studied Efficacy of dexmedetomidine compared with midazolam for sedation in adult intensive care patients: a systematic review and concluded. The benefits of dexmedetomidine vs. midazolam for sedation remain inconclusive, while dexmedetomidine showed clinical effectiveness for some secondary outcomes (10)

ESKO RUOKONEN et al. This is a multicentre, prospective, randomized, double-blind, double-dummy, active comparative study where Dexmedetomidine was compared with propofol/midazolam for long-term sedation during mechanical ventilation and concluded. Dexmedetomidine appears safe and comparable to current sedation practice for long-term sedation, but not suitable as the sole agent for deep sedation (RASS -4 or less). Dexmedetomidine enhances the patient's ability to communicate. (11)

PRATHIK ET AL Effect of Sedation With Dexmedetomidine vs. Lorazepam on Acute Brain Dysfunction in Mechanically Ventilated Patients and concluded that use of a dexmedetomidine infusion in mechanically ventilated ICU patients managed with individualized targeted sedation, resulted in more days alive without delirium, coma and more time at the targeted level of sedation when compared with a lorazepam infusion.(12)
PRASAD et al. The comparative study between dexmedetomidine and fentanyl for sedation during mechanical ventilation in postoperative pediatric cardiac surgical patients and concluded Dexmedetomidine facilitates adequate sedation and also early extubation for mechanical ventilation as compared with fentanyl
In our study, we observed that there was a significant difference in HR reduction from baseline to 24 hrs within each group. However, the mean reduction of HR from baseline was extremely significant statistically for dexmedetomidine. (13)
In our study, it we observed that there was a significant difference in MAP reduction from baseline to 24 hrs within each group, But the mean reduction of MAP from baseline was extremely significant statistically for Dexmedetomidine.

We observed that there has been significant difference in RSS reduction from baseline to 24 hrs for Dexmedetomidine group, which was extremely significant statistically for dexmedetomidine

We also observed that there was a significant difference in BPS reduction from baseline to 24 hrs within each group, and the mean reduction of BPS from baseline was extremely significant statistically for both dexmedetomidine group and butorphanol group.

V. Conclusion

In the present study, we found that Dexmedetomidine is more efficacious than Butorphanol as a sole sedative and analgesic in intubated patients.

We conclude that Dexmedetomidine at a dose of 1 mcg/kg for 15min followed by 0.25 mcg/kg/hr has turned out to be an excellent sedative and analgesic agent without any significant adverse effects which can be used as a sole agent for mechanically ventilated patients in ICU.

Caution must be exercised while infusing Dexmedetomidine in patients with hypotension where Butorphanol can be used as a sole sedative and analgesic

Butorphanol can also be used as a sole sedative and analgesic in ICU as it is cost effective and does reduce the requirement of rescue sedation to some extent.

Both are well tolerated and safe for use in intubated patients. There have been limited studies designed specifically to evaluate the efficacy of Dexmedetomidine and nearly no studies investigating Butorphanol for sedation and analgesia in mechanically ventilated patients.

Acknowledgments

We are thankful to Dr USSA VARA PRASAD Hod and Staff of the Department of Anesthesia and Critical care Dr. P.S.I.M.S. & R.F

References

[1]. Jerrold H. Levy, MD, Dexmedetomidine: Clinical Applications and Considerations; Powerpoint presentation.
[2]. Thomas J. Ebert, Current strategies in ICU Sedation, special report, Anaesthesiology News.
[3]. Kress JP, Pohlman AS, O'Connor MF et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000; 342:147177.
[4]. Thomas J. Ebert, Current strategies in ICU Sedation, special report, Anaesthesiology News.
[5]. Jean-Francois Payen, GéraldChanques, Jean Mantz, Christiane Hercule, Igor Auriant, Jean-Luc
[6]. Leguillou, MichèleBinhas, Céline Genty, Carole Rolland, Jean-Luc Bosson; Current Practices in Sedation and Analgesia for Mechanically Ventilated Critically Ill Patients: A Prospective Multicenter Patient-based Study. Anesthesiology 2007;106(4):687-695. doi:10.1097/01.anes.0000264747.09017.da.
[7]. Tukenmez, B., Memis, D. & Pamukcu, Z. Crit Care (2006) 10(Suppl 1): P435. https://doi.org/ 10.1186/cc 4782
[8]. Paul BS, Paul G. Sedation in the neurological intensive care unit. Ann Indian Acad Neurol 2013;16:194-202.
[9]. Lerch, C. and Park, G. (1999). Sedation and analgesia. British Medical Bulletin, 55(1), pp.76-95.
[10]. Zhang X, Wang R, Lu J, et al. Effects of different doses of dexmedetomidine on heart rate and blood pressure in intensive care unit patients. ExpTher Med. 2015;11(1):360-366.
[11]. R. Adams, G. T. Brown, M. Davidson, E. Fisher, J. Mathisen, G. Thomson, N. R. Webster; Efficacy of dexmedetomidine compared with midazolam for sedation in adult intensive care patients: a systematic review, BJA: British Journal of Anaesthesia, Volume 111, Issue 5, 1 November 2013, Pages 703–710.
[12]. Ruokonen E, Parviainen I, Jakob SM, et al. Dexmedetomidine versus propofol/midazolam for long term sedation during mechanical ventilation. Intensive Care Med 2009; 35: 282–290.
[13]. Pandharipande PP, Sanders RD, Girard TD, McGrane S, Thompson JL, Shintani AK, et al. Effect of dexmedetomidine versus lorazepam on outcome in patients with sepsis: an a priori-designed analysis of the MENDS randomized controlled trial.Critical Care 2010;14: R38.
[14]. Prasad SR, Simha PP, Jagadeesh AM. A comparative study between dexmedetomidine and fentanyl for sedation during mechanical ventilation in post-operative pediatric cardiac surgical patients. Indian J Anaesth 2012;56:547-52.