COMPARISON BETWEEN DEXMEDETOMIDINE AND FENTANYL+MIDAZOLAM FOR ANALGESIA AND SEDATION IN MECHANICALLY VENTILATED PATIENTS IN INTENSIVE CARE UNIT.

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ABSTRACT

INTRODUCTION: Pain is defined as an unpleasant sensory or emotional experience.Nearly all patients in ICU experience pain.

AIM: Evaluation of efficacy of dexmedetomidine vs fentanyl+midazolam as sedative andanalgesic agents in mechanically ventilated patients.

MATERIALS AND METHODS:

This prospective observational study was conducted in 60 critically ill intubated patients belonging to both sexes and ages 18 years and above.Patients were divided into 2 groups;

Group A: Dexmedetomidine 1mcg/kg loading followed by 0.25mcg/kg/hr

Group B: Fentanyl-1mcg/kg bolus followed by 1.5mcg/kg/hrMidazolam-0.02mg/kg bolus followed by 0.02mg/kg/hr

Participants were evaluated at baseline,and every 6hrs upto 24 hrs for heart rate,mean arterial pressure,ramsay sedation scale(RSS) and behavioural pain scales(BPS).

RESULTS: Patients who recieved Dexmedetomidine infusion were hemodynamically more stable andwere easily arousable when compared to patients receiving fentanyl+Midazolaminfusion.Mean reduction in HR, MAP, RSS, BPS is more in dexmedetomidinegroup.

DISCUSSION: Present study was conducted to explore and evaluate efficacy and safety of dexmedetomidine VS fentanyl+midazolam for sedation and analgesia in mechanically ventilated patients.Main aim of sedation is to relieve anxiety, discomfort ,minimize pain, facilitate treatment and care. Nocturnal sedation will reduce sleep deprivation.Over sedation is associated with worse clinical outcomes like longer time on mechanical ventilation, long stay in

ICU and increased brain dysfunction(delirium, coma).Under sedation can lead to anxiety,hyperactivity of sympathetic system etc.

CONCLUSION: Dexmedetomidine at a dose of 1mcg/kg for 15min followed by 0.25mcg/kg/hr is anexcellent sedative and analgesic agent without significant adverse effects, which canbe used as sole agent for mechanically ventilated patients in ICU.Fentanyl+midazolam can be used as sedative and analgesic in ICU as it is costeffective and reduce the requirement of rescue sedation to some extent.

Keywords: SEDATION AND ANALGESIA, RAMSAY SEDATION SCORE, BEHAVIOURAL PAIN SCORE,HEART RATE.

INTRODUCTION:

Pain is defined as “an unpleasant sensory or emotional experience” which highlights the subjective nature of pain[1]

Mechanically ventilated patients in ICU will require analgosedation due to numerous reasons, such as, to prevent respiratory fighting and facilitate specific procedures such as tracheal aspiration, physiotherapy and catheter placements[2]However, some commonly-used sedatives, such as propofol, midazolam and lorazepam, might decrease blood pressure, depress breathing, and delay awakening after a long-term infusion3

Alpha-2 agonists have a range of effects including sedation, analgesia and antianxiety. They sedate, but allow staff to interact with patients and do not suppressrespiration[3].

Dexmedetomidine is a highly selective α2-adrenergic receptor agonist, is the newest agent introduced for sedation in intensive care unit (ICU)[4]Dexmedetomidine is used for prolonged sedation and anxiolysis in the ICU, as well as outside the ICU in various settings, including sedation and adjunct analgesia in the operating room and sedation in diagnostic and procedure units, as well as for other applications such as withdrawal or detoxification amelioration in adult and pediatric patients[5,6]

Opiates which are used more frequently have rapid onset, ease of titration, lack of accumulation of the parent drug or its metabolites, and low cost but also have, Side-effects

which includes respiratory depression, hypotension, Sympatholysis (Volume depleted), vagally-mediated bradycardia, histamine release (morphine) ileus, depression of sensorium[7]

The sedative strategy for critically ill patients has emphasized minimal sedation with daily awakening and assessment for neurologic, cognitive, and respiratory functions, since SCCM guidelines were presented in 2002 and concerns on adverse effects associated with oversedation emerged[8]

Intensivists require tools that measure the effectiveness of sedation and analgesia in an individual patient about the objectives; such an instrument should be simple and user-friendly at the bed side[9]

Objective methods like an electroencephalogram (EEG), auditory evoked potential and signal-processed EEG - bispectral index (BIS) monitors and subjective methods - sedation scores like Riker sedation-agitation scale (SAS), Richmond agitation-sedation scale (RASS), motor activity assessment scale (MAAS), Adaptation to the intensive care environment scale (ATICE), Ramsay Sedation Scale[10]

Payen et al. (2001) described the Behavioral Pain Scale (BPS) to assess pain in criticallyill ventilated patients, having three subscales: facial expression, upper limb movement, and compliance with mechanical ventilation[9]

Materials and methodology

This was a prospective, observational study comparing dexmedetomidine and fentanyl+midazolamin mechanically ventilated patients in ICU for sedation and analgesia.

After obtaining approval from the institutional ethics committee (IEC-Dr PSIMS AND RFAPPROVAL NO. PG/856/22) ,study was conducted from october2023 to july 2023 in 60 critically ill patients intubated in ICU in Dr.PSIMS & RF.

INCLUSION CRITERIA

1. Patients aged 18 years and above
2. Mechanically ventilated patients in intensive care unit

3. Both sexes

EXCLUSION CRITERIA

1. Patients in surgical ICU who are on mechanical ventilation
2. Neurological procedures and severe hepatic or renal disease
3. Known allergy to fentanyl or dexmedetomidine
4. Known or suspected pregnancy and gross obesity

After obtaining ethical clearance from the ethical committee study was conducted at our institute.

Patients were divided into 2 groups:

Group A : Dexmedetomidine 1 mcg/kg bolus followed by 0.25mcg/kg/hr

Group B: Fentanyl- 1mcg/kg bolus followed by 1.5mcg/kg/hr+Midazolam-0.02mg/kg bolus followed by 0.02mg/kg/hr

Participants were evaluated at baseline ,6th hour,12th hour,18th hour and 24th hour for, Heart rate,Mean arterial pressure, Ramsay sedation scale (RSS), Behavioural pain scales (BPS).

OBSERVATION AND RESULTS

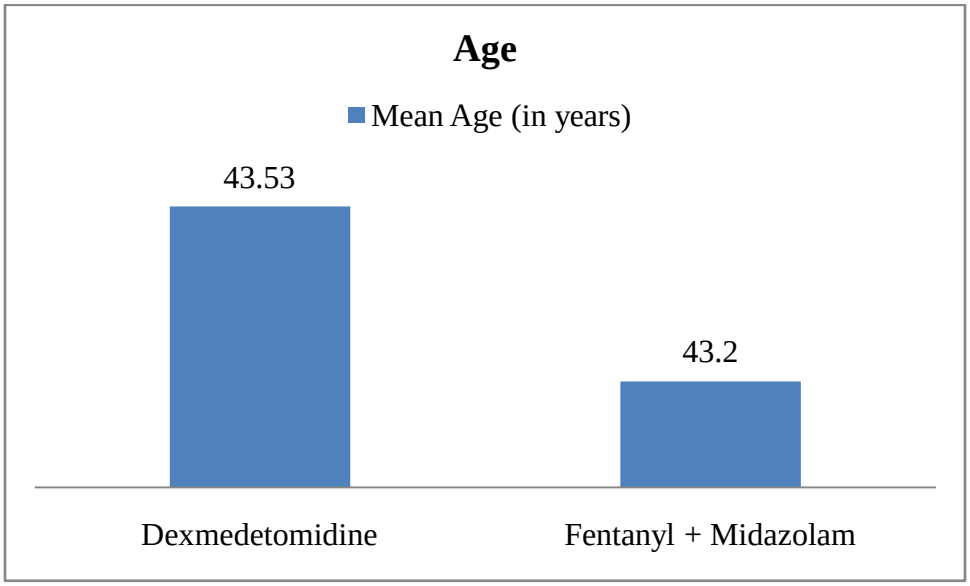
Patients who participated in this study were 39males accounting for65% and 21females accounting for 35%.

The mean age of the patients in dexmedetomidine group was 43.53 ± 11.383 years, and the mean age of the patients in Fentanyl + Midazolam group was 43.20 ± 12.823 years. On statistical comparison the two groups were comparable according to their age with p valueof 0.916.

Table 1:Distribution of patients according to age

Variable	Dexmedetomidine		Fentanyl + Midazolam		p value
	Mean	SD	Mean	SD	
Age(in years)	43.53	11.383	43.20	12.823	0.916

Graph 1: Age distribution of patients



Graph 2:Gender distribution of patients

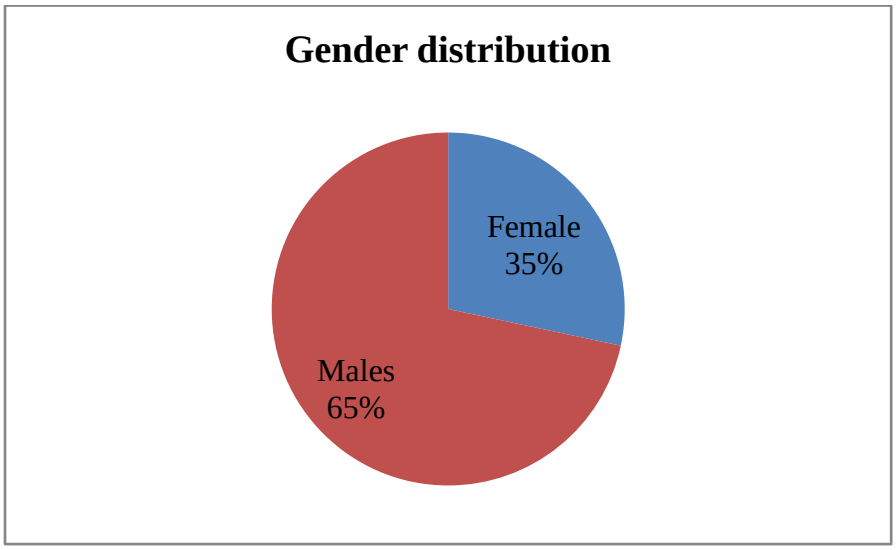
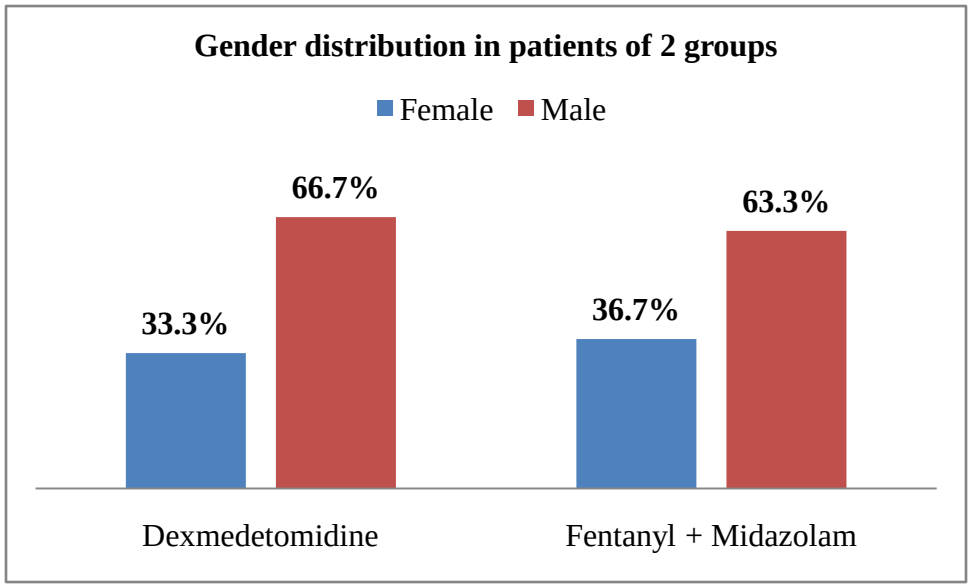


Table 2: Gender distribution in patients of 2 groups

Gender	Dexmedetomidine		Fentanyl + Midazolam	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Female	10	33.3%	11	36.7%
Male	20	66.7%	19	63.3%
Total	**30**	**100%**	**30**	**100%**

Graph 3: Gender distribution in patients of 2 groups



EFFICACY

Heart rates in the 2 groups were studied and statistically significant values were obtained between Dexmedetomidine and Fentanyl + Midazolam at 6 hr, 12 hr, 18 hr and 24 hrs.

Table 3:Comparison of Heart rate in 2 groups

Heart Rate(HR) (bpm)	Dexmedetomidine (Mean ±SD)	Fentanyl + Midazolam (Mean ± SD)	p value
0 Hrs	109.60 ± 6.526	109.03 ± 8.927	0.780
6 Hrs	96.40 ± 12.065	105.77 ± 10.385	0.002*
12 Hrs	93.17 ± 11.588	100.93 ± 10.144	0.008*
18 Hrs	88.03 ± 10.242	97.63 ± 8.743	0.002*
24 Hrs	80.83 ± 10.242	92.23 ± 7.960	< 0.001*

Graph 4: Comparison of Heart rate in 2 groups

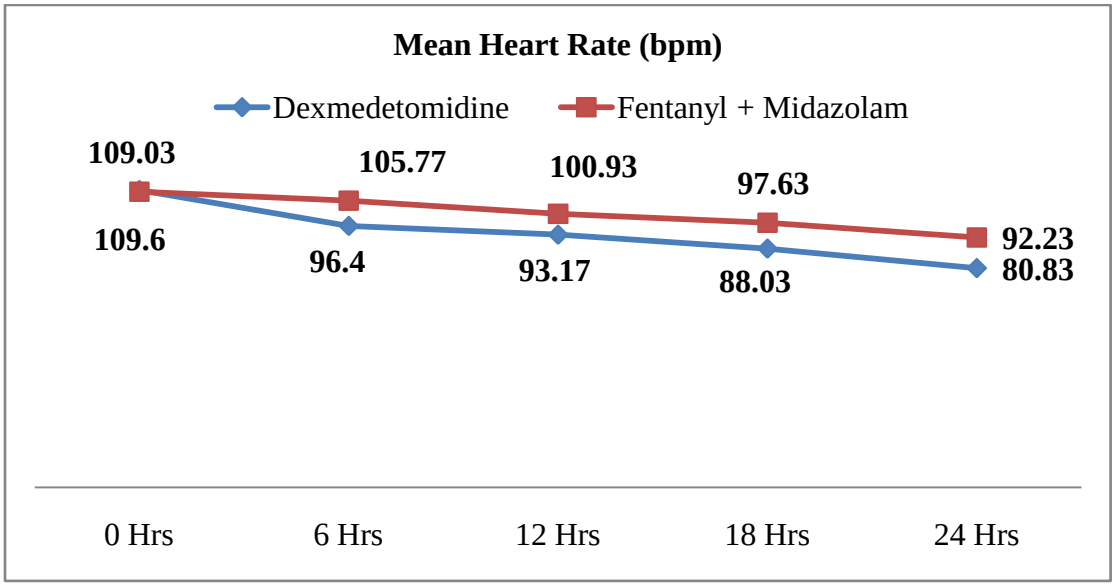


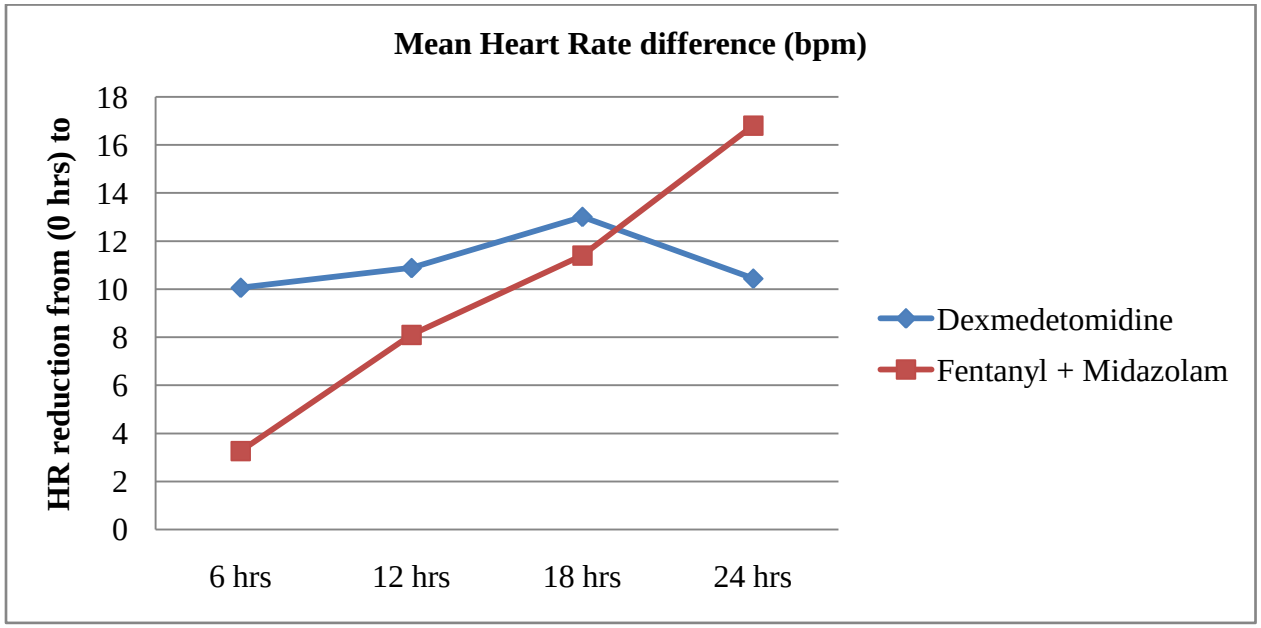
Table 4: Heart rate comparison

Study Group	Heart rate reduction from base line (0HRS)	Mean difference	SE of Difference	p - value
Dexmedetomidine	**6 hrs**	10.060	1.837	<0.001*
	12 hrs	10.881	1.987	<0.001*
	18 hrs	13.008	2.375	<0.001*
	24 hrs	10.441	1.906	<0.001*
Fentanyl + Midazolam	**6 hrs**	3.267	1.655	0.058
	12 hrs	8.100	1.814	<0.001*
	18 hrs	11.400	1.904	<0.001*
	24 hrs	16.800	2.170	<0.001*

On using Paired-t-test, we observed there was a significant difference in HR reduction from baseline to 24 hrs within each group. But the mean reduction of HR from baseline was significant statistically for dexmedetomidine during all the recorded times and for Fentanyl +

Midazolam during all the recorded times except for 6 hrs from the baseline recording with p-value <0.0001. These observations are tabulated in Table 4

Graph 5: Heart rate comparison



The mean of MAP was statistically compared and 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 were obtained at 18 hr and 24 hrs.

Table 5: Comparison of MAP in 2 groups

MAP (mm of Hg)	Dexmedetomidine (Mean ±SD)	Fentanyl + Midazolam (Mean ± SD)	p value
0 Hrs	113.13 ± 14.567	101.80 ± 18.310	0.010*
6 Hrs	101.60 ± 15.487	99.97 ± 16.900	0.698
12 Hrs	91.90 ± 14.194	94.37 ± 13.540	0.494
18 Hrs	86.10 ± 12.707	94.67 ± 11.839	0.009*
24 Hrs	82.43 ± 11.599	91.57 ± 13.219	0.006*

Graph 6: Comparison of MAP in 2 groups

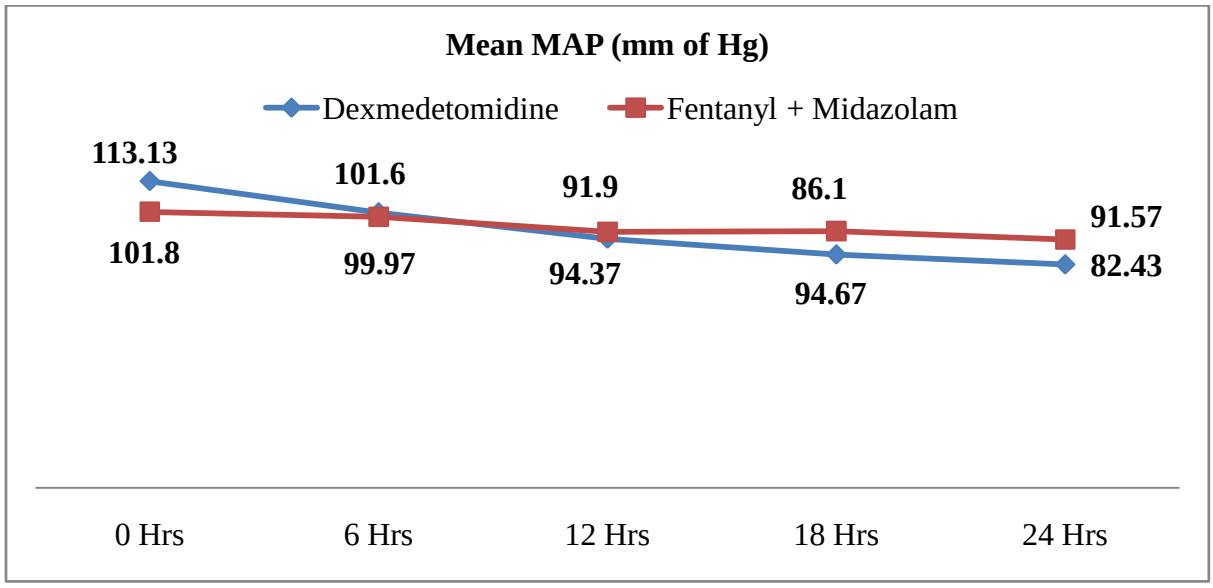


Table 6: MAP reduction within groups from baseline

Study Group	MAP reduction from (0 hrs) to	Mean difference	SE of Difference	p - value
Dexmedetomidine	**6 hrs**	11.533	1.837	<0.0001*
	12 hrs	21.233	2.145	<0.0001*
	18 hrs	27.033	2.094	<0.0001*
	24 hrs	30.700	2.475	<0.0001*
Fentanyl + Midazolam	**6 hrs**	1.833	2.373	0.446
	12 hrs	7.433	2.726	0.011*
	18 hrs	7.133	2.595	0.010*
	24 hrs	10.233	2.806	0.001*

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 significant statistically for dexmedetomidine with p-value <0.0001.

Graph 7: MAP reduction between groups from baseline

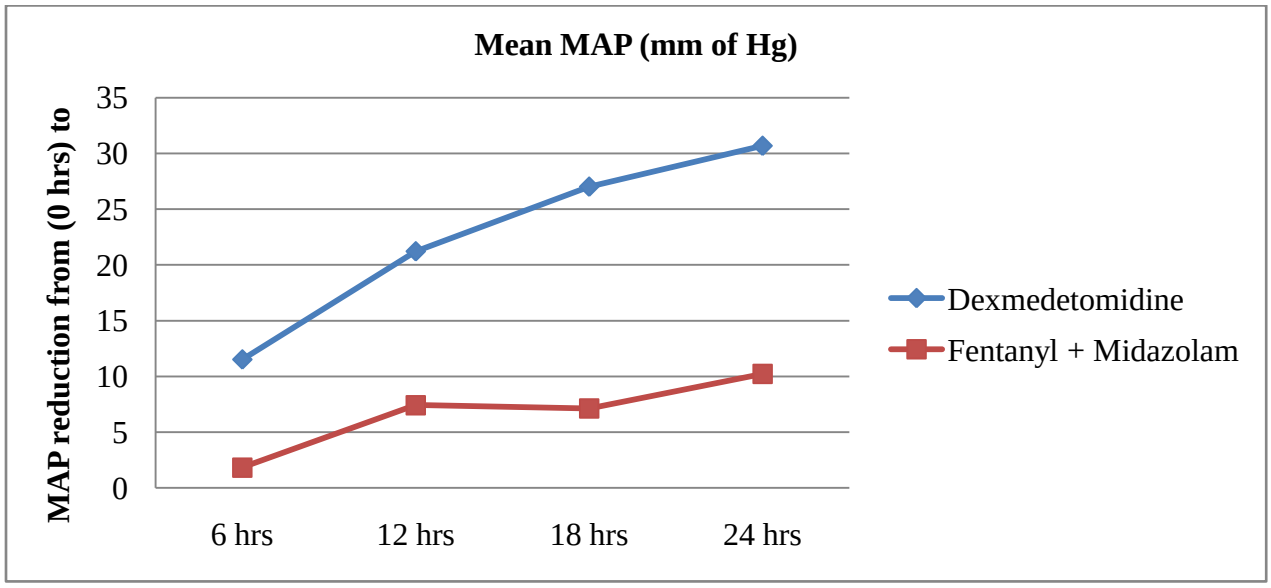
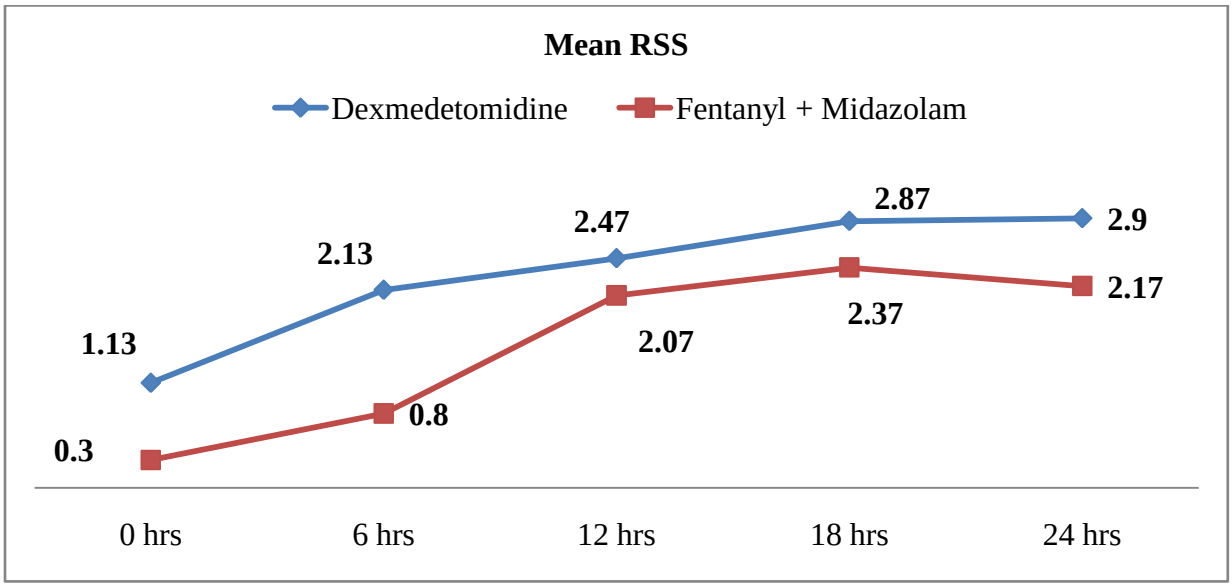


Table 7: Comparison of RSS in 2 groups

RSS	Dexmedetomidine (Mean ±SD)	Fentanyl + Midazolam (Mean ± SD)	p value
0 hrs	1.13 ± 0.571	1.30 ± 0.952	0.414
6 hrs	2.13 ± 0.900	1.80± 1.126	0.210
12 hrs	2.47 ± 0.973	2.07 ± 1.015	0.125
18 hrs	2.87± 0.819	2.37 ± 0.850	0.024*
24 hrs	2.90± 1.094	2.17± 0.913	0.007*

Graph 8: Comparison of RSS in 2 groups



There is a variation in RSS between 2 groups. Significant difference was not found between Dexmedetomidine and Fentanyl + Midazolam groups at baseline, 6 and 12 hrs.

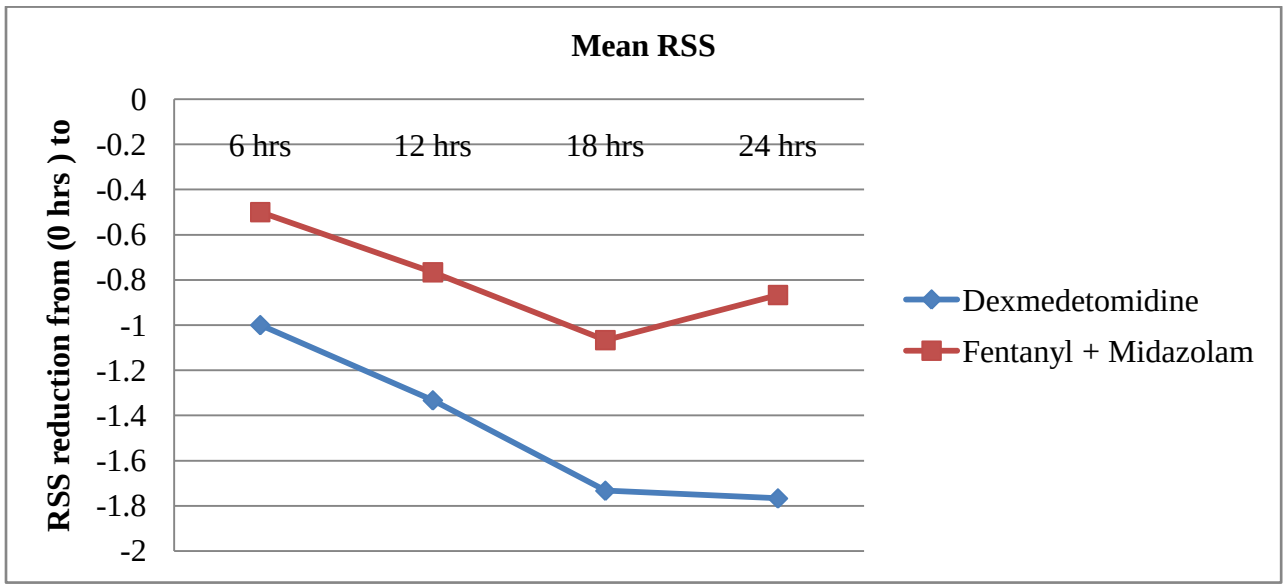
But on using Paired-t-test, we observed that there was a significant difference in RSS reduction from baseline to 24 hrs for Dexmedetomidine group and Fentanyl + Midazolam group, which was significant statistically with p-value <0.0001. These observations are tabulated in Table 7 and 8.

Table 8: RSS reduction in each group from baseline

Study Group	RSS reduction from (0 hrs) to	Mean difference	SE of Difference	P - value
Dexmedetomidine	**6 hrs**	-1.000	0.159	<0.001*
	12 hrs	-1.333	0.175	<0.001*
	18 hrs	-1.733	0.179	<0.001*
	24 hrs	-1.767	0.190	<0.001*
Fentanyl + Midazolam	**6 hrs**	-0.500	0.178	0.009*
	12 hrs	-0.767	0.164	<0.001*
	18 hrs	-1.067	0.179	<0.001*
	24 hrs	-0.867	0.150	<0.001*

* - statistically significant

Graph 9: RSS reduction within each group from baseline



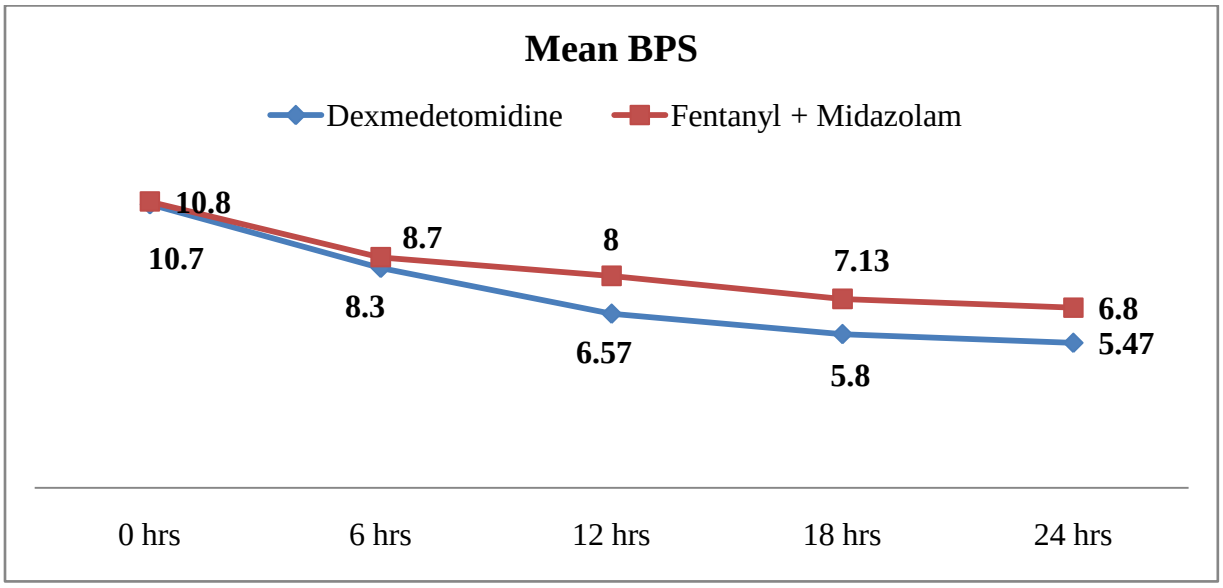
There is a little variation in BPS between 2 groups. Significant difference was found between Dexmedetomidine and Fentanyl + Midazolam groups at 12 hr, 18 hr and 24 hrs. These observations are tabulated in Table 9.

Table 9: Comparison of BPS in 2 groups

BPS	Dexmedetomidine (Mean ±SD)	Fentanyl + Midazolam (Mean ± SD)	p value
0 hrs	10.70±1.512	10.80 ± 1.648	0.807
6 hrs	8.30 ± 2.054	8.70 ± 1.643	0.408
12 hrs	6.57 ± 1.794	8.00 ± 1.838	0.003*
18 hrs	5.80 ± 1.495	7.13 ± 1.776	0.003*
24 hrs	5.47 ± 1.306	6.80 ± 1.750	0.001*

* - statistically significant

Graph 10: Comparison of BPS in 2 groups

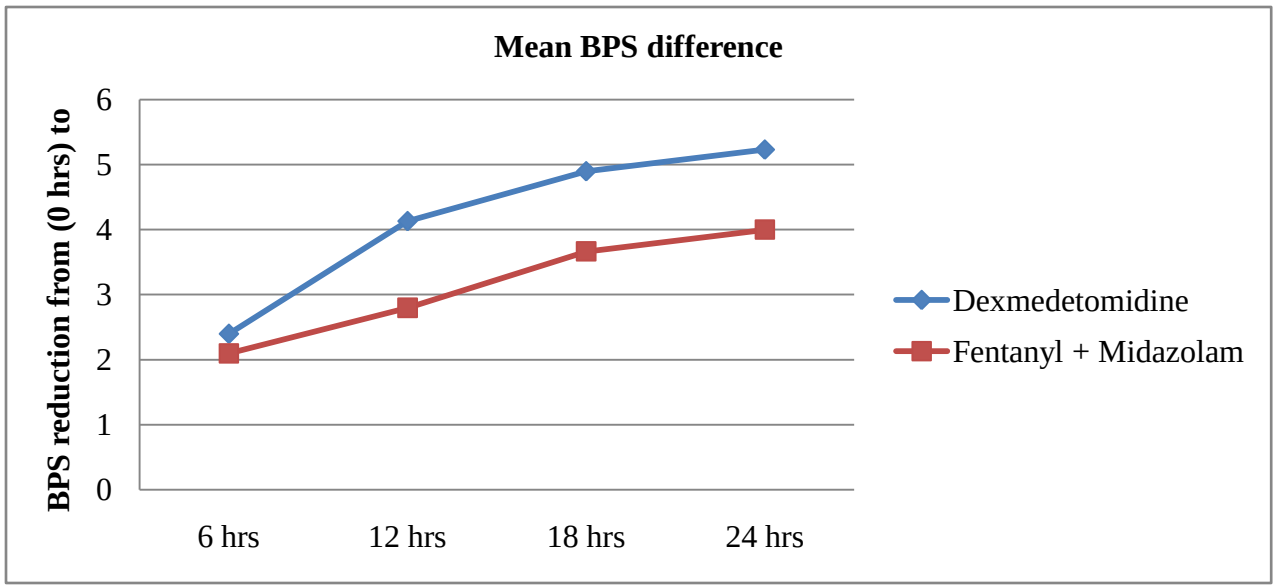


On using Paired-t-test, we observed that there was a significant difference in BPS reduction from baseline to 24 hrs within each group, and the mean reduction of BPS from baseline was extremely significant statistically for both Dexmedetomidine group and Fentanyl + Midazolam group with p-value <0.001

Table 10: BPS reduction in each group from baseline

Study Group	BPS reduction from (0 hrs) to	Mean difference	SE of Difference	P – value
Dexmedetomidine	**6 hrs**	2.400	0.243	<0.001*
	12 hrs	4.133	0.321	<0.001*
	18 hrs	4.900	0.326	<0.001*
	24 hrs	5.233	0.310	<0.001*
Fentanyl + Midazolam	**6 hrs**	2.100	0.188	<0.001*
	12 hrs	2.800	0.273	<0.001*
	18 hrs	3.667	0.308	<0.001*
	24 hrs	4.000	0.318	<0.001*

Graph 11: BPS reduction in each group from baseline



Discussion

The present study was conducted to explore and evaluate the efficacy and safety of dexmedetomidine over fentanyl and midazolam for sedation and analgesia in mechanically ventilated patients in ICU.

Pain is a common experience for most ICU patients[11,12,13]. With a sedative-based regimen, hypnotic agents aretitrated to maintain patient comfort despite them having almost no analgesic effect, and the opioid dose is usually minimised[14]. When interviewed about their ICU stay, many patients recall significant unrelieved pain[15,16,17].

So analgosedation should be provided for ventilated patients in ICU. The main aim of analgosedation is to relieve anxiety, patient – ventilator discomfort, minimize pain, facilitate treatment and provide adequate nursing care thereby improving patient outcomes.

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[18] A continuous infusion of sedatives is found to be an important predictor of longer duration of mechanical ventilation as well as longerstay in ICU[19]

An ideal sedative agent must have the following qualities. It should have short half-life without cumulative effects on cardiorespiratory systems. It should be titratable and allow for rapid recovery once discontinued[20]

Dexmedetomedine is almost an ideal sedative and analgesic for ICU owing to its no respiratory depressive action and minimal delirium and agitation[20]

In patients sedated with dexmedetomidine patients remain easily arousable combined with the minimal influence on respiration, makes dexmedetomidine an ideal drug sedation .

In our study, we evaluated Dexmedetomidine with fentanyl and midazolam because it is one of the most commonly used regimens in IndianICUs.Second reason is there are very few studies done in Indian population comparing both drugs.

Comparison with other studies

In our study, Heart rates were studied and statistically significant values were obtained between Dexmedetomidine and Fentanyl + Midazolam at 6 hr, 12 hr, 18 hr and 24 hrs

It was also observed that there was a significant difference in reduction of heart rate from baseline to 24 hrs within each group. But the mean reduction of HR from baseline was extremely significant statistically in dexmedetomidine group and for Fentanyl + Midazolam group during all the recorded times except for 6 hrs from the baseline recording with p-value <0.0001.

NEHA PANSE[21] et al in their study comparing dexmedetomidine and butorphanol sedation in icu patients showed statistically significant reduction in heart rate at T1 and T2 time points.

Basha s j et al[22] in their study comparing dexmedetomidine and butorphanol sedation in icu patients showed statistically significant reduction in heart rate at 6, 12,18 and 24 hrs.

Prasad S R et al[23] in their study comparing dexmedetomidine vs fentanyl in postoperative pediatric cardiac surgical patients showed frequency of bradycardia in the fentanyl group was significantly less. In the dexmedetomidine group, even though heart rate decreased in the first

few hours, it was not more than 10 to 15% from the baseline and did not require any intervention, where as in our study no patient showed bradycardia

Ashwin kumar d et al[20] in their study showed reduction in heart rate while comparing dexmedetomidine and fentanyl at 6 , 12,18 and 24 hrs. which was not statistically significant.

In our study, the mean of MAP was statistically compared and 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 were obtained at 18 hr and 24 hrs.

In Ashwin kumar d et al [20] in their study showed no statistical significant difference between the mean score for MAP measured at all intermittent time interval among Dexmedetomidine and Fentanyl.

NEHA PANSE[21] et al in their study comparing dexmedetomidine and butorphanol showed patients in dexmedetomidine group showed a higher systolic blood pressure before starting the infusion which was not clinically significant. Contrary to the usual belief, there was no significant difference in the systolic and diastolic blood pressure between both groups.

Basha s j et al[22] in their study comparing dexmedetomidine and butorphanol showed mean of MAP was statistically compared and 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 were obtained at 18 hr and 24 hrs.

In Prasad s r et al [23]There was no statistical as well as clinically significant difference in the hemodynamic parameters, i.e. the pulse, systolic blood pressure and diastolic blood pressure

In our study it was observed that there was a significant difference in RSS reduction from baseline to 24 hrs for Dexmedetomidine group and Fentanyl + Midazolam group, which was significant statistically with p-value <0.0001.

Samia elbaradie et al[24] in their study compared ramsay sedation scores.Ramsay sedation score was 4.1+/-1 and 4+/-0.9 for propofol and dexmedetomidine, respectively with a value of p=0.59 which is not statistically significant.

R M VENN ET AL[25] Over the whole study period, compared propofol with dexmedetomidine and found no significant statistical difference between the two groups.

PRASAD et al concludes 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"[23]

R M VENN ET AL concludes "Dexmedetomidine as a safe and acceptable sedative agent in the intensive care unit. The rate pressure product is reduced in patients receiving dexmedetomidine,which may protect against myocardial ischemia"[25]

Prathik et al concludes 'Use of a dexmedetomidine infusion in mechanically ventilated ICU patients managed with individualized targeted sedation, resulted in more days alive without delirium or coma"[26]

LIMITATIONS:

Small sample size: The sample size of our study was 60 which is less and it may affect the power of thestudy which interferes with translation of the results of this study into general population.

This current study was a single center study and replication and extension of this work are needed todetermine how generalizable the findings are.

The limitation of use of dexmedetomidine is its cost.

Rescue sedation and analgesia was not studied.

We have not studied the effect of inotropes on heart rate and blood pressure.

CONCLUSION:

In the present study we found that, dexmedetomidine is more efficacious than fentanyl+midazolam as a sole sedative and analgesic in intubated patients.

We conclude that dexmedetomidine at a dose of 1mcg/kg over 15minutes followed by 0.25mcg/kg/hr has turned out to be an excellent sedative and analgesic agent without any significant adverse effects.

Fentanyl+Midazolam can also be used as a sole sedative and analgesic in ICU and is cost effective.

Both are well tolerated and safe for use in intubated patients.

REFERENCES:

1.Pain terms: A list with definitions and notes on usage, recommended by the IASP subcommittee on taxonomy. Pain 1979; 6:249

2.Venn RM, Bradshaw C, Spencer R. Preliminary UK Experience of dexmedetomidine, a novel Agent for postoperative sedation in the intensive care unit. Anaesthesia.1999; 54: 1136-114.

3. Chen K, Lu Z, Xin YC, Cai Y, Chen Y, Pan SM. Alpha-2 agonists for long-term sedation during mechanical ventilation in critically ill patients. Cochrane Database Syst Rev. 2015 Jan 6;1(1):CD010269. doi: 10.1002/14651858.CD010269

4. Yu SB. Dexmedetomidine sedation in ICU. Korean J Anesthesiol. 2012 May;62(5):405-11. doi: 10.4097/kjae.2012.62.5.405. Epub 2012 May 24. PMID: 22679535; PMCID: PMC3366305.

5 .Gerlach AT, Dasta JF: Dexmedetomidine: an updated review, Ann Pharmacother41:245-252, 2007.368.

6.Tobias JD: Dexmedetomidine: applications in pediatric critical care and pediatric anesthesiology, PediatrCrit Care Med 8:115-131, 2007.

7. Kumar A, Mukund M, Jamal J. Comparison between Dexmedetomidine and Fentanyl Infusion for Short Term Sedation in Mechanically Ventilated Patients in Intensive Care Unit. European Journal of Molecular & Clinical Medicine.;9(07):2022.

8. Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med.* 2002;30:119–141.

9. Naithani U, Bajaj P, Chhabra S. Assessment of Sedation and Analgesia in Mechanically Ventilated Patients in Intensive Care Unit. Indian J Anaesth 2008;52:519

10. Gurudatt CL. Sedation in intensive care unit patients: Assessment and awareness. Indian J Anaesth 2011;55:553-5.

11.Novaes MA, Knobel E, Bork AM, Pavao OF, Nogueira-Martins LA, Ferraz MB. Stressors in the ICU: perception of the patient, relatives and healthcare team. *Intensive Care Med* 1999;25:1421–1426.

12. Puntillo KA. Pain experiences of intensive care unit patients. *Heart Lung* 1990;19:526–533.

13.Turner JS, Briggs SJ, Springhorn HE, Potgieter PD. Patients' recollection of intensive care unit experience. *Crit Care Med* 1990;18:966–968.

14. Muellejans B, Matthey T, Scholpp J, Schill M. Sedation in the intensive care unit with remifentanil/propofol versus midazolam/fentanyl: a randomised, open-label, pharmacoeconomic trial. Crit Care. 2006;10(3):R91. doi: 10.1186/cc4939. Epub 2006 Jun 15. PMID: 16780597; PMCID: PMC1550941.

15. Novaes MA, Knobel E, Bork AM, Pavao OF, Nogueira-Martins LA, Ferraz MB: Stressors in ICU: perception of the patient, relativesand health care team. *Intensive Care Med* 1999, 25:1421-1426.

16. Carroll KC, Atkins PJ, Herold GR, Mlcek CA, Shively M, Clopton P, Glaser DN: Pain assessment and management in critically illpostoperative and trauma patients: a multisite study. *Am J CritCare* 1999, 8:105-117.

17. Ferguson J, Gilroy D, Puntillo K: Dimensions of pain and analgesic administration associated with coronary artery bypass grafting in an Australian intensive care unit. *J Adv Nurs* 1997,26:1065-1072.

18. Lerch, Constance and Gilbert R. Park. “Sedation and analgesia.” *British medical bulletin* 55 1 (1999): 76-95.

19.Kollef MH, Levy NT, Ahrens TS, et al. The use of continuous I.V. sedation is associated with prolongation of mechanical ventilation. Chest. 1998; 114:541-548

20.Comparison between Dexmedetomidine and Fentanyl Infusion for Short Term Sedation in Mechanically Ventilated Patients in Intensive Care Unit. European Journal of Molecular & Clinical Medicine, 2022; 9(7): 968-975

21. Dr. Neha panse, to compare the sedation and analgesia produced by continuous infusions of dexmedetomidine and butorphanol in critically ill patients on mechanical ventilation: a randomized double-blind controlled trial., indian journal of applied research: volume-7 | issue-12 | december-2017

22. Basha SJ, Sanam R, Rekha KD. Comparison of Sedation and Analgesia Produced By Dexmedetomidine and Butorphanol in Critically Ill Patients on Mechanical Ventilation: A Prospective Observational Study.

23. Prasad SR, Simha PP, Jagadeesh AM. 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

24.Elbaradie S, El Mahalawy FH, Solyman AH. Dexmedetomidine vs. propofol for short-term sedation of postoperative mechanically ventilated patients. *J Egypt Natl Canc Inst*. 2004;16(3):153-158.

25.R. M. Venn, R. M. Grounds; Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions[†], *BJA: British Journal of Anaesthesia*, Volume 87, Issue 5, 1 November 2001, Pages 684–690.

26..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: