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SEDATION AND ANALGESIA IN THE MECHANICALLY VENTILATED PATIENTS: A COMPARISON BETWEEN DEXMEDETOMIDINE AND MIDAZOLAM PLUS FENTANYL.

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ABSTRACT **Background:** Sedation and analgesia are now regarded as an integral part of treatment of patients in the intensive care unit (ICU) instead of being an unpleasant but necessary and minor issues.

Material And Method: In this present comparative, randomized, prospective, double blind study total of 60 patients in ICU with surgical diagnosis who required ICU stay between ages 18-60 years of either sex of ASA grade I-II were included. Patients were divided into two group via computer generated random number (30 patients each):Group A: DEXMEDETOMIDINE-1µg/kg loading iv over 10-20 min followed by 0.2-0.7µg/kg/hr.) and Group-B: MIDAZOLAM PLUS FENTANYL- Loading dose of Midazolam 1mg i.v. and followed by 2-3 mg/hr and Fentanyl 25-50µg i.v. every 30 minute to 1 hour followed by 25-50µg /hr till Ramsay Sedation Score 3.

Result: In the group Midazolam plus Fentanyl shows wider range of Ramsay Sedation Score (2-5) than Dexmedetomidine group (2-4) which was statistically significant at 16 hr ($p<0.007$) and 24 hr ($p<0.005$).Thus at the end of 24 hr, Midazolam plus Fentanyl infusion provided deep level of sedation. Behavioral Pain Scale in both group was comparable which was not statistically significant ($p>0.05$). Side effects like bradycardia and hypotention was more in Dexmedetomidine group and delirium was more in Midazolam plus Fentanyl group.

Conclusion: Patients treated with Dexmedetomidine had earlier weaning and removal from mechanical ventilation, shorter ICU stay. So Dexmedetomidine can be preferred over Midazolam plus Fentanyl in achieving effective sedation and analgesia.

KEYWORDS : Dexmedetomidine, Midazolam, Fentanyl, Ramsay Sedation Score, Behavioral Pain Score

INTRODUCTION:

Sedation and analgesia are now regarded as an integral part of treatment of patients in the intensive care unit (ICU). Nearly all patients in the ICU experience pain, whether it is result of procedures performed, the disease process, catheters or endotracheal tubes insertion, or because they are immobile and cannot shift position[1]. Analgesia[2] is defined as pain control in the form of diminution or elimination of pain. American Society of Anesthesiologists[3] defines level of sedation according to responsiveness of patients into Awake, Moderate or conscious sedation, Deep sedation, General anaesthesia.

A large number of sedative drugs have been used eg. Benzodiazepines, Propofol and analgesic drugs like opioid, NSAIDS via intravenous route, patient controlled analgesia, intrathecal and epidural routes. Ideally a sedative and an analgesic agent used in ICU should have following criteria like easy administration, rapid onset of action, effective response, predictable duration of action, no adverse effect on vital organs mainly cardiac and respiratory system and antidote should be available. Now a days moderate or conscious of sedation is preferred for mechanically ventilated patients.

Dexmedetomidine is S-enantiomer of Medetomidine, a substance that has been used for sedation and analgesia[4].It shows a high specificity for alpha-2 receptor (alpha-2/alpha-1,1600:1) compared with Clonidine (alpha-2/alpha-1,220:1) thus making a complete alpha-2 agonist[5]. It belongs to the imidazole subclass of alpha-2 receptor agonist. It have sedative, analgesic, anxiolytic, sympatholytic effect and lack of respiratory depression attributed to action on Locus Coeruleus, a small nucleus located in dorsal horn of Pons. Analgesic effect are mediated by alpha-2 adrenergic receptor present on superficial dorsal horn in substantia gelatinosa by inhibiting nociceptive transmitter Substance P and Glutamate. It was introduced in clinical practice in the united states in 1999 and was approved by the Food and Drug Administration only as a short term <24 hours sedative for mechanically ventilated patients in ICU[6].

Midazolam is a benzodiazepine which is used as anxiolytic, sedative and anticonvulsant**.** It has rapid onset of action of 2-4 minutes, distribution half life of 6-15 minutes, elimination half life of 2 to 4 hrs. It has short duration of action. It is highly lipophillic. It is the most commonly used sedative agent which can be used for continuous infusion. Alpha hydroxy Midazolam is the active metabolite which accumulates in prolonged infusion. It is metabolized in the liver by hepatic microsomal oxidation and glucuronidation. Its metabolism may be impaired in elderly and in patients with liver disease[7].

Fentanyl citrate is commonly used opioid in anaesthesia which is a centrally acting synthetic opioid , a μ_1- and μ_2-receptor agonist. Fentanyl is a lipophilic opioid and is 100 times more potent than Morphine.It has replaced Morphine as the most popular opioid analgesic in ICU. The advantages of Fentanyl over Morphine includes more rapid onset of action, less risk of hypotension, the abscence of active metabolites and the relative lack of adverse hemodynamic effects Fentanyl is a lipophilic opioid. Lipophilicity of Fentanyl minimises its rostral migration to respiratory centre, thereby not causing delayed respiratory depression[8].

OBJECTIVES –

Primary objectives in our study were to assess sedation and analgesia level while change in hemodynamic parameters and side effects secondary objectives.

MATERIALAND METHOD :

Present study was conducted in Anaesthesia intensive care unit, Swaroop Rani Nehru Hospital associate to Moti Lal Nehru Medical College, Prayagraj over a period of one year. A total 60 patient in ICU with surgical diagnosis who required ICU stay at least 1 week, age between 18-60 years of either sex of ASA grade I and II.

Study Design:

It was comparative, randomized, double blind, hospital based study.

Sample Size:

The required sample size was calculated using the following formula as proposed by Kirkwood BR et al[9]**.**

Randomization:

Patients were randomized on the basis of a computer generated table of random number generated by using Microsoft Excel, SPSS Version 24.0.

Double Blinding:
Double blinding was achieved by three different anaesthesiologists – one for preparation of the study drug, second for administration of the drug and third for data collection. Hence the observer and patient both were unaware of the study.

Group Allocation
Patients were randomly allocated and divided into two groups using computer generated random number table(30 patients each):

GROUP A (DEXMEDETOMIDINE)	30 Patients	Each received a loading dose of injection Dexmedetomidine 1µg/kg(100µg/ml) iv over 10-20 min followed by an infusion at 0.2-0.7µg/kg/hr.
GROUP B (MIDAZOLAM PLUS FENTANYL)	30 Patients	Each received a loading dose of 1mg i.v Midazolam and followed by an infusion at 2-3 mg/hr and Fentanyl 25-50µg i.v.every 30 minute to 1 hour followed by an infusion at 25-50µg /hr.

The study included the patients who confirm the following:

Inclusion Criteria :
1) Patients with written informed consent
2) ASA grade I-II patients.
3) Adult patients between 18 – 60 years of age, of either sex.
4) Adults weighing between 45 to 90kgs.
5) Patient on ventilatory support
6) Patient should not have received any systemic analgesics or sedation in the last 4 hours

Exclusion Criteria :
1) Patient refusal.
2) Patient belonging to ASA physical status >II
3) Uncontrolled cardiovascular disease.
4) History of cerbro vascular disease.
5) Patients with severe hepatic and renal disease.
6) History of bleeding disorders.
7) Patients on oral anticoagulants/aniplatelet drugs.
8) Adverse reactions to any drugs used in the study.
9) Patient having neurological disorder.
10) Patients having spinal and epidural anaesthesia

METHODOLOGY
After approval from The Ethical Committee of the institution Registration no. ECR/922/inst/UP/2017, This Randomized control study was conducted at Swaroop Rani Nehru Hospital associated to Moti Lal Nehru medical college, Prayagraj over a period of one year from June 2019 to May 2020. Patients were shifted from surgical OT to ICU and put on mechanical ventilation after obtaining informed written consent. For all the patients age and weight were noted. Patients were randomly divided into 2 groups and study drug was started within 24 hours of the start of mechanical ventilation. In ICU Monitors attached as per standard ASA monitoring like pulse oximeter, NIBP and ECG were connected. Vital parameters like pulse rate, blood pressure (SBP,DBP), SpO_2 and baseline investigations like Complete Blood Count, Random blood sugar, Kidney Function Test, Liver Function Test, X- Ray Chest and E.C.G were noted. Double blind was achieved and preparation were made by the Post graduate colleague and given by other colleague hence the observer and the patient were unaware of the content of the preparation.

- Ramsay Sedation Scale (RSS) was used to assess the sedation level. RSS measures sedation in six points with score one being the Anxious, Agitated and six was patients with unresponsive to stimulus.

Ramsay Sedation Scale[10]

Sedation Level	Description level
1	Anxious, Agitated
2	Cooperative, oriented, tranquil
3	Responds only to verbal commands
4	Asleep with brisk response to light stimulation or loud auditory stimulus
5	Asleep without response to light stimulation (glabellar tap)
6	Non-responsive

- Behavioral pain scale was used to assess the intensity of pain as patient were intubated. BPS measures in 12 points with score 3 for no pain and 12 for maximum pain.

Behavioral Pain Scale[11]

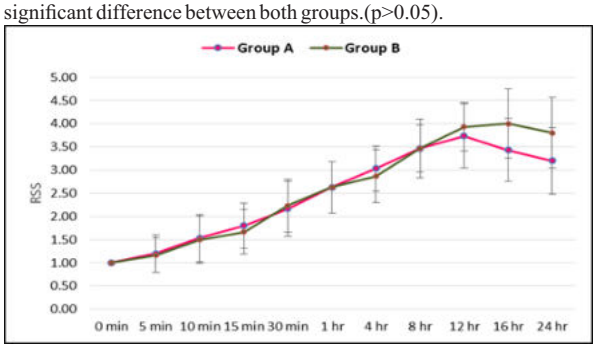
Item	Description	Sore
Facial expression	Relaxed	1
	Partially tightened (for example, brow lowering)	2
	Fully tightened (for example, eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation for most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Statistical Analysis-
Data was analysed by using coGuide software, V.1.0[12], Mean and Standard Deviation by sample t-test and quantitative variable like BPS, RSS by Mann-Whitney U test. P Value < 0.05 was considered as statistically significant.

OBSERVATION
Table 1: Comparison Of Demographic Profile

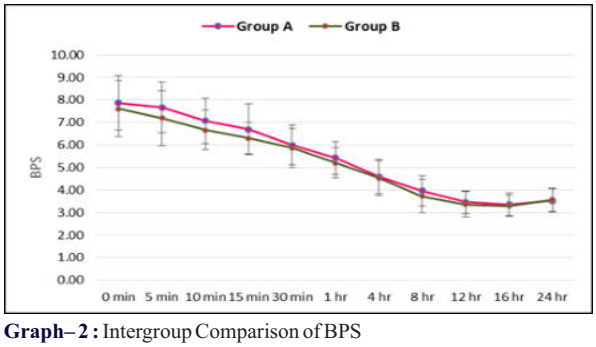
Variable		Group A	Group B	p-value
Age in years (mean±S.D)		46.60±8.32	42.43±10.73	0.20
Weight in kg (mean±S.D)		57.17±7.84	59.77±6.87	0.17
Sex (Female/Male)		60%/40%	46.7%/53.3%	0.30
ASA	Grade I	63.3%	56.7%	0.59
	Grade II	36.7%	43.3%	

Demographic profile in both groups were comparable with no significant difference between both groups.(p>0.05).



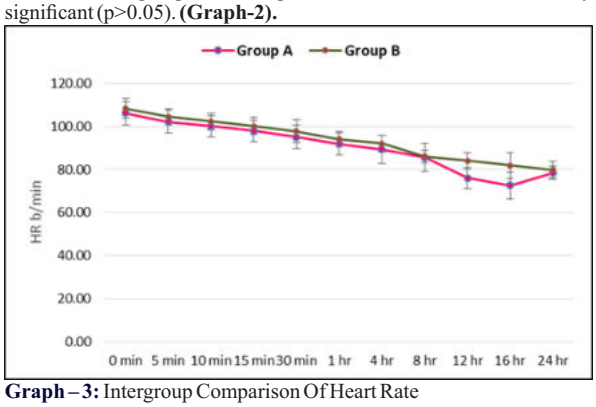
Graph – 1 : Intergroup Comparison of RSS

In our study mean value of RSS at 16 hr in group A was 3.43±.68 as compared to group B was 4±.74 which was statiscally significant where as at 24 hr RSS in group A 3.20±.71 and group B was 3.80±.76 which was statiscally significant**.** Ramsay Sedation Score in the group Midazolam plus Fentanyl shows wider range of RSS (2-5) than Dexmedetomidinegroup (2-4) which was statistically significant at 16 hr (p<0.007) and 24 hr (p<0.005). Thus at the end of 24 hr, Midazolam plus Fentanyl infusion provided deep level of sedation. **(Graph-1)**



Graph– 2 : Intergroup Comparison of BPS

In our study the intergroup comparison of BPS of two group A and B where the mean value of BPS of group A was 7.87±1.20 which gradually decreases and goes to minimum value of BPS 3.53±.51 at 24 hr while in group B mean value of BPS was 7.6±1.25 at 0 min which also decreases and goes to a minimum value of BPS 3,57±.50 at 24 hr. No significant difference was found at any time point. Behavioral Pain Scale in both group was comparable which was not statistically significant (p>0.05). **(Graph-2).**

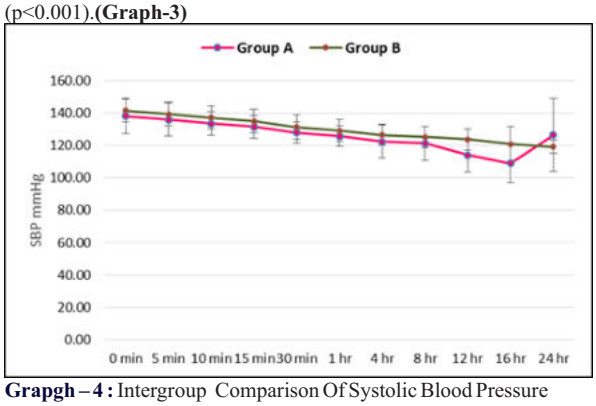


Graph – 3: Intergroup Comparison Of Heart Rate

The mean value of heart rate of Group A was 106.13±5.46 at 0 min which decreases and goes to a mean value 72.57 ± 6.15 at 16 hours again it increased and reached a mean value 78.43±3.05 at 24 hrs.

In group B the mean value of heart rate at 0 min was 108.40±4.50 it gradually decreases and reached a minimum mean value of 79.97±3.94 at 24 hrs.

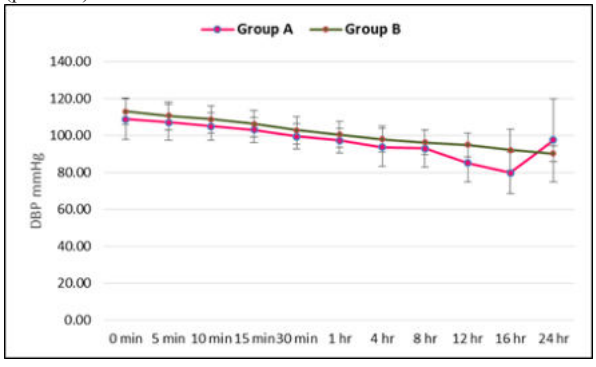
The significant differences were found at 12hr and 16 hr (p<0.001).**(Graph-3)**



Grapgh – 4 : Intergroup Comparison Of Systolic Blood Pressure

In above **Graph-4** the mean value of SBP in group A was 138.30±10.99 at 0 min which gradually decreased and goes to a minimum mean value 126.60±22.54 at 24 hr while the mean value of SBP of Group B was found 141.77±7.24 at 0 min which also gradually decreased and reached a minimum mean value 119.20±4.11 at 24hr.

The significant differences were found in both groups at 12 hr and 16hr (p<0.001).



Graph – 5 : Intergroup Comparison of Diatolic Blood Pressure

Graph 5 shows comparison of DBP of two groups A and B where in Group A the mean value of DBP of Group A was 109.03±11.11 at 0 min which decreases and goes to the mean value of DBP 97.57±22.76 at 24 hr, while in Group B the mean value of DBP was found 113.13±7.22 at 0 min which also gradually decreased and goes to a mean DBP value 90.33±4.18 at 24 hr.

No significant diffences were found at all the points except 12hr and 16 hr.

Table – 2 : Distribution Of Side Effects

Side effect	Group A		Group B	
	No.	%	No.	%
Bradycardia	3	10.0%	1	3.3%
Delirium after extubation	2	6.7%	6	20.0%
Hypotension	4	13.3%	2	6.7%

Table 2 shows that in Group A 13.3% shows Hypotension while Bradycardia and Delirium after extubation were(10.0% 6.7% respectively) while in Group B Delirium after extubation was showns by 20.0% person, hypotension (6.7%) and Bradycardia (3.3%).

RESULT-

Following results were drawn from the study :

- Demographic and baseline clinical characteristics were comparable between both the groups in respect of age, sex, weight and ASA status with no significant difference. (p>0.05)**(Table 1)**
- Ramsay Sedation Score in the group Midazolam plus Fentanyl shows wider range of RSS (2-5) than Dexmedetomidine group (2-4) which was statistically significant at 16 hr (p<0.007) and 24 hr (p<0.005).Thus at the end of 24 hr, Midazolam plus Fentanyl infusion provided deep level of sedation.**(Graph-1)**
- Behavioral Pain Scale in both group was comparable which was not statistically significant (p>0.05) **(Graph-2)**
- Dexmedetomidine group causes more bradycardia than Midazolam plus Fentanyl group which was statistically significant at 12 and 16 hr (p<0.001) **(Graph-3)**
- Dexmedetomidine group causes more decrease in systolic and diastolic pressure than Midazolam plus Fentanyl group which was statistically significant at 12 and 16 hr (p<0.001) **(Graph 4,5)**
- Side effects like bradycardia (10%) and hypotention (13.3%) was more in Dexmedetomidine group than Midazolam plus Fentanyl group (3.3%,6.7%, respectively).**(Table 2)**
- Post extubation delirium (20%) was more in Midazolam plus Fentanyl group than Dexmedetomidine group (6.7%). **(Table 2).**

DISCUSSION-

Dexmedetomidine, Midzolam and Fentanyl are the drugs that have been used very frequently to achieve adequate sedation and analgesia in mechanically ventilated patients.

Dexmedetomidine promotes the decrease in motor activity, mental stability, allowing better care by the physician, nurse and physical therapist. Its metabolites are inactive and the clearance is urinary and fecal. Analgesia and sedation are related to the binding to central noradrenergic receptors. It can modulate the descending inhibition from the locus coeruleus with noradrenaline release. Dexmedetomidine reduces the incidence of delirium and the duration of mechanical ventilation. It causes little respiratory depression and it is administered at a dose of 1 µg/kg, followed by an infusion of 0.1-0.7 µg/kg/h for analgesia and sedation, with the dose being titrated. With the infusion, hypotension occurs due to the central sympatholytic effect and noradrenaline decrease. The sympatholytic effect can be beneficial as it reduces tachycardia and arterial hypertension, or undesirable, as they cause hypotension and bradycardia..Although both Midazolam and Fentanyl have a rapid onset and a short clinical duration with single dose, accumulation and prolonged sedative effects may be observed after continuous administration, which is also indicated by a significantly longer context-sensitive half time of these drugs.

In our study mean value of RSS at 16 hr in group A was 3.43±.68 as compared to group B was 4±.74 which was statiscally significant where as at 24 hr RSS in group A 3.20±.71 and group B was 3.80±.76 which was statiscally significant**.**

Lalit Kumar Rajbanshi et al[13]. observed that Dexemedetomidine provided a comparatively narrower range of sedation level (2 to 4) than Midazolam infusion (2 to 5) and at the end of 24 hours, the range of the sedation score for the patient in Dexmedetomidine infusion was again

2 to 4 while it was 3 to 5 in midazolam group producing deep sedation.Thus Dexmedetomidine provided a uniform pattern of sedation level in comparison to Midazolam.

Santosh Kumar Sharma, Shahbaz Ahmad, Zulutena Jamir et al[14] observed that Dexmedetomidine provided an effective alternative to Midazolam in producing and maintaining controlled (RSS 2-3) short-term sedation in mechanically ventilated eclampsia patients and stable haemodynamics.

In our study the intergroup comparison of BPS of two group A and B where the mean value of BPS of group A was 7.87±1.20 which gradually decreases and goes to minimum value of BPS 3.53±.51 at 24 hr while in group B mean value of BPS was 7.6±1.25 at 0 min which also decreases and goes to a minimum value of BPS 3,57±.50 at 24 hr.No significant difference was found at any time point**.**

SR Prasad, Parimala Prasanna Simha, and AM Jagadeesh[15] studied the efficacy of sedation, analgesia and time required for extubation during Dexmedetomidine sedation were compared with that of Fentanyl. They observed that Dexmedetomidine provides comparable sedation, analgesic and stable haemodynamic effects as Fentanyl.

Devangi A Parikh, Sagar N Kolli, Hemangi S Karnik, Smita S Lele, and Bharati A Tendolkar[16] compared the satisfaction scores and effectiveness of sedation and analgesia with Dexmedetomidine with a combination of Midazolam-Fentanyl. Dexmedetomidine is a comparable alternative to the combination of Midazolam-Fentanyl for sedation and analgesia in tympanoplasty surgery under local anesthesia.

In our study the mean heart rate of group A was 106.13±5.46 at 0 min which decreases to mean value 76±4.90 at 12 hr and 72,57±6.15 at 16 hr as compared to group B where the decrease in mean heart rate at 12 hr was 84.17±3.83 and at 16 hr 81.93±5.98. The difference in mean heart rate in both the group at 12 and 16 hr was statistically significant**.**

In the study of **Richard R. Riker et al**[17] compared the efficacy and safety of prolonged sedation with Dexmedetomidine vs Midazolam for mechanically ventilated patients. Dexmedetomidine treated patients were more likely to develop bradycardia (42.2% [103/244] vs 18.9% [23/122]; *P*_.001), with a nonsignificant increase in the proportion requiring treatment (4.9% [12/244] vs 0.8% [1/122]; *P*=.07), but had a lower likelihood of tachycardia (25.4% [62/244] vs 44.3% [54/122]; *P*_.001) or hypertension requiring treatment (18.9% [46/244] vs 29.5% [36/122]; *P*=.02).

In the study of **Vinit K. Srivastava et al**[18]**.** compared the efficacy of Dexmedetomidine, Propofol and Midazolam for sedation in neurosurgical patients for postoperative mechanical ventilation. In group Dexmedetomidine there was a decrease in HR after Dexmedetomidine infusion (p<0.05), but there was no significant difference in HR between group Propofol and group Midazolam.

In our study at 12 hr mean fall in the systolic and diastolic blood pressure in group A was 114.10±10.5 and 85.23±10.15 respectively as compared to group B where mean SBP was 123.77±6.34 and DBP 95±6.36 and the difference was statistically significant. At 16 hr mean fall in SBP and DBP in group A was 108±11.86 and 79.90±11.43 respectively as compared to group B where mean SBP was 120.97±10.80 and DBP 92.33±11.14 and the difference was statistically significant**.**

Santosh Kumar Sharma, Shahbaz Ahmad, Zulutena Jamir et al compared the efficacy of Dexmedetomidine and Midazolam for sedation of eclamptic patients on mechanical ventilation in ICU. Both (Dexmedetomidine and Midazolam) groups showed decrease in heart rate (HR) and blood pressure (SBP, DBP, MAP) at all-time intervals, but the decrease was statistically significant.

Lalit Kumar Rajbanshi et al. compared Dexmedetomidine and Midazolam for sedation in mechanically ventilated patients and observed the Dexmedetomdine infusion produced greater fall in the blood pressure as compared to Midazolam infusion. There was maximum decrease in blood pressure at 12 to 16 hours of infusion and the difference between the groups was statistically significant (P< 0.001) which support our study.

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In adverse effect hypotension and bradycardia was more in group A (13.3%,10%) as compared to group B (6.7%,3.3%) respectively where as delirium after extubation was more in group B (20%) as compared to group A (6.7%).

Li Wang , Tiejun Zhang, Lili Huang , and Wei Peng[19] observed that the incidence of delirium in the Dexmedetomidine group was significantly lower than that in the Midazolam group, and the difference was statistically significant ($p = 0.003$).

Neeraj Kumar, Amarjeet Kumar, Ashish Kumar, Mumtaz Hussain, Anil Kumar[20] observed that the incidence of delirium was more in patient receiving Propofol group (6.6% vs. 20%, P = 0.346) than Dexmedetomidine group.

LIMITATIONS:-

1) Very small sample size was taken and further research was needed to know sedation analgesia effect in both drugs in mechanically ventilated patients.

2) We did not measure the patient satisfaction score and biochemical and haematological variables during study period.

3) The study had evaluated the sedation level only in the first 24hrs of starting infusions.This might have potentially biased the result in favour of Dexmedetomedine.

4) The study period was designed to last only during the administration of Midazolam and Fentanyl information of patient regarding adverse events after drug discontinuation such as withdrawl symptoms or dependency was not included.

CONCLUSION

As both group (Dexmedetomidine and Midazolam plus Fentanyl) were considered effective in achieving adequate level of sedation and analgesia for mechanically ventilated patients. Dexmedetomidine provided lighter plane of sedation that helped to make the patient awake earlier. Patients treated with Dexmedetomidine had earlier weaning and removal from mechanical ventilation, shorter ICU stay and less chance of developing ICU delirium. So Dexmedetomidine can be preferred over Midazolam plus Fentanyl in achieving effective sedation and analgesia with better outcome.

Conflict Of Interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Bader MK, Burns SM, Campbell M, et al. Consensus Conference on SedationAssessment – A Collaborative Venture by Abbott Laboratories, AmericanAssociation of Critical Care Nurses, and Saint Thomas Health System. Critical Care Nurses 2004; 24:33-41.
2. Carol A Warfield, Zahid HBajwa Principles & Practice of Pain medicine.2005; (2nd edition), Vol 1. Tata McGraw-Hill,
3. Practice guidelines for Sedation and Analgesiaby Non-anesthesiologists: An updated report by the American Society of Anesthesiologists Task Force on sedation and analgesia by Non-Anesthesiologists. Anesthesiology2002; 96: 1004-1017,
4. BhanaN,etal:Drugs 2000 59:263,
5. Virtanen R,etal:Eur J Pharmacol 1988; 150:9,
6. Gerlach AT,Dasta JF : Ann Pharmacother 2007; 41:245,
7. Tobias JD: Pediatr 2007 Cric Care Med 8:115,
8. Devlin JW,Roberts RJ pharmacology of commonly used analgesic and sedative in the icu: benzodiapines,propolfol and opiods.2009; crit care clin25(3):439-449.
9. Kirkwood BR. Essentials of medical statistics: Blackwell Scientific Publications; 1988.
10. Masaki K, Akira S, Asako I, Keiko K, et al. Study on sedation levels using Ramsay sedationscore and administration methods of propofol. Japanese Journal of Intensive Care Medicine 2005; 29:139-144.

11. Payen JF, Bru O, Bosson JL, et al. Assessing pain incritically ill sedated patients by using a behavioural pain scale. Crit Care Med 2001; 29:2258-63.
12. ADSS Corp . Released 2020. coGuide Statistics software, Version 1.0, India: ADSS corp.
13. Rajbanshi LK, ArjyalB,Bajracharya A, Khanal K, Sharma A. Comparison of dexmedetomidine and midazolam infusion for sedation in patients admitted in intensivecare unit. Journal of Chitwan Medical College. 2018 Sep 30;8(3):3-10.
14. Sharma, Santosh Kumar, et al. "A study of efficacy of dexmedetomidine and midazolam for sedation of eclamptic patients on mechanical ventilation in ICU." Journal of Evolution of Medical and Dental Sciences, 2017,vol. 6, no. 30, , p. 2415
15. Prasad, S. R., Parimala Prasanna Simha, and A. M. Jagadeesh. "Comparative study between dexmedetomidine and fentanyl for sedation during mechanical ventilation in post-operative paediatric cardiac surgical patients." Indianjournal of anaesthesia(2012),56(6): 547.
16. Parikh, Devangi A., et al. "A prospective randomized double-blind study comparingdexmedetomidine vs. combination of midazolam-fentanyl for tympanoplasty surgery under monitored anesthesia care." Journal ofanaesthesiology& clinical pharmacology(2013),29(2): 173.
17. Riker, Richard R., et al. "Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial." *Jama* (2009),301(5): 489-499.
18. Srivastava, Vinit K., et al. "Comparison of dexmedetomidine, propofol and midazolam for short-term sedation in postoperatively mechanically ventilated neurosurgical patients." *Journal of Neuroanaesthesiology and Critical Care* (2015), 2(02): A24.
19. Li Wang, Tiejun Zhang, Lili Huang, Wei Peng, "Comparison between Dexmedetomidine and Midazolam for Sedation in Patients with Intubation after Oral and Maxillofacial Surgery", BioMed Research International, 2020, vol. 2020, 6 pages,
20. Kumar, Neeraj, et al. "Comparison between dexmedetomidine and propofol for sedation during mechanically ventilated patients after major intraabdominal surgeries: An observational study." *Indian Journal of Clinical Anaesthesia* (2018), 5(2): 210-215.