Comparison between the Efficacy of Dexmedetomidine, Propofol and Midazolam for Sedation of Mechanically Ventilated Patients in ICU

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Abstract
Introduction: *Patients are treated with many interventionsin intensive care units (ICUs) mostly endotracheal intubation and invasive mechanical ventilation that are considered to be stress conditions. Pain is the commonest bad memorythat patients have during the period of their ICU admission. Agitation may cause accidental events such asremoval of endotracheal tubes or intravascular catheters used for monitoring or injection of life-saving medications. Consequently, sedatives and analgesics are widely used in ICUs.*

Benzodiazepines like midazolam and lorazepam, Non-benzodiazepines like the short-acting intravenous anesthetic agent like propofol orα2-adrenoceptor agonist sedation like dexmedetomidine. Remifentanil, an opioid, is also used as aunique agent due to its sedative properties. Benzodiazepines action occurs on γ-aminobutyric acid type A (GABAa) receptors, as in part does propofol, however dexmedetomidine is an α2-adrenoceptor agonist, on the other hand remifentanil is a μ-opioid receptor agonist.

Benha University Hospitals in the year of 2018. Patients were divided equally into 3 groups according to receiving of Dexmedetomidine, Propofol or Midazolam.

Group 1: *20 mechanically ventilated patients received Dexmedetomidine with loading dose 1 µg/kg over 10 minutes with I.V injection and follow by maintaining dose 0.2-0.7 µg/kg/h with continuous I.V infusion.*

Group 2: *20 mechanically ventilated patients received Propofol with loading dose 1 mg/kg over 5 minutes with I.V injection and follow by maintaining dose 1-3 mg/kg/min with continuous I.V infusion.*

Group 3: *20 mechanically ventilated patients received Midazolam with loading dose 0.05 mg/kg with I.V injection and follow by maintaining dose 0.05-0.1 mg/kg/h with continuous I.V infusion.*

Studying the efficacy of Dexmedetomidine, Midazolam and Propfol amongmechanically ventilated patient was done according to:

Respiratory rate (RR),Heart rate (HR),Mean arterial blood pressure (MAP),Changes in arterial blood oxygen saturation (SpO2,Length of staying on MV, time of extubation and Occurrence of delirium.

Conclusion: *Dexmedetomidine provides hemodynamic stability and has no clinically important adverse effects on respiration also provide less number of patients suffering from delirium.*

Introduction

The ICU environment is filled with uncomfortable procedures which may be invasive including endotracheal intubation, central venous catheterization and physical restraint. Also, ICU is a noisy atmosphere which amplifies anxiety of conscious patient[1]. It's thought that stress and anxiety worse the clinical outcome of the patients and exposure prevention of this noise can help enhancement of outcome[2].

Mechanical ventilation (MV) considered one of the most common procedures in ICU which being invasive, uncomfortable, stressful and even painful maneuver. Hence, the international guidelines recommend routine use of sedative drugs to reach and sustain optimal level of comfort to prevent these streesful effects.[3] It was found that reaching a low level of sedation that offers analgesia, comfort, mentain day/night cycle and avoiding discomfort is associated with improved clinical outcomes[4].

Benzodiazepines like midazolam, propofol and opioids are among the drugs commonly used for sedation ICU. Dexmedetomidine, and α2-adrenoceptor agonist, has also been accepted for use as a short-term sedative medication in ICU.[5]

The suggestion performed by the recent studies to change the conceptof being benzodiazepines as the backbone of therapy in compare of non-benzodiazepine including dexmedetomidine or propofol.[6]

Aim of the work

The aim is to study the comparison between the efficacy of Dexmedetomidin, Propofol and Midazolam in sedation of mechanically ventilated patients in ICU in respect to the changes in heart rate (HR), respiratory rate (RR), mean arterial pressure (MAP) and oxygen saturation of arterial blood (Spo2) during sedation with each drug during period of MV till the time of extubation and the comparison included the length to stay on MV and associated delirium with

Patients and Methods

- ❖ This prospective observational consisted of sixty patients who were admitted to the Critical Care Department, Benha University Hospitals in the academic year of 2018.

Patients were divided into 3 groups

Group 1: 20 mechanically ventilated patients received Dexmedetomidine with loading dose 1 µg/kg over 10 minutes with I.V injection and follow by maintaining dose 0.2-0.7 µg/kg/h with continuous I.V infusion.

Group 2: 20 mechanically ventilated patients received Propofol with loading dose 1 mg/kg over 5 minutes with I.V injection and follow by maintaining dose 1-3 mg/kg/min with continuous I.V infusion.

Group 3: 20 mechanically ventilated patients received Midazolam with loading dose 0.05 mg/kg with I.V injection and follow by maintaining dose 0.05-0.1 mg/kg/h with continuous I.V infusion.

Dosing adjustment

To compare between the effects of the 3 drugs we must reach the same degree of sedation by each one. As The Richmond Agitation-Sedation Scale (RASS) and Ramsay Sedation-Agitation Scale (RSS) are the most reliable sedation assessment of depth and quality of sedation in adult ICU patients, we applied them to estimate the level of sedation.

The target RASS between 2:4 and the target RSS 2:3 and by hourly careful follow up of both actual and target levels we titrated the sedative infusing doses.

Studying the efficacy of Dexmedetomidine, Midazolam and Propfol among mechanically ventilated patient was done according to:

- Respiratory rate (RR).
- Heart rate (HR).
- Mean arterial blood pressure (MAP).
- Changes in arterial blood oxygen saturation (SpO2).

- Length on staying on MV and time of extubation.
- Occurrence of delirium

Inclusion criteria

The study included patients who meet the following conditions:

- Both genders.
- Aged more than 18 years.
- Needing sedation to initiate and to sustain mechanical ventilation.

Exclusion criteria

The study excluded patients who meet the following conditions:

- Allergy or intolerance to used drug in each group.
- Pregnancy.
- Patients recently treated with α2 agonist or blocker.
- Post cardiac arrest encephalopathy from different causes.
- Acute coronary syndromes.
- Coma of neurological origin.
- Coma of unknown etiology.

Results

There was no statistically significant difference in age distribution ,gender and weight between the groups (P >0.05).

Heart rate (HR)

As regard heart rate table (1) show p value = 0.001 this means statistically significant difference is present among the groups.
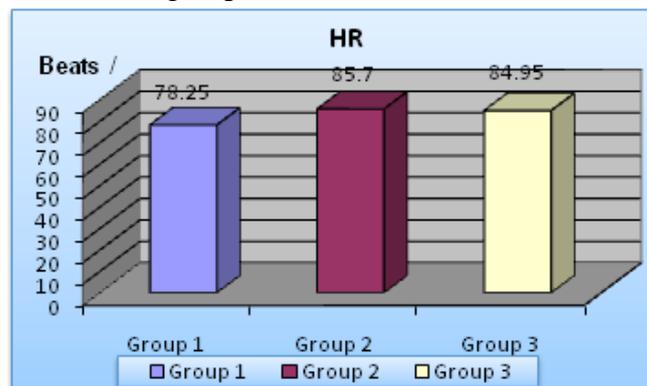
There was highly statistical significance between group 1& group 2 and between group 1& group 3 p value =0.001 but there was no statistical significance between group 2 & group 3 P-value > 0.050 non-significant.

Table 1: follow up of heart rate during MV in between the groups

HR (Beats / min.)	Group 1	Group 2	Group 3
Range	73 – 87	80 – 90	80 – 90
Mean ± SD	78.25 ± 4.83	85.70 ± 3.25	84.95 ± 2.87
F. test	23.950		
p. value	0.001*		

Group 1 & Group 2	Group 1 & Group 3	Group 2 & Group 3
0.001*	0.001*	0.529

Figure (1) follow up of heart rate during MV in between the groups

Respiratory rate

No statistical significant differences between three groups as regard respiratory rate, P-value > 0.050 non-significant.

Changes in arterial blood oxygen saturation (SpO2)

There was no statistical significance difference between the studied groups as regard the changes in arterial blood oxygen saturation (SpO2) p value > 0.050.

No significant difference between three groups as regards the systolic blood pressure , diastolic blood pressure and MAP p value > 0.050.

Duration from cessation of sedation to extubation

Table (2): Duration from cessation of sedation to extubation.

Duration from cessation of sedation to extubation (hours)	Group 1	Group 2	Group 3
Range	6 – 8.5	4.2 – 7	4.5 – 25
Mean ± SD	7.40 ± 0.76	5.65 ± 0.96	16.42 ± 6.74
F. test	42.648		
p. value	0.001*		
Group 1 & Group 2		Group 1 &Group 3	Group 2 &Group 3
0.169		0.001*	0.529

Table (2) showing comparison between the studied groups as regard duration from cessation of sedation to extubation.
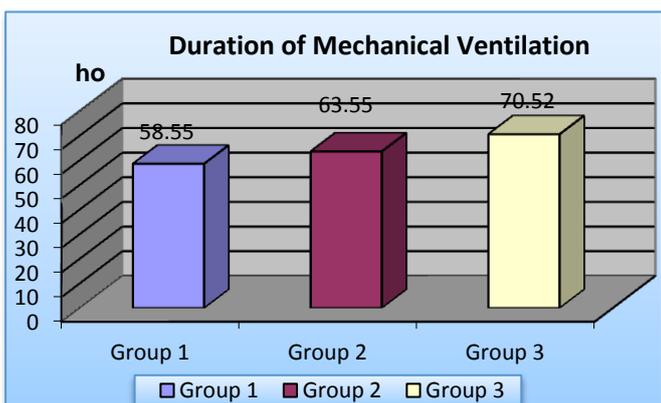
There was statistical significant differences between three groups p value =0.001.

There was statistical significant differences between group 1& group 3 p value =0.001 but no statistical significant differences between group 1&2 and group 2&3 p value > 0.050.

Duration of Mechanical Ventilation
Table (3) Duration of Mechanical Ventilation

| Duration of Mechanical Ventilation	Group 1	Group 2	Group 3
Range	36.6 – 80.5	38.8 – 88.5	45.2 – 132
Mean ± SD	58.55 ± 16.66	63.55 ± 17.22	70.52 ± 25.0
F. test	1.809		
p. value	0.173		

Figure (2) Duration of Mechanical Ventilation
As regard duration of mechanical ventilation there was no statistical significant differences between the studied groups p value > 0.050. Table 3 fig 2.

Prevalence of delirium
Table (4) and figure (3) shows the number of patient suffering from delirium in each groups higher number of patients in group 3 and lower number in group .

There was no statistical significant differences between the studied groups p value > 0.050

Figure (3): Prevalence of delirium
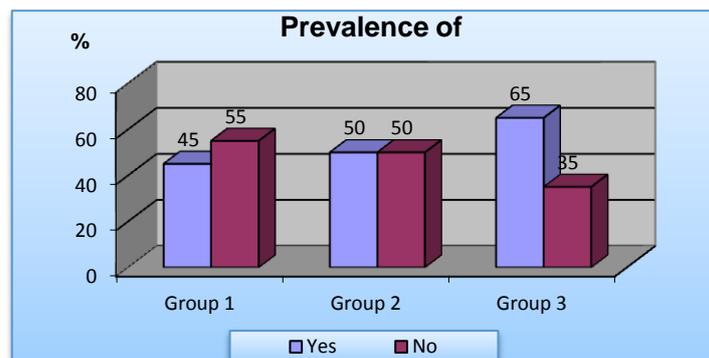
Table (4) Prevalence of delirium

Prevalence of delirium		Group 1	Group 2	Group 3	Total
Yes	N	9	10	13	32
	%	45.0%	50.0%	65.0%	53.3%
No	N	11	10	7	28
	%	55.0%	50.0%	35.0%	46.7%
Total	N	20	20	20	60
	%	100.0%	100.0%	100.0%	100.0%
Chi-square	X^2	1.741			
	P-value	0.419			

Conclusion
From the result of this study we can conclude that
Dexmedetomidine a new sedative agent is safe to be used in the mechanically ventilated in ICU. Dexmedetomidine provides hemodynamic stability and has no clinically important adverse effects on respiration also provide less number of patients suffering from delirium. Tracheal extubation was earlier in patients receiving, dexmedetomidine and propofol than from midazolam

Recommendations
✧ The number of patients in this study is small, so studies on large numbers of patients might have an effect on the different variables.

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