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Impact of Dexmedetomidine Infusion on Hemoglobin, Liver Enzymes, Serum Glucose in Patients with Sepsis in the Intensive Care Unit

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Abstract

Sepsis is a widespread multi-system severe inflammatory response to a stressor (infection, trauma and surgery). Diffuse cellular injury due to the massive release of inflammatory mediators (interleukins and tumor necrosis factor) is the hallmark with the release of stress hormones – corticosteroid and adrenaline- are the mainstay for the development of stress hyperglycemia, acute liver injury. Dexmedetomidine is a centrally acting highly selective alpha receptor agonist possess anti-inflammatory action through its sympatholytic action. To determine whether dexmedetomidine can decrease sepsis induced liver injury, stress hyperglycemia and its effect on serum hemoglobin and Glasgow coma scale. This prospective randomized single blinded study conducted on 40 patients with sepsis on mechanical ventilation in ICU at Minia university hospital classified into two groups Group I: (control group): Undergo loading dose of midazolam (0.05-0.3mg/kg followed by maintenance dose (0.05-0.2mg/kg/hour). Group II: (Dexmedetomidine group): Undergo loading dose of 1 µg/kg dexmedetomidine over 10 minutes followed by a continuous IV infusion at 0.2–0.7 µg/kg/hour**.** Dexmedetomidine can significantly decrease serum glucose level at day 4 and 5 with p value= 0.04 and 0.03 respectively and liver enzymes at 3, 4, and five days from admission. No significant impact over GCS and hemoglobin level. Dexmedtomidine infusion could successfully decrease serum glucose and liver enzymes levels in patients with sepsis in intensive care unit**.**

Keywords: Sepsis, mechanical ventilation, stress hyperglycemia, liver injury

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1. Introduction

Pro-inflammatory mediators released in the context of sepsis are the cornerstone for the process of tissue injury. Continuous inflammation can provoke cellular apoptosis. Stress hyperglycemia mediated by endogenous steroid can enhance this injury [1]. Sedation via many drugs can ameliorate this process. Dexmedetomidine is a highly selective alpha 2 agonist. It mediates decrease release of noradrenaline creating a state of sympatholysis. Moreover, Dexmedetomidine can decrease inflammatory prostaglandin and tumor necrosis factor [2].

2. Materials and Methods

This prospective randomized single blinded study conducted on 40 patients of Patients with sepsis undergoing mechanical ventilation in ICU at minia university hospital classified into two groups Group I: (control group): Undergo loading dose of midazolam: 0.05-0.3mg/kg in increments of 1-2.5mg followed by Maintenance dose: 0.05-0.2mg/kg/hour. Group II: (Dexmedetomidine group): Undergo loading dose of 1 µg/kg dexmedetomidine for 10 minutes followed by a continuous IV infusion at 0.2–0.7 µg/kg/hour**.**

2.1. Sample size calculation

Sample size was calculated using online programmer for odds ratio sample size calculation. Using the following parameters:

- Relative precision (49%)
- Confidence interval (89.8%)
- Expected prevalence of the outcome in absence group (59.5%)

Accordingly, estimates sample size was 40 patients.

2.2. Inclusion Criteria for study group

Age being between 18 & 80 years old, both male and female included, intubated, and mechanically ventilated patients.

2.3. Exclusion Criteria for groups

1. Patient's relative's refusal.
2. Pregnancy or lactation.
3. Serious central nervous system pathology.

2.4. Ethical Consideration

Study protocol had been submitted for approval by the ethics committee on research involving human subjects of faculty of Medicine at Minia University**.** Informed written consent had been obtained from relatives of each participant sharing in the study. Confidentiality and personal privacy had been respected in all levels of the study.

2.5. Methods

The eligible subjects included in this study were subjected to the following: Full history taking, clinical examination and laboratory investigations.

2.6. Statistical analysis

Data were analyzed using SPSS version 22 (Statistical Software package version 22). Data were presented using descriptive statistics in the form of mean and standard deviation for quantitative variables, while median and interquartile range were used for scores. Independent sample t test was used to compare means. Mann-Whitney test to compare medians. Statistical significance was considered at p-value <0.05.

3. Results and discussion

Table 1 showed that there was statistically significant difference between the studied groups regarding liver enzymes at third, fourth and fifth day (p value= 0.04, 0.03 and 0.02 respectively). However, regarding serum glucose, there was significant difference inbetween 2 groups at fourth and fifth day of admission (p value= 0.04 and 0.03 respectively). Table 2 showed that there was no statistically significant difference between the studied groups regarding hemoglobin and hematocrit.

Table 1. Represents changes of SGOT, SGPT and glucose overtime (difference measured from baseline 1st reading at 1st day) among different study group

Variable (mean difference)	**Dexmedetomidine group n = 20**	**Control group n = 20**	**Significance**
SGOT (day 2)	2.1±4.75	7.25±16.2	P=0.19
SGOT (day 3)	6.25 ± 17.7	19.05 ±22.2	**P=0.04**
SGOT (day 4)	16.65±35.1	30.9 ±35.2	**P=0.03**
SGOT (day 5)	19.1 ±38.4	29.7 ± 43.9	**P=0.02**
SGPT (day 2)	1.15 ±4.36	2.8 ±10.5	P=0.52
SGPT (day 3)	8.95±13.7	9.8± 14.4	**P=0.04**
SGPT (day 4)	5.45 ± 21.6	13.55 ±25.8	**P=0.03**
SGPT (day 5)	7.6 ±25.8	16.01 ±33.4	**P=0.02**
Glucose (day 2)	-15.9 ±47.5	-5.45 ± 61.8	P=0.55
Glucose (day 3)	-20.6 ± 43.8	-22.7 ±59.8	P=0.47
Glucose (day 4)	-17.06 ±55.9	-12.2 ± 47.6	**P=0.04**
Glucose (day 5)	-18.76± 63.3	-10.6 ±61.5	**P=0.03**

Table 2. Offers data about changes of hematocrit and hemoglobin overtime (difference measured from baseline 1st reading at 1st day) among different study group

Variable	Dexmedetomidine group n = 20	Control group n = 20	Significance
Htc (day 2)	-0.1±.05	-0.49±0.05	P=0.78
Htc (day 3)	-0.34±0.09	-1.07±0.15	P=0.65
Htc (day 4)	-1.1±1.04	-1.97±0.16	P=0.67
Htc (day 5)	-2.35±1.1	-1.94±0.5	P=0.84
Hb (day 2)	-0.49±0.2	-0.58±0.37	P=0.83
Hb (day 3)	0.13±0.05	-1.41±0.15	P =0.22
Hb (day 4)	-0.49±0.06	-1.38±0.68	P=0.1
Hb (day 5)	-1.08±0.95	-1.59±0.99	P=0.42

Table 3. Medians, interquartile ranges of GCS scale overtime between two study groups

Variable	Dexmedetomidine group n = 20	Control group n = 20	Significance
GCS admission	8 (6-13)	7 (6- 9.25)	P=0.32
GCS 12 hours	7 (6-12)	7 (6- 9.25)	P=0.35
GCS 24 hours	7 (6-12.25)	7 (6-9.75)	P=0.25
GCS day 2	7 (6-11.75)	6 (5-9)	P=0.11
GCS day 3	6 (5-10)	6 (5-8.5)	P=0.13
GCS day 4	6 (5 -9)	5 (4-8)	P=0.17
GCS day 5	6 (5-9)	5 (4-8.25)	P=0.25

Data presented by median, IQR. Mann-Whitney test to compare medians

Table 3 showed that there was no significant difference between the studied groups regarding Glasgow coma scale. Dexmedetomidine as the active isomer of medetomidin, was licensed by the Food and Drug Administration (FDA) in 1999 to sedate patients admitted to intensive care units (ICUs). Accordingly, the use of alpha-2 agonist agents as DXM to common septic shock treatments could reduce vasopressor dose requirements via decreasing the output of noradrenergic neurons from the locus cereulus while increasing the activity of inhibitory neurons such as gamma aminobutyric acid [3]. Furthermore, several studies have shown that DXM can suppress inflammatory reactions and protect organs in humans [4]. The current study compared between DEX and midazolam infusion in septic patients. No statistically significant differences were seen in the current study with respect to hemoglobin, hematocrit, GCS, while serum glucose and liver enzymes was significant at day 4 and 5 and 3,4 and 5 days respectively from admission of ICU. Dexemedtomidine with its alpha 2-receptor agonistic activity and sympatholytic action could decrease anti-insulin hormones (noradrenaline and adrenaline) which can explain the significant decrease in serum glucose. These results match those of lin et al., 2022 who conducted a single center placebo-controlled clinical trial about peri-operative hepatic protection of dexemedetomidine in 44 type II diabetic patients. They concluded that dexmedetomidine can attenuate oxidative stress with decreasing serum glucose and prevent elevation of liver enzymes without any potential risk [5]. In contrast to our results, Matthias et al., 2019 in their randomized trial which enrolled sixty four child undergoing elective general anesthesia under dexmedetomidine infusion in multi-dosing fashion (0.25 µg/kg dexmedetomidine , dexmedetomidine 0.5 µg/kg, dexmedetomidine 0.75 µg/kg). They noticed slight elevation of serum glucose after 15 minutes after induction of anesthesia. This difference can be attributed to dose change beside the use og glicose 5% as a maintenance fluid therapy intra-operative [6]. In the current study, dexmedetomidine didn't affect hemoglobin nor hematocrit. However, Doaa et al., 2015 reported significant rise in HB and hematocrit in adult population with open nephrolithotomy postoperative in dexmedetomidine group in comparison to control group. This discrepancy can be explained by the use of dexmedetomidine as a deliberate hypotensive agent which can decrease intraoperative blood loss [7].

4. Conclusions

Dexmedtomidine infusion could successfully decrease serum glucose and liver enzymes levels in patients with sepsis in intensive care unit.

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