

*Research Article***The efficacy of combination of Terlipressin and Norepinephrine Versus Norepinephrine in Septic Shock****Ibrahim A. Yousef, Assist. Jozef Z. Attia, and Moustafa R. Iaky**

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Abstract

Introduction: Sepsis is the clinical syndrome defined by the presence of systemic inflammatory response syndrome (SIRS) in the setting of an infection. **Aim of the work:** Aim of this study is to evaluate and compare the effect of terlipressin and norepinephrine versus norepinephrine in septic shock. **Patients and methods:** After obtaining the local ethics committee of EL-Minia University Hospital . approval and written informed consent was taken from the relatives, this prospective double blind study was conducted on 40 adult patients of both gender admitted to our ICU with septic shock. Septic shock was defined by the presence of two or more diagnostic criteria for systemic inflammatory response syndrome, proven or suspected Infection, and hypotension despite adequate fluid resuscitation (defined as systolic blood pressure <90 mmHg or MAP <70 mmHg in absence of other causes of hypotension. The patients were allocated into two equal groups (20 patients in each group) by using a computer- generated table. **Group A (Norepinephrine group):** Two syringe pumps were prepared one containing NE (8mg) was dissolved in a 50ml syringe containing 5% dextrose in water and the other containing saline. The NE infusion started at .05ug/kg/min (at rate 1.3ml/hr) with maximum infusion rate of 0.8ug/kg/min till reached the target mean arterial blood pressure of 65-75mmHg. **Group B (Terlipressin plus NE):** Two syringe pumps were prepared terlipressin (1mg) was dissolved in a 50ml syringe containing 5% dextrose in water. And NE (8mg) was dissolved in a 50ml syringe containing 5% dextrose in water. Terlipressin infusion started at 20-160ug/h (at rate 1ml/hr) with maximum infusion rate of 4mg/day) in addition to norepinephrine whereas the NE infusion started at .05ug/kg/min which uptitrated if the target mean arterial pressure not reached after maximum dose of terlipressin. **Results:** Combination of terlipressin with norepinephrine improve hemodynamics, renal function, lactate clearance, reduce norepinephrine requirement.

Keywords: Terlipressin, Norepinephrine, systemic inflammatory**Introduction**

Sepsis is the clinical syndrome defined by the presence of systemic inflammatory response syndrome (SIRS) in the setting of an infection. SIRS is defined by the presence of at least two of the following, fever or hypothermia; leukocytosis, leukopenia, or bandemia; heart rate >90 bpm or tachypnea or hypocapnia.

When acute organ dysfunction, such as acute renal failure, altered mental status, or acute lung injury (hypoxemia) is present, Sepsis is classified as severe sepsis.

Septic shock is a state of sepsis associated with acute circulatory collapse characterized by persistent arterial hypotension (defined as a systolic blood pressure <90mmHg, a mean

arterial pressure <60mmHg, or a reduction in systolic blood pressure of >40 mmHg from baseline) despite fluid resuscitation.

The incidence and mortality due to sepsis and septic shock is directly related to the age of patient, many of whom require ICU hospitalization. Initial management of a patient with sepsis/septic shock is a goal directed therapy, which consist of early administration of broad spectrum antibiotic, crystalloid or colloid fluid resuscitation, and use of vasopressor support to improve hemodynamics and maintain MAP >65mmHg. Use of continuous infusion of terlipressin, when given as first line vasopressor agent in septic shock is effective in reversing sepsis induced arterial hypotension and in reducing norepinephrine Requirement.

Aim of the work

The primary aim of this study is to evaluate and compare the effect of terlipressin and norepinephrine versus norepinephrine on mortality rate in patients with septic shock. The secondary aim of this study is evaluation and comparison the effect of terlipressin and norepinephrine on hemodynamics (MAP, HR), lactic acid clearance, NE requirement, renal function (urea, creatinine) and ALT.

Patients and methods

After obtaining the local ethics committee of EL-Minia University Hospital approval and written informed consent was taken from the relatives, this prospective double blind study was conducted on 40 adult patients of both gender admitted to our ICU with septic shock.

Septic shock was defined by the presence of two or more diagnostic criteria for systemic inflammatory response syndrome, proven or suspected infection, and hypotension despite adequate fluid resuscitation (defined as systolic blood pressure <90 mmHg or MAP <70 mmHg) in absence of other causes of hypotension. The patients were allocated into two equal groups (20 patients in each group) by using a computer-generated table. Group A (Norepinephrine group): Two syringe pumps were prepared one containing NE (8mg) was dissolved in a 50ml syringe containing 5% dextrose in water and the other containing saline.

The NE infusion started at .05ug/kg/min (at rate 1.3ml/hr) with maximum infusion rate of 0.8ug/kg/min till reached the target mean arterial blood pressure of 65-75mmHg. Group B (Terlipressin plus NE): Two syringe pumps

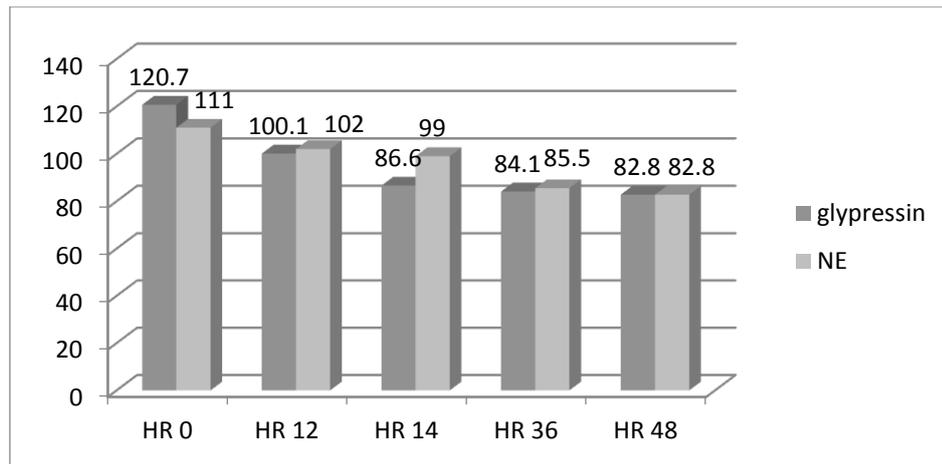
were prepared terlipressin (1mg) was dissolved in a 50ml syringe containing 5% dextrose in water. And NE (8mg) was dissolved in a 50ml syringe containing 5% dextrose in water.

Terlipressin infusion started at 20-160ug/h (at rate 1ml/hr) with maximum infusion rate of 4mg/day) in addition to norepinephrine whereas the NE infusion started at 0.05ug/kg/min which uptitrated if the target mean arterial pressure not reached after maximum dose of terlipressin. On arrival a careful medical history was taken from patient and relatives.

General examination including pulse (HR), arterial blood pressure (systolic, diastolic), temperature, central venous pressure (CVP) if present and peripheral arterial oxygen saturation. Physical examination including chest, heart, abdomen, lower limb, back. Routine investigations including Complete blood picture (Hb, platelet), coagulation profile (PC, PT, INR), renal function test (urea, creatinine), liver function test (AST, ALT, albumin, bilirubin), random blood sugar, blood culture was taken on arrival before starting antibiotics, CVP was inserted, arterial blood gases (ABG) was done, treatment started with broad spectrum antibiotics, fluid resuscitation with 30 ml/kg over an hour and vasopressor if needed.

Results

As regard Patient's characteristics age, sex and mortality were comparable in all studied groups with p value > 0.05. There is significant difference in HR at 24h, and NE requirement. No significant difference in mortality, MAP, lactic acid clearance, urea, creatinine, ALT.



Changes in HR (bpm) in the study group.

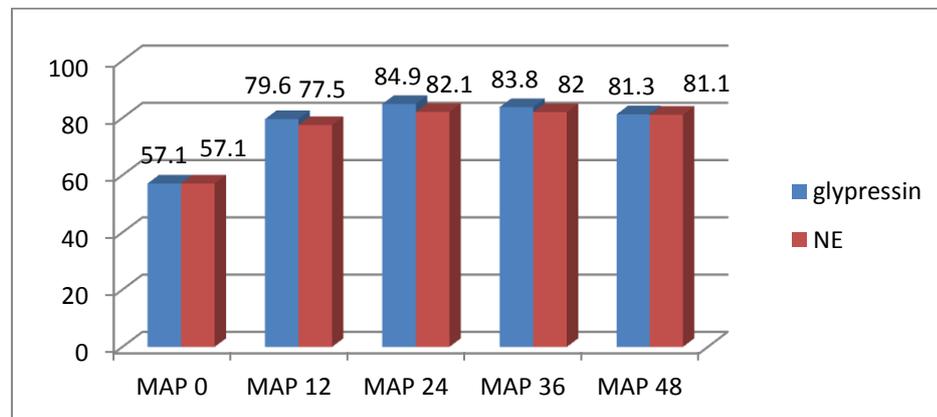


Figure (2): Changes in MAP (mmHg) in the study group.

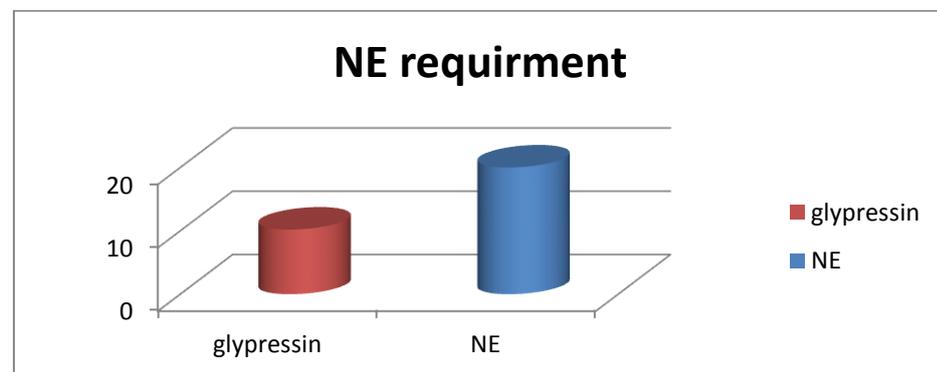


Figure (3): Changes in NE requirement.

Discussion

Our study found no significant difference in mortality, MAP, urea, creatinine ALT and lactic acid clearance. There is significant difference in HR at 24h, and NE requirement. In partial agreement with our study Labib et al., 2016, they conducted a study to compare adrenaline to terlipressin as a 2nd vasopressor to noradrenaline in septic shock, they divided the patients into two groups **Group (A)** received adrenaline infusion as a second-line vasopressor Adrenaline was given according to the following protocol (0.2µg/kg/min) and **Group (T)** received terlipressin infusion as a second-line vasopressor. Terlipressin was given by means of continuous infusion at a rate of 1.3µg/kg/h.

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