Monitoring of The Effect of Synthetic Vasopressin in Vasodilatory Shock Using Esophageal Doppler Probe

Thesis
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Abstract

Background: Septic shock is a form of vasodilatory shock chractrized by arteiolar vasodilation the objective of treatment is to elevate tissue perfusion & mean arterial pressure to allow adequate organ perfusion. Noradrenaline and dopamine were the usual catecholamines used in the treatment of septic shock. Loss of response was the common problem that lead to patient loss after large continous doses of noradrenaline which was termed as catecholamine refractory septic shock. Recently vasopressin and its alnalog namely terlipressin were used in the treatment of such catastrophic condition.

Methods and Results: In a prospective controlled study we included 40 patients with catecholamine resistant septic shock i.e. noradrenaline dose exceeded 0.6 μg/kg/min divided into two groups: 20 patients were treated conventionally according to survving sepsis campaign 2008 who served as a control group and the other 20 patients were treated conventionally and when noradrenaline dose exceeded 0.6 mic/kg/min terlipresin in a dose of 1 mg I.V bolus every 12 hours for a study time of 48 hours was started. Terlipressin therapy was associated with increased MAP from 58±14 mmHg at baseline to 73±20 mmHg with P value: 0.008 after 48 hours that allowed significant reduction of noradrenaline dose from 50 mic/min on day 0 to <25±8 mic/min after 48 hours. Terlipressin therapy was associated with increased systemic vascular resistant from 546±260 dyne.sec/cm^{-5} to 986±390 dyne sec/cm^{-5} after 48 hour which represent normalized arterilor tone that is expected to allow better organ bed perfusion.

There was reduction of both stroke volume and cardiac output (from 63±16 ml/beat to 51ml/beat and from 78 liter/min to 5.3 litre/min, respectively) yet this was not associated with abnormal organ perfusion marked by improved urine output from 49 ml/hour to 133 ml/h and improved global perfusion as marked by improved base deficit which represent lactic acidosis from 9.3±3 mEq/L to 5.7±3 mEq/L P value: <0.002. Terlipressin therapy was not associated with deleterious effect on PO_2/FiO_2 ratio (from 208±74 to 211±118 after 48 hours. Yet there was significant reduction of oxygen delivery (Do_2 from 848 ml/min to 610±47 ml/min after 48 hours (P> 0.02).

There was no effect on length of ICU stay in both groups (16±6 in the terlipressin group and 12±6 days in control group, P< 0.06). This shorter length of stay in control group may be due to the rapid deterioration of hemodynamics and death without terlipressin support, shown true as mortality in control group of 70% versus 60% (12/20) in terlipressin group with absolute risk reduction of 10% and relative risk reduction of 25%. Regarding organ function, terlipressin could improve SOFA score form 11±3.2 to 8±5 with P value: <0.02.

Conclusion: Terlipressin is a rather safe inexpensive easy to administer alternative in the treatment of septic shock. Further studies are needed to decide the ideal timing for initiation of this therapy early vs late, adjuvant or as an initial treatment.

Key words: Terlipressin, catecholamine resistant septic shock.

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List Of Abbreviations

APACHE:	Acute Physiology and chronic healthy evaluation
CD:	Cluster Determinant
CO:	Cardiac output
CSA:	Cut sectional area
CVP:	Central venous pressure
DIC:	Disseminated intravascular coagulopathy
DNA:	Deoxyribonucleic acid
DO2:	Oxygen delivery per minutes
ED:	Emergency Department
EDM:	Esophageal Doppler Monitoring
EGDT:	Early goal directed therapy
FiO2:	Fractional of oxygen in inspired air
FTc:	Flow time corrected for heart rate
HLA:	Human leukocyte antigen
ICU:	Intensive care unit
IFNα:	Interferone Gamma
IL:	Interleukin
iNOS:	Nitric oxide synthase "inducible subtype"
MAP:	Mean arterial pressure
MD:	Minutes distance
nNOS:	Nitric oxide synthase "neuronal subtype"
NO:	Nitric oxide
PAC:	Pulmonary artery Catheter
PAOP:	Pulmonary artery occlusion pressure
PO2:	Parametric pressure of oxygen
PV:	Peak velocity
SBP:	Systolic blood pressure
ScvO2:	Central venous blood oxygen saturation
SD:	Standard deviation

SD:	Stroke Distance
SOFA:	Sequential organ failure score
SV:	Stroke volume
TF:	Tissue factor
TGF:	Transforming growth factor
TGF-β:	Transforming Growth factor β
Th:	T lymphocytes helper cells helper cells
TVI:	Time-velocity integral
VO2:	Oxygen consumption
WBC:	White blood cells

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Abbreviations of Master Table

BSA	Body surface area
MAP	Mean arterial pressure
0	Base line
1	12 hours
2	24 hours
3	36 hours
4	48 hours
HR	Heart rate
CVP	Central venous pressure in mmHg
UOP	Urine output in ml/hour
SOFA	Sequential organ failure score
COP-edp	Cardiac output measured by esophageal Doppler probe at day 0
SV	Stroke volume ml/beat
FTc	Flow time corrected for heart rate by m.sec
SVR	Systemic vascular resistance
Echo-Co	Cardiac output measured by transthoracic echo at day 0
NA	Noradrenaline dose in mic/min
PAC-CO	Cardiac output measured by pulmonary artery catheter in litre/min
FiO2	Fraction of oxygen in inspired air
DO2	Oxygen delivery in ml/min
VO2	Oxygen consumption in ml/min
ALT	Alamine transfrange
DM	Diabetes mellitus
LOS	Length of stay
0	No
1	yes

Introduction

- Endotoxic shock is a syndrome of cardiovascular collapse and multiple organ failure in response to bacterial product s ***(Parrillo et al., 1990).***
- The central characteristic of septic shock is systemic vasodilatation, the cause of which is multifactorial the most common cause is excessive nitric oxide synthesis and activation of vascular smooth muscle K^+ ATP channel. ***Kilbourn et al., 1990, Landry et al., 1992.***
- Vascular smooth muscle is poorly responsive to noradrenaline (NA) in septic shock ***Meadow et al., 1988,*** and vasopressin doesn't play a significant role in the control of vascular smooth muscle in normal conditions ***Schwortz et al., 1981,*** but becomes critical when blood pressure is threatened ***(Schwartz et al., 1981).***
- Recent studies showed that some patients in advanced vasodilatory septic shock are exquisitely sensitive to the pressure effect of the exogenous vasopressin therapy.
- This unexpected finding raised the possibility that endogenous plasma vasopressin is inappropriately low in these patients.
- The most common theories for vasopressin deficiency is first, deficent baroreflex-mediated secretion of vasopressin i.e. primary autonomic failure ***Kautmann et al., 1999*** the second explanation is depletion of secretory stores of the neurohypophysis ***(Jones CW et al., 1969, Cook et al., 1993).***

- The above findings are the new concept of treatment of catecholamine resistant septic shock by replacement of the deficient vasopressin in this group of patients.