Comparative Study between Norepinephrine and Dopamine in the management of septic shock using noninvasive cardiac output monitoring

Thesis
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List of Abbreviations

- **ICU:**Intensive care unit
- Protease-activated receptors (PARs)
- **ANOVA:** Analysis Of Variance
- **APACHE:** Acute Physiology and Chronic Health Evaluation
- acute respiratory distress syndrome (ARDS),
- central venous pressure (CVP)
- dopamine (DA) or
- norepinephrine (NE).
- **CKD:**Chronic Kidney Disease
- mean arterial pressure (MAP)
- **ECG:** Electrocardiogram
- The Surviving Sepsis Campaign (SSC)
- mixed venous oxygen saturation (SvO_2).
- guanosine monophosphate (GMP)
- pulmonary artery catheter (PAC)
- **ESRD:** End Stage Renal Disease
- stroke volume (SV)

- **FSGS:** Focal and Segmental Glomerulosclerosis
- cardiac output
- **GI:** Gastrointestinal
- **GFR:** Glomerular Filtration Rate
- **GLN:** Glutamine
- **HD:** Hemodialysis
- **ICU:** Intensive Care Unit
- **IDPN:** Intradialytic Parenteral Nutrition
- **IGF-1:** Insulin-like Growth Factor
- **MAC:**Mid Arm muscle Circumference
- **MCT:** Medium-Chain Triglycerides
- **MIA:** Malnutrition, Inflammation, and Atherosclerosis
- **MICS:** Malnutrition-Inflammation Complex Syndrome
- **MPGN:** Membrano-Proliferative Glomerulonephritis
- **N:** Nitrogen

- **NKF-K/DOQI:** The National Kidney Foundation–Kidney Disease Outcomes and Quality Initiative
- **ONS:** Oral Nutritional Support
- **PEG:** Percutaneous Endoscopic Gastrostomy
- **PEJ:** Percutaneous Endoscopic Jejunostomy
- **PEM:** Protein-Energy Malnutrition
- **PN:** Parenteral Nutrition
- **PPN:** Peripheral Parenteral Nutrition
- **PTH:** Parathyroid Hormone
- **REE:** Resting Energy Expenditure
- **SD:** Standard Deviation
- **SPSS:** Statistical Package for the Social Science
- **TPN:** Total Parenteral Nutrition
- **TSF:** Triceps Skin Fold
- **UF:** Ultrafiltration
- **USRDS:** United States Renal Data System
- **UUN:** Urinary Urea Nitrogen

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Abstract

Background:

Circulatory shock is a life-threatening condition that is associated with high mortality. The administration of fluids, which is the first-line therapeutic strategy, is often insufficient to stabilize the patient's condition, and adrenergic agents are frequently required to correct hypotension. Among these agents, dopamine and norepinephrine are used most frequently. Both of these agents influence alpha-adrenergic and beta-adrenergic receptors, but to different degrees.

Method:

Patients enrolled in the study were blocked randomly allocated to two groups according to the vasoactive agent used. ***Group A***(37 patients received dopamine infusion as a vasopressor Dopamine was given by the following protocol : 15mcg/kg/min up to a maximum of 20 mcg/kg/min). ***Group B:***(39 patients received norepinephrine infusion 1.5 -2.5 mcg/kg/min up to a as a vasopressor).

The goal of therapy was to achieve and maintain for six hours, all of the following:

1. systolic blood pressure*(* SBP) more than 90 mm Hg

2. Systemic vascular resistance index (SVRI) more than 1100 dynes.S/Cm^5 $m^{2.}$

3. Cardiac Index (CI) more than 4.0L/min/ $m^{2.}$

The patients were classified into responders and non-responders to the vasoactive agent used. (The "responder" is a patient who achieves and maintains all the predefined goals of therapy for a period of six hours, in the specified dose range).

results:

There was no significant difference between dopamine and noradrenaline as regards SBP, MBP, CVP, CI, lactate and UOP. As regards H.R, DO_2I and SVRI there were highly significant difference between the two groups.

Dopamine group showed significant increase in DO_2I at the end of the study while norepinephrine group showed highly significant decrease in HR and highly significant increase in SVRI at the end of the study.

Arrhythmia was more prevalent among dopamine group compared to norepinephrine group with highly significant difference .As regards incidence of coma and ARF, there was no significant difference between the 2 groups.

Comparison of the 2 groups as regards number of responders showed highly significant difference .Number of responders were higher in norepinephrine group (29 patients) than in dopamine group (16 patients).

Conclusion:

We suggest that, at the doses tested, norepinephrine is more effective and reliable than dopamine in reversing systemic vasodilatation which is the main issue in the pathophysiology of septic shock.

Key Words:

Septic shock, Norepinephrine, dopamine, impedence cardiography.

Introduction

Sepsis develops in ~750,000 people annually and accounts for more than 210,000 deaths per year. Evolving definitions of sepsis including predisposing factors, host response, and end-organ damage emerged in recent years leading to our improved understanding of the path physiology of the disorder and targeted treatments (***Sharad et al.,2007*****).**

Severe sepsis and septic shock develop when infectious agents or induced inflammatory mediators lead to circulatory abnormalities including peripheral vasodilatation, reduced mean arterial pressure, myocardial depression, and intravascular volume depletion. Despite adequate fluid resuscitation, misdistribution of blood flow may cause an imbalance between oxygen delivery and demand, leading to global tissue hypoxia, shock, and, if not reversed, death

(Michael and Mitchell ,2004).

Goals of early resuscitation in patients with sepsis include restoration of tissue perfusion, reversal of oxygen supply dependency, and normalization of cellular metabolism. When appropriate fluid administration fails to

restore adequate tissue perfusion and arterial pressure, vasopressors are usually necessary to increase mean systemic pressure, cardiac output, and oxygen delivery (***Gaurav and Singh,2010).***

These agents have the ability to reduce organ flow through their vasoconstrictive action, their utility depends on the balance between increased organ specific perfusion pressure (by increased mean systemic pressure and stroke volume) and their direct effect on the microvasculature, Thus the goal with vasopressor agent is to increase the perfusion pressure to the point at which blood flow is optimized***(Stephen and James ,2002).***

Among the available vasopressors, dopamineand norepinephrine are used mostfrequently. These adrenergic agentshave different pharmacologic properties.

Both agents stimulate α adrenergic receptors,resulting in vasopressor effects, but this effect is weaker for dopaminethan for norepinephrine. However, dopaminestimulates β adrenergic receptorsmore than norepinephrine, and this mayresult in a greater increase in cardiacoutput. However, this β adrenergic stimulationcan also promote tachycardia and arrhythmic events, increase cellular metabolism, and may be immunosuppressive***(Backer et al., 2012).***

The more recent trend in monitoring of septic shock focuses on monitoring the variables that have a direct influence on the outcome of septic shock such as ,Systolic and mean arterial pressure (SBP and MAP), Systemic vascular resistance index (SVRI) ,Cardiac index (CI)***(Sharad etal.,2007).***

These variables may be monitored either invasively or noninvasively. Impedance cardiography, the non-invasive method of cardiac output monitoring, has been found to be a satisfactory substitute for invasive monitoring as it provides essentially similar information and is easier, quicker, cheaper and much safer to use (***Hanan et al.,,2007***).

Bioreactance is a novel technology platform which analyses changes in frequency of electrical impulses as they traverse the chest. NICOM (non invasive cardiac out put(CO) measurement) enables a highly precise, highly accurate,continuous, stable and non-invasive method to measure CO and other parameters such as SVRI and CI ***(Fortinaet al.,2006).***

Aim of the work

The purpose of this study is to compare the effects of dopamine and norepinephrine in the treatment of septic shock with pre-defined end-points using continuous non-invasive cardiac output monitoring with impedance cardiography.

Septic shock

Sepsis is one of the oldest and most elusive syndromes in medicine. Hippocrates claimed that sepsis was the process by which flesh rots, swamps generate foul airs, and wounds fester.Galen later considered sepsis a laudable event, necessary for wound healing***(Derek et al., 2013).***With the confirmation of germ theory, sepsis was recast as a systemic infection, often described as “blood poisoning,” and assumed to be the result of the host's invasion by pathogenic organisms that then spread in the bloodstream.

However, with the advent of modern antibiotics, germ theory did not fully explain the pathogenesis of sepsis: many patients with sepsis died despite successful eradication of the inciting pathogen. Thus, researchers

suggested that it was the host, not the germthat drove the pathogenesis of sepsis***(Funk et al., 2009).***

In 1992, an international consensus panel defined sepsis as a systemic inflammatory response to infection, noting that sepsis could arise in response to multiple infectious causes and that septicemia was neither a necessary condition nor a helpful term. Instead, the panel proposed the term “severe sepsis” to describe instances in which sepsis is complicated by acute organ dysfunction, and they codified “septic shock” as sepsis complicated by either hypotensionthat is refractory to fluid resuscitation or by hyperlactatemia***(Derek et al., 2013)***.

In 2003, a second consensus panel endorsed most of these concepts, with the caveat that signs of a systemic inflammatory response, such as tachycardia or an elevated white-cell count, occur in many infectious and noninfectious conditions and therefore are not helpful in distinguishing sepsis from other conditions. Thus, “severe