Vasoplegic Syndrome in Cardiac Surgery

Essay

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Anesthesia

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا
عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ
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List of Abbreviations

AAC	:	Area above the MAP curve
ACE	:	Angiotensin-converting enzyme
ANP	:	Atrial natruretic peptide
ATP	:	Adenosine triphosphate
AVP	:	Arginine-vasopressin
BMI	:	Body mass index
Ca	:	Calcium
CABG	:	Coronary artery bypass graft
cGMP	:	Cyclic guanosine monophosphate
CGRP	:	Calcitonin gene related peptide
CO	:	Carbon monoxide
CO	:	Cardiac out put
CPB	:	Cardiopulmonary bypass
CSE	:	Cystathionine lyase
eNOS	:	Endothelial isoform
EuroSCORE	:	European system for cardiac operative risk evaluation
G6PD	:	Glucose-6-phosphate dehydrogenase deficiency
GC	:	Guanylate cyclase
GFR	:	Glomerular filtration rate
H2S	:	Hydrogen sulfide
ICU	:	Intensive care unit
IFN	:	Interferon gamma
IL-1	:	Interleukin 1
iNOS	:	Inducible nitric oxide synthases
IQR	:	Interquartile range
K-ATP	:	ATP-sensitive potassium channels
LPS	:	Lipopolysaccharide

List of Abbreviations (Cont.)

MAP	:	Mean arterial pressure
MB	:	Methylene blue
MMAP	:	Median mean arterial pressure
NADPH	:	Nicotinamide adenine dinucleotide phosphate
nNOS	:	Neuronal nitric oxide synthases
NO	:	Nitric oxide
NOS	:	Nitric oxide synthases
O_2	:	Oxygen
PVS	:	Postoperative vasoplegic syndrome
SIRS	:	systemic inflammatory response
SVR	:	Systemic vascular resistance
TNF-α	:	Tumor necrosis factor alpha
VASST	:	Vasopressin and septic shock trial
VS	:	Vasoplegic syndrome

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Introduction

Vasoplegic syndrome is a syndrome that is characterized by severe hypotension, tachycardia, normal or increased cardiac output, decreased systemic vascular resistance and low filling pressures. It is poorly responsive or unresponsive to volume with fluid infusion ***(Senol G, 2011).***

Vasoplegic syndrome has been observed in different clinical settings. It is associated with cardiac pulmonary bypass, severe sepsis, anaphylaxis and hemodialysis ***(Kwok E and Hokwes D, 2006).***

Incidence may reach 10 % in postcardiac surgery patients and up to 50% in patients who die from sepsis as well as in association with anaphylaxis and protamine administration for reversal of systemic heparinization ***(Takakura K et al., 2006).***

Vasoplegic syndrome is multifactorial, resulting on one hand from pathologic activation of several vasodilator mechanisms and on the other hand from resistance to vasopressors. These pathways are dynamic and an interaction between them is commonly seen ***(Surks H et al., 1999).***

Mortality rates as high as 25% were reported when postoperative vasoplegia persisted for 36 to 48 hours ***(Shanmugam G, 2005).***

Management of Vasoplegic syndrome is controversial. But treatment is based on the use of drugs with vasoconstrictor effect for the purpose of supporting the organs' perfusion pressure. The currently used drugs are catecholamine with adrenergic alpha effects, such as norepinephrine, epinephrine, and dopamine but the effectiveness of these drugs is limited by frequent catecholamine resistance, as well as severe toxic effects at high dosage ***(Ulusoy H et al., 2008).***

An interesting alternative that has emerged as an option for the treatment of vasopressor-resistant vasoplegia is methylene blue. Methylene blue was classically employed as a medication for the treatment of methemoglobinemia as well as a dye in various medical procedures ***(Shanmugam G, 2005).***

Several studies have shown that single-dose postoperative administration of methylene blue in response to vasoplegic syndrome can restore systemic vascular resistance. Recently, it has been shown that preoperative methylene blue administration reduces the incidence and severity of the vasoplegic syndrome in high-risk patients ***(Ozal E et al., 2005).***

A few adverse effects of methylene blue in the treatment of norepinephrine refractory vasoplegia have been described, such as cardiac arrhythmias, coronary vasoconstriction, decreases in cardiac output, renal blood flow, mesenteric blood flow, increases in pulmonary vascular pressure, and deterioration in gas exchange. However, most of these side effects are dose dependent and do not occur when a dose of methylene blue not greater than 2 mg/kg is administered ***(Bjoern W et al., 2003).***

Aim of the Work

The aim of the work is to focus spotlight on vasoplegic syndrome, etiology, risk factors, management, and rule of methylene blue in treatment of vasoplegic syndrome.

Pathophysiology of Vasoplegic Syndrome

Organ homeostasis is maintained by providing adequate systemic blood flow and perfusion pressure. This depends upon a balance of vasoconstrictor and vasodilator influences. Under pathologic conditions the influence of one of the antagonists can outweigh the other, leading to perfusion compromise at the end organ level. When blood flow falls below a critical level resulting in inadequate oxygen delivery to peripheral tissue, the situation is referred to as "shock." One form of shock that is encountered under conditions of extreme vasodilation is referred to as "vasoplegia" ***(Gregory W and Mathew A, 2010).***

Shock was classified into four states: hypovolemic, cardiogenic, obstructive, and distributive shock. In the first three states, tissue hypoperfusion is a result of decreased cardiac output. In distributive shock, however, hypoperfusion results from circulatory dysfunction, leading to an abnormal distribution of a normal or even increased cardiac output. Vasodilatory shock, which could be considered a form of distributive shock, is characterized by two major factors: hypotension, due to failure of the vascular smooth muscle to constrict, and poor response to vasopressor therapy, due to

hyporeactivity to catecholamines ***(Sotiria G and Spyros D, 2011).***

The underlying mechanism of Vasoplegic Syndrome (VS) appears very complex and is not completely understood, but it may be mainly related to activation of systemic inflammatory response (SIRS). Numerous pathophysiologic mechanisms for VS have been suggested, and the most widely accepted cause is release of inflammatory cytokines ***(Ulukaya S et al., 2007).***

Sepsis should be considered a common cause of VS, although it is uncommon on the first postoperative day except in the setting of surgery for active endocarditis, but VS is also the final common pathway for prolonged and severe shock of any cause ***(Foot C et al., 2005).***

However, VS due to a non-septic mechanism can be thought of as a kind of "pure" SIRS. Fundamentally, vasodilatation is due to inappropriate activation of the vasodilator mechanism and failure of the vasoconstrictor mechanism in vascular smooth muscle despite high plasma catecholamine levels and activation of the renin-angiotensin system ***(Shanmugam G, 2005).***

At this point, three mechanisms have been implicated; The first is the activation of adenosine triphosphate activated and calcium regulated potassium channels (KATP and K Ca^{++} channels) in the membrane of vascular smooth muscle. The second is impairment of the arginine vasopressin (AVP) system and the third is increased level of nitric oxide (NO) due to activation of the inducible form of NO synthase ***(Holmes C and Walley K, 2008).***

(A)-Activation of ATP-Sensitive Potassium Channels in Vascular Smooth Muscle

Adequate vasoconstriction requires that hormonal or neuronal ligands such as angiotensin II and norepinephrine bind to and activate receptors on the surface of vascular smooth-muscle cells and, by way of second messengers, increase the concentration of calcium in the cytosol (Fig. 1). This increase results from the release of calcium from intracellular stores and the entry of extracellular calcium into the cell through voltage-gated calcium channels. At high cytosolic concentrations, calcium forms a complex with calmodulin, and this complex activates a kinase that phosphorylates the regulatory light chain of myosin. The phosphorylation of myosin allows the activation of myosin ATPase by actin and the cycling of myosin crossbridges along