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Hemodynamic Changes during Sepsis among Pediatrics: Review Article

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ABSTRACT

Background: Peripheral dilatation and shunting between arteries and capillaries characterize the circulatory maldistribution known as septic distributive shock. Yet, there are both hyperdynamic (warm) and hypodynamic (cool) forms of septic shock.

Objective: The aim of the current study is to assess the hemodynamic changes during sepsis among pediatric population.

Methodology: We searched PubMed, Science Direct and Google Scholar for information on "Hemodynamic Changes with Sepsis". However, only the most current or comprehensive study from January 2010 to May 2022 was considered. The authors also assessed references from pertinent literature. Documents in languages other than English have been disregarded since there aren't enough resources for translation. Unpublished manuscripts, oral presentations, conference abstracts, and dissertations were examples of papers that weren't considered to be serious scientific research. **Results**: Despite a high Left ventricular ejection fraction (LVEF; typically >55%), stroke volume is reduced in the early stages of sepsis due to inadequate cardiac preload brought on by increased vascular permeability and vasodilation. Even though left ventricular (LV) systolic dysfunction is common in septic patients, it may be reversible in survivors. Those who die from sepsis have a lower left ventricular end-diastolic volume (LVEDV) than those who do, even if they receive more fluids than those who do later in the disease.

Conclusion: Our result is in keeping with the hypothesis of a continuing preload deficit. Some studies have found an association between sepsis and cardiac depression, with survivors having a higher prevalence of cardiac depression than no survivors.

Keywords: Sepsis, Hemodynamic changes, Left ventricular end-diastolic volume.

INTRODUCTION

Sepsis is a major source of morbidity and mortality in pediatric patients, even in the most advanced intensive care units (PICUs). Even in affluent nations, it presents a clinical challenge as a leading cause of visits to the pediatric emergency room and the pediatric critical care unit [(1)].

Systemic sclerosis is a connective tissue disorder that can cause fibrosis of internal organs and the skin. Because there are currently no effective particular medications for scleroderma, treating the disease remains challenging. Research investigating the effectiveness of alternative drugs such intravenous immunoglobulins (IVIG), and ultraviolet (UVA-1) phototherapy for the treatment of scleroderma-related dermatological disease is encouraging, despite methotrexate's prolonged dominance. Medication for scleroderma treatment should be selected and managed with the patient's unique organ problems in mind [(2)].

A staggering 7.5 million children each year lose their lives due to sepsis, making it the top cause of death in the pediatric population worldwide. As published it includes the four leading causes of death in children: pneumonia, diarrhea, malaria, and measles, all in severe forms [(3)].

Rates of sepsis have not decreased despite the widespread use of next-generation conjugate vaccinations; this is likely because the majority of cases of sepsis occur in babies before they have had a chance to get a full series of vaccines [(4)].

Hyperdynamic shock, also known as warm shock, is the initial stage of septic shock and is characterized by high cardiac output (CO), low peripheral vascular resistance, and warm extremities. In the last stages, the patient experiences hypotension and hypodynamic shock characterized by low carbon monoxide levels, inadequate peripheral blood flow, cold extremities, and ultimately death. There was likely insufficient fluid therapy and inappropriate use of vasopressors that led to the cold sepsis situation with low CO [(5)].

Historically, it was thought that patients in a state of hypodynamic shock had a hemodynamic profile consisting of inadequate resuscitation, relative hypovolemia, and high afterload. Patients with sepsis often have a cardiac index that is normal or slightly higher after appropriate volume resuscitation and the drastically decreased systemic vascular resistance. A person in septic shock may have a normal SV and a high CO, yet their heart may be severely dysfunctional. Shock survivors were shown to have a higher end-diastolic volume (EDV) and a lower ejection fraction (EF) than shock non-survivors. This lends credence to the idea that dilation of the ventricles is a compensatory mechanism that protects against myocardial depression and helps maintain a healthy cardiac output [(6)].

Patients who did not make a full recovery were shown to be insensitive to volume loading, whereas those who did make a recovery had a much higher EF and a significantly lower left ventricular EDV. Cardiac compliance and function may also be affected by myocardial edema brought on by inflammation-induced vascular leakage. Alterations in afterload also

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affect ventricular performance. Right-heart dilatation worsens right-heart function, while pulmonary hypertension worsens left-heart function. Septic shock is characterized by the impairment of endothelial cells' ability to produce vasoactive chemicals that regulate peripheral vascular resistance. This is due to the fact that reduced endothelium-derived nitric oxide (NO) release may alter the physiological regulation of blood flow distribution by causing coronary vasospasm, elevated peripheral vascular resistance, and elevated cardiac workload and myocardial oxygen demand [(7)].

Although left ventricular ejection fraction (LVEF) is normally high (>55%) in the early stages of sepsis, low stroke volume results from increased vascular permeability and vasodilation, lowering cardiac preload. Evidenced by elevated lactate levels, compensatory tachycardia during early sepsis is generally insufficient to maintain appropriate cardiac output.

The left ventricular ejection fraction (LVEF) drops dramatically (typically by 45 percent) after fluid loading over the first three days of hemodynamic support. Even though left ventricular (LV) systolic dysfunction is common in septic patients, it may be reversible in survivors. In the later stages of sepsis, despite receiving more fluids than those who did not survive, those who did not show lower LVEDV, indicating a persistent preload shortage. Some studies have found an association between sepsis and cardiac depression, with survivors having a higher prevalence of cardiac depression than non-survivors [(8)].

Hemodynamic alterations during sepsis:

1. Decreased intravascular volume (reduced preload)

Absolute or relative hypovolemia causes the decreased intravascular volume characteristic of septic conditions. Reduced preload, a crucial component determining cardiac function in septic patients, may result from both situations. Venous pooling, especially in the splanchnic compartment, is induced by endotoxemia in experimental animals, and this decreases the effective compliance of the entire vascular bed [(9)].

2. Decreased vascular tone (reduced afterload)

Systemic resistance decreases when vascular tone is low, especially in the mesenteric area. It's possible that in this situation, myocardial depression is temporarily masked, keeping LV systolic function intact despite the myocardial infarction. A normal LVEF may be identified in septic shock despite drastically diminished intrinsic LV contractility due to the shock's effect on arterial tone. This is because LVEF represents the relationship between LV afterload and LV contractility [(10)].

It is well accepted that an unfavorable ratio of vasoconstrictor to vasodilator factors is responsible for these shifts in systemic resistance. Patients with sepsis frequently experience vascular hyporesponsiveness, which is characterized by a reduced pressure response to vasopressor medications [(11)].

Desensitization to the effects of catecholamines, which may occur in severe sepsis due to down-regulation of 1-adrenergic receptors or uncoupling between receptors and their intracellular messengers, may contribute to the vascular hypotension that characterizes this condition. In a septic state, plasma vasopressin levels fall and the vasopressin 1 receptor is downregulated. Different chemicals that cause blood vessels to dilate are released by the body when sepsis sets in. Low vascular tone can also be caused by a lack of corticosteroids or a decreased sensitivity to steroids [(12)].

3. Microcirculatory alterations

Microcirculation is altered by severe sepsis and septic shock; vascular density is decreased and perfusion is altered in a dynamic fashion (intermittent, reduced, or stopped blood flow). Clinical outcomes are associated with these pathological alterations, which resolve rapidly in survivors but remain stable in non-survivors. Dissociation between cardiac depression and elevated mixed venous oxygen saturation (SvO2) levels, commonly reported in septic patients, may be connected to poor oxygen extraction and may be explained by microcirculatory changes [(13,14)].

4. Oxygen extraction/oxygen delivery dependency

Even in the presence of normal DO2, VO2 becomes dependent on DO2 due to the impairment of oxygen extraction that commonly occurs in sepsis (so-called VO2/DO2 dependency). It's possible that changes in vascular tone and secondary blood flow redistribution, microcirculatory changes, and cellular oxygen use are all to blame for this occurrence (also called cytopathic hypoxia) [(15)].

5. Lactate

Glycolysis (the production of lactate) and oxidation (the consumption of lactate) and gluconeogenesis (the conversion of lactate to glucose) occur continuously in all cells. Plasma lactate concentrations are <1.5 mmol/L in a healthy infant or child and less than 2 mmol/L in a very unwell infant or child when production and consumption are balanced. One of the key indicators for assessing and following shock conditions is lactate levels. The most common reason for elevated lactate levels is increased anaerobic metabolism due to circulatory failure, while this can also result from highly aerobic glycolysis (seizures, hyperventilation, liver failure, mitochondrial inhibition, etc.). Failure to normalize lactate levels within the first 6-12 hours of monitoring is associated with an increased risk of significant consequences [(16)].

6. Mechanical ventilation (MV) and septic cardiomyopathy

Among the many ways that MV can affect cardiac function and hemodynamics is by decreasing venous return (due to an increase in right atrial pressure), raising pulmonary vascular resistance (PVR), and decreasing cardiac output (CO). The ventilator settings [positive end-expiratory pressure (PEEP), tidal volume, respiratory rate] and the degree of pulmonary distension and hypoxic pulmonary vasoconstriction influence these hemodynamic repercussions of MV [(17)].

It is common for lung injury and/or acute respiratory distress syndrome to occur during sepsis, necessitating the use of breathing techniques designed to prevent further damage to the lungs. Combinations of a high respiratory rate, a low tidal volume, and a high amount of positive end-expiratory pressure (PEEP) are examples of these techniques. Hyperinflation brought on by PEEP, in turn, may change autonomic tone and heighten PVR. Further exacerbating PVR is the fact that hypoxia is caused by the decreased lung capacity and consequent alveolar collapse that result from lung-protective ventilation (hypoxic pulmonary vasoconstriction) [(15)].

In order to reverse hypoxic pulmonary vasoconstriction and reduce pulmonary artery pressure, recruitment techniques and positive-pressure breathing are used. The right ventricle may be more susceptible to pulmonary vascular dysfunction and increased afterload due to adult respiratory distress syndrome if its intrinsic contractility is decreased due to sepsis [(17)].

Although it reduces LV afterload and raises pulmonary arterial pressure, the effects of positive-pressure ventilation on the left side of the heart are counteracting (i.e., improving LV ejection). Hemodynamic goal-directed therapy based on fluid administration may mask myocardial dysfunction in critically ill individuals (i.e., preload and CO decrease) [(15)].

Septic Myocardial Dysfunction (SMD):

If not diagnosed and treated promptly, SMD is a substantial risk factor for sepsis-related death. Myocardial dysfunction occurs in 40%-44% of adults and 80% of children with septic shock. In children with septic shock, myocardial dysfunction is the leading cause of death [(18)]**.** Patients with sepsis who do not also have cardiovascular impairment have a 20% chance of survival, whereas those with cardiovascular dysfunction have a 70-90% chance of death [(19)].

Myocardial dysfunction in septic shock: management:

Hemodynamic improvement and infection control are the cornerstones of treatment for myocardial dysfunction. Early control of the source and monitoring of blood cultures in addition to early sufficient antibiotic therapy are critical for minimizing pathogen associated molecular patterns (PAMPs) induced by invasive bacteria [(20,21)].

In addition, vigorous fluid replacement appears to be a reasonable method to treat hypovolemia, guided by monitoring fluid response measures. It's certainly good to give patients fluids promptly and adequately, but giving too much can be counterproductive. Increased pulmonary microcirculatory permeability and LV diastolic dysfunction both contribute to an increased risk of pulmonary edema development [(22)].

Rapid and targeted administration of life-saving measures, such as fluid resuscitation, vasopressor and inotropic therapy, red blood cell transfusion, mechanical ventilation, and renal support, is essential. Regulating arterial pressure as soon as possible in patients with septic shock is essential for restoring organ perfusion pressure, which maintains blood flow to tissues and reduces DAMP release [(23)].

Dobutamine is the first-line inotropic medication suggested by the Surviving Sepsis Campaign guidelines (SSCG) 2012 for patients with myocardial depression who need to acquire adequate tissue perfusion and improve hemodynamics. Inotropes can be used to boost cardiac output when volume status has been optimized. Reversing shock and restoring appropriate organ perfusion may require the use of catecholamines, but their continued use, especially in very high dosages, may be hazardous and worsen myocardial damage. Septic shock patients with myocardial depression have a suboptimal response to beta adrenergic [(24)].

Hemodynamic assessment and cardiac evaluation of the critically ill patients:

The assessment of newly admitted sepsis patients using two-dimensional echocardiograms is vital because it permits the estimation of left ventricular function and can advise in fluid resuscitation. Left ventricular (LV) contractility is impaired in children with septic shock, although this impairment is reversible, and there is an inverse relationship between ejection fraction (EF) and fractional shortening [(25)].

The prognosis was favorable for patients with left ventricular enlargement and decreased LVEF. Despite this apparent paradox, numerous echocardiographic investigations have linked a reduced LVEF to a worse prognosis. It's possible that this is because LVEF alone does not adequately reflect the underlying hemodynamic pattern in individuals with septic shock and that the outcome is dependent on characteristics other than LVEF [(25)].

Doppler echocardiography's measurement of diastolic filling is a noninvasive method of learning about the health of the LV. The early diastolic velocity of the mitral annulus as a percentage of the mitral velocity (E/E') by tissue Intravascular measures of left ventricular (LV) diastolic performance are correlated with Doppler imaging that incorporates both

transmitral driving pressure and myocardial relaxation and have been found to predict mean LV diastolic pressure (M-LVDP) [25].

Role of echocardiography in management of septic shock:

Although echocardiography had been around since the 1950s, it wasn't until the late 1980s that some forward-thinking intensivists began to promote it as the primary method for assessing patients with hemodynamic instability. Interest in using echocardiography in the critical care unit (ICU) has risen in the past decade [26].

Due to its capacity to quickly diagnose the causes of hemodynamic instability and direct subsequent treatment accordingly, echocardiography is now widely considered as a vital method for the hemodynamic assessment in the intensive care unit (ICU). This method has many advantages, including being noninvasive, risk-free, serial, real-time, and able to be evaluated alongside clinical data by intensivists [27].

It has been shown in multiple studies that echocardiography is useful in the care of critically ill patients, leading to adjustments in treatment in 30–60% of instances. Recent expert consensuses and reviews on shock highlight the value of echocardiography in classifying the many types of shock (distributive, hypovolemic, obstructive, and cardiogenic) that can occur in septic patients [28].

In the intensive care unit, echocardiography is a must-have diagnostic tool due to the unique insights it provides into cardiovascular function. Hemodynamic monitoring with noninvasive methods is lacking significantly in children, making echocardiography an even more attractive option [29].

Septic shock is one of the most difficult hemodynamic failure syndromes because it can cause a reduction in central blood volume (absolute or relative), significant peripheral vasodilation, and RV/LV myocardial failure. Echocardiography is a powerful tool that can answer all of these issues and guide the use of fluid and vasoconstrictor/inotropic drugs [25].

CONCLUSION

Even though the Left ventricular ejection fraction (LVEF; generally >55%) is high in early sepsis, the stroke volume is low because of inadequate cardiac preload brought on by excessive vascular permeability and vasodilation. Systolic dysfunction of the left ventricle (LV) is common in septic patients, but it might be reversible in those who make it. Those who do not make it through the later stages of sepsis have a lower LVEDV, even if they receive more fluids than those who do. This result is in keeping with the hypothesis of an ongoing preload scarcity. Some studies have found an association between sepsis and cardiac depression, with survivors having a higher prevalence of cardiac depression than non-survivors.

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