Rev Bras Anestesiol. 2015;65(5):395–402

REVISTA BRASILEIRA DE ANESTESIOLOGIA
Official Publication of the Brazilian Society of Anesthesiology
www.sba.com.br

REVIEW ARTICLE

Current concepts on hemodynamic support and therapy in septic shock

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Received 23 September 2014; accepted 11 November 2014
Available online 9 July 2015

KEYWORDS
Septic shock;
Hemodynamics;
Resuscitation;
Fluid therapy;
Vasoconstrictor agents

Abstract Severe sepsis and septic shock represent a major healthcare challenge. Much of the improvement in mortality associated with septic shock is related to early recognition combined with timely fluid resuscitation and adequate antibiotics administration. The main goals of septic shock resuscitation include intravascular replenishment, maintenance of adequate perfusion pressure and oxygen delivery to tissues. To achieve those goals, fluid responsiveness evaluation and complementary interventions – i.e. vasopressors, inotropes and blood transfusion – may be necessary. This article is a literature review of the available evidence on the initial hemodynamic support of the septic shock patients presenting to the emergency room or to the intensive care unit and the main interventions available to reach those targets, focusing on fluid and vasopressor therapy, blood transfusion and inotrope administration.

PALAVRAS-CHAVE
Choque séptico;
Hemodinâmica;
Reposição volêmica;
Fluidoterapia;
Agentes vasoconstritores

Conceitos atuais sobre suporte hemodinâmico e terapia em choque séptico

Resumo A sepse grave e o choque séptico são um grande desafio para a assistência médica. Grande parte da melhora na taxa de mortalidade associada ao choque séptico está relacionada ao reconhecimento precoce em combinação com a reposição volêmica oportuna e a administração adequada de antibióticos. Os principais objetivos da reanimação do choque séptico incluem reposição intravascular, manutenção adequada da pressão de perfusão e fornecimento de oxigênio para os tecidos. Para atingir esses objetivos, a avaliação da responsividade do volume e das intervenções complementares (vasopressores, inotrópicos e transfusão de sangue) pode ser necessária. Este artigo é uma revisão da literatura para identificar as evidências disponíveis do suporte hemodinâmico inicial aos pacientes com choque séptico admitidos em sala de emergência ou unidade de terapia intensiva e as principais intervenções disponíveis

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http://dx.doi.org/10.1016/j.bjane.2014.11.006

para atingir essas metas, com foco em terapia com reposição de líquidos e vasopressores, transfusão de sangue e administração de inotrópicos.

Introduction

Sepsis, a systemic inflammatory response associated to an infection, is a common disease with an estimated incidence of 300 cases per 100,000 people and with an incidence increase of 13% per year.[1,2] Approximately half of septic patients will develop the most severe spectrum of this disease, i.e. severe sepsis and septic shock.[3]

Septic shock carries an average in-hospital mortality rate around 20% and a 90 day mortality rate between 20% and 50%.[4–10] In Brazil, the 28 day mortality rate achieves around 50% with an incidence density of thirty cases per thousand patient-days.[11]

Septic shock is also associated with high burden of morbidity and costs. The average cost per patient is US$ 22,100, which accounts for an annual expenditure of approximately seventeen billion dollars in the United States alone.[1] Additionally, the quality of life and cognitive function of sepsis survivors may be permanently compromised.[12–14] Key interventions to improve outcomes in this population of critically ill patients include early recognition and early onset of adequate therapy, mainly broad-spectrum antibiotics and fluids.[15]

The initial attempts to optimize hemodynamics in critical care patients were deemed ineffective, increasing the risk of death.[16,17] During the past decade, the early goal-directed therapy principle encompassing early series of protocolized interventions, i.e. antibiotics, fluids, vasopressors, inotropes, red blood transfusion, etc., showed significant reduction of mortality rate.[18] This strategy has been recommended by specialty societies in their guidelines for severe sepsis and septic shock treatment and has been implemented in emergency departments and intensive care units in a global scale.[15]

According to these guidelines, septic patients presenting with signs of persistent hypotension (i.e. mean arterial blood pressure <65 mmHg despite initial adequate fluid resuscitation) or tissue hypoperfusion (i.e. arterial lactate concentration equal to or higher than 4.0 mmol/L) have a high risk of death and therefore must be promptly resuscitated.[15]

Nevertheless, there is increasing evidence coming from new randomized clinical trials challenging the efficacy of the early goal-directed therapy for septic patients.[8,9] Therefore, we propose a narrative review of the literature supporting the management of the early stages of septic shock, with special attention to hemodynamics evaluation and evidence-based interventions, taking into account the recently published data.

Objective

Our objective was to perform a narrative review of the available evidence on hemodynamic support for septic shock patients and provide an overview of the key available interventions for resuscitation, e.g. fluid therapy, vasopressors, inotropes and red blood transfusion.

Methods

We performed a systematic search in MEDLINE/Pubmed, Embase/OVID, LILACS/Bireme and Cochrane Library up to October 2014 using the Medical Subject Headings (MeSH) terms ''sepsis'', ''severe sepsis'' AND/OR ''septic shock'' combined with ''central venous pressure'', ''lactate'', ''lactate clearance'', ''mean arterial pressure'', ''blood pressure'', ''vasopressors'', ''norepinephrine'', ''epinephrine'', ''vasopressin'', ''central venous oxygen saturation'', ''blood transfusion'', ''transfusion'', ''dobutamine'', ''fluid responsiveness''.

We have limited our search to articles written in English, human subjects and clinical trials. We also reviewed the current Surviving Sepsis Campaign Guidelines for the Treatment of Severe Sepsis and Septic Shock and their key related articles.[15] Additional studies were added at authors' discretion. One hundred and seventy-nine articles were retrieved from this search and further filtered for quality and originality before being included in this review.

Hemodynamic goals

The imbalance between oxygen consumption and oxygen delivery is the main determinant of the development and progression of organ dysfunction in septic shock patients. Therefore, the aim of the hemodynamic interventions commonly applied to these patients is to increase oxygen delivery to match oxygen demand (Fig. 1).

The currently recommended hemodynamic targets to be achieved during the initial six-hour of resuscitation include a central venous pressure (CVP) between 8 and 12 mmHg in spontaneously breathing patients or between 12 and 15 mmHg in mechanically ventilated patients or in those with reduced ventricular compliance, a mean arterial blood pressure (MAP) $\geq$65 mmHg, a central venous (ScvO2) or mixed venous (SvO2) oxygen saturations $\geq$70% and 65% respectively, a lactate clearance $\geq$10% and an urinary output $\geq$0.5 mL/kg/h (Fig. 2).[15]

Recently, two large randomized clinical trials confronted the efficacy of early goal-directed therapy in septic shock.[8,9]