Sepsis: Control and Treatment

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4.1 Introduction

Sepsis is a complex, multifactorial syndrome which can evolve into conditions of varying severity. If left untreated, it may lead to the functional impairment of one or more vital organs or systems. Therefore its adequate treatment is crucial already in the emergency room.

Early detection and timely therapeutic intervention can improve the overall clinical outcome of septic patients; reducing time to diagnosis of sepsis is thought to be a critical component in reducing mortality from multiple organ failure. However, early diagnosis of sepsis can be difficult; determining which patients presenting with signs of infection during an initial evaluation do currently have, or will later develop, a more serious illness is challenging.

Despite decades of sepsis research, no specific therapies for sepsis have emerged. Without specific therapies, management is based on control of the infection and organ support. Fluid resuscitation and support of vital organ function, early antibiotics, and source control are the cornerstones for the treatment of patients with sepsis.

In February 2016, the Journal of the American Medical Association (JAMA) published a proposal for new definitions and criteria for sepsis, called Sepsis-3 [1], updating previous sepsis definitions.

Sepsis is now defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. It can be clinically represented by an increase in the Sequential Organ Failure Assessment (SOFA) score of 2 points or more [1].

Septic shock is defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mmHg

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or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia [1].

Under this terminology, "severe sepsis" becomes superfluous.

Furthermore, the consensus group proposed the introduction of qSOFA as an alert system. Patients with at least 2 of 3 clinical abnormalities including Glasgow coma score of 14 or less, systolic blood pressure of 100 mmHg or less, and respiratory rate 22/min or greater may be prone to have the poor outcome typical of sepsis. Importantly, qSOFA does not define sepsis but provides simple bedside criteria to screen adult patients with suspected infection.

Sepsis should generally warrant greater levels of monitoring and intervention.

In patients with severe sepsis or septic shock, the Surviving Sepsis Campaign (SSC) guidelines recommend [2]: (1) that treatment and resuscitation begin immediately, (2) that administration of IV antimicrobials be initiated as soon as possible after recognition and within 1 h for both sepsis and septic shock, and (3) that a specific anatomic diagnosis of infection requiring emergent source control be identified or excluded as rapidly as possible in patients with sepsis or septic shock.

4.2 Hemodynamic Resuscitation

It is well known that early treatment with aggressive hemodynamic support can limit the damage of sepsis-induced tissue hypoxia and prevent the overstimulation of endothelial activity.

Early, adequate hemodynamic support of patients in shock is crucial to prevent worsening organ dysfunction and failure.

Fluid therapy to improve microvascular blood flow and increase cardiac output is an essential part of the treatment of sepsis.

A fluid challenge incorporates four determinant elements [3]:

1. Crystalloid solutions should be the first choice, because they are well tolerated and cheap.
2. Fluids should be infused rapidly to induce a quick response but not so fast that an artificial stress response develops.
3. The goal should be an increase in systemic arterial pressure.
4. Pulmonary edema is the most serious complication of fluid infusion and appropriate monitoring is necessary to prevent its occurrence.

Vasopressor agents should be administered to restore organ perfusion if fluid resuscitation fails to optimize blood flow in various organs.

It may be acceptable practice to administer a vasopressor temporarily while fluid resuscitation is ongoing, with the aim of discontinuing it, if possible, after hypovolemia has been corrected although the benefit of this approach is unclear [3].

Norepinephrine is now the first-line vasopressor agent used to correct hypotension in the event of septic shock [2]. It is more efficacious than dopamine and is

more effective for reversing hypotension in patients with septic shock [2]. Moreover, dopamine may cause tachycardia more frequently and may be more arrhythmogenic than norepinephrine.

Dobutamine is another inotropic agent that increases cardiac output, regardless of whether norepinephrine is also being given. With predominantly β-adrenergic properties, dobutamine is less likely to induce tachycardia than either dopamine or isoproterenol [3].

Hypotension is the most common indicator of inadequate perfusion and restoring a mean arterial pressure of 65–70 mmHg is a good initial goal during the hemodynamic support of patients with sepsis [3].

Hemodynamic resuscitation has been the cornerstone of management for severe sepsis and septic shock in Surviving Sepsis Campaign guidelines since its first draft [4].

Rivers et al. [5] demonstrated that early goal-directed therapy (EGDT), initiated in the emergency department, reduced the in-hospital mortality rates of patients in septic shock. However, results of recent multi-center prospective randomized trials [6–8] have been unable to reproduce the Rivers' results [9].

EGDT involved reaching a target ScvO2 ≥ 70% (through transfusion of red cells and dobutamine). Patients should otherwise have: central venous pressure (CVP) ≥8–12 mmHg (through crystalloid boluses), mean arterial pressure (MAP) ≥65 mmHg (through vasopressor administration), urine output ≥0.5 mL/kg/h (whenever possible). Early identification of sepsis and prompt administration of intravenous fluids and vasopressors are always mandatory. However, initial resuscitation should not be based on a simple, predetermined protocol.

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4.3 Antimicrobial Therapy

A key component of the initial management of the septic patient is the administration of IV empiric antimicrobial therapy. An insufficient or otherwise inadequate antimicrobial regimen is strongly associated with unfavorable outcomes in critically ill patients [10].

Empiric broad-spectrum antimicrobial therapy should be started as soon as possible in all patients with sepsis or septic shock. In these patients, dosing strategies of antimicrobials should be always optimized based on accepted pharmacokinetic/pharmacodynamic principles and specific drug properties [2].

Accurate diagnostic tests are essential for the correct identification of microorganisms causing sepsis.

The performance of antimicrobial susceptibility testing by the clinical microbiology laboratory is crucial both to confirm susceptibility to the empirical therapy, and to detect resistance in bacterial isolates. At least two sets of blood cultures for both aerobic and anaerobic bacteria and fungal organisms should always be obtained before starting empirical antimicrobial therapy.

4.4 Source Control

Source control encompasses all measures undertaken to eliminate the source of infection, reduce the bacterial inoculum, and correct or control anatomic derangements to restore normal physiologic function [11, 12].

Patients with sepsis need to be carefully examined to ensure that all drainable foci have been identified. Infected fluid collections, devitalized tissue, and devices may act as a persistent source of sepsis until removed.

It is well known that inadequate source control at the time of the initial operation has been associated with increased mortality in patients with severe intra-abdominal infections [13].

4.5 Conclusion

Sepsis is a complex condition that is often life-threatening. Early recognition of sepsis and early intervention are paramount in improving outcomes.

A systematic, organized approach to identify and control sepsis is mandatory to improve the outcomes of patients.

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