Meeting report

Haemodynamic management of severe sepsis: recommendations of the French Intensive Care Societies (SFAR/SRLF) Consensus Conference, 13 October 2005, Paris, France

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Abstract

We present a consensus report from the SFAR/SLRF (Société Française d'Anesthésie et de Réanimation/Société de Réanimation de Langue Française) Consensus Conference, held on 13 October 2005 in Paris, France. The consensus report made recommendations on five topics relevant to the treatment of circulatory failure in sepsis and its underlying rationale. These topics are as follows: therapeutic goals of haemodynamic support in sepsis; goals of fluid resuscitation (including transfusion); role of inotropes and vasoactive drugs; role of other treatments; and treatment strategy. This report is reproduced from a translation of the original in *Annales Françaises of Anesthésie and Réanimation*.

Introduction

This consensus report is reproduced from a translation of the original [1], which was published in French. It is limited to the management of haemodynamic consequences of severe sepsis. The treatment of associated organ failure (renal, hepatic and haematological) is beyond the scope of this report.

The recommendations were made by the panel using available scientific data and studies. The scientific value of studies is divided into five levels as follows: level 1 includes large randomized controlled trials with clear results, and low risk for false positives (α error) or false negatives (β error); level 2 includes smaller randomized controlled trials with less clear results, and medium to high risk for false positives (α error) or false negatives (β error); level 3 includes nonrandomized studies with contemporaneous controls; level 4 includes nonrandomized studies with historical controls or expert opinion; and level 5 includes case reports, noncomparative studies, or expert opinion.

The strength of the recommendations is graded on the basis of the level of evidence of the studies on which they are based. Grade A recommendations are based on at least two studies of level 1 evidence; grade B recommendations are based on one level 1 study; grade C recommendations are based on level 2 studies; grade D recommendations are based on level 3 studies; and grade E recommendations are based on level 4 or 5 studies. However, there may be situations in which the level of scientific evidence available is of insufficient quality to support the recommendation (i.e. grade D or E) but the recommendation is considered essential on clinical grounds.

Question 1: what are the therapeutic goals of haemodynamic support in sepsis?

The different stages of sepsis are characterized by certain circulatory changes. Circulatory changes exist at both 'macrovascular' and 'microvascular' (capillary) levels, but presently there is no way to monitor microcirculatory changes directly, and neither are any direct therapeutic interventions available. Therefore, at present the therapeutic goals are limited to the measurable macrocirculatory endpoints (arterial pressure, cardiac function and vascular resistance of large vessels).

Hourly urine output, lactate levels and biochemical markers of renal function are the only markers of microvascular perfusion available (grade E). Correction of arterial hypotension increases oxygen delivery to tissues and improves the prognosis of patients with severe sepsis; therefore, early and aggressive fluid loading is recommended (grade B). Apart from

MAP = mean arterial pressure; $ScvO_2$ = vena cava oxygen saturation.

the specific treatment of vasodilatation with vasoconstrictors, there is no specific treatment for vascular dysfunction.

Except for coronary blood flow, all cardiac indices are potentially modified by sepsis. However, only 10-20% of adults with sepsis develop cardiac failure as characterized by a persistently low cardiac index and mixed venous oxygen saturation, despite adequate volume expansion. Treatment with positive inotropes is indicated in these cases (grade B).

Specific differences in paediatric patients

Severe sepsis in children is more often characterized by cardiac failure and hypovolaemia, which responds well to fluid loading. However, the diagnosis is more difficult to establish because hypotension develops later than in adults.

Prognosis is dependent on prompt diagnosis and intervention with aggressive fluid therapy and early use of antibiotics (grade D). The mortality rate in children is lower than in adults, although fulminant purpuric sepsis warrants consideration as a separate entity.

Question 2: What are the goals of fluid resuscitation (including transfusion)?

Diagnosis and monitoring of volume deficit

The initial phase

Systematic intravenous fluid loading is the primary management option in severe sepsis. There is no single measurement required before commencing fluid resuscitation. The recommended goal is to achieve and maintain a mean arterial blood pressure (MAP) above 65 mmHg (grade C). However, in cases of life-threatening hypotension (i.e. diastolic blood pressure <40 mmHg), treatment with vasopressors must be started immediately (grade E).

Ongoing fluid management

After the initial phase of fluid therapy, if intravenous filling is still required then it must be done while monitoring and aiming for specific haemodynamic targets (grade D).

Choice of fluids

Blood products, albumin, dextrans and starches with molecular weights above 150 kDa should not be used as first-line fluids for fluid resuscitation. When crystalloids and colloids are titrated to the same haemodynamic target, they have been shown to be equally efficacious. Crystalloids have fewer potential side effects and are less expensive than colloids; they are therefore recommended as first-choice treatment for intravenous fluid resuscitation in managing the initial phase of shock (grade B).

Volume and frequency of fluid boluses

Intravascular filling is achieved by 500 ml boluses of crystalloids every 15 min (grade E). These boluses should be repeated to achieve a MAP above 65 mmHg (without developing signs of pulmonary oedema). If this target blood pressure is not reached then the use of vasopressors is indicated (grade E).

Blood transfusion

In the case of acute anaemia the target haemoglobin is between 8 and 9 g/dl. There are situations in which different haemoglobin levels may be acceptable, either in cases in which it is not tolerated clinically or dependent on the vena cava oxygen saturation ($Svco_2$; grade E).

Specific differences in paediatric patients

During the first hour, intravascular fluid replacement up to a volume of 60 ml/kg has been shown to reduce mortality and is therefore recommended (grade E). For the reasons given above for adults, crystalloids are the fluids of choice (grade B).

Question 3: what is the role of inotropes and vasoactive drugs?

Vasoconstictors

If despite adequate intravascular filling a MAP in excess of 65 mmHg cannot be achieved, then vasoconstrictors must be used (grade B). Early use of vasoconstrictors is recommended because it reduces the incidence of organ failure (grade E). Noradrenaline (norepinephrine), a potent vasoconstrictor, should be used in the first instance (grade E). Vasopressin (0.01-0.04 units/min) or terlipressin (boluses of 1-2 mg) are rescue therapies in cases of refractory shock (grade E).

Positive inotropes

Routine use of inotropes is not recommended (grade E). In patients undergoing optimal management (adequate fluid resuscitation, appropriate correction of anaemia and use of vasoconstrictors), the indication for using inotropes cannot be based on an isolated measurement of cardiac output. It is, however, recommended when a low cardiac output is accompanied by a $Svco_2$ below 70% (grade E). Inotrope therapy must be titrated to a targeted response, such as improvements in $Svco_2$ and in myocardial function indices, and a reduction in lactate. The combination of dobutamine and noradrenaline stimulates both α_1 and β_2 adrenergic receptors, and it is recommended as first-line treatment (grade E). Adrenaline appears equally efficacious but, because of its metabolic side effects, it is not routinely used.

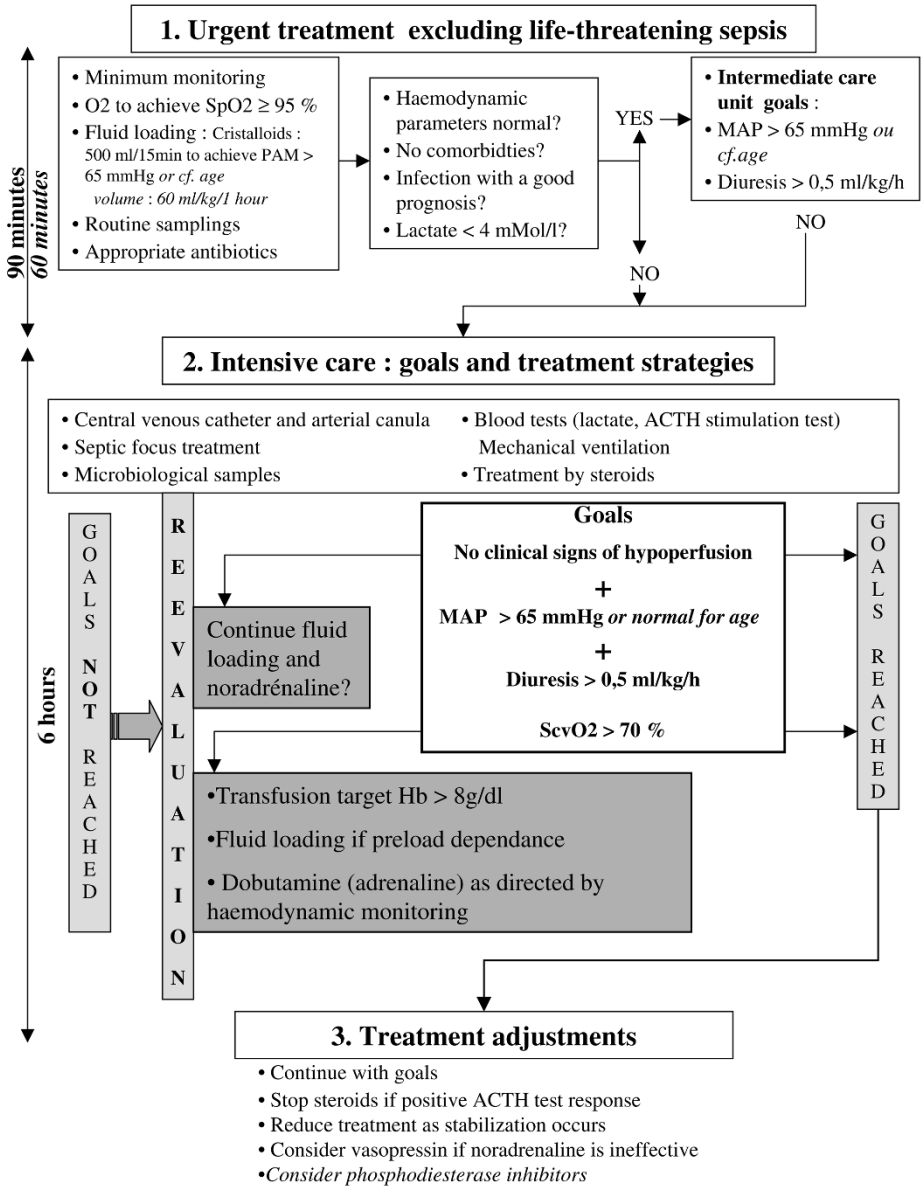
Specific differences in paediatric patients

Noradrenaline is recommended as the first-line vasoactive drug treatment. Phosphodiesterase III inhibitors may also be considered in cases of low cardiac output and normal arterial pressure.

Question 4: what is the role of other treatments?

The use of steroids is recommended in the treatment of septic shock in patients who do not respond to a dose of

Figure 1



Algorithm outlining the therapeutic strategy in sepsis. ACTH, adrenocorticotrophic hormone; MAP, mean arterial pressure; Scv_{O_2}, vena cava oxygen saturation.

250 µg of adrenocorticotrophic hormone (an appropriate response is an increase in cortisol level by 9 µg/dl). The recommended dose of hydrocortisone is 200-300 mg/day for at least 5 days, followed by a tapering dose (grade E). There is no role for activated protein C solely for the management of haemodynamic parameters.

Haemofiltration is not recommended for the management of haemodynamic shock (unless renal failure is present). There is no place for other treatments aimed at removing inflammatory mediators, such as plasmopheresis (grade E).

An increased mortality rate has been described with the use of one nitric oxide synthase inhibitor. Therefore, there is no role for its use in the management of sepsis (grade B).

Specific differences in paediatric patients

The recommended dose of hydrocortisone is 1 mg/kg every 6 hours.

Question 5: what is the treatment strategy?

The speed at which treatment is started influences prognosis, and so patients with septic shock must be managed promptly

and using a standardized treatment algorithm (Figure 1). Patients with life-threatening signs (decompensated blood pressure, acute respiratory distress, or coma) must be admitted directly to an intensive care unit.

Competing interests

The authors declare that they have no competing interests.

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Panel members included A de Lassence, R Gauzit, S Jaber, M Jourdain, E L'Her, C Lejus, F Plouvier and S Renolleau.

Reference

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