Sepsis in the intensive care unit

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Abstract

Sepsis remains a major cause of mortality in intensive care. The past 15 years has seen a more uniform, world-wide approach to the management of sepsis, severe sepsis and septic shock with improved survival. Recognizing the early symptoms and signs of sepsis are key: the confused, hypoxic, hypotensive patient with pyrexia, tachycardia, tachypnoea and leucocytosis. Examination must include search for a source of infection and early drainage or debridement. Next to take appropriate cultures, give fluids and broad-spectrum antibiotics. If the picture does not improve over the next 6 hours step-up the treatment to include urine output monitoring, blood gases for base excess, lactate, haemoglobin and glucose. These will guide the management of vasopressors, insulin, fluids, transfusion and bicarbonate. If the hypotension persists (septic shock) the patient should be moved to intensive care. The most recent recommendations include the withdrawal of starch based colloids, dobutamine in place of dopamine and a higher threshold for the use of steroids. This should be instituted within 24 hours of the start of sepsis. Advanced care includes mechanical ventilation using the ARDSnet protocol. Prevention by screening, stopping cross infection and appropriate use of antibiotics remains the first priority.

Keywords Intensive care; sepsis; septic shock; severe sepsis

Introduction

Sepsis covers a wide range of conditions which usually do not require admission to the intensive care unit (ICU) unless it becomes severe. When this occurs patients will often need ICU and broadly account for about 30% of admissions according to the patient population. This will impact on the type of septic problems such as community-acquired infection versus nosocomial or hospital-acquired infection. A medical ICU will have far more community-acquired infections than an ICU admitting elective surgical patients. Whatever the source, infection leading to sepsis remains a major intensive care problem that has a mortality of at least 38%.[1]

Definitions

Sepsis is infection with systemic manifestations (Box 1).

Severe sepsis is when sepsis induces significant organ dysfunction or tissue hypoperfusion (Box 2). **Septic shock** is when there is induced hypotension that persists despite adequate fluid resuscitation.[2] Systemic inflammatory response syndrome (SIRS) is a syndrome of two or more of the general variables shown in Box 1. It does not mean the patient is septic. Thus sepsis can be defined as, 'SIRS with evidence of infection'.

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Sepsis is a response not a disease. Defining the level of response and managing each level as it manifests provides the opportunity to start treatment early and influence outcome.

Pathophysiology

The normal immune and physiological response is to eradicate pathogens. In sepsis, there is an imbalance in the normal regulation. This may be caused by continual activation by the pathogen. There are high levels of circulating anti-inflammatory cytokines and impaired immune function. We see rapid lymphocyte apoptosis, delayed apoptosis of neutrophils and enhanced necrosis of cells. The coagulation system is also affected. There is increased coagulation and diminished fibrinolytic activity in conjunction with the excessive inflammatory response. The loss of homoeostatic balance among these systems results in generalized coagulopathy and microvascular thrombosis which can lead to acute organ failure and death.[3]

Various treatments aimed at modifying this response or using biomarkers to direct treatment and predict outcome have been

Systemic manifestations associated with sepsis

General variables

- Core temperature >38.3°C or <36°C
- Heart rate >90 bpm
- Tachypnoea (may not feel respiratory distress but a rate >30 pm)
- Significant oedema or positive fluid balance (>20 ml/kg over 24 hours)
- Hyperglycaemia-plasma glucose >7.7 mmol l^{-1}. Diabetics are higher risk

Inflammatory variables

- Leucocytosis (WBC count >12,000 μl^{-1})
- Leukopenia (WBC count <4000 μl^{-1})
- Plasma C-reactive protein: 2 SD above the normal value
- Plasma procalcitonin: 2 SD above the normal value (not routine in all hospitals)

Heamodynamic variables

- Arterial hypotension: SBP <90 mmHg; MAP <65 mmHg

Organ dysfunction variables

- Arterial hypoxaemia: SaO_2 <93% on air or (PaO_2/FiO_2 <300)
- Acute oliguria: urine output <0.5 ml/Kg/hr or <45 ml in 2 hours, despite fluid resuscitation
- Creatinine increase: >44 μmol l^{-1} in 24 hours
- Coagulation abnormalities: INR >1.5 or APTT >60 seconds
- Ileus (absent bowel sounds)
- Thrombocytopenia: platelet count <100,000 μl^{-1}
- Hyperbilirubineamia: plasma total bilirubin >34 μmol l^{-1}
- Hyperlactatemia >4 mmol l^{-1}
- Decreased capillary refill

WBC, white blood cell; SBP, systolic blood pressure; MAP, mean arterial blood pressure.

Box 1

Signs of organ dysfunction associated with severe sepsis

- Sepsis-induced hypotension
- Lactate greater than 4 mmol l^{-1}
- Urine output <0.5 ml/kg/hr for >2 hours, despite fluid resuscitation
- ALI with PaO_2/FiO_2 <250 in the absence of pneumonia as infection source
- ALI with PaO_2/FiO_2 <200 in the presence of pneumonia as infection source
- Creatinine >176 mmol l^{-1}
- Bilirubin >34 mmol l^{-1}
- Platelet count <100,000 μl^{-1}
- Coagulopathy INR >1.5

ALI, acute lung injury; INR, international normalized ratio.

Box 2

tried. Antithrombin III and activated protein C are two such proteins that have been tested in clinical practice but are not currently recommended.

Modern approach

15 years ago a collaborative approach to the 'septic patient' was started by the Society of Critical Care Medicine, the European Society of Intensive Care Medicine and the International Sepsis Forum. Together they formed the 'Surviving Sepsis Campaign' www.survivingsepsis.org which published a four phase plan to tackle sepsis world-wide.

Phase I

- Awareness amongst professionals, governments, health agencies and the public.
- Early and accurate diagnosis.
- Appropriate treatments and interventions.
- Educating all healthcare professionals about diagnosis, treatment, and management of sepsis.
- Improving access to ICU care for septic patients.
- Developing global standards of care.

Phase II

- Publication of guidelines following the Barcelona meeting in 2003.

Phase III

- Translating the guidelines into clinical practice. Establishing a world-wide database that would enable the campaign to achieve its aim of a 25% reduction in mortality.

Phase IV

- Maintaining the database and refining treatments and publishing results.

In compliance with phase IV, results from the database from 218 centres world-wide have been published showing significant improvement in survival when protocol compliant.[4]

Though well known amongst intensivists, the campaign is less well known to doctors working more widely in the hospital. As most patients come from the wards or via 'accident and emergency' and there is an emphasis on the first 6 hours of care, it is important that all doctors are aware of what are the best current guidelines for treating sepsis.[5] In particular 'time zero' for the protocol starts on admission to the 'accident and emergency' department and not when the patient arrives on the ICU. Some of the management seems prescriptive and care bundles are used. Both are inevitable in the drive for global standards and making treatment protocols that are easy to use, remember and audit.

Diagnosis

Recognizing a septic patient is easy once the diagnosis has been considered. However, the longer the patient remains untreated or receives inadequate treatment the worse the prognosis.

History

The patient may have another underlying condition such as arthritis, diabetes, ischaemic heart disease, etc., but that is not the cause of feeling 'unwell'. Ask about fever, chills, lethargy, confusion, weakness, bowel habit, appetite, headache, etc. The doctor needs to cover all the systems. For example, lung infection will cause shortness of breath and purulent sputum, urinary tract infection may cause dysuria and pungent smelling urine and abdominal infection will cause pain.

Physical signs of infection

Look at the whole patient (Figure 1): pyrexia, tachycardia, tachypnoea, pain and swelling. At this stage identifying site specific infection is crucial in the choice of antibiotics and obtaining cultures.

Diagnostic criteria for suspected sepsis:[5] these define whether the patient has sepsis or not and if it is uncomplicated or severe. This will determine the treatment plan. The patient that is septic without the criteria for 'severe sepsis' should have cultures taken (blood, screening and site specific), antibiotics, fluids and supplemental oxygen according to SaO_2 values. The patient with severe sepsis moves into a more advanced paradigm.

Management of severe sepsis

A patient suspected of severe sepsis should be managed in at least a higher dependency area where there is access to central venous pressure monitoring and supplemental oxygen therapy.

Diagnostic: full screening swabs must include urine, sputum, drains, and pus from any apparent source.

Also blood cultures from vascular lines and direct from a peripheral vein. The successful isolation of a pathogen is more likely if cultures are taken prior to antibiotic therapy.

Antibiotics: antibiotic prescribing should be according to hospital protocol. But the principle is to start broad-spectrum antibiotics early. This should continue for 3–5 days or until there is a culture or other evidence of the source at which time de-escalation to narrow spectrum should begin. Overall therapy should be for 7–10 days unless it is determined that infection was not the source of the illness.