Sepsis management based on recent treatment guidelines

## Introduction

Septic shock and subsequent death remain one of the most important problems encountered in the Intensive Care Units of hospitals all over the world (Kaukonen, Bailey, Suzuki, Pilcher, & Bellomo, 2014). The current mortality rate of sepsis patients in Australia alone is 4.6% (Kaukonen et al., 2014). However, the recent inculcation of the Surviving Sepsis Campaigns has led to a decrease in mortality rates in a number of countries (Kaukonen et al., 2014). This report focuses on the management strategies of sepsis as per the Australian guidelines with detailed procedures, rationales and recommendations for trending and evolving treatments for sepsis.

## Surviving Sepsis Campaign

The Surviving Sepsis Campaign guidelines, first published in 2004, is a collaborative effort of the European Society of Intensive Care Medicine and the Society of Critical Care Medicine (Dellinger et al., 2012). These guidelines aim to lay down a set of rules and principles that can be followed by a healthcare provider in taking care of a patient with sepsis (Dellinger et al., 2012). Based on ongoing evidence from trials regarding the best management strategies for sepsis, improvement bundles have been devised to make it easy to incorporate the latest strategies into the sepsis management framework (Dellinger et al., 2012). For a patient presenting with septic shock, a number of normal physiologic parameters have been devised and early resuscitation is given to the patient to achieve these goals (Dellinger et al., 2012). This is known as early goal-directed therapy and is implemented within the first 6 hours of presentation (Dellinger et al., 2012). According to the sepsis improvement bundles, within 3 hours of

presentation of a sepsis patient to the ICU, the lactate levels should be measured, blood cultures should be done before the administration of antibiotics, broad-spectrum antibiotics should be administered, and 30 ml/kg crystalloid should be administered for hypotension or lactate levels above 4 mmol/L (Dellinger et al., 2012). Between 3 to 6 hours of presentation, vasopressors should be administered for hypotension such that the mean arterial pressure is above 65 mm Hg, volume status and tissue perfusion should be re-assessed if hypotension persists, and lactate levels should be monitored if the initial lactate value was elevated (Dellinger et al., 2012).

## Pharmacological management of sepsis

### Antimicrobial therapy

Antimicrobial therapy for the treatment of sepsis should be administered within the first hour of diagnosis and should include drugs against the common microbial causes of sepsis (Salomao et al., 2011). Broad-spectrum antibiotics commonly used include β-lactam antibiotics, fluoroquinolones, and aminoglycosides (Salomao et al., 2011). The use of these classes of antibiotics ensures that the critically ill patient receives antimicrobial drugs that target a wider range of microorganisms and curb the growth of resistant microorganisms (Salomao et al., 2011). Once blood cultures confirm the causative microorganism and the efficacy of the antimicrobial regimen is assessed, the drugs may be modified to provide a narrower and more focused management of sepsis (Salomao et al., 2011). In order to estimate the duration of antimicrobial therapy, levels of procalcitonin are used as important biomarkers (Agarwal and Schwartz, 2011). Procalcitonin levels are found to be elevated in patients with sepsis, and monitoring these levels can indicate when to reduce or stop antimicrobial treatment (Agarwal and Schwartz, 2011).

### Hemodynamic support and adjunctive therapy

Apart from antimicrobial therapy, there are a number of other adjunctive therapies that help management of sepsis (Keh, Weber-Carstens, & Ahlers, 2008). This is necessary because sepsis leads to a number of conditions such as hyperglycemia, acute renal failure, and sepsis-induced lactic acidosis, and these conditions need targeted treatment (Keh et al., 2008). Here is a list of adjunctive therapies that are used in sepsis management.

- **Fluid therapy**

Sepsis often results in an enormous loss of fluids due to vomiting, diarrhea, edema and sweating, or other mechanisms such as extravasation of bodily fluids and vasodilation (Rivers, Jaehne, Eichhorn-Wharry, Brown, & Amponsah, 2010). The consequences of this enormous fluid loss include hypotension, reduction in systemic oxygen delivery, reduction in ventricular preload, reduction in stroke volume, and constriction of blood vessels (Rivers et al., 2010). Listed below are some of the fluids used for sepsis management.

- Normal saline (0.9%) – It is a slightly hyperosmolar solution comprising 154 mEq/l each of both sodium and chloride (Rivers et al., 2010). As part of fluid therapy, 500 ml of saline is administered over 10 minutes (Glassford, Eastwood, & Bellomo, 2014).
- Ringer's lactate solution – This solution is administered at 33 ml per kg of body weight per day (Perner et al., 2012).
- Albumin (5%) – This is given at the rate of 250 ml over 15 minutes (Glassford et al., 2014).
- Hydroxyethyl starch – This is administered as a 6% solution at the rate of 7 ml/kg over 30 minutes (Glassford et al., 2014).
- Blood – Blood is usually administered in the form of packed red blood cells to achieve a final hematocrit concentration of ≥ 30% (Dellinger et al., 2012).

- **Vasopressor therapy**

The most important characteristic of septic shock is hypotension, where the mean arterial pressure falls below 65 to 70 mm Hg (Hollenberg, 2009). Hence, if a patient is suffering septic shock, it is essential to use an arterial catheter to continuously monitor the arterial blood pressure, which should normally be between 70 to 100 mm Hg (Hollenberg, 2009). The most common vasopressors used when the arterial pressure is less than normal include norepinephrine, dopamine, epinephrine, phenylephrine, hydrocortisone, and vasopressin (Hollenberg, 2009). Dopamine is usually administered at 10 $\mu g.kg^{-1}.min^{-1}$, norepinephrine at 0.2 – 1.3 $\mu g.kg^{-1}.min^{-1}$, phenylephrine at 0.5 – 5 $\mu g.kg^{-1}.min^{-1}$, and vasopressin at 0.01 – 0.04 units/min (Hollenberg, 2009).

- **Inotropic therapy**

During septic shock, patients undergo a state of tissue hypoxia, which needs to be reverted immediately with the use of inotropes (Westphal, Silva, Salomao, Bernardo, & Machado, 2010). Inotropes function by restoring the blood flow and hence, allowing the passage of oxygen into the tissues (Westphal et al., 2010). The goal of inotrope therapy is to establish normal values of $SvcO_2$ and the agent most commonly used is dobutamine (Westphal et al., 2010). It is strongly recommended that the use of inotropes should be coupled with vasopressors such as epinephrine, especially if the patient has hypotension (Westphal et al., 2010).

- **Corticosteroids**

Severe sepsis also results in widespread systemic inflammation which, if left untreated, can lead to multiple organ failure and death (Annane, 2011). The administration of

corticosteroids leads to reduction in tissue inflammation, initiation of tissue repair, improvement in tissue perfusion, and restoration of renal oxygen uptake (Annane, 2011). Corticosteroid therapy should only be considered when the patient has undergone septic shock as this leads to uncontrolled inflammation, and hydrocortisone should be preferred over other synthetic corticosteroids (Annane, 2011). This is usually given intravenously at the rate of 200 mg per day until the systemic inflammation is cured (Annane, 2011).

- **Blood products administration**

In patients with sepsis, anemia or low hemoglobin usually occurs secondary to hemorrhage or coagulation disorders (Murthy, 2014). Red blood cell transfusion is considered when hemoglobin levels fall below 7 g/dl and it is administered at the rate of 8 – 10 ml/kg over 1 – 2 hours (Murthy, 2014). Fresh-frozen plasma may be transfused if there is a deficiency of coagulation factors due to active bleeding as a result of sepsis or just prior to surgery (Murthy, 2014). Rapid infusion is usually done to achieve factor levels of 10 – 15 ml/kg (Murthy, 2014). Some patients might be diagnosed with thrombocytopenia due to increased bleeding, and in such cases, platelets are transfused when the levels fall to 5000 – 30,000/$mm^3$ (Murthy, 2014).

- **Mechanical ventilation**

Almost 50% of patients who have sepsis also develop acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) and require endotracheal intubation and/or mechanical ventilation to provide oxygen to the tissues and allow the patient to discontinue using the accessory muscles for breathing (Dellinger et al., 2012). Supplemental oxygen should be provided to maintain an oxygen saturation of ≥ 90% (Dellinger et al., 2012). Mechanical ventilation is usually administered when the respiratory rate is greater than 40, the patient is

using accessory muscles for breathing, and has extreme hypoxemia and metabolic acidosis (Dellinger et al., 2012). When administering mechanical ventilation, the tidal volume targeted should be 6 ml/kg of body weight, plateau pressure of the lung should be ≤ 30 cm $H_2O$, and there should be a weaning protocol in place to decide when to take the patient off respiratory support (Dellinger et al., 2012).

- **Blood glucose**

Use of hydrocortisone in sepsis patients often leads to an increase in blood glucose (Dellinger et al., 2012). Hence, blood glucose management should be initiated in patients with sepsis when the levels go above 180 mg/dl (Dellinger et al., 2012). Blood glucose levels should be monitored every 2 hours until they reach normal, and then every 4 hours to ensure they remain stable (Dellinger et al., 2012).

- **Renal replacement therapy**

Septic patients often face multi-organ failure due to an imbalance between the mediators and inhibitors in the body and as a consequence, acute renal failure, which cannot be treated with hemodialysis due to hemodynamic instability and hypotension (Garcia-Miguel, 2012). In such cases, the strategy of choice is continuous arteriovenous hemofiltration (Garcia-Miguel, 2012). Continuous renal replacement techniques work by simultaneously removing several inflammatory mediators from the plasma over a period of 24 – 48 hours without affecting the hemodynamic balance of the body (Garcia-Miguel, 2012). The removal happens by simple diffusion and/or convection and is equally efficient for solutes with a relatively smaller size leading to rapid clearance of factors contributing to sepsis complications such as organ failure (Garcia-Miguel, 2012).

- **Prophylaxis treatment**
- Deep vein thrombosis prophylaxis – Sepsis patients are at a high risk for developing deep vein thrombosis due to the possibility of development of infection within a vein leading to subsequent blockage (Dellinger et al., 2012). Hence, they need to be protected against venous thromboembolism by administration of low molecular weight heparin every day (Dellinger et al., 2012). However, if the rate of creatinine clearance is less than 30 ml/min, it is important to use an agent that has low rate of renal metabolism, such as dalteparin (Dellinger et al., 2012). In cases where the patient has coagulopathy, hemorrhage or thrombocytopenia, heparin should not be administered and instead, compression stockings or other devices should be used (Dellinger et al., 2012).
- Stress ulcer prophylaxis – Prophylaxis for stress ulcers should be commenced to reduce the possibility of bleeding from the upper gastrointestinal tract as a result of hypotension or administration of mechanical ventilation (Dellinger et al., 2012). This can be done by using proton pump inhibitors or H2 blockers which offer protection by suppressing acid production in the stomach (Dellinger et al., 2012).
- Nutrition –The patient should be given nutrition either orally or enterally at the rate of 500 calories per day for the first week after diagnosis (Dellinger et al., 2012). The advantages of enteral feeding in the initial stages include conserving integrity of the gut mucosa and preventing translocation of bacteria (Dellinger et al., 2012). The supplements of choice are arginine, glutamine and omega-3-fatty acids as they are good for the immune system of the patient and help recovery (Dellinger et al., 2012). Intravenous glucose may also be administered during the first week to avoid loading the patient with complex nutrients which cannot be digested easily (Dellinger et al., 2012).

## Non-pharmacological management of sepsis

### Nursing interventions

There are a number of things a nurse needs to keep in mind in order to ensure optimum care for a septic patient (Dellacroce, 2009). Fluid resuscitation should be started immediately with the intravenous infusion of saline (Dellacroce, 2009). A Foley catheter may be inserted for monitoring the patient (Dellacroce, 2009). Blood cultures need to be obtained to identify the cause of sepsis, after which antimicrobial therapy can be initiated (Dellacroce, 2009). In case the patient goes into septic shock, vasopressor therapy should be commenced (Dellacroce, 2009). Blood glucose levels should also be maintained by the infusion of insulin (Dellacroce, 2009). Changes in a patient's condition should be closely monitored and promptly reported (Dellacroce, 2009).

### Conclusion

Given that sepsis is one of the major causes of death worldwide, it is of no surprise that a number of committees all around the world are working together to chart out management strategies that will improve prognosis of a septic patient. The Surviving Sepsis Campaign is one such attempt and it lays down the steps in detail that should be used for treatment of sepsis. They include both pharmacological and non-pharmacological methods with emphasis on regular monitoring of the patient, ensuring multisystem stability and management of all sepsis complications.

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