Chapter 175

Role of Physician in Surgical Sepsis

S Asokan

Infection, sepsis, severe sepsis, shock, systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS) are the same whether it is a medical problem or surgical problem. Severe surgical sepsis assumes significance where the patient may be primarily handled by surgeons and may be in surgical intensive care units, still having a plethora of medical problems.

Surgical infections may be one of the followings:

- Infections requiring surgeon's attention still can be managed medically
- Infections requiring surgical procedures
- Infections followed by surgical procedures.

Severe surgical sepsis and septic shock require intensive surgical care management. The much feared SIRS (systemic inflammatory response syndrome) requires another SIRS (systematic informed response system) for an effective management with multidisciplinary arrangements and a physician's role is a very vital one in this.

Continued research and updating of the knowledge, newer techniques, efficient devices, effective drugs, etc. in handling severe sepsis and septic shock have not reduced the mortality rate drastically and still they top the list of noncoronary deaths. An international conference on sepsis rolled out the following definitions in 2001 which are relevant even today.

Infection: A pathologic process caused by the invasion of normally sterile tissue fluid or body cavity by pathogenic or potentially pathogenic microorganisms.

Sepsis: Infection, documented or suspected and some of the signs and symptoms of an inflammatory response.

Severe sepsis: Sepsis complicated by organ dysfunction.

Septic shock: Severe sepsis plus acute circulatory failure characterized by persistent arterial hypotension despite adequate volume administration, unexplained by causes other than sepsis.[1]

Organ failure is a sequelae of septic shock. Usually single organ failure does not lead to death but multiple organs failure has been the leading cause of death occurring in 50–60% patients of severe sepsis. MODS being a significant cause of death, physicians need to be involved at the earliest opportunity.

INITIAL ASSESSMENT AND RESUSCITATION

It should be started at the earliest preferably within 6 hours of onset of septic shock, samples for blood and urine cultures, central venous pressures, serum lactate/procalcitonin, acid-base assessment are the few more tests required to be done along with the usual biochemical tests.

Early goal directed therapy (EGDT) has been shown to improve survival by 15% in patients of septic shock.[2-5]

HEMODYNAMIC STABILIZATION

Vasodilatation, venous pooling and capillary leak in septic shock lead to profound intravascular fluid deficit, thus leading to hypotension and setting the train of events to follow. So, fluid needs to be replaced; both crystalloids and colloids may be used.

It is desirable to work towards achieving the following goals:

- Central venous pressure (CVP): 8–12 mm of Hg
- Mean arterial pressure (MAP): More than 65 mm of Hg
- Urine output: More than 0.5 ml/kg/hr
- Central venous oxygenation: More than 70% or mixed venous 65%.

In the event of adequate fluid challenge (1,000 mL of crystalloids or 300–500 mL of colloids over 30 minutes) failing to evoke the desired response and persistent hypotension, vasopressors like dopamine, noradrenaline, adrenaline, and vasopressin may be used. Noradrenaline and dopamine centrally administered are the initial vasopressors of choice.[6-10]

ANTIBIOTIC THERAPY

Timely administration of empirical antibiotic with relatively broad spectrum of coverage with good penetration into presumed source may be started in the absence of microbiologic data, as early as 4–6 hours of presentation is essential. Around 10% of septic patients do not receive prompt antibiotic therapy, resulting in a 10–15% higher mortality rate among these patients than those who received appropriate therapy promptly.[11-14] The surviving sepsis campaign (SSC) guidelines gave the recommendations for initiating intravenous (IV) antibiotics within 1 hour of recognition of severe sepsis.

The following frame work can be used to classify organisms and assist in the initial selection of antibiotics:

- Gram-positive organism with or without *Enterococcus* and with or without methicillin-resistant *Staphylococcus aureus* (MRSA)
- Gram-negative organisms with or without *Pseudomonas*
- Atypical organisms including *Legionella*
- Anaerobic organisms like *Bacteroides.*

In selecting the appropriate antibiotic for a septic patient, the clinician should consider the patient's immune status and prior antibiotic use, whether the patient has an indwelling IV catheter line and the types and antibiotic susceptibilities of bacteria that frequently occur in the hospital where the patient is being treated. Consider combination therapy in *Pseudomonas* infections and in neutropenic patients. Combination therapy less than 3–5 days and de-escalation following susceptibilities. Total Duration of therapy typically limited to 7–10 days; it will be longer if response is slow or there are undrainable foci of infection or immunologic deficiencies.

Fungal infections pose serious problems for clinicians because they carry higher risks for morbidity, such as respiratory failure, compared with bacterial infections and have a mortality rate of 40–60%. Clinicians should, therefore, closely monitor patients with high index of suspicion for nosocomial fungal sepsis and treat presumptively.[15]

DIABETIC CONTROL

Patients with severe surgical sepsis especially postoperative sepsis need to be maintained with continuous insulin infusion to maintain sugars less than 150 mg/dL. However, this intensive insulin therapy is associated with frequent episodes of hypoglycemia which needs to be carefully monitored with blood glucose values every 1–2 hours (4 hours when stable).[16]

ACUTE LUNG INJURY/RESPIRATORY DYSFUNCTION

About 40–60% of septic shock patients develop acute lung injury, which left untreated may lead to *acute respiratory distress syndrome*, with a mortality rate of 25–50%. Normal arterial oxygen saturation but sustained respiratory rate of more than 30/min is a warning sign. Early intubation and mechanical ventilatory support thus enhancing perfusion of vital organs, prevents diversion of significant amount of cardiac output to the respiratory muscles. In ventilated patients, target a tidal volume of 6 mL/kg (predicted) body weight with plateau pressure less than 30 cm H_2O and positive end-expiratory pressure (PEEP) more than 5 cm H_2O is usually required to avoid lung collapse.[17-19] Sedation and paralysis if necessary have shown to lower oxygen consumption and CO_2 production.[20,21] Use a weaning protocols regularly to evaluate the potential for discontinuing mechanical ventilation. Surfactant therapy can improve gas exchange.

CARDIAC DYSFUNCTION

Sepsis-induced cardiac dysfunction is by a combination of hypovolemia and peripheral vascular dysfunction resulting in hypotension, cardiac failure and cell dysfunction; sepsis-induced cardiac dysfunction occurs early and leads to both systolic and diastolic dysfunction. Systolic dysfunction affects both the ventricles by the impairment in contractility whereas the diastolic dysfunction is due to reduced biventricular distensibility related to myocardial interstitial edema. This needs to be addressed to aggressively. Dobutamine is the drug of choice as an inotropic in patients with myocardial dysfunction as supported by elevated cardiac filling pressures and low cardiac output

ACUTE KIDNEY INJURY

Acute kidney injury (AKI) is a syndrome characterized by an abrupt decrease in glomerular filtration rate that leads to decrease in urinary output causing acidosis through accumulation of nitrogenous and non-nitrogenous waste products. In septic shock, 60% of cause for AKI is pre-renal due to decreased cardiac output, hypovolemia or raised intra-abdominal pressure, etc. If this is left unchecked, it may leads to AKI, renal.

Removal or treating the cause and maintaining physiological homeostasis while recovery are the principles of management. Restoration of plasma volume, perfusion pressure and replacement therapies like intermittent hemodialysis and continuous venovenous hemofiltration (CVVH) are the therapies required, both are considered equivalent but CVVH offers easier management in hemodynamically unstable patients.

SOURCE CONTROL IN SEVERE SURGICAL SEPSIS

Intra-abdominal sepsis starting from a perforated appendix, inflamed gallbladder, necrosed pancreas, perforation of any hallow viscus leading to generalized peritonitis are all the majority of surgical causes for severe sepsis. Skeletomuscular sepsis, burns and trauma are the other causes apart from postoperative sepsis.

Cardinal principle in source control is wherever there is pus, it has to be drained. Necrotic tissue should be debrided. In case of intra-abdominal sepsis, the source of sepsis should be removed. In this context, two entities have to be remembered:

1. Intra-abdominal hypertension
2. Abdominal compartment syndrome.

Intra-abdominal Hypertension

It is defined as a sustained or repeated pathologic elevation of intra-abdominal pressure more than 12 mm Hg.

Abdominal Compartment Syndrome

Abdominal compartment syndrome (ACS) is sustained intra-abdominal pressure more than 20 mm Hg that is associated with organ dysfunction or failure.

Primary ACS is a surgical cause associated with injury or disease in the abdominopelvic region that frequently requires early surgical or interventional radiological intervention.

Secondary ACS refers to conditions that are secondary to sepsis other than causes of abdominopelvic region diseases.

Recurrent ACS refers to the condition in which ACS redevelop following previous surgical or medical treatment of primary or surgical ACS.

There are several methods of measuring intra-abdominal pressure using the routes of stomach, bladder, uterus, inferior vena cava and peritoneal cavity. None of them have been able to reach the status of a gold standard.

Properly timed abdominal decompression after taking adequate care to maintain the fluid balance is the definitive treatment to tackle ACS. ACS due to surgical causes requires definite decompression preferably with temporary abdominal closure or laparostomy facilitating relook whenever required, is beneficial.

NUTRITIONAL SUPPORT

The nutritional support in severe surgical sepsis patients is aimed at correcting the ill effects of preoperative weight loss if any, to support wound healing, immune function and prevent malnutrition and its comorbid consequences. The desirable goal is to provide adequate substrate to support organ function, wound healing and immune competence without causing metabolic derangement or increasing infection risk.

In general, well-nourished or mildly malnourished medical or surgical patient can withstand 7–10 days of starvation but severely malnourished and severely stressed patients need prompt nutritional intervention because they are at high risk of developing sepsis, wound infections and prolonged SICU stay without nutritional support. If the patient has a functional gastrointestinal tract, hemodynamically stable and unable to take oral nutrition, enteral feeding may be resorted. If the patient has splanchnic hypoperfusion, acute shock, and on high-dose vasopressors or problems with the small bowel leak, obstruction or massive resection, parenteral nutrition can be employed. Suitable formulations having required protein, carbohydrates, lipid, fluids, electrolytes, minerals and vitamins need to be chosen. Caloric support should be based on measured energy expenditure or 20–25 kcal/kg/BW/day, protein 1.5 to 2.5 g/kg/IBW/day, will be suitable for most of the patients.

DEEP VEIN THROMBOSIS PROPHYLAXIS

- Use either low-dose unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH), unless contraindicated.

- Use a mechanical prophylactic device, such as compression stockings or an intermittent Compression device, when heparin is contraindicated.
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high-risk for deep vein thrombosis.
- In patients at very high risk, LMWH should be used rather than UFH.

STRESS ULCER PROPHYLAXIS

Provide stress ulcer prophylaxis using H2 blocker or proton pump inhibitor. Benefits of prevention of upper gastrointestinal bleed must be weighed against the potential for development of ventilator-acquired pneumonia.

BLOOD PRODUCT ADMINISTRATION

Give red blood cells when hemoglobin decreases to 7.0 g/dL to target a hemoglobin of 7.0–9.0 g/dL in adults. A higher hemoglobin level may be required in special circumstances (e.g. myocardial ischemia, severe hypoxemia, acute hemorrhage, cyanotic heart disease, or lactic acidosis)

- Should not use erythropoietin to treat sepsis-related anemia. Erythropoietin may be used for other accepted reasons
- Should not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures
- Administer platelets when
  - Counts are less than 5,000/mm^3 regardless of bleeding
  - Counts are 5,000–30,000/mm^3 and there is significant bleeding risk
  - Higher platelet counts (>50,000/mm^3) are required for surgery or invasive procedures.

RECENT ADVANCES

PMX-B Hemofiltration

Polymyxin B-immobilized fiber column meant for extracorporeal direct hemoperfusion, developed in Japan for the purpose of selectively adsorbing endotoxin especially in surgical sepsis, is useful. It interrupts sepsis cascade without systemic side effects by:

- Adsorbing/reducing blood endotoxin levels
- Interference with apoptotic signal pathways
- Modulating levels of pro- and anti-inflammatory mediators
- Removal of activated inflammatory cells.

Thus, improving gas exchange (PaO_2/FiO_2 ratio), improve systemic vascular resistance and cardiac output, there by increases blood pressure and reduces vasopressor use, and in overall it helps to reduce mortality.

REFERENCES

1. Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International sepsis definitions conference. Crit Care Mad. 2003;(4):1250-6.
2. Shapiro NI, Howell MD, Talmor D, et al. Implementation and outcomes of the multiple urgent sepsis therapies (MUST) protocol. Crit Care Med. 2006;34:1025-32.
3. Micek SST, Roubinian N, Heuring T, et al. Before-after study of a standardized hospital order set for the management of septic shock. Crit Care Med. 2006;34:2707-13.
4. Nguyen HB, Corbett SW, Steele R, et al. Implementation of a bundle of quality indicators for the early management of severe sepsis and septic shock is associated with decreased mortality. Crit Care Med. 2007;35:1105–12.
5. Shorr AF, Micek ST, Jackson WL Jr, et al. Economic implications of an evidence based sepsis protocol: Can we improve outcomes and lower costs? Crit Care Med. 2007;35:1257-62.
6. Bendjelid K, Romand JA. Fluid responsiveness in mechanically ventilated patients: A review of indices used in intensive care. Intensive Care Med. 2003;29:352-60.
7. Malbrain ML, Deeren D, De Potter TJ. Intra-abdominal hypertension in the critically ill: It is time to pay attention. Curr Opin Crit Care. 2005;11:156-71.
8. Varpula M, Tallgren M, Saukkonen K, et al. Hemodynamic variables related to outcome in septic shock. Intensive Care Med. 2005;31:1066-71.
9. Kortgen A, Niederprum P, Bauer M. Implementation of an evidence-based "standard operating procedure" and outcome in septic shock. Crit Care Med. 2006;34:943-9.
10. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345:1368-77.
11. Pappas PG, Rex JH, Sobel JD, et al. Guidelines for treatment of candidiasis. Clin Infect Dis. 2004;38:161-89.
12. McCabe WR, Jackson GG: Gram negative bacteremia. Arch Intern Med. 1962;110:92-100.
13. Kreger BE, Craven DE, McCabe WR. Gram negative bacteremia: IV. Re-evaluation of clinical features and treatment in 612 patients. Am J Med. 1980;68:344-55.
14. Leibovici L, Shraga I, Drucker M, et al. The benefit of appropriate empirical antibiotic treatment in patients with bloodstream infection. J Intern Med. 1998;244:379-86.
15. Ibrahim EH, Sherman G, Ward S, et al. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. Chest. 2000;118:146-55.
16. Pappas PG, Rex JH, Sobel JD, et al. Guidelines for treatment of candidiasis. Clin Infect Dis. 2004;38:161-89.
17. Brunkhorst FM, Engel C, Bloos F, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med. 2008;358(2):125-39.
18. Tobin MJ. Culmination of an era in research on the acute respiratory distress syndrome. N Engl J Med. 2000;342:1360-1.
19. Marini JJ, Gattinoni L. Ventilatory management of acute respiratory distress syndrome: A consensus of two. Crit Care Med. 2004;32:250-5.
20. Hager DN, Krishnan JA, Hayden DL, et al. Tidal volume reduction in patients with acute lung injury when plateau pressures are not high. Am J Respir Crit Care Med. 2005;172:1241-5.
21. Brook AD, Ahrens TS, Schaiff R, et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. Crit Care Med. 1999;27:2609-15.