ORIGINAL RESEARCH PAPER

Anaesthesiology

KEY WORDS:

SEVERE SEPSIS AND ANAESTHESIA: WHERE WE ARE STANDING AT PRESENT

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ABSTRACT

Sepsis, is a a common cause of morbidity and mortality affecting all age groups throughout the world, especially in resource limiting settings such as india. Anaesthetists play a central role in the multidisciplinary management of patients with severe sepsis from their initial deterioration at ward level, transfer to the diagnostic imaging suite, and intraoperative management for emergency surgery. The timely administration of appropriate i.v. antimicrobial therapy is a crucial step in the care of patients with severe sepsis who may require surgery to control the source of sepsis. Preoperative resuscitation, aimed at optimizing major organ perfusion, is based on judicious use of fluids, vasopressors, and inotropes. Intraoperative anaesthesia management requires careful induction and maintenance of anaesthesia, optimizing intravascular volume status, avoidance of lung injury during mechanical ventilation, and ongoing monitoring of arterial blood gases, lactate concentration, haematological and renal indices, and electrolyte levels. Postoperative care overlaps with ongoing management of the severe sepsis syndrome patient in the intensive care unit. These patients are by definition, high risk, already requiring multiple supports, and require experienced and skilful decision-making to optimize their chances of a favourable outcome. Similar to acute myocardial infarction, stroke, or acute trauma, the initial hours (golden hours) of clinical management of severe sepsis represent an important opportunity to reduce morbidity and mortality. Rapid clinical assessment, resuscitation and surgical management by a focused multidisciplinary team, and early effective antimicrobial therapy are the key components to improved patient outcome.

Epidemiology

Severe sepsis and septic shock are major healthcare problems with an estimated 11 million cases a year with a close to 3 million deaths in India[1,2] Sepsis is the most common cause of admission in ICU and is associated with significant morbidity and mortality but data on epidemiology of sepsis in Indian ICU is limited. In 2001, a consensus conference (Society of Critical Care Medicine, Euro- pean Society of Intensive Care Medicine, American College of Chest Physicians, American Thoracic Society, and Surgical Infection Society) concluded that the basic definitions of systemic inflammatory response syndrome (SIRS), as originally described in 1992 by the American College of Chest Physicians and the Society of Critical Care Medicine,[3] should remain largely unchanged[4] (Table 1).

Table 1 - 2001 Sepsis Definition By The American College Of Chest Physicians (accp) And The Society Of Critical Care Medicine(sccm)

Pathological entity	Definition
Bacteraemia	Presence of bacteria in the bloodstream
Septicaemia	The presence of large numbers of bacteria in the bloodstream often associated with systemic signs and symptoms such as fever, rigors, and headache
SIRS	The threshold definition is two or more of the following criteria: o temperature >38°C or <36°C o heart rate >90 beats min^{-1} o ventilatory frequency >20 bpm or Pa_{CO_2} <4.3 kPa o WBC $<4 \times 10^9$ $litre^{-1}$ or $>12 \times 10^9$ $litre^{-1}$ or >10% immature forms
Sepsis	SIRS with clinical evidence of infection
Severe sepsis	Sepsis associated with organ dysfunction, hypotension, or hypoperfusion abnormalities
Septic shock	Sepsis-induced hypotension, despite fluid resuscitation, plus hypoperfusion abnormalities
Sepsis-induced hypotension	A systolic arterial pressure <90 mm Hg or a reduction of > 40 mm Hg from baseline in the absence of other causes for hypotension

Because of the limitations of the definitions of SIRS and infection, the 2001 consensus conference suggested an expanded list of possible signs of systemic inflammation that may be observed in 'septic-looking 'patients (Table 2).

Table 2 - Diagnostic Criteria For Sepsis

Documented or suspected infection with some of the following clinical signs or laboratory data
1. Infection: documented or suspected infection
2. Signs of systemic inflammation
(a) General parameters
Fever (core temp. >38.8°C)
Hypothermia (core temp. <36°C)
Tachycardia (>90 beats min^{-1})
Tachypnoea (>30 bpm)
Altered mental status
Significant positive fluid balance (>20 ml kg^{-1} over 24 h)
Hyperglycaemia (>7.7 mmol $litre^{-1}$) in non-diabetic patients
(b) Inflammatory parameters
WCC <4 or >12, >10% immature forms
C-reactive protein >2 SD above normal value
Plasma procalcitonin >2 SD above normal value
(c) Haemodynamic parameters
Arterial hypotension (SAP <90 mm Hg)
Sv_{O_2} >70%
CI>3.5
(d) Organ dysfunction parameters:
Hypoxic (Pa_{O_2}/FI_{O_2} <40)
Oliguria (<0.5 ml kg^{-1} h^{-1})
Creatinine increase (>0.5 mg dl^{-1})
Coagulopathy (INR >1.5, aPPT>60 s, plt count<100)
Absent bowel sounds
Hyperbilirubinaemia
(e) Tissue hypoperfusion parameters
Lactate>3 mmol $litre^{-1}$
Decreased capillary refill
Mottling of skin

Severe sepsis occurs in 1–2% of all hospitalizations and accounts for as much as 25% of intensive care unit (ICU) bed

utilization. It is common in elderly, immune- compromised, and critically ill patients and is a major cause of death in ICUs worldwide.[5] Sepsis is the second leading cause of death in non-coronary ICU patients. Mor- tality remains high at 30–50% despite improved care in the past 10–15 yr.[156]

Causes Of Sepsis

Severe sepsis may have infective and non-infective causes. Infections are common and amenable to treatment; therefore, in patients presenting with clinical signs of systemic inflammation (SIRS), an infective cause should be actively sought.(Table 3)

Table 3 - Aetiology Of Severe Sepsis

Infective causes	Non-infective causes
CNS infections	Severe trauma
CVS infections	Haemorrhage
Respiratory infections	Complication of surgery
Renal infections	Complicated aortic aneurysm
GIT infections	Myocardial infarction
Skin and soft tissue infections	Pulmonary embolism
Bone and joint infections	Cardiac tamponade
	Subarachnoid haemorrhage
	Burns
	Acute pancreatitis
	Drug overdose/toxicity
	Diabetic ketoacidosis
	Adrenal insufficiency
	Anaphylaxis

Anaesthetic Management

Anaesthetists are frequently involved in the care of severely septic patients in the emergency department, operating theatre, or ICU. Infection source control, involving surgical drainage of an abscess or debridement of necrotic tissue coupled with early effective antimicrobial therapy, is central to the successful treatment of a patient with severe sepsis. In high-risk surgical or trauma patients with sepsis, early haemodynamic optimisation before the development of organ failure reduced mortality by 23% in comparison with those who were optimised after the development of organ failure.[9,10]

Pharmacokinetics In Sepsis

Sepsis and septic shock are accompanied by profound changes in the organism that may alter both the pharmacokinetics and the pharmacodynamics of drugs. The mechanisms by which sepsis-induced pathophysiological changes may influence pharmacological processes. Drug absorption following intramuscular, subcutaneous, transdermal and oral administration may be reduced due to a decreased perfusion of muscles, skin and splanchnic organs. Compromised tissue perfusion may also affect drug distribution, resulting in a decrease of distribution volume. On the other hand, the increase in capillary permeability and interstitial oedema during sepsis and septic shock may enhance drug distribution. Changes in plasma protein binding, body water, tissue mass and pH may also affect drug distribution. For basic drugs that are bound to the acute phase reactant alpha(1)-acid glycoprotein, the increase in plasma concentration of this protein will result in a decreased distribution volume. The opposite may be observed for drugs that are extensively bound to albumin, as the latter protein decreases during septic conditions. For many drugs, the liver is the main organ for metabolism. The determinants of hepatic clearance of drugs are liver blood flow, drug binding in plasma and the activity of the metabolic enzymes; each of these may be influenced by sepsis and septic shock. For high extraction drugs, clearance is mainly flow-dependent, and sepsis-induced liver hypoperfusion may result in a decreased clearance. For low extraction drugs, clearance is determined by the degree of plasma binding and the activity of the metabolic enzymes. Oxidative metabolism via the cytochrome P450 enzyme system is an important clearance mechanism for many drugs, and has been shown to be markedly affected in septic conditions, resulting in decreased drug clearance. The kidneys are an important excretion pathway for many drugs. Renal failure, which often accompanies sepsis and septic shock, will result in accumulation of both parent drug and its metabolites. Changes in drug effect during septic conditions may theoretically result from changes in pharmacodynamics due to changes in the affinity of the receptor for the drug or alterations in the intrinsic activity at the receptor. The lack of valid pharmacological studies in patients with sepsis and septic shock makes drug administration in these patients a difficult challenge. The patient's underlying pathophysiological condition may guide individual dosage selection, which may be guided by measuring plasma concentration or drug effect.

Preoperative Assessment

Although not all patients with severe sepsis have an infective focus, it is prudent to examine patients systematically looking for a source of infection. The primary source may be self-evident (e.g. trauma, burns, recent surgery) or may be more difficult to identify (e.g. empyema of the gall bladder, pancreatitis, gynaecological sepsis, soft tissue, and bony infections), particularly in agitated un-cooperative patients. The examination should focus on the severity of SIRS, the state of intravascular hydration, the presence of shock or multi-organ dysfunction, and the adequacy of haemodynamic resuscitation.

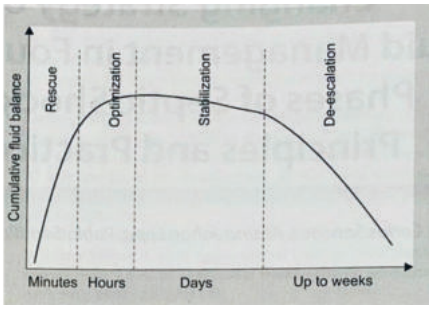
Surviving Sepsis Campaign

Following an international process of consultation to standardize the management of critically ill septic patients, the Surviving Sepsis Campaign suggested that therapies be grouped or 'bundled 'for particular subsets of patients. The concept is not unlike that of Advanced Trauma Life Support (ATLS), where somewhat didactic therapies are proposed in given clinical situations. Although its detractors point out that bundled therapies are not individualized to a particular patient's needs, and the lack of evidence-based medicine to underpin its guidelines, there is nonetheless some evidence that the process of care and outcomes improved after educational programmes were instituted based on the Surviving Sepsis Campaign.[11–13]

For sepsis, a range of biomarkers is identified, including fluid phase pattern recognition molecules (PRMs), complement system, cytokines, chemokines, damage associated molecular patterns (DAMPs), non-coding RNAs, miRNAs, cell membrane receptors, cell proteins, metabolites, and soluble receptors.

Antibiotic Therapy

It is imperative that i.v. antibiotics should be started as early as possible after the diagnosis of severe sepsis and septic shock. There is no evidence that delaying until the start of the surgical procedure or until microbiology culture results are available is beneficial. Appropriate samples should be obtained for culture before giving first-line anti-microbial therapy.[14] Anti-microbial drugs are best given i.v. and in sufficient dosage to achieve therapeutic concentration. The choice of agents should be based on the clinical history, physical examination, likely pathogen(s), optimal penetration of anti-microbial drugs into infected tissues, and the local pattern of sensitivity to anti-microbial agents. Broad-spectrum agents should be used initially with one or more agents active against all likely bacterial/fungal pathogens.



Graph 1: Four Phases Of Intravenous Fluid Therapy

Haemodynamic Resuscitation

The objective of preoperative resuscitation measures is to rapidly restore adequate oxygen delivery to peripheral tissues. If the patient is haemodynamically unstable, invasive arterial pressure monitoring, central venous access, and ICU or high dependency unit admission must be considered. Placement of a central venous catheter will allow measurement of central venous pressure (CVP), mixed venous oxygen saturation, administration of i.v. fluids, and vasopressor medication.[15–17] Resuscitation measures begun in the emergency room can be continued even if the patient requires diagnostic imaging studies or admission to the ICU before transfer to the operating theatre. The first 6 h of resuscitation of septic patients, the so-called 'golden hours', are crucial and frequently coincide with the time for emergency surgery.[11,18]

Table 4: Goal Directed Therapy: A Summary Of Clinical Targets

Clinical parameter	Goal
Central venous pressure	8-12 mm Hg (≥8 mm Hg in spontaneously breathing patient, ≥12 mm Hg in ventilated patients)
Mean arterial pressure	Between 65 and 90 mm Hg
Central venous oxygen saturation	≥70 mm Hg
Urine output	≥0.5 ml kg^{-1} h^{-1}
Haematocrit	≥30%

Four Phases of intravenous fluid therapy: Rescue, Optimization, Stablization,De-escalation as proposed by Vincent and De Backer or Rescue, Optimization, Stablization and evacuation as proposed by Malbrain et al.

There is little disagreement among clinicians that in the hypotensive septic patient with lactate >3 mmol litre□1, volume resuscitation using crystalloids or colloids should be used initially, aiming to reach the following clinical endpoints: CVP 8–12 mm Hg, mean arterial pressure 65 mm Hg, urine output 0.5 ml kg□1 h□1, central venous oxygen saturation: >70%. There is no evidence-based support for one type of i.v. fluid over another with regard to ICU stay, duration of mechanical ventilation, duration of renal replacement therapy, and 28 day outcome.[11,16] Colloid with pentastarch therapy was associated with higher rates of acute renal failure and renal-replacement therapy than Ringer's lactate and its toxicity is increased with accumulating doses.[7] Vasopressor support with norepinephrine may be considered even before optimal i.v. fluid loading has been achieved. Low-dose vasopressin (0.03 units min□1) may be subsequently added to reduce the requirement for high-dose norepinephrine alone.[10,18,19] Inotropes are added to volume resuscitation and vasopressors, if there is evidence of continued low cardiac output despite adequate cardiac filling and fluid resuscitation. The Surviving Sepsis Campaign recommends that dobutamine is the first-line inotrope therapy to be added to vasopressors in septic patients.[11] However, a study in septic patients showed no difference in efficacy and safety with epinephrine alone compared with norepinephrine plus dobutamine (28 day mortality: 40% vs 34% respectively, P=0.31) in the management of septic shock.[19] There is no evidence to support the use of dobutamine to achieve supernormal oxygen delivery in terms of improving outcomes.[16–18] Resuscitation efforts should be continued as long as haemodynamic improvement accompanies each step in the process. Further i.v. fluid administration should be stopped when filling pressures are high and no further improvement seen in tissue perfusion is seen (e.g. serum lactate not decreasing). Transfusion of red blood cells may be considered if tissue oxygen delivery remains inadequate.[20,21]

Table 5 - Fluid terminology

- **Fluid bolus**: A rapid infusion to correct hypotensive shock.It typically includes the infusion of at least 500ml opera maximum of 15minutes.
- **Fluid Challenge:** 100-200ml over 5-10 with a reassessment to optimise surgical perfusion.
- **Fluid infusion:** Continuous delivery of intravenous fluids maintain homeostasis, replace losses, or prevent organ injury(e.g.,pre-hydration before operation or contrast nephropathy)
- **Maintenance:**Fluid administration to provide fluids for patients who cannot meet their needs by oral route.this should be titrated to patient need and context and should include the replacement of ongoing losses.In a patient without ongoing losses, this should probably >1-2ml/kg/h.
- **Daily fluid balance**: Daily sum of all intakes and outputs.
- **Cumulative fluid balance:**The total fluid accumulate on over a set period of time.
- **Fluid Overload**: Cumulative fluid balance expressed as a proportion of baseline body weight.A value of 10% is associated with adverse outcomes.

Levosimendan may be a useful adjunct to conventional inotropic therapy in cases of refractory myocardial dysfunction in sepsis. Its inotropic effect is attributable to increased cardiac troponin C sensitivity to calcium. The systemic and pulmonary vasodilator effect is attributable to its opening of ATP-dependent potassium channels.[22] A single randomized controlled trial in 28 patients with septic shock and ejection fraction <45% persisting >48 h after conventional treatment found that cardiac index and renal function indices improved after levosimendan, compared with dobutamine.[22,23] However, further larger clinical studies are required before levosimendan becomes a widely accepted therapy in septic shock.

Supplemental oxygen therapy is valuable in severely septic patients even if they do not have signs of respiratory distress. Immediate tracheal intubation and mechanical ventilation of the lungs can be considered if the patient's level of consciousness is low or if there is progressive distress and hypoxia.24 If there is an inadequate response to these resuscitation measures, it is important to consider the presence of an alternative diagnosis. The non-infective causes of SIRS or an iatrogenic complication, for example, tension pneumothorax after CVC placement, should also be considered (Table 3).

Cardiac Dysfunction in Sepsis

Cardiac dysfunction is a consequence of severe sepsis and is characterized by impaired contractility, diastolic dysfunction, as well as reduced cardiac index and ejection fraction (EF). Cardiac dysfunction is an important component of multiorgan failure that is caused by severe sepsis. Septic patients with either systolic or diastolic dysfunction or a combination of both have higher mortality than those diagnosed with sepsis but without diastolic or systolic dysfunction.[21] The mechanisms that underlie myocardial depression during septic shock are not well known. Circulating inflammatory cytokines interleukin (IL)-1, IL-8, and tumor necrosis factor (TNF)□, which are increased during septic shock, may account for cardiac dysfunction as they have been associated with altered production of nitric oxide and altered calcium homeostasis. Impaired □-adrenergic signaling leading to reduced cardiac contractility is also present in sepsis. Moreover, growing evidence associates septic cardiac dysfunction with impaired metabolism and reduced energy production in cardiomyocytes. The heart produces ATP primarily via fatty acid and glucose oxidation, which both are strongly decreased in experimental animal models of sepsis. Despite reduced cardiac lipid uptake, sepsis leads to intracellular lipid accumulation. Lipid accumulation must therefore result from impaired fatty acid oxidation and conversion of non-oxidized fatty acids into triglycerides.[21]

Intraoperative Management

The primary goal of the anaesthetist during the intraoperative

period is to provide safe and optimal care for critically ill septic patients so that they may benefit maximally from the surgical or radiological source control procedure. The majority of surgical source control procedures are optimally carried out in the operating theatre under general anaesthesia.

Before Induction

Many source control procedures are done out of hours, so it is important that the anaesthetist has appropriate help available in the operating theatre. Some thought should be given early to whether the patient may require ICU management after operation. Awareness of the microbiological samples sent for culture, the anti-microbial agents which were started, and timing of the next scheduled dose is important to optimize type and timing of intraoperative antimicrobial therapy.[28] Therapeutic concentrations of effective antimicrobial agents should be maintained throughout the perioperative period as the procedure itself may cause further bacteraemia and clinical deterioration. Invasive haemodynamic monitoring is likely to be indicated in addition to standard intraoperative monitoring. Serial measurements of arterial blood gases and lactate concentration should be readily available from near-patient testing equipment. If large volume loss is anticipated during the surgical procedure, it is worth considering placement of an appropriate volume resuscitation intravascular device.

Induction of anaesthesia and initiation of mechanical ventilation

Patients undergoing source control procedures are in an inherently unstable cardiovascular state due to the combined effects of sepsis, anaesthesia, intravascular volume loss, bleeding, and surgical stress. De-nitrogenation of the lungs, breathing 100% O_2 through a tightly fitted facemask for up to 3 min, may be considered before induction of anaesthesia. Because many surgical procedures on severely septic patients occur on an emergency basis, a modified rapid sequence induction, perhaps using rocuronium rather than succinylcholine to facilitate tracheal intubation, may be required. Options for the induction technique are many, including ketamine, etomidate, and slow administration of more commonly used agents such as propofol. Most i.v. or inhalation anaesthetic agents cause vasodilation or impaired ventricular contractility. Induction of anaesthesia is ideally a deliberate step-wise process, using small doses of i.v. anaesthetic agents, titrated to clinical response. The choice of induction agent or narcotic is less important than the care with which they are administered. Ketamine or midazolam may provide a degree of haemodynamic stability and short-acting opioids such as fentanyl will enable a reduction in the dose of anaesthetic induction agent.[29] Placement of a cuffed tracheal tube is facilitated by the use of neuromuscular blocking agents (preferably non-histamine releasing agents).

Maintenance Of Anaesthesia

There is no evidence to suggest an outcome benefit when anaesthesia is maintained by the inhalation or i.v. route. Options for maintaining anaesthesia include inhalation agents, i.v. agents, and opioids, for example, fentanyl infusion using 2 to 2.5 □g kg□1 min□1. The anaesthetist should choose the technique which they believe best fits with their assessment of the individual patient's risk factors and co-morbidities, and their own experience and expertise. The MAC of inhalation anaesthetic agents is reduced in severe sepsis.[32] In patients with significant lung dysfunction, maintenance of stable concentrations of anaesthetic agents in the brain may be more reliably achieved when using i.v. rather than inhalation agents. Whatever technique is used, the depth of anaesthesia achieved can be estimated using bispectral index monitoring. During surgery, the haemodynamic state may be further complicated by blood loss or systemic release of bacteria or endotoxins. Transfusion of blood products should proceed without delay if the surgical procedure is complicated by excessive blood loss.

Intravascular volume resuscitation should continue as indicated throughout the surgical procedure. Although a CVP of 8–12 cm H_2O is a commonly used haemodynamic goal in the initial resuscitation of septic patients, intraoperative CVP values may be increased by raised intra-thoracic and intra-abdominal pressure. Changes in dynamic markers (pulse pressure variation, stroke volume variation) have been shown to predict volume responsiveness more accurately than pressure-based estimates (CVP or pulmonary artery occlusion pressure). Changes in dynamic markers of volume responsiveness can be used intraoperatively to guide i.v. volume therapy, especially in patients with regular sinus heart rhythm and whose lungs are ventilated by controlled mechanical ventilation

Hypercarbia should be avoided specifically in patients with raised intracranial pressure, compensated metabolic acidosis, or the later stages of pregnancy. In all other circumstances, hypercarbia may be well tolerated and there is some evidence that permissive hypercapnia may have inherent protective effects.[31,35]

Protective lung strategies are advisable for mechanical ventilation of the lungs. The difference between the pressure inside and outside the alveolar air space at end-inspiration is the transpulmonary pressure. Plateau airway pressure, measured during volume-control mechanical ventilation when an end-inspiratory pause has been applied, is an indicator of the maximal pressure applied inside the alveolar sac. The pressure outside the alveolar sac cannot be measured directly but is estimated clinically by assessing changes in pleural pressure. Extra-alveolar or pleural pressure can be abruptly increased by placing the patient in the Trendelenberg position or by the increased intra-abdominal pressure associated with inflation of a pneumoperitoneum for laparoscopic surgery. Pulmonary gas exchange may deteriorate if pleural pressure is increased and plateau pressure remains constant (i.e. a reduction in transpulmonary pressure). On the other hand, high transpulmonary pressures are associated with lung injury.

Postoperative Management Of Patients With Severe Sepsis

It is important to note that pre-resuscitation measurements should be used to calculate the Intensive Care admission APACHE score and not those that have improved after resuscitation and the surgical procedure. Ongoing infusions of vasopressor medication should be adjusted to match the present intravascular volume and the new mechanical ventilator settings. Having secured the patient's airway, mechanical ventilation settings can be decided, with the objective of minimizing ventilation-induced volutrauma and barotraumas to the lungs. This is most likely to be achieved using low-pressure settings, a high fractional inspired oxygen concentration, and suitably set alarm limits. Low tidal volumes (up to 6 ml kg□1 of the predicted body weight) and permissive hypercapnia may be considered, provided that arterial pH does not decrease below 7.20.[36]

Nutrition is one of the cornerstones of management in critically ill septic patients. Enteral nutrition via a nasogastric tube is the best choice to maintain enterocyte integrity and nourish the patient. Gastrointestinal protective measures (stress ulcer prophylaxis) and antiemetic drugs are also prescribed. Total parenteral nutrition (TPN) should be considered if there is a surgical contraindication to enteral nutrition or if nutritional requirements are not fully met by enteral nutrition alone. Patients may become rapidly hypoglycaemic if TPN or enteral nutrition is stopped during the perioperative period.[44]

I.V. hydrocortisone may be considered when hypotension

responds poorly to fluid resuscitation and vasopressors. A 7 day trial treatment with low doses of hydrocortisone and fludrocortisone significantly reduced the risk of death in patients with septic shock and relative adrenal insufficiency without increasing adverse events (P<0.05).[30] In this study, there were 81 deaths (70%) in the placebo group and 66 deaths (58%) in the corticosteroid group at the end of ICU stay [relative risk (RR) 0.82; 95% CI 0.68–1.00; adjusted odds ratio (OR) 0.50; 95% CI 0.28–0.89; P=0.02]. Although this study was conducted in the ICU setting, it seems prudent to extrapolate the finding to appropriately selected patients in the perioperative period.[45]

Hydrocortisone in a dose of 200 mg per day in four divided doses or as a continuous infusion in a dose of 240 mg per day (10 mg h□1) for 7 days is recommended for septic shock in the ICU setting.[10,45]

Regional Anaesthesia In Sepsis

Performing or not regional anaesthesia or NRA in the patient with an active infection is not supported by strong evidence. Only the presence of infection at the puncture site or catheter insertion may be contraindicated. Single-puncture techniques can be safe. The available information so far indicates that the insertion of catheters requires an antibiotic pretreatment of the infection followed by a clinically appropriate response.

Regarding thoracic epidural anaesthesia use in SIRS or in surgical or non-surgical sepsis, numerous experimental studies and a few clinical studies provide some evidence that its effects can be beneficial depending on the time of its establishment. Although it may be ethically conflicting, randomised studies are necessary in selected patients or groups of patients to assess the aforementioned advantages and indications. The future use of regional anaesthesia in patients with sepsis is open, both through clinical and experimental investigations.[27]

Vitamin C in Sepsis

Sepsis is associated with enormous stress to the organism. In animals exposed to stress, an increased endogenous synthesis of ascorbate was found as a compensatory mechanism to maintain the homeostasis. However, for critically ill patients, neither do we know an optimal vitamin C plasma concentration nor is it known whether supernormal plasma concentrations are more beneficial. However, a number of studies demonstrated that parenteral administration of vitamin C is more effective to increase plasma levels and reduce multi-organ failure.[41]

Acute renal failure occurs in 23% of patients with severe sepsis. Renal replacement therapy may be initiated to correct acidosis, hyperkalaemia, or fluid overload and may be continued until acute tubular necrosis has recovered. Sodium bicarbonate is not recommended for correcting acidosis unless pH <7.1.

Analgesia and sedative medication is continued by infusion, but excessive use of sedation or neuromuscular blocking agents is not recommended. Finally where applicable, it is wise to raise the subject of advanced care planning with the patient and his family, and realistic expectations and outcomes targeted.

In conclusion, severe sepsis is a major healthcare issue, with a persistently high mortality. Patients with severe sepsis syndrome often require surgery for source of infection control. The anaesthetist has a crucially important role in coordinating and delivering resuscitation and therapeutic strategies to optimize patient survival outcome. Early i.v. administration of effective antimicrobial therapy is essential. Preoperative resuscitation, aimed at optimizing major organ perfusion, is based on judicious use of fluids, vasopressors, and inotropes. Intraoperative management requires careful induction of anaesthesia, using lowest effective doses of a range of agents. Maintenance of anaesthesia is challenging, requiring achievement of optimal volume status, avoidance of lung injury during mechanical ventilation, and ongoing monitoring of arterial blood gases, haematological and renal indices, and electrolyte levels. Postoperative care overlaps with ongoing management of the severe sepsis syndrome patient in the ICU. The care of critically ill septic patients requiring anaesthesia and surgery will be further enhanced by testing promising therapeutic strategies, e.g. use of levosimendan for intraoperative inotropic support, in well-designed clinical trials.

Conflict Of Interest: None

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