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Review Article

Septic shock diagnosis and its treatment

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ABSTRACT

In critical care, sepsis continues to be a major cause of mortality. The pathogenic, diagnostic, and therapeutic panorama of sepsis is no longer restricted to the critical care unit: many patients who enter treatment through other doors, both inside and outside the hospital, develop severe illness. Next, administer fluids and broad-spectrum antibiotics after taking the proper cultures. Step up the treatment to include monitoring urine output, blood gases for base excess, lactate, haemoglobin, and glucose if the situation does not get better within the following six hours. These will dictate how bicarbonate, insulin, fluids, transfusions, and vasopressors are managed. The patient should be sent to intensive care if the hypotension doesn't improve (septic shock). Sepsis can now be treated with methods that have produced better results with other illnesses. New medicines have been created as a result of a better understanding of the biology of severe sepsis and septic shock, placing a strong emphasis on early detection and aggressive treatment. The major priorities continue to be prevention through screening, preventing cross infection, and prudent antibiotic usage.

Keywords: Intensive care unit, Septic shock, Pathophysiology, Treatment

INTRODUCTION

One of the most common reasons for admission to the intensive care unit (ICU) is sepsis. It is described as a potentially fatal organ malfunction brought on by an improperly controlled host response to an infection. Every year, septic shock kills between one in three and one in six victims, making it a serious public health issue.[1] It is one among the main causes of death worldwide. A life-threatening circulatory collapse with insufficient tissue perfusion is known as shock.[1] Hypotension (low systolic ≤90 mm Hg) or mean arterial blood pressure (≤65 mm Hg) with clinical indications of hypoperfusion characterise the typical presentation.[2] According to Kaukoken et al, the overall mortality rate for sepsis patients hospitalised can be as high as 24.2%, and it is higher for patients with concomitant conditions (33.1 versus 19.1%). The mortality rate for septic shock is 40%. Antibiotics are used to treat the infection and limit the infection's source while providing enough multi-organ support in the treatment of sepsis and septic shock. In addition to relative hypovolaemia caused by fluid leakage through vessels or absolute hypovolaemia when the patient has had significant fluid loss or intolerance to oral fluids (e.g., sepsis of the abdominal or post-surgic type), the haemodynamic changes that accompany septic shock include a severe decrease in systemic vascular resistance (SVR), an initial increase in cardiac output (CO) due to decreased left ventricular (LV) afterload, and increased cellular metabolic needs Chronic inflammation can also cause cardiomyopathy and (relative) adrenal insufficiency. Despite advances in medicine, managing all of these changes remains difficult for the intensivist, who must concentrate on restoring tissue perfusion to boost oxygen delivery (DO_2) to tissues and prevent organ failure.[1]

PATHOPHYSIOLOGY

Pathogens are eliminated as part of the normal immunological and physiological response. There is an imbalance in the regular regulation in sepsis. The pathogen's on-going activation may be to blame for this. High amounts of anti-inflammatory cytokines are circulating, and immunological function is compromised. We see accelerated necrosis of cells, delayed neutrophil apoptosis, and fast lymphocyte apoptosis. In addition, the coagulation system is impacted. The excessive inflammatory response is accompanied by increased coagulation and decreased fibrinolytic activity. Acute organ failure and mortality may ensue from the loss of homoeostatic balance across these systems, which causes generalised coagulopathy and microvascular thrombosis Figure 1.[3]

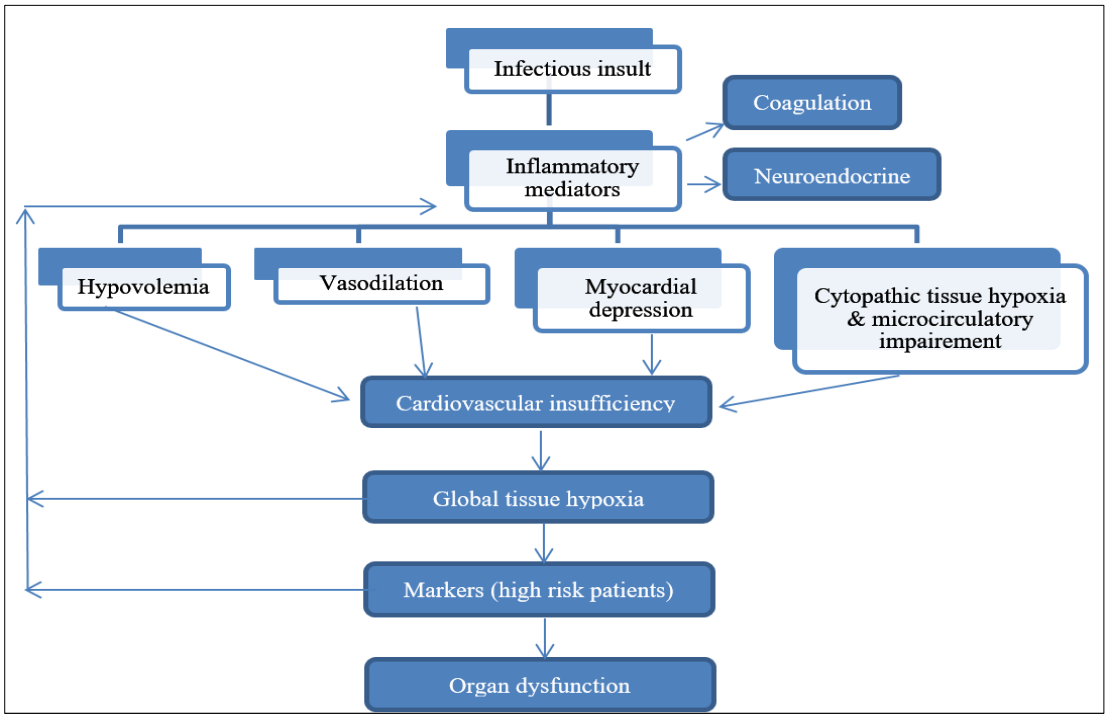

Figure 1: Pathophysiology.

FIRST SIX HOURS CRUCIAL

Sepsis patients are frequently transferred to the ICU from general medical-surgical practise units (GPUs), operating rooms (ORs), emergency departments (EDs), long-term care homes, and other hospitals. Even for individuals that were admitted to GPUs or the ICU, the diagnosis and care given to these patients may not have been optimal. In the first six hours following ICU admission, delays in the identification, transfer, and management of critically sick patients have been linked to higher fatality rates 4 and greater hospital resource utilisation. New treatments for this illness have been made available in the last five years thanks to developments in the management of severe sepsis and septic shock. Although these studies were ICU-based, Rivers and colleagues ability to demonstrate a significant mortality advantage when hemodynamic optimisation was administered during the first few hours of disease presentation made the timeliness of treatment a more crucial issue. Severe sepsis and septic shock can now be treated with early resuscitation in the "golden hour" and "silver day" manner that has historically been used for trauma. The phrase "golden hour" refers to the period of time immediately following a trauma patient's initial diagnosis when treatment has the best chance of producing positive results. The remaining hours of the first day were referred to as the "silver day" because it was discovered that prompt treatment of shock and organ malfunction reduced the need for medical resources and enhanced results. The surviving sepsis campaign, a global movement, has incorporated these principles into its 24-hour sepsis pathway, which includes a crucial 6-hour course of action.[4]

DIAGNOSIS

A dysregulated host response to infection is what is known as sepsis, which is characterised as a life-threatening organ malfunction. The ability to recognise sepsis can be difficult. It necessitates a precise history collecting, physical examination, and laboratory data interpretation. Several sepsis screening techniques have been created over the years to assist clinicians in accurately identifying patients with sepsis. The quick sequential organ failure score (qSOFA), systemic inflammatory response syndrome (SIRS), and national early warning score (NEWS) are the most widely used and standardised ones. These ratings, nevertheless, are incredibly general. While the SIRS criteria identify patients who have the signs of a

systemic inflammatory response without the obvious signs of organ dysfunction or an infectious cause for the inflammation, the qSOFA quickly identifies the signs of organ dysfunction without taking a possible infectious cause into account. Therefore, as indicated in the most recent worldwide sepsis recommendations, clinical assessment, comprising a history taking and physical examination, remains the key component for the proper diagnosis of sepsis. Nevertheless, a variety of technologies, including point-of-care ultrasound, biomarkers, and laboratory measures might support this approach. The identifying and accurate identification of the septic focus is one of the important components in the diagnosis of sepsis. The most frequent primary sources of infection in sepsis patients are respiratory, urinary, and intra-abdominal sources. These are followed by less frequent causes like skin and soft tissue infections, meningitis, and infections linked to indwelling catheters (Figure 2).[5]

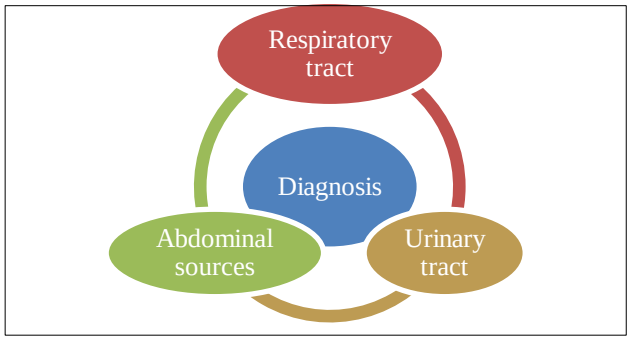

Figure 2: Diagnosis.

Respiratory tract

Lung ultrasonography performed remarkably well in the diagnosis of pneumonia, according to a sizable systematic review and meta-analysis conducted several years ago. The combined sensitivity and specificity for the diagnosis of pneumonia using LUS were 94% (95% CI, 92-96%) and 96% (94-97%), respectively.[6] Additionally, a sizable meta-analysis looked at the utility of lung ultrasound in the assessment of ED patients with undifferentiated dyspnea in order to correctly determine the underlying cause and discriminate between pneumonia, COPD/asthma exacerbation, and heart failure.[7] For the diagnostic examination of patients with dyspnea in the ED and ICU, numerous ultra sound methods, such as the BLUE protocol, have established themselves as standard practise.[8]

In addition, independent of the original source of infection, acute respiratory distress syndrome (ARDS) is a frequent and terrifying consequence of sepsis and septic shock.[9] In critically ill septic patients with respiratory distress, lung ultrasonography may be able to detect this severe consequence and direct the doctor to more aggressive treatments for respiratory failure, such as high-flow oxygen administration or mechanical ventilation.[10]

Urinary tract

The second most typical infection in sepsis is urinary tract infections. The primary method of choice for the evaluation of the kidneys and excretory organs is ultrasound because it is widely available, reasonably straightforward, and quick to diagnose hydronephrosis and renal abscesses.[11] However, the clinical presentation may be sufficient for the emergency physician to make a correct diagnosis of UTI.

Abdominal sources

Contrary to the organs and systems previously stated, abdominal infections are a reasonably frequent cause of sepsis. However, the clinical examination of the abdomen is difficult and frequently deceptive.[12] Abdominal ultrasound is a commonly available, reasonably priced test that can be done at the patient's bedside. When performed by a skilled ultra-sonographer, it can identify a variety of abdominal pathologies that may be the cause of infection, such as cholecystitis, cholangitis, pancreatitis, small bowel obstruction, or perforation.[13] When diagnosing patients with suspected acute cholangitis or gallbladder disease, a frequent and extremely dangerous source of abdominal infection that needs to be treated right once, ultrasound is the imaging modality of choice.[14] For the diagnosis of acute appendicitis, it is widely agreed that clinical findings in association with an ultrasound are sufficient, but a CT scan should only be performed on individuals who have inconclusive sonographic results.[5]

TREATMENT

Antimicrobial therapy

In the ICU setting, a link between prompt and effective antibiotic administration and reduced morbidity and death has been demonstrated. When antibiotics are given between 4 and 8 hours after a patient arrives at the hospital, according to observational studies there is a significantly lower mortality rate ($p<0.01$). Antibiotics should be given within an hour of receiving a sepsis diagnosis, according to the most recent Surviving Sepsis Campaign recommendations.

The focus of this study does not extend to specific antibiotic methods; reviews of antibiotic strategies can be obtained elsewhere. However, we advise comprehensive coverage initially, adapted to the suspected source of infection and in line with sensitivity and resistance trends observed at the neighbourhood hospital.

When a patient has an intra-abdominal source of sepsis or an undrainable abscess, surgical consultation for source control is necessary. When patients reside in nursing homes or use intravenous medications, the likelihood of resistant microorganisms should also be taken into account.[4]

Hemodynamic optimization

Strategies for resuscitating patients with severe sepsis or septic shock have been the subject of extensive research and discussion for years. Studies that used techniques to reach supernormal physiologic endpoints in ICU patients up to 72 hours into their hospital stay had unfavourable, if not harmful, outcomes. Sepsis resuscitation studies meta-analyses have shown that early therapies that happen before organ dysfunction.[4,15,16] have superior results. A recent trial 7 examining hemodynamic resuscitation to normal physiologic parameters or early goal-directed therapy (EGDT) in ED patients with severe sepsis or septic shock found a statistically significant mortality decrease of 16.5%.

Within the first six hours of receiving care in the ED, the EGDT algorithmic approach to hemodynamic optimisation (Figure 5) seeks to reestablish the equilibrium between oxygen supply and demand in situations of severe sepsis or septic shock. By optimising intravascular volume (preload) with the aid of central venous pressure (CVP) monitoring, blood pressure (afterload) with the aid of mean arterial pressure monitoring, contractility with the aid of monitoring to avoid tachycardia, and restoration of the balance between systemic oxygen delivery and oxygen demand (guided by $ScvO_2$ measurements to resolve global tissue hypoxia), the strategy seeks to achieve adequate oxygen delivery. The Society of Critical Care Medicine's recommendations for hemodynamic support in sepsis served as the basis for the components of EGDT.[17,18]

Hemodynamic monitoring

Monitoring of CVP, arterial blood pressure, and $ScvO_2$ is necessary for early hemodynamic optimisation. Although vasopressor medicines may cause central arterial pressure to be overestimated when measured from the radial artery, intra-arterial pressure monitoring is generally advised for patients who are prescribed them $ScvO_2$ can be monitored continuously with a fiber-optic central venous catheter and monitor (Edwards Life sciences, Irvine, California) or intermittently from venous gas samples obtained from the distal port of a normal central venous catheter. The pulmonary artery is still a reliable measurement location in the hands of experts, although it has yet to demonstrate any positive outcomes.[4]

Fluid treatment

In sepsis, numerous proteins and toxins produced by bacteria cause vasodilatation, which causes capillary leakage, a decrease in the amount of blood that is really circulating, and a decrease in venous return. These organ dysfunction and reduced tissue perfusion are the results of these macro hemodynamic consequences. It is now controversial to treat these individuals with intravenous (IV) fluids because of these hemodynamic changes. In the first three hours of resuscitation for patients with sepsis-induced hypoperfusion or septic shock, intravenous crystalloids should be administered at a dose of at least 30 ml/kg, according to the Surviving Sepsis Campaign 2021 guidelines. Although the document highlights a shift in the strength of the recommendation and quality of the evidence (from a strong recommendation with low quality of evidence in 2021), its inclusion in the guideline as a standard dose may result in incorrect fluid prescriptions, which could be harmful to patients, especially those who have comorbidities. The majority of the available information, which supports the recommendation of initial bolus IV fluids, is based on retrospective research. Recent research on the initial bolus of IV fluids has shown conflicting findings.[1]

ICU length of stay is directly impacted by the detrimental effects of IV fluid boluses and persistent positive fluid balance for longer than two days, which cause multi-organ oedema and the global increased permeability syndrome (GIPS), increase the number of days spent on mechanical ventilation (MV), and increase the number of days spent in the hospital, which can result in multi-tissue oedema.

According to experts, the fluid dose required for both the initial and follow-up resuscitation of patients with septic shock should always be tailored to the patient's clinical characteristics and based on dynamic assessments of fluid responsiveness. A young patient without comorbidities, as opposed to a fragile elderly patient with chronic cardiac or renal disease, is more likely to tolerate receiving a significant volume of fluid. The response to fluids decreases significantly over the period of time following the start of resuscitation in patients with sepsis and septic shock (liquid responders: at 0 hours, only 57%; at 2 hours, only 22%; at 4 hours, only 11%; at 6 hours, only 10%; and at 8 hours, only 3%). This is just one of the many drawbacks of maintaining a fixed dose of fluids for these patients.[1]

The use of static measurements to evaluate the volume status and response in these individuals, such as central venous pressure, is not advised. It is best to employ dynamic metrics to gauge the impact of the increased volume on heart filling pressures and stroke volume (SV) in order to determine which patients will or won't respond to fluid administration. Practical options include passively raising the legs (which would result in a return of 200–300 ml of venous blood from the lower limbs) or giving a bolus of crystalloid fluids (typically no more than 500 ml, e.g., 3–4 ml/kg), and then directly measuring the change in systolic volume (e.g., with thermodilution, echocardiography, or pulse wave analysis). A sufficient fluid response is associated with an SV rise of 10% to 15%. Heart-lung interaction in patients on MV can also be evaluated for these changes using pulse pressure variation (PPV), systolic volume, velocity-time integral (VTI) with Doppler ultrasound at LV outflow tract or arterial vessel level (e.g., carotid artery), and variation in the diameter of the inferior vena cava (ICV) or internal jugular vein (IJV). In the absence of right ventricular dysfunction, frequent arrhythmias, considerable tachycardia, and spontaneous

and forceful ventilations, the response to IV fluids is typically stronger the greater the fluctuation of any of these measures (PPV, SV, and VLT), typically above 10-15%. Physiologically reported fluid and vasopressor resuscitation using passive leg raise induced systolic volume change to guide treatment was found to be safe and effective in reducing net fluid balance, with a reduced risk of renal and lung injury in a recent randomised clinical trial in patients with sepsis, hypotension, and shock.[1]

In terms of the type of solutions to be supplied, balanced solutions (which are more expensive) have no advantage over 0.9% saline. When a considerable dose of crystalloid solutions has previously been delivered or in cases of severe hypoalbuminemia, IV albumin may be helpful.[1]

Vasopressor and inotropes

Even though there are numerous research on the best inotrope or vasopressor to use, there isn't much actual science to differentiate between the two. The medication that is frequently used and is known to nursing staff is noradrenaline. It is well recognised that overusing any vasoconstrictor can result in renal and splanchnic hypoperfusion. However, in the case of sepsis and adequate filling pressures, noradrenaline has the most advantageous profile. Vasopressin is listed as a backup option because studies have revealed that septic individuals have low plasma levels of the hormone. Dobutamine, which has tended to supplant dopamine, is the second inotrope of choice after adrenaline. When no central venous access is available, adrenaline should also be taken into consideration alongside noradrenaline, however it cannot be utilised outside of intensive care. Despite worries regarding its effects on other hormones, the therapeutic importance of which is uncertain, dopamine has a rather excellent cardiac safety profile if less potent inotrope support is needed outside of the ICU.[19]

Steroids

Over time, there have been changes in how steroids are used in septic shock. However, if hypotension persists despite fluids and pressor therapy, a Cochrane Review supports the use of steroids (typically hydrocortisone 200 mg every day for seven days).[20] However, a European trial that supported the use of low-dose steroids in the treatment of shock was unable to demonstrate a reduction in mortality.[21] The mineralocorticoid action of hydrocortisone makes it preferred to dexamethasone. The Sepsis Campaign advises only sparingly using steroids.

Blood and blood products

Trials involving septic patients have used a variety of transfusion protocols. Therefore, an ideal haemoglobin is unknown. A target haematocrit (Hct) of 30% was adopted in River's study.[13] A haemoglobin range of 7-9 g/dl has been compared with greater haemoglobins in other research, and the lower values have not been found to be detrimental. Thus, 7-9 g/dl or Hct 21-27% is the recommended objective, while greater values may be preferred in particular patient populations.[14] Fresh frozen plasma and platelets are used for bleeding patients or when surgery is anticipated; in these situations, platelets are administered if the count is below 50,000/mm^3. Cryoprecipitate should not be used for measured values of fibrinogen degradation products, according to current recommendations.[6] However, when dealing with coagulopathy, both fresh plasma and cryoprecipitate are employed.[19]

Mechanical ventilation

There has been a shift towards protective lung breathing techniques over the past 15 years. Mechanical ventilation will be necessary for many septic patients. Although ideal, non-invasive ventilation is less efficient in sepsis than in other respiratory conditions. The effects of septicemia will result in an acute lung damage in half of these patients. They are now susceptible to barotrauma brought on by operating room ventilation techniques. Acute respiratory distress syndrome (ARDS), which has a very high mortality and morbidity rate, will then develop as a result of this, especially in people over the age of 45. The 'ARDSnet strategy' is based on the core tenets of using low tidal volumes of 6 ml/kg or less, maintaining inspired plateau pressures of 30 cm H_2O or less, recruiting techniques, and allowing permissive hypercapnia.[22] Although exact $PaCO_2$ values have not been established, it is thought reasonable to permit a respiratory acidosis of about pH 7.25.

Infection control and prevention

Preventing sepsis in the first place is the best course of action. Everyone who works with patients has a responsibility to halt infection before it begins and to stop its spread. To make this work, consideration of the likely pathogens is necessary. The unit's layout and organisation play a key role. As long as staffing permits sufficient care, side rooms are ideal for patients. To ensure that everyone can efficiently hand-wash, design should also take into account washing facilities. It is now well acknowledged that screening for methicillin-resistant *Staphylococcus aureus* (MRSA) is necessary and effective in lowering the incidence of MRSA infections.[19]

While MRSA may be detected by screening and is declining in frequency, other infections are rising. The multi-resistant Gramme negative microbes in the ICU are noteworthy. *Acinetobacter spp., Gramme* negatives that produce extended spectrum elactamases (ESBL), *Stenotrophomonas maltophilia,* and gentamicin-resistant *Pseudomonas aeruginosa* are the main culprits. Numerous bacteria, including *Salmonella, Escherichia coli, Pseudomonas, Klebsiella pneumonia*, and others, include the ESBL enzyme. Given the prevalence of these pathogens, it is crucial to distinguish between colonisation and infection before making treatment decisions.

Microbiology and the infection control team must be involved in the antibiotic selection process. Treatment will frequently require isolation and should last for three weeks or longer. Antibiotic therapy is crucial for preventing infections throughout the hospital and, in a perfect world, should be carried out by the infection control team in compliance with stringent hospital regulations.

On the ICU, *Clostridium difficile* is a serious issue. Since 1990, there have been more cases reported in the UK, going from 2500 to 65,000 by 2007. Most occurrences affect people over the age of 65; 23% of adults are carriers, but the number is substantially greater in newborns. The majority of hospital patients contract the virus through consuming the spores. The spores survive the stomach's acid and then multiply in the big intestine's antibiotic-reduced flora. Toxins that range in severity from mild diarrhoea to pseudomembranous colitis are created here. This is always followed by prolonged isolation in the ICU and, in the case of a susceptible patient, can be a fatal situation. Once more, its spread and prevalence are controlled by good hand hygiene, cleaning, isolation, and stringent antibiotic prescription regulations.

Central lines and invasive catheters have always been implanted using a semi-sterile technique. They can end up being the patient's source of bacteremia. Various organisations, most recently Matching Michigan, have succeeded in raising awareness of the issue and changing the approach to line insertion in general. Work done in Michigan demonstrated that sepsis from lines was an issue and that this problem might be avoided by using a package of care or bundle to cover all aspects of line insertion.[21]

CONCLUSION

In the initial hours of severe sepsis and septic shock, timely diagnosis and resuscitation improve outcomes. The use of corticosteroids, activated protein C, mechanical ventilation with small tidal volumes, and strict glycemic control are other treatments that can reduce mortality in patients with severe sepsis and septic shock. The clinician faces a challenge when managing the hemodynamics of patients who are in septic shock. The prognosis of these patients can be improved by identifying haemodynamic abnormalities and taking the proper therapeutic action using fluids, vasopressors, inotropes, corticosteroids, and/or beta-blockers, along with infection treatment. The launch of a coordinated and collaborative effort by the primary treating doctor and the intensivist depends critically on the specific emphasis on adequate triage to ensure rapid diagnosis of the high-risk patient. The appropriate therapy of sepsis should not be restricted to the confines of an ICU because the disease's potential for reversibility and the resulting mortality may be greatest during the first stages of presentation.

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