Extended Abstract

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Pharmacology 2019: Strategies for the detection, treatment and management of sepsis - Maannashon Prabaharan - King's College London

Maannashon Prabaharan
King's College London, UK

Abstract

Sepsis may be a complex condition characterized by the simultaneous activation of inflammation and coagulation in response to microbial insult. These events manifest as systemic inflammatory response syndrome or sepsis symptoms through the discharge of proinflammatory cytokines, procoagulants, and adhesion molecules from immune cells and/or damaged endothelium. Today, sepsis may be a severe multisystem disease with difficult treatments for its manifestations and high mortality rates. Within the last 20 years especially, many studies are conducted on sepsis that cause shock, multiorgan dysfunction, and organ failure by especially resulting in hemodynamic changes. In sepsis, increasing antibiotic resistance and medicine-resistant hemodynamic changes have resulted in further research on new treatment modalities additionally to classical treatments. Within the last decade, the sepsis physiopathology has been elucidated. Various therapeutic agents are utilized in addition to antibio therapy, but no satisfactory results are obtained. This review summarizes the sepsis pathophysiology, current treatment protocols, and new approaches.

Described for hundreds of years, sepsis may be a maladaptive inflammatory response to infection, creating profound symptoms and poor outcomes, including high short-term mortality . Even into the late 1990s, our experiences, expectations, and insight into the care of the septic patient were dismal and grim. We knew that inflammatory mediators, coagulation, cellular oxygen processing, and both macro- and micro-circulation could be disturbed the cascading interaction(s) created the dismal outcomes that we dutifully reported and lamented. Half or more of those afflicted died during hospitalization, and that we intervened after organ failure was clear using promising biologics that appeared to fix some facets but did not improve mortality or function after recovery. In 2001, Rivers et al. explored a newer approach, termed Early Goal-Directed Therapy (EGDT). The conceptual model of EGDT was that sepsis and, in some instances, septic shock are under-recognized and hence under-treated. Rather than target mediators and individual organ or cellular events, Rivers et al. sought to limit the worldwide oxygen deficits accompanying sepsis tothwart the cycle of 'evil humors running amok' and creating dysfunction. EGDT attempted to achieve this by guiding the first 6 hours of resuscitation with central venous pressure and saturation measures. The structured EGDT approach delivered more fluids (5 L mean)in the first 6 hours, more inotropic support, and more frequent red blood cell transfusion than an unstructured approach. This EGDT use translated into a 16% absolute mortality benefit compared to controls, the most stark noted in sepsis care. Based on this, many involved central catheter-driven EGDT look after all with septic shock .Follow-up work replicated the overall observation that earlier recognition, including resuscitative care, improved outcomes. Often, the sites involved had little pre existing focus on sepsis recognition and care; even when the full EGDT protocol was not implemented a common event –outcomes improved, suggesting that one path to improved care was possible .At an equivalent time, others noted a parallel opportunity with another sepsis care target –source control with antibiotics. Delays in delivering appropriate antibiotics led to higher mortality, akin to delayed resuscitation .Coupling these therapeutic insights with the observation hat much of the hospitalized sepsis population receives initial care in the emergency department reinforced the importance of early care

Sepsis is caused by the host's over-response to an infection, which leads to organ failure. This affects many areas of the body, including the cardiovascular, renal, GI and pulmonary systems. Sepsis has high mortality rates, but even survivors are affected by complications, including cognitive decline and increased cardiovascular events.

Current methods for diagnosing sepsis include the use of physical biomarkers such as heart rate (HR), and serological biomarkers such as C-Reactive Protein (CRP) and Procalcitonin (PCT). Clinical trials were found through a literature search using the PubMed and Ovid databases. The cumulative evidence suggests that other serological biomarkers such as presepsin, Pentraxin-3 (PTX3) and micro-RNA have potential for future clinical use. Heart rate variability (HRV) is a newer physical biomarker that has good evidence for diagnosing sepsis patients.

The Surviving Sepsis Campaign has annual updates on guidelines for clinicians in treating sepsis. The latest guidelines have included the empirical use of broad-spectrum antimicrobials to be given immediately, as part of the 1-hour bundle. The growing evidence suggests of a trend in increasing antimicrobial resistance, and new alternatives should be found. This text has evidence for alternative methods, such as the use of antimicrobial stewardship (responsible use of

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antibiotics) and the main alternative to antibiotics-bacteriophages.

Recent innovations in technology over the past decade have been integrated into clinical practice, and there is great hope for the near future with new innovations in predictive algorithms and consumer technology in treating patients.

This review aims to summarise the current developments that have occurred in the diagnosis, treatment and management of septic patients. This review also aims to show the reader what future developments hold for improving the quality of sepsis management.

Survival in sepsis has improved over the last 40 years. However, we still lack a specific molecular therapy for this condition, other than antimicrobial therapy. Numerous trials of promising biological agents targeting different mediators of sepsis have failed. This article will focus on the immediate management of sepsis – the management of patients in a critical care setting is not covered here.

Resuscitation

Immediate resuscitation of a critically ill septic patient is not appreciably different from non-septic patients. Adequate oxygen to take care of saturations in more than 95% should tend . Although there is no high quality randomised controlled trial evidence, it is considered standard care to give intravenous saline to all patients with sepsis.13 For patients with hypotension, this should be a bolus of 500 mL of saline over 15 minutes. Further fluids should be titrated to response. Starch based fluids should be avoided14 and there's no evidence to support the utilization of albumin.15 Persistent hypotension despite adequate fluid resuscitation will almost certainly require admission to a critical care facility and therefore the use of vasopressors – noradrenaline is that the preferred agent.16

Prompt and appropriate antimicrobial therapy

Studies have shown a clear benefit of rapid use of antimicrobials that target the likely causative pathogens.17 Although the exact timing required is not entirely clear, every effort should be made to offer such drugs as quickly as possible, ideally within 1 hour of admission. Prior to administering antibiotics, blood cultures should be taken. Although there are no trials showing the benefit or not of such cultures, identification and characterisation of antibiotic sensitivities of cultured pathogens is crucial in further management.

Accurate fluid balance

Urine output should be recorded, together with all fluids administered. A urinary catheter should be placed if required for patient management but it is not essential.

Blood glucose

In the event of hyperglycaemia, blood sugar should be kept

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Biography:

Maannashon Prabaharan is an intercalating student who has interests in pharmacology, and its uses in clinical practice. This paper vocalises his opinions about the current clinical scenario regarding sepsis (Levy et al. 2018), and potential future changes that could be implemented in all aspects of clinical care.

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