Section 26  Geriatrics

Chapter 176

Treatment of Sepsis and Related Syndromes in the Elderly: Indian Scenario

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SUMMARY
Sepsis and related syndromes are most common causes for admission to intensive care units (ICUs) across the world. Infections, sepsis syndrome and septic shock are a major threat to the health of the geriatric population. Estimates suggest that the global burden of elderly population with sepsis syndrome and septic shock is expected to be on the rise in the ensuing years. A similar scenario is expected in India as well. Recognition of sepsis and related syndromes in elderly patients is a diagnostic challenge, because infections can present in the elderly in unusual ways. Thus, sepsis and related syndromes in the elderly are often not suspected, and are often missed or diagnosed late. The basic principles of initial resuscitation, localization and treating the focus of infection and giving hemodynamic support, are described in the updated version of Surviving Sepsis Campaign Guidelines for management of severe sepsis and septic shock 2008. These guidelines are applicable to the elderly also. However, the fact is that dedicated geriatric ICUs are seldom found in India and most elderly patients with sepsis neither have access to the state-of-the-art ICUs nor can afford care in this setting, and are frequently treated in general wards with devastating consequences. While implementing the treatment guidelines, due consideration should be given for the presence of comorbid conditions such as, cardiac disease, underlying renal and hepatic dysfunction, occurrence of fluid overload in elderly patients with sepsis and related syndromes. While documenting and monitoring treatment response, it should be remembered that in the elderly, values of several biomarkers of sepsis may be elevated at the base line, and can remain elevated subsequently, due to associated comorbid conditions and may not accurately guide in the treatment. Clinicians should have a low threshold for suspecting sepsis in elderly patients as this will facilitate a focused diagnostic work-up and institution of specific treatment.

INTRODUCTION
Septic shock being the most common cause for hospitalization in the ICU around the world, patients are often hospitalized for extended periods of up to 2–3 weeks. In spite of the use of appropriate antimicrobial therapy and advanced life-support, mortality in patients with sepsis has remained high during the past 2 decades. Elderly subjects are a vulnerable population who are susceptible to a wide range of infectious diseases. The number of hospitalizations in older adults, with an infectious disease as the primary diagnosis has been estimated to be 21.4 million from 1990 to 2002. Furthermore, it has been estimated that by 2050, globally, 21.4% of people will be aged 60 years or older. Thus, the burden of elderly population with sepsis syndrome and septic shock is expected to be on the rise. Infections, sepsis syndrome and septic shock are a major threat to the health of the geriatric population.

With the starting of respiratory care units in the mid-1970s and medical ICUs in the 1980s, critical care medicine has come a long way in India, to emerge as a specialty in its own rights. Presently, several corporate and government sectors provide critical care facilities not only in large metros but also in smaller cities. While reliable published epidemiological data are not available, experienced clinicians opine that the number of elderly patients being admitted for treatment of sepsis and related syndromes in the ICUs across the country is on the rise. Given that the mortality in patients with septic shock is high (up to 50%) and the mortality in those with multiple organ dysfunction syndrome (MODS) is even higher (~ 80%) in the general population, these figures are likely to be considerably higher in the elderly subjects.

SEPSIS AND RELATED SYNDROMES: DEFINITIONS
Sepsis and related syndromes are complex disease states affecting a diverse group of patients. They can originate from multiple sites, and can be triggered as a result of infection by a variety of microorganisms. Patients with sepsis and related syndromes present with a wide spectrum of symptoms and signs. In 1992, the American College of Chest Physicians (ACCP) and the Society of Critical Care (SCC) first brought out definitions for systemic inflammatory response stress (SIRS), sepsis and related syndromes. SIRS was defined as the presence of at least two of the four clinical criteria: (1) body temperature greater than 38°C or less than 36°C; (2) heart rate greater than 90 beats/minute; (3) respiratory rate greater than 20 breaths/minute or hyperventilation with an arterial carbon dioxide tension (PaCO₂) less than 32 mm Hg; and (4) white blood cell count greater than 12,000/mm³, or less than 4,000/mm³ or with greater than 10% immature neutrophils. Sepsis was defined as the presence of SIRS caused by a confirmed infectious process. Severe sepsis was defined as sepsis associated with organ dysfunction, hypoperfusion abnormality or sepsis-induced hypotension. Severe sepsis with sepsis-induced hypotension persisting despite adequate fluid resuscitation was defined as septic shock.

In the ensuing decade, with increasing understanding of the pathophysiology, recognition of new biomarkers, dissatisfaction with the Australian College of Pharmacy Practice (ACPP)/Society of Critical Care Medicine (SCCM) definitions was felt world over.
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Subsequently, definitions of sepsis and related syndromes were revised by the SCCM, the European Society of Intensive Care Medicine (ESICM), the ACCP and the Surgical Infection Societies (SIS) (Table 1).10 Severe sepsis and septic shock reflect the end result of complex interactions between infecting microorganisms and the host response, and signify a primarily inappropriate response by the host to a microbial insult. The “mismatch” of the host response to the intensity of the pathogenic stimuli is the key component that describes the pathophysiological events in septic shock that eventually result in organ injury or dysfunction with or without hypotension. This mismatch results in an immune profile that could be predominantly proinflammatory (SIRS), mixed [mixed antagonistic response syndrome (MARS)] or predominantly anti-inflammatory [compensatory anti-inflammatory response syndrome (CARS)].11-13

The system of grading patients according to four key components, namely, (1) the predisposing factors, (2) insult or infection, (3) the host response and (4) organ dysfunction (PIRO grading system) facilitates more homogenous stratification of patients with sepsis and thereby, facilitate delivery of better targeted interventions (Table 2).14

Recognition of Sepsis and Related Syndromes in Elderly Patients

Recognition of sepsis and related syndromes in elderly patients is a diagnostic challenge because infections can present in the elderly in unusual ways. Fever is often absent and other biomarkers of sepsis may be elevated due to comorbid conditions in elderly patients with sepsis. Diagnosing urinary tract infections in older adults are caused by an increased prevalence of asymptomatic bacteremia and frequent use of urinary catheters. In elderly subjects with bacterial pneumonia, the classic signs such as fever, shaking chills are also less frequently seen with increasing age. Published data support the view that the diagnostic yield of blood cultures in elderly subjects with bacteremia is similar to that observed in young individuals.15

However, world over including India, data suggest that sepsis and related syndromes are often not suspected, and are often missed or diagnosed late. Therefore, there is a significant delay in the institution of treatment. A study conducted in afebrile geriatric patients, (n = 27) found bacteremia-fungemia and diagnosis was correctly made in only one-third of the patients, after blood cultures were drawn, and almost one-half were already receiving antibiotics.16

Principles of Treatment of Sepsis

Presently, the updated Surviving Sepsis Campaign Guidelines for management of severe sepsis and septic shock (2008)1 are considered as standard of care. However, in resource limited countries, implementation of all the components of these guidelines is not possible. In India, while affordable patients with access to ICUs may be treated as per the standard of care, many other critically ill patients are cared for, in less comprehensive settings. A tentative treatment algorithm for patients with sepsis is shown in Flow chart 1.

Treatment of Sepsis and Related Syndromes: Implications for the Elderly

Hemodynamic Support and Adjunctive Therapy

While fluid-resuscitation using crystalloids or colloids is carried out, a target central venous pressure (CVP) of 8 mm Hg or more

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TABLE 1 | Definition of sepsis and related syndromes1,10

| Infection | Infection is a pathologic process caused by the invasion of normally sterile tissue or fluid by pathogenic or potentially pathogenic microorganisms. |
| Sepsis | Sepsis is the systemic response to infection. It is defined as the presence of several clinical, hematologic, biochemical and immunologic variables associated with an infection. |
| Severe sepsis | Severe sepsis is complicated by organ dysfunction. |
| Septic shock | Septic shock refers to a state of acute circulatory failure characterized by arterial hypotension despite adequate fluid resuscitation so that vasoppressor therapy is necessary to restore a minimally acceptable arterial pressure. Hypotension is defined by a systolic arterial pressure below 90 mm Hg or a reduction of more than 40 mm Hg from baseline, and it is associated with signs of altered tissue perfusion such as oliguria, altered mental status, or altered skin perfusion and a metabolic marker (i.e. increased blood lactate levels) |

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TABLE 2 | Suggested clinical and laboratory variables for the four components of the predisposition, insult or infection, response and organ dysfunction (PIRO) grading system13

<table>
<thead>
<tr>
<th>Variables</th>
<th>Clinical</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predisposing factors</td>
<td>Age, pre-existing diseases, gender, use of corticosteroid or immunosuppressive therapy, etc.</td>
<td>Genetic polymorphisms</td>
</tr>
<tr>
<td>Infection</td>
<td>Site of focus of infection (e.g. pneumonia, catheter related), type of infection (e.g. community acquired/hospital acquired)</td>
<td>Virulence, resistance profile of infecting organism</td>
</tr>
<tr>
<td>Response</td>
<td>Temperature, heart rate, blood pressure, cardiac output, etc. parameters</td>
<td>White blood cell count, prothrombin time, augmented partial thromboplastin time, blood lactate levels, biomarkers of sepsis</td>
</tr>
<tr>
<td>Organ dysfunction</td>
<td>Blood pressure, urine output, Glasgow coma scale</td>
<td>PaO₂/FiO₂, serum creatinine, serum bilirubin, platelet count</td>
</tr>
</tbody>
</table>

Abbreviations: PaO₂, Arterial oxygen tension; FiO₂, Fraction of inspired oxygen
(≥ 12 mm Hg if mechanically ventilated) is aimed at. Elderly patients with septic shock, receiving fluid resuscitation often have comorbid conditions, such as, coronary artery disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease, etc. and therefore, should be carefully monitored for fluid overload, especially while administering “fluid challenge”. Similarly, cardiac and hemodynamic status should be carefully monitored. Caution should be exercised while administering vasopressors and inotropic support.

**Antibiotic Therapy**

While initiating antibiotic therapy in elderly subjects with sepsis, due consideration should be given to dosage adjustments as per the renal function and hepatic function status.

**Monitoring Response**

While documenting and monitoring treatment response, it should be remembered that several biomarkers of sepsis, such as the
erythrocyte sedimentation rate (ESR) are frequently elevated slightly due to age itself, or increased by comorbid conditions that are often found in older adults. Similarly, in elderly patients, lack of normalization of ESR following antibiotic treatment can occur secondarily to undiagnosed comorbidities, and may be interpreted as unresponsiveness. In the elderly, it should be remembered that biomarkers are likely to be most useful if they are combined with data from history, physical examination, imaging and other diagnostic and laboratory testing.15,17

INDIAN SCENARIO
Sparse data are available from India regarding the treatment outcomes of critically ill elderly patients with sepsis and related syndromes. In contrast to western countries where Gram-negative sepsis is the predominant cause of sepsis, other uncommon causes such as falciparum malaria, leptospirosis, enteric fever, tuberculosis are also important causes of sepsis, septic shock and MODS in elderly patients in India who are critically ill. In a study from New Delhi,32 of 387 patients with sepsis, who fulfilled the criteria for severe sepsis/septic shock were considered for analysis. The most common suspected site of infection was the lung (45.5%), followed by urinary tract (21.2%) and abdomen (16.7%). While the ICU mortality in young patients (< 60 years of age) was 45.6%, the mortality was 60.7% in the old (> 60 years of age but < 80 years of age) and 78.9% in very old (> 80 years of age) patients (P = 0.035). The relative risk (RR) for dying in the old and very old subjects was 1.125 and 1.487, respectively as compared to the young patients. There was an increased need for organ support in the elderly and very elderly population as compared to the younger population. On multivariate analysis, the age of patient was the only variable found to be an independent predictor of ICU mortality [P = 0.002, OR: 1.038, 95% confidence interval (CI): 1.014–1.062]. These observations suggest that increasing age is an important independent predictor of death in critically ill patients in the Indian scenario.

Treatment of Elderly with Sepsis in India: Future Directions
There is a need to sensitize clinicians to have a low threshold for considering sepsis and related syndromes as a diagnostic possibility in older patients, even in the absence of fevers. This will facilitate a focused work-up and initiation of specific goal-directed treatment. While implementing the treatment guidelines, due consideration should be given for presence of comorbid conditions such as, cardiac disease, lung disease, underlying renal and hepatic dysfunction, occurrence of fluid overload in elderly patients with sepsis and related syndromes. Comorbid conditions also contribute to prolonged recovery and delayed hospital stay in elderly patients with sepsis. While documenting and monitoring treatment response, it should be remembered that in the elderly, several biomarkers of sepsis can be elevated at the baseline and can remain elevated subsequently due to associated comorbid conditions, and may not accurately guide treatment. Furthermore, there is a need for capacity building, in terms of developing dedicated geriatric ICUs with trained experts, nursing and other support staff with appropriate subsidy built into account for the astronomical costs associated with ICU care. There is also the need to validate the prognostic grading (e.g. PIRO) and scoring [e.g. Acute Physiology and Chronic Health Evaluation II (APACHE II)] systems in the Indian elderly population. While treating critically ill elderly patients, the clinicians should focus on aggressively investigating and treating the acute critical illness but not terminal pathology.

REFERENCES