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EDITORIAL

Treatment of sepsis; evidence-based medicine, protocol-guided management, is it effective?

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Sepsis affects millions of patients worldwide each year and results in the death of up to one-half of those afflicted, depending on age, severity of illness, the adequacy and timeliness of therapy, and a host of other factors. The cost is staggering and is estimated to be in the tens of billions of dollars in the USA alone (1,2). Beginning in 2003, the Surviving Sepsis Campaign made a commitment to reduce the mortality rate of sepsis by one-third by protocol-guided care (1,2).

The overarching goal is improved processes and delivery of care that lead to better outcomes; however, many believe that good care is also cost-effective care (3), owing to the avoidance of unnecessary diagnostics and therapeutics and the elimination of iatrogenic morbidity (among other factors). If improved care and better outcomes can also be cost-effective care, so much the better.

Shorr et al. have reported a retrospective economic analysis (4) of a prospective before–after study (5) that examined the clinical impact of the introduction of a protocol for sepsis care. The protocol was developed from the Surviving Sepsis Campaign guidelines (2) and recent literature, and emphasized identification of patients with septic shock, aggressive fluid resuscitation, timely and appropriate antibiotic administration, and other adjunctive and supportive measures such as vasopressor/inotrope therapy, transfusion of red blood cell concentrates, and use of drotrecogin alfa (activated) and corticosteroids. The study was conducted in adult patients with septic shock presenting to the emergency department of a single institution between December 2004 and November 2005, with protocol implementation beginning in July 2005. Patients who died in the emergency department were excluded from the analysis.

The primary endpoint for the economic analysis was total hospital costs, as determined from hospital billings converted to costs by cost/charge ratios. Hospital length of stay was a secondary endpoint. Sensitivity analysis was performed to assess the impact of in-hospital mortality on costs and length of stay, stratifying for survival to attempt to control for confounding due to the timing of death.

One hundred and twenty patients were studied and divided equally into the two time periods. There was no difference between groups with respect to age, gender, ethnicity, source of infection or severity of illness. Pneumonia (28%) was the most common cause of septic shock, followed by intra-abdominal infection (27%) and urinary tract infection (26%). The median APACHE II score was 22.5 points, with 20% of patients having an APACHE II score >30 points. The 28-day

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mortality rate was 48% prior to use of the protocol and 30% thereafter (p=0.04). The cost of implementing the protocol was estimated to be US$ 5000. The median estimated per-patient cost before protocol implementation was US$ 21,985 (range, US$ 3610–99,795), but only US$ 16,103 (range, US$ 3445–102,440) afterwards (p=0.008). Total cost savings were estimated to be US$ 573,000 despite higher rates of survival after protocol implementation. The main drivers of decreased costs were ICU and hospital ward costs due to the 5-day reduction in median length of stay.

The median length of stay among survivors decreased from 13 days (range, 3–37 days) before protocol implementation to 8 days (range, 2–35 days) afterwards. Protocol implementation reduced mortality, length of stay and, thus, the cost of care for critically ill patients with septic shock. The tendency of early mortality to reduce costs artifactually had no impact in this study, because reduced costs were documented even among survivors. New therapies and technologies are usually demonstrated to improve outcomes at increased cost, as has been demonstrated for renal replacement therapy for acute renal failure (6) and mechanical ventilation for acute respiratory distress syndrome (7). In contradistinction, why might protocol-driven sepsis care improve outcomes at a lower cost? It is possible that earlier, more aggressive fluid resuscitation, an emphasis on appropriate administration of antibiotics, and the use of adjunctive therapies may limit the physiological derangements that develop, and thus diminish the incidence and magnitude of multiple organ dysfunction syndrome. Alternatively, the protocol itself may focus the efforts of the healthcare team in a unidirectional, more productive manner. For example, education of staff may facilitate the earlier identification of patients who meet the entry criteria for the protocol.

There are many potential limitations of this study among which lack of controls, small sample size, and availability of results of a single center may be noted.

In Iran, with respect to the establishment of Emergency Medicine as a post-graduate course during the recent decade, this should be managed by emergency medicine specialists, however, since graduated fellows could not suffice the need of public or even private hospitals till the next two or three decades, training general practitioners, internists, and infectious disease specialists on how to manage septicemia seems logical. On the other hand, lack of related evidence-based studies in Iran is our main limitation, for which practical researches towards appropriate management of septicemia should be set as our priority.

Overall, the study suggests that protocolised implementation of basic aspects of sepsis care can result in improved outcomes at substantial cost savings. It is unknown whether more elaborate protocols that include, for example, increased usage of drotrecogin alfa (activated) would yield the same cost benefit.

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