Epidemiology of severe sepsis in the intensive care unit

Severe sepsis affects large numbers of intensive care unit patients and is associated with high mortality rates. Understanding the epidemiology of sepsis is important to effectively allocate adequate resources. However, differences in definitions and in studied populations must be taken into consideration when interpreting and comparing the available epidemiological data.

One of the big problems when we talk about the epidemiology of sepsis is that 'sepsis' is not well defined. The underlying concept of sepsis as a syndrome, i.e. the host response to infection, is good, but sepsis can be manifest by a whole constellation of clinical signs, symptoms and biological abnormalities and that is the problem: it is very difficult to identify objective criteria that accurately define the syndrome of sepsis.

In 1991, a North American consensus conference suggested that the presence of just a few elements was sufficient to diagnose sepsis (Bone et al, 1992). Just two of four variables (temperature > 38°C or < 36°C; heart rate >90 beats per minute; respiratory rate >20 breaths per minute or PCO_2 <32 mmHg; white blood cell count >12x10^9/litre or <4.0x10^9/litre) was sufficient to diagnose systemic inflammatory response syndrome and sepsis was defined as systemic inflammatory response syndrome plus infection.

The idea behind the introduction of the systemic inflammatory response syndrome criteria was to raise awareness of the fact that the same inflammatory response seen in sepsis can occur in conditions where there is no clear infection, e.g. pancreatitis or burns. However, this definition makes sepsis a very common event and indeed we would all be septic several times a year, e.g. a simple dental abscess with a slight fever, or a mild case of 'flu! When physicians refer to a septic patient we do not mean someone with such a mild infectious illness, but rather a patient who is seriously ill and whose condition is likely to deteriorate if we do not intervene rapidly and effectively.

Severe sepsis

If we focus on severe sepsis, however, these facets of definition are less important, as severe sepsis is associated with a clearer clinical picture being defined as sepsis plus the presence of at least one organ dysfunction attributed to the sepsis. For purposes of defining organ dysfunction, various organ dysfunction scoring systems have been developed, one of the most widely used, especially in Europe, being the sequential organ failure assessment (SOFA) (Vincent et al, 1998). The SOFA score enables the (dys)function of six organ systems (cardiovascular, respiratory, renal, hepatic, neurological, and coagulation) to be evaluated individually and repeatedly over time.

Interpreting the data

In reviewing the frequency of severe sepsis, however, we must consider the differences in the criteria used to define organ failure. In addition, it is often difficult to separate organ dysfunction which can be directly attributed to the presence of sepsis from organ dysfunction which has occurred for another reason. For example, a patient with worsening heart failure or cirrhosis develops pneumonia and renal failure – is the deterioration of the renal function really related to the infection or is it caused by the heart failure or the liver disease? In many situations it is difficult to determine precisely the cause of the organ dysfunction, which may often be partly related to several factors including the sepsis.

In addition to considerations of definition, when one reviews the published epidemiological data, there are two key considerations to remember:

1. Did the study consider data only on admission, or throughout the intensive care unit (ICU) stay? This is important, as many patients will develop severe sepsis while in the ICU and studies evaluating the incidence of severe sepsis on admission may thus underestimate the true incidence of this syndrome. Alberti et al (2005), for example, reported that 20% of ICU patients with infection or sepsis developed severe sepsis or septic shock by day 10 of their ICU stay
2. Did the study include all patients admitted to the ICU or just a select group? In most hospitals, some patients are admitted to the ICU for postoperative surveillance after major surgery (e.g. cardiac surgery or neurosurgery), but these patients generally remain only for a short time and are not likely to develop sepsis. Epidemiological studies that include these postoperative patients in their analysis are, therefore, likely to report lower rates of sepsis than patients who exclude these postoperative patients from their analyses.

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Incidence of sepsis

Bearing in mind the above differences among studies in definitions and study populations, it is not surprising that the incidence of severe sepsis reported in the ICU varies considerably in the literature. Some of the best, recent information probably comes from the Sepsis Occurrence in Acutely ill Patients (SOAP) database (Vincent et al, 2006), which included data on patients throughout their ICU stay and excluded postoperative patients. In the SOAP study, severe sepsis was defined as the presence of sepsis associated with organ failure, except when that organ failure was present 48 hours before the onset of the sepsis, in an attempt to limit the number of patients being included with non-sepsis related organ dysfunction.

The SOAP study reported that 30% of the 3147 ICU patients from 198 western European ICUs had severe sepsis at some point during their ICU stay and half of these (15% of the total population) had septic shock (Vincent et al, 2006). Not surprisingly, as scheduled admissions for postoperative monitoring were excluded, the reported numbers for the incidence of severe sepsis are higher than for some other studies where these patients were included (Brun-Buisson et al, 2004; Engel et al, 2007; Karlsson et al, 2007). For example, the Episepsis study (Brun-Buisson et al, 2004) reported an incidence of severe sepsis of 17% (suspected) or 15% (documented) in French ICUs, but postoperative patients were included in the study population. Importantly, these authors suggested an increase in the frequency of sepsis compared to a study conducted 10 years earlier (Brun-Buisson et al, 1995).

Harrison et al (2006) also reported an increase in the number of patients diagnosed with severe sepsis in the first 24 hours after ICU admission, rising from an incidence of 24% in 1996 to 29% in 2004. Alberti et al (2002) reported a frequency of severe sepsis of 34% in 14 364 patients after excluding patients admitted for routine postoperative monitoring, a similar rate to that reported by the SOAP study. Importantly, several large epidemiological studies (Angus et al, 2001; Martin et al, 2003; Sundararajan et al, 2005) used the *International Classification of Diseases*-based criteria (World Health Organization, 2007), which may result in an overestimation of the frequency of sepsis (Wenzel and Edmond, 2001).

Conclusions

Despite the different study designs, definitions and populations, severe sepsis affects large numbers of ICU patients. This is even more worrying when one considers the elevated associated mortality rates. Patients in the SOAP study (Vincent et al, 2006) had ICU mortality rates of 32% for patients with severe sepsis and 54% for patients with septic shock. Other studies have reported similar mortality rates (Brun-Buisson et al, 2004) and, although some have suggested a slight decrease in mortality rates in recent years (Harrison et al, 2006), a recent study in Italy noted ICU mortality rates of 47 and 71% for severe sepsis and septic shock respectively (Malacarne et al, 2008). With the high incidence of severe sepsis, there is an urgent need to develop new therapies that can reduce morbidity and mortality in these patients. **BJHM**

Conflict of interest: none.

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KEY POINTS

- When comparing epidemiological data from studies of severe sepsis, one must consider differences in the definitions used and the populations studied.
- Severe sepsis is defined as sepsis plus sepsis-associated organ dysfunction, but in critically ill patients it can be difficult to determine whether organ dysfunction is the result of the sepsis or another cause.
- Severe sepsis affects about 30% of intensive care unit patients (if routine postoperative admissions are excluded).
- Severe sepsis is associated with mortality rates of about 30–40%.
- The incidence of sepsis is increasing so even if mortality rates have decreased slightly in recent years, the number of deaths from severe sepsis continues to increase.