Abstract

BACKGROUND AND OBJECTIVES:

Severe sepsis and septic shock have posed significant treatment challenges for many years. Recently, a number of circulating apoptosis biomarkers have emerged, such as full-length and caspase-cleaved cytokeratin 18 (CK18) and nucleosomal DNA (nDNA), that may be predictive of likely outcome. This non-interventional study aimed to assess the ability of enzyme-linked immunosorbent assays (ELISAs) for these biomarkers to provide clinically useful information to guide the management of sepsis.

METHODS:

This study was conducted in patients admitted to the intensive care unit with severe sepsis at five US centres. Blood samples for assessment of plasma levels of full-length CK18 (measured by the M65® ELISA) and caspase-cleaved CK18 (measured by the M30-Apoptosense® ELISA) and nDNA (measured by ELISA) were collected from patients within 2 hours of consent (baseline) and on days 2, 4 and 8. Blood samples from 17 healthy volunteers acted as controls. Levels of each biomarker were presented descriptively.

RESULTS:

A total of 22 patients (mean age 60 [range, 24-83] years; 50% male) were included in the study. The mean APACHE II score was 24.4 (range 7-50). One-third of patients had three organ system failures and over one-half had septic shock. Three patients died during the study. Full-length and caspase-cleaved CK18 levels decreased within 48 hours following initiation of treatment of sepsis in patients who survived, whereas increases were observed in the same timeframe in patients who died within 28 days of admission. Baseline nDNA and total soluble CK18 levels (caspase-cleaved and total intact) were significantly (p ≤ 0.05) higher in patients who required renal support than those who did not.

CONCLUSIONS:

Despite the small numbers of subjects assessed in the current study, these results confirm that measurement of apoptosis biomarkers may help to provide clinically useful information to manage sepsis and expedite development of novel therapeutics. However, further investigations to fully assess their prognostic value are required.