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Effectiveness of sepsis bundle application in cirrhotic patients with septic shock: a single-center experience

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Abstract

Purpose: To evaluate the effect of adherence to evidence-based guidelines of the Surviving Sepsis Campaign (SSC) on the outcome of cirrhotic patients with septic shock admitted to the intensive care unit.

Methods: This prospective observational cohort study included 38 patients with documented liver cirrhosis and septic shock admitted to a multidisciplinary intensive care unit at a University Hospital from January 2005 to June 2009. In each patient, the compliance to 4 resuscitation (ie, 6-hour bundle) and to 3 management (i.e. 24-hour bundle) interventions recommended by the SSC guidelines and the 30-day mortality were measured.

Results: The 6-hour, 24-hour, and all bundles were completed in 50 %, 52%, and 39% of the patients, respectively. The characteristics at admission and the 30-day mortality of patients with all-bundle compliance (n = 15; mortality 86.6%) were similar to those of patients without bundle compliance (n = 23; mortality 78.2%), except for central venous O_2 saturation. Unadjusted and adjusted regression analysis showed that none of the single sepsis interventions and bundles were independently associated with 30-day mortality.

Conclusions: In our observational study, the adherence to the interventions recommended by the SSC evidence-based guidelines did not provide an improvement in the survival rate of cirrhotic patients with septic shock.

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Abbreviations: SSC, Surviving Sepsis Campaign; ICU, intensive care unit; PaO_2/FiO_2, arterial O2 partial pressure to inspired O2 fraction ratio; MAP, mean arterial pressure; ALI, acute lung injury; ARDS, Adult respiratory distress syndrome; $ScvO_2$, central venous oxygen saturation; SAPS, Simplified Acute Physiology Score; SOFA, simplified organ failure assessment; MELD, Model End-stage Liver Disease score.

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1. Introduction

Liver cirrhosis is one of the most frequent chronic disease over the world. In 2002, more than 300,000 adult men in the European Union have died from liver cirrhosis complications such as hemorrhage and sepsis [1]. End-stage liver disease is a well-defined risk factor for development of infections and sepsis in cirrhotic patients is frequently associated with encephalopathy, renal failure, and gastrointestinal bleeding [2-4]. The mortality rate of cirrhotic patients with sepsis greatly exceeds that of septic patients without liver disease, approaching to 100% in patients requiring intensive care unit (ICU) admission with 3 or more organ dysfunctions [5,6].

In 2004 and in 2008, the guidelines of the Surviving Sepsis Campaign (SSC) [7,8] recommended a series of evidence-based interventions (ie, sepsis bundles) whose application ought to improve the outcome of patients with severe sepsis and septic shock. Numerous recently published articles showed that the application of the SSC was effective in decreasing the hospital mortality of septic shock patients [9,10], and this was the case also in our experience [11]. However, the effectiveness of these interventions has never been assessed in population with specific comorbidities that can interfere with the normal inflammatory responses to infection, as for instance, liver cirrhosis. In this study we evaluated the effects of the sepsis interventions proposed by SSC guidelines on the all-cause 30-day mortality in cirrhotic patients with septic shock admitted to the intensive care unit (ICU).

2. Methods

2.1. Patients

This prospective observational study enrolled patients with liver cirrhosis and septic shock admitted from January 2005 to June 2009 to ICU of a University Hospital with a liver transplantation program. The study was approved by the local ethical committee. Most patients (90%) were in waiting list for liver transplantation and had histological documentation and/or a clear medical history of chronic liver failure. The patient was considered to be in septic shock if all the following conditions were satisfied: (i) mean arterial pressure was less than 60 mmHg despite adequate fluid resuscitation, (ii) there were signs of tissue hypoperfusion (eg, oliguria, acidosis, worsening of mental status), (iii) there was evidence of systemic inflammatory response syndrome (eg, body temperature >38°C or <36°C; tachycardia, tachypnea, leukocytosis, or leukopenia), and (iv) there was a microbiologically documented infection. Patients with shock of uncertain etiology and with do not resuscitate order or end-life decisions were not included in the study. Only the first episode of septic shock was considered for each patient.

2.2. Data collection

In each patient, the compliance to 4 resuscitation interventions (6-hour bundle) and 3 management interventions (24-hour bundle) was evaluated. The 6-hour bundle includes (1) blood cultures collection before antibiotic administration and (2) empiric antibiotic therapy within 3 hours from diagnosis, adequate fluid resuscitation before vasopressor administration, and central venous oxygen saturation ($ScvO_2$) optimization within 6 hours ($ScvO_2$ >70 %). The 24-hour bundles includes: (1) blood glucose median <150 mg/dL in the first 24 hours, (2) low-dose hydrocortisone administration in association with vasopressor support, (3) plateau inspiratory pressure <30 cm H_2O in patients with acute lung injury/adult respiratory distress syndrome. The term adequate fluid resuscitation indicates a central venous pressure >6 mm Hg (>8 mm Hg if mechanically ventilated) or a global end-diastolic volume by trans-pulmonary thermodilution (PiCCO system, Pulsion, Germany) >700 mL/m^2. The use of recombinant human activated protein C was not considered because of its contraindications in patients with chronic liver disease.

Two of the authors (L.R. and L.D), not involved in the management of the patients, collected the above interventions by analysis of clinical charts, and any uncertain data were reviewed with the attending physician. The interventions were classified in a dichotomous way, that is, completed or not completed. If an intervention was not applied because it not applicable (eg, low inspiratory pressure in patient without acute lung injury/adult respiratory distress syndrome), it was defined as completed. The time zero for bundles timing was the time in which signs of septic shock were documented by clinical notes. Grade of sepsis, primary site of infection, SAPS II and SOFA scores [12,13], and 30-day mortality were also recorded for each patient. The grade of liver failure was assessed at ICU admission using the Model End-Stage Liver Disease (MELD) score [14].

2.3. Statistical analysis

χ^2 Test and ANOVA single-factor analysis were used when appropriate. Kaplan-Meier curves and log-rank tests were used for the comparison of 30-day survival curves between patients with and without sepsis bundles completion. To estimate the independent effect of each single intervention and bundle on 30-day mortality, univariate unadjusted and multivariate logistic regression adjusted for age, MELD, and SOFA scores were used. Data analyses were performed by means of SPSS version 15.0 (SPSS, Chicago, IL) and $P < .05$ was considered significant.

3. Results

Thirty-eight patients with liver cirrhosis and septic shock were studied (Table 1). Apart from steroids administration

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