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Toward a personalized response approach in sepsis 4.0

Hacia una estrategia de respuesta personalizada en sepsis 4.0

Dear Editor,

Sepsis is one of the leading causes of mortality worldwide.[1] However, mortality rates widely vary among different countries when patients have been enrolled in prospective septic shock trials.[2] For this and other reason, including sepsis recognition, new definitions of septic shock were launched. Now, shock is a clinical condition defined by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia.[3] Our hypothesis is that lactate level is not sufficient for defining shock progression but timing within the first 24 h of resuscitation. The aim of the present study is to determine the prognostic value of a predefined lactate clearance in the first 24 h of sepsis. A total of 544 consecutive patients with sepsis were included from a tertiary University Hospital (Parc Tauli Hospital, Sabadell, Spain). The vast majority presented an abdominal (37.9%) or respiratory source of sepsis (31.3%) and 62.8% were admitted through emergency department. Patients presented were 66.6 (SD 14.8) years old, 63.2% male and presented an APACHE II score of 18.4 (SD 7.7) with a mortality rate of 29.8%. We calculated the optimal cutoff for a lower mortality during the first 24 h of sepsis using the Youden index. With our data, this optimal cutoff was 10%, with a sensitivity of 51% and specificity of 71%. Patients with a lactate clearance ≥ 10% within the first 24 h of sepsis had a lower mortality in a univariate analysis than patients without that clearance (21.2% vs. 39.1%; $p < 0.001$). We adjusted lactate clearance for confounding factors, as initial lactate value and severity (APACHE II score), and we observed that lactate clearance ≥ 10% during the first 24 h of sepsis was identified as a protective factor for mortality (OR 0.49: 95% CI 0.30–0.81; $p < 0.05$) (Fig. 1). We, therefore, analyzed the relationship between lactate clearance and the fulfillment of the Surviving Sepsis Campaign (SSC) bundles. The group of patients with a lactate clearance ≥ 10% trended toward a better fulfillment of SCC bundles (5.1% vs. 2.2%; $p = 0.12$). We performed a multivariate analysis including all the SCC bundles (antibiotic treatment, fluid administration, vasopressors and initial lactate value and fluid administration) and lactate clearance ≥ 10% (OR 6.41; 95% CI 2.01–20.45; $p < 0.05$) was associated independently with a lower mortality. Despite the new incorporation of serum lactate levels for shock definition, we consider that the most important approach to reflect current ICU mortality would be the use of lactate clearance in the definition.[4] Therefore, a personalized approach is lacking in the current definitions and a lactate clearance equal or greater than 10% within the first 24 h of sepsis evolution is independently associated with lower mortality. Nguyen et al.[5] discovered that early lactate clearance within the first 6 h was associated with a decrease mortality however the 10% decrease was chosen after analyzing sensitivity and specificity of different thresholds. In our study, the implementation of a mathematical model (Youden index) helped us to find the ''ideal threshold''. Interestingly, in accordance with recently published studies, in our cohort, fluid administration during the first hours of sepsis is independently associated with lactate clearance.[6] Effort should be done to identify patients with shock and determinant of response, rather than to flag them only shocked.

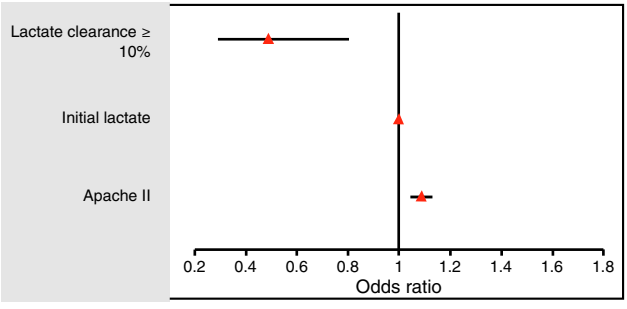

Figure 1 Odds ratio for mortality in patients included in the study. *Abbreviation*: OR, odds ratio.

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Conflict of interest

The authors have no conflict of interest to disclose.

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Successful treatment of Panton–Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* pneumonia with high doses of linezolid administered in continuous infusion

Tratamiento eficaz de una neumonia comunitaria producida por un *Staphylococcus aureus* resitente a meticilina leucocidina Panton-Valantin con altas dosis de linezolid en perfusión continua

Pneumonia caused by methicillin-resistant *Staphylococcus aureus* (MRSA) strains producing a cytotoxin known as Panton–Valentin leukocidin (PVL) is a severe and difficult to treat disease.[1–4] Linezolid has excellent epithelial lining fluid (ELF) penetration rates but drug concentrations in critically ill patients are highly variable.[5–8] We describe the clinical case of a patient with septic shock secondary to a community-acquired PVL-secreting MRSA pneumonia, in which linezolid plasma concentration within the therapeutic range were only reached with the use of higher than recommended doses (600 mg every 8 h) administered in continuous infusion.

A 56-year-old Caucasian man was admitted on February 2, 2015 with a 4-day history of dyspnea, mucopurulent expectoration, and fever (>38 °C). His weight was 80 kg (body mass index [BMI] 27.7 kg/m^2), smoked 2–3 cigarettes a day, and consumed approximately 7 standard drinks daily. Physical examination revealed sinus tachycardia (160 beats/min), diaphoresis, hypertension (blood pressure [BP] 154/92 mmHg), and marked respiratory distress as well as bilateral crackles and disperse rhonchi up to the apex on lung auscultation. This caused a hypoxemic respiratory insufficiency with an initial PaO_2 of 55 mmHg that did not improve despite an elevated inspired oxygen fraction (FiO_2 0.5) and noninvasive mechanical ventilation, for which he needed orotracheal intubation and ICU admission. Blood urea nitrogen was 32 mg/dL, serum creatinine 0.88 mg/dL, and glomerular filtration rate (Cockcroft–Gault equation) 106 mL/min, C-reactive protein 25.6 mg/L, procalcitonin 24.17 ng/mL, and lactic acid 5 mmol/L. Other laboratory data were unrevealing. Chest radiography revealed bilateral alveolar and interstitial infiltrates and alveolar condensation in the right upper lobe. The patient was tentatively diagnosed with CAP and was treated empirically with intravenous ceftriaxone (2 g every 24 h), intravenous levofloxacin (0.5 g every 12 h) (positive urinary detection of