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Recent lactate findings: is repeated serum lactate testing necessary in septic shock patients?

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Within the broader category of sepsis, septic shock is a distinct clinical entity characterized by circulatory and metabolic (i.e., cellular) dysfunction; its mortality rate (more than 40%) is higher than that of either hyperlactatemia alone (less than 30% mortality) or patients treated with vasopressors alone (30% mortality) [1]. The clinical criteria of septic shock are a serum lactate level >2 mmol/L (18 mg/dl) continuing in spite of adequate volume resuscitation and persistent hypotension for which vasopressors are required to maintain a mean arterial pressure ≥65 mmHg [1].

Shock is presented by hyperlactatemia and abnormal tissue hypoperfusion [2]. Early resuscitation is an essential aspect of treating septic shock [3]. Serum lactate can serve as a surrogate marker of tissue perfusion, even though it is not a direct indicator of perfusion [4], because elevated serum lactate levels are associated with hypoxia in the tissues and higher rates of aerobic glycolysis resulting from abnormally high beta-adrenergic stimulation or other causes; as such, hyperlactatemia is associated with a poor prognosis [5]. Lactate-guided resuscitation has been shown to lead to a significantly lower risk of mortality, with a relative risk of 0.67 (95% confidence interval, 0.53 to 0.84) [6-9]. Two meta-analyses enrolling 647 patients demonstrated that implementing a strategy focusing on early lactate clearance led to lower rates of in-hospital mortality than either a strategy focusing on $ScvO_2$ normalization or usual care [10,11].

As increased serum lactate levels, lactate kinetics are associated with mortality [12], the Surviving Sepsis Campaign has suggested that hemodynamic resuscitation should be guided by repeated assessments of serum lactate levels at intervals of 2 to 4 hours until lactate levels normalize [13]. However, sometimes other causes rather than tissue hypoperfusion, may persistently increase serum lactate levels [14], lactate kinetics may gradually return to normal even in survivors [12,15], and it may not be possible to measure lactate levels in all circumstances. Thus, the identification of alternative targets for resuscitation is a major desideratum of research in the field of sepsis [16].

In pediatric patients with septic shock, the lactate area score, which is defined as the area under the curve of measured lactate levels, was established to be an independent factor that predicted mortality [17]. However, few studies have investigated the role of the lactate area score in predicting the prognosis of septic shock [17,18] and pediatric or geriatric patients were enrolled in intensive care unit (ICU). In a single tertiary medical center, 362 adult septic shock patients were enrolled in the emergency department. The authors found that serial

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lactate measurements with five times within 12 hours and lactate area score were independently associated with 28-day mortality. Unfortunately, the lactate area score showed a lower odds ratio than had been reported in previous studies or that of the SOFA score for predicting mortality [19].

Increased serum lactate level and lactate kinetics are well-known prognostic factors for mortality in patients with septic shock. However, it remains controversial how many serum lactate level checks should be performed and at what time intervals for prediction of mortality in septic shock patients. To reach firmer conclusions on these issues, it will be necessary to conduct prospective multicenter interventional studies in the future.

Recently, ANDROMEDA-SHOCK trial was reported [20]. Randomized 424 adult patients with septic shock were included at 28 ICUs in five countries between March 2017 and March 2018. A protocolized resuscitation with capillary refill time (CRT; to less than 3 seconds, n=212) guided or lactate guided (aiming to reduce lactate levels by more than 20% each 2 hours, n=212) was used during initial 8-hour period. Both resuscitation strategy failed to decrease all-cause mortality at 28 days (P=0.06), but showed clinically meaningful results. A CRT targeting resuscitation was associated with lower Sequential Organ Failure Assessment (SOFA) score at 72 hours (P=0.045). A lactate-guided resuscitation group received an excess of 400 mL of crystalloid over the 8-hour period as compared to the CRT group [20].

Gattinoni L et al. [21] showed that post-hoc analysis of baseline variables in a multicenter trial, named ALBumin Italian Outcome Sepsis (ALBIOS) study, enrolled 1,741 septic patients. A lactate concentration and $ScvO_2$ were divided by sextiles. Only 35% patients among them, $ScvO_2$ was lower than 70%. The highest lactate levels, frequency of organ dysfunction, and mortality rate were observed in the first and sixth sextiles of $ScvO_2$. Acidemia only showed an association with lactate levels in patients with renal dysfunction (creatinine >2 mg/dl), which was detected by negative values of alactic base excess. They concluded that increased lactate level is strongly associated with severity of sepsis. The current resuscitation strategy could be modified according to the origin of hyperlactatemia because major cause is an impairment of tissue oxygen utilization rather than that of oxygen transport [21].

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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