Editorial

New clinical criteria for septic shock: serum lactate level as new emerging vital sign

Su Mi Lee, Won Suk An

Department of Internal Medicine, Dong-A University, Busan, Korea

Correspondence to: Won Suk An. Department of Internal Medicine, Dong-A University, 3Ga-1, Dongdaesin-Dong, Seo-Gu, Busan 602-715, Korea. Email: anws@dau.ac.kr.

Submitted Apr 10, 2016. Accepted for publication Apr 18, 2016.
doi: 10.21037/jtd.2016.05.55
View this article at: http://dx.doi.org/10.21037/jtd.2016.05.55

Sepsis is leading cause of acute hospital mortality and commonly results in multi-organ dysfunction secondary to culture-positive or negative infection. Septic shock is defined as unrecovered hypotension despite adequate fluid replacement in the Surviving Sepsis Campaign (SSC) Guidelines (1). Sepsis-induced arterial hypotension is defined as a systolic blood pressure (SBP) <90 mmHg or mean arterial pressure (MAP) <70 mmHg or a SBP decrease >40 mmHg or less than two standard deviations below normal for age in the absence of other causes of hypotension (1).

Until recently, septic shock was considered to be composed of three components, including systemic arterial hypotension, tissue hypoperfusion associated with organ dysfunction, and hyperlactatemia (2). According to the new definition of this issue (3), septic shock can be diagnosed under two conditions. The first condition is persistent hypotension after fluid resuscitation and requiring vasopressors to maintain MAP >65 mmHg. The second condition is serum lactate level >2 mmol/L. Since heart rate, respiration rate, and other laboratory data are not included, the diagnosis and recognition of septic shock have become simplified. This very new definition implies that increased serum lactate level may represent tissue hypoperfusion associated with signs of organ dysfunction in critically ill patients. In addition, it is of note that the serum lactate cut off level was decreased from 4 to 2 mmol/L. Serum lactate level as a clinical tool was described approximately half a century ago by Broder and Weil (4). At that time, serum lactate level >4 mmol/L was associated with shock status. Since the serum lactate level was decreased to 2 mmol/L, serum lactate level is a more sensitive marker for septic shock.

Notably, serum lactate level >2 mmol/L indicates a condition that is similar to sepsis with low BP in this issue of *Journal of the American Medical Association* (*JAMA*) (3). The SSC data base (n=18,840 patients) showed that acute hospital mortality in group 3, 4 and 5 (serum lactate level >2 mmol/L and without requiring vasopressors) was similar to that in hypotensive patients requiring vasopressors with serum lactate level <2 mmol/L (group 2) (5). Thus, a serum lactate level >2 mmol/L may be a new emerging vital sign of septic shock. Importantly, serum lactate level can be greatly increased under conditions of low BP requiring vasopressors because vasopressors constrict vessels resulting in tissue hypoxia. Based on this pathophysiology, new definition of septic shock can be explained although serum lactate level of 2 mmol/L (18.2 mg/dL) is normal value. Therefore, if a patient has a serum lactate level >2 mmol/L, BP or serum lactate level should be carefully monitored.

Lactate is important source of energy, particularly during starvation. Therefore, when lactate is not produced, humans cannot survive. Lactate also contributes to acidic environment by converting to lactic acid. Next, lactate is converted to bicarbonate and becomes a main source of alkalemia under normal conditions. Lactate of 1,400–1,500 mmol/L per day is formed from the reduction of pyruvate which is generated largely by anaerobic glycolysis (6). In tissue hypoxia, lactate is overproduced by increased anaerobic glycolysis. Lactate clearance typically occurs in the liver (60%), followed by the kidney (30%) and to a lesser extent by other organs (heart and skeletal muscle). Lactate clearance cannot overcome lactate production and may be worsened during critically ill status. Septic shock status with liver dysfunction and acute kidney injury elevate lactate levels because of decreased lactate

Table 1 Acute hospital mortality according to serum lactate level in septic patients requiring vasopressors

Hospital mortality	Initial serum lactate level (mmol/L)			P value
	<4	4–8	>8	
24-hour mortality, n (%)	1 (10.0)	14 (35.0)	19 (52.8)	0.011
48-hour mortality, n (%)	3 (30.0)	26 (65.0)	26 (72.2)	0.033

clearance. Lactate clearance at a discrete time point is an important prognostic factor compared to initial serum lactate level in severe sepsis (7). Some patients recovering from septic shock show normalized serum lactate levels, although vasopressors are still necessary to maintain a MAP of 65 mmHg or greater. Additionally, decreasing or normalized lactate levels are important signs of recovery from septic shock. Although there is no data related to this, we commonly detect lactate levels before stopping vasopressor treatment or detect normalized inflammatory markers such as C-reactive protein. This clinical finding supports that serum lactate level is a more sensitive vital sign reflecting anaerobic metabolism and acidosis than BP. Further clinical studies are necessary to support this.

Lactic acidosis caused by increased lactate levels, typically derived from tissue hypoxia in common clinical situations. Ischemic colitis and narrowed intestinal arteries induce lactic acidosis, particularly in the elderly (8). Shock status, such as cardiogenic or septic shock, is an important source of lactate production. Acidic conditions caused by lactic acidosis depress cardiac function and decrease the response of vasopressors. In contrast, sodium bicarbonate, which is used to correct metabolic acidosis, may aggravate lactic acidosis and increase mortality (9). Therefore, the early detection of septic shock based on a new definition is very important because early management of infection can reverse lactic acidosis and shock status.

Septic shock occurs when there is insufficient circulation to maintain adequate metabolism because of sepsis. Increased lactate production caused by anaerobic metabolism can reflect shock status. The number of elderly patients and bed-ridden patients with cardiovascular complications such as stroke or myocardial infarction is increasing. Since these patients are at risk of chronic kidney disease and volume overload, too rapid replacement of fluid to elevate BP may be harmful in septic shock. The new definition of septic shock can affect the treatment modality, and thus physicians must prepare for the new therapeutic guideline according to cellular metabolism and cardiovascular complications.

The mortality rate of patients with both hypotension and lactate ≥4 mmol/L is 46.1%, septic patients with hypotension alone is 36.7% and lactate ≥4 mmol/L alone is 30% (10). We recently published one article related with severe sepsis (7) and reanalyzed 86 septic shock patients with lactic acidosis supplementing sodium bicarbonate according to new septic shock definition. It was found that acute hospital mortality was significantly higher in patients with higher serum lactate level than those with lower serum lactate level (*Table 1*). The new septic shock definition will be updated and can be distinguished according to the BP or serum lactate level because high lactate level indicates higher mortality. This new definition should evolve, and precise dosages and types of vasopressors should be also determined. In conclusion, new definition of septic shock accurately reflects cell-based metabolism and lactate level can be used in place of vital signs.

Acknowledgements

This work was supported by the Dong-A University research fund.

Footnote

Provenance: This is an invited Editorial commissioned by the Section Editor Zhongheng Zhang (Department of Critical Care Medicine, Jinhua Municipal Central Hospital, Jinhua Hospital of Zhejiang University, Jinhua, China).
Conflicts of Interest: The authors have no conflicts of interest to declare.

Comment on: Shankar-Hari M, Phillips GS, Levy ML, *et al.* Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:775-87.

References

1. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013;41:580-637.
2. Vincent JL, De Backer D. Circulatory shock. N Engl J Med 2013;369:1726-34.
3. Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:775-87.
4. Broder G, Weil MH. Excess Lactate: An Index of Reversibility of Shock in Human Patients. Science 1964;143:1457-9.
5. Abraham E. New Definitions for Sepsis and Septic Shock: Continuing Evolution but With Much Still to Be Done. JAMA 2016;315:757-9.
6. Jeppesen JB, Mortensen C, Bendtsen F, et al. Lactate metabolism in chronic liver disease. Scand J Clin Lab Invest 2013;73:293-9.
7. Lee SM, Kim SE, Kim EB, et al. Lactate Clearance and Vasopressor Seem to Be Predictors for Mortality in Severe Sepsis Patients with Lactic Acidosis Supplementing Sodium Bicarbonate: A Retrospective Analysis. PLoS One 2015;10:e0145181.
8. Park WM, Gloviczki P, Cherry KJ Jr, et al. Contemporary management of acute mesenteric ischemia: Factors associated with survival. J Vasc Surg 2002;35:445-52.
9. Kim HJ, Son YK, An WS. Effect of sodium bicarbonate administration on mortality in patients with lactic acidosis: a retrospective analysis. PLoS One 2013;8:e65283.
10. Levy MM, Dellinger RP, Townsend SR, et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. Crit Care Med 2010;38:367-74.

Cite this article as: Lee SM, An WS. New clinical criteria for septic shock: serum lactate level as new emerging vital sign. J Thorac Dis 2016;8(7):1388-1390. doi: 10.21037/jtd.2016.05.55