Editorial

The potential of lipopolysaccharide-binding protein to predict the severity and prognosis of cirrhotic patients with severe sepsis

Bacterial translocation and episodic endotoxemia are common phenomena in cirrhotic patients and animals. Lipopolysaccharides (LPSs), which can promote the synthesis of LPS-binding protein (LBP) in the liver, intestine, and lungs, play a central role in the pathophysiology of sepsis. LBP is an acute phase protein that plays an important role in LPS signaling. In cirrhosis, cytokines and LBP levels are increased and responsible for the hyperdynamic circulation. Albillos et al reported that the subset of ascitic cirrhotic patients with marked immune and hemodynamic derangement can be identified by increased LBP levels. High LBP levels have also been found to be predictive of severe bacterial infections in cirrhotic patients with ascites. Previous studies suggested that the serum level of cytokines including LBP can serve as surrogate markers for the prognosis of cirrhosis. It has been reported that elevated LBP levels may be related to bacterial passage from the gut to the circulation without overt infection in cirrhotic patients with ascites. A recent study including 286 cirrhotic patients and 100 controls discovered that cirrhotic patients with increased serum LBP levels were four times more likely to have severe bacterial infection during follow-up than cirrhotic patients with normal LBP.

In this issue of the Journal of the Chinese Medical Association, Chen and colleagues evaluated the serum LBP, inflammatory cytokines, and the relationship between LBP concentrations, liver function reserve, and outcome in 58 critically ill cirrhotic patients with severe sepsis. Their study concluded that the concentration of LBP is inversely associated with disease severity scores and 28-day outcomes in critically ill cirrhotic patients with severe sepsis. A previous similar study reported that increased LBP levels inhibited LPS-mediated cytokine release and prevented hepatic failure, resulting in a significantly improved survival rate of experimental mice. Thus, it has been suggested that low or constitutive levels of LBP facilitate the recognition of LPS and early activation of immune cells, whereas acute phase elevated LBP levels serve to neutralize LPS to prevent overstimulation of the immune system. Another investigation similar to the Chen et al study reported that high concentrations of LBP in serum of patients with severe sepsis or septic shock inhibit the LPS response in human monocyte/sera of patients. Zeweigner et al reported that the inhibition of LPS effects by high concentrations of LBP is a defense mechanism of the host in severe sepsis and bacterial infections.

However, two recent studies reported that LBP levels were not clearly correlated with severity and prognosis of sepsis. Conversely, Villar et al reported that serum LBP offers a clinically useful biomarker for the identification of patients with severe sepsis having the worst outcomes and the highest probability of developing sepsis-induced acute respiratory distress syndrome.

The discrepancies about the prognostic significance of serum LBP level in cirrhotic and noncirrhotic patients might be explained by the dynamic changes in serum LBP during sepsis. In 180 patients with severe sepsis, serum LBP levels were serially measured at study entry, at 48 hours, and at 7 days. Villar et al revealed that the higher LBP levels were observed at the initial test and decreased thereafter, with the lowest recorded at the last test (7 days). In patients with sepsis and septic shock, Prucha et al measured the time-course changes in LBP levels by repeated measurement at 3–5-day intervals for 30 days or until death. Their fifth to seventh measurements of serum LBP levels showed a similar trend to that in Villar et al’s study. By contrast, it is clear that LBP can have either activating or inhibitory LPS actions depending on its concentration. At low concentrations, LBP typically potentiates the cells’ response to LPS by facilitating the transfer of LPS to its receptor, whereas high levels of LBP have been shown to inhibit cell responses to LPS by transferring the LPS to high-density lipoproteins or by facilitating the internalization of LPS without triggering inflammatory cell stimulation. It is noteworthy that the sample size of Chen et al’s study was relatively small compared with previous studies. Other limitations of their study are the lack of a noncirrhotic group and the single measurement of serum LBP level in cirrhotic patients with sepsis.

This is the first study to explore the role of serum LBP level in the prognostic values in cirrhotic patients with sepsis. The current study provides a novel marker LBP that might help clinicians to identify cirrhotic patients who are at risk of deterioration and in need of timely intervention. Nonetheless,
larger sample size prospective studies are needed to clarify the impact of serum LBP levels on the severity and prognosis at different time points of cirrhotic patients with sepsis prior to further clinical application.

Conflicts of interest

The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

References


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