Effect of Terlipressin on Renal Function in Liver Cirrhosis With Ascites: A Pilot Study

Ascites is one of the common decompensation events in cirrhosis,¹ which causes vasodilatation of visceral arteries, reduction of effective circulation volume, activation of endogenous vasoconstriction system, and sodium and water retention and hypoperfusion in the kidney,² thereby increasing the risk of acute kidney injury (AKI)³ and hepatorenal syndrome (HRS).⁴ Terlipressin has an effect on systemic vasodilatation and renal dysfunction in patients with portal hypertension.⁵ Common adverse reactions of terlipressin include hyponatremia, hypertension, abdominal pain, intestinal peristalsis or abdominal colic, nausea, diarrhea, and headache, but severe adverse events are rare in our clinical practice.^{6,7} Previous studies have confirmed the efficacy of terlipressin for improving renal function in HRS⁸ and suggested the potential benefits of terlipressin in improving the severity of ascites and preventing postparacentesis circulatory dysfunction.^{9,10} A recent study suggests that terlipressin may be beneficial on preventing renal function impairment in patients with cirrhosis and acute upper gastrointestinal bleeding,¹¹ and the role of terlipressin for improving renal function and preventing from HRS/AKI in patients with ascites remained controversial. Our recent survey of Chinese hepatologists suggested that terlipressin would be a potential choice of treatment for ascites if conventional treatment failed.¹² Herein, we have further conducted a pilot study to investigate the dynamic change of renal function after the administration of terlipressin in patients with ascites. It may be useful to further elucidate the possibility of early use of terlipressin in patients with cirrhosis and ascites.

METHODS

We retrospectively reviewed the medical records of patients with cirrhosis who were admitted to the General Hospital of Northern Theater Command from September 2018 to September 2019. The inclusion criteria were as follows: (1) a diagnosis of ascites with or without renal dysfunction and (2) use of terlipressin during hospitalization. The exclusion criteria were as follows: (1) acute upper gastrointestinal bleeding at admission or during hospitalization, (2) hemodialysis during hospitalization, and (3) lacking of posttreatment renal function. We evaluated whether or not patients were diagnosed with HRS before using terlipressin. The diagnostic criteria of HRS-AKI

were in accordance with the current practice guideline¹³: (1) cirrhosis with ascites, (2) an increase in serum creatinine ≥ 0.3 mg/dl within 48 h or $\geq 50\%$ from baseline value, (3) absence of response after at least 2 days of diuretic withdrawal and volume expansion with albumin, (4) absence of shock, (5) neither current nor recent treatment with nephrotoxic drugs, and (6) absence of parenchymal disease as indicated by proteinuria >500 mg/day, microhaematuria (>50 red blood cells per high power field), urinary injury biomarkers (if available), and/or abnormal renal ultrasonography. Owing to the retrospective nature of this study, the indications for the use of terlipressin were not restricted. We calculated the changes in sCr and cystatin-C (Cys-C) concentrations in patients with ascites.

RESULTS

A total of 11 patients were included. The median age was 63.00 years (range: 51.00 to 88.00). Most of patients were men (72.70%). The median MELD score was 12.00 (range: 7.00 to 40.00), and most patients had Child-Pugh class B (72.70%). Mild, moderate, and large ascites were observed in 5, 4, and 2 patients at admission, respectively. Four of these patients had abnormal urine tests (>50 red blood cells per high power field), which were inconsistent with the diagnostic criteria of HRS-AKI. The sCr concentrations at different time points were shown in the [Supplementary Table 1](#). Only one patient met the diagnostic criteria for HRS-AKI before the use of terlipressin, which were indicated by $\geq 50\%$ increase in sCr within 3 months in the absence of substantial kidney changes or shock. The median sCr concentration before the use of terlipressin was $77.79 \mu\text{mol/L}$, and Cys-C concentration before the use of terlipressin was 2.70 mg/L .

According to the sCr concentration before the use of terlipressin, there were 6 patients in the sCr concentration $>133 \mu\text{mol/L}$ group (mild ascites [$n = 3$], moderate ascites [$n = 1$], and large ascites [$n = 2$]) and 5 patients in the sCr concentration $<133 \mu\text{mol/L}$ group (mild ascites [$n = 3$] and moderate ascites [$n = 2$]). The median duration of terlipressin was 2 days (range: 1 to 8), and the median dosage was 6 mg (range: 2 to 15) during hospitalization. Terlipressin was given in all patients by continuous pumping. Among them, 10 (90.90%) patients were treated with diuretics and 8 (72.70%) patients were treated with albumin infusion.

In the sCr concentration $>133 \mu\text{mol/L}$ group, the median change of sCr concentration was $-59.23 \mu\text{mol/L}$

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Figure 1 The changes of sCr (panel A) and Cys-C (panel B) concentrations before and after use of terlipressin.

(95% confidence interval [CI]: -1.26 to 0.09 , $P = 0.0321$) (Figure 1A), and the median change of Cys-C concentration was -0.725 mg/L (95% CI: -1.12 to -0.25 , $P = 0.0067$) (Figure 1B).

In the sCr concentration <133 $\mu\text{mol/L}$ group, the median change of sCr concentration was $+12.38$ $\mu\text{mol/L}$ (95% CI: -0.09 to 0.37 , $P = 0.1570$) (Figure 1A), and the median change of Cys-C concentration was $+0.058$ mg/L (95% CI: -0.58 to 0.70 , $P = 0.4139$) (Figure 1B).

Our preliminary findings suggested that the use of terlipressin would improve renal function in patients with ascites when sCr concentration was >133 $\mu\text{mol/L}$. In contrast, the benefits of terlipressin seemed to disappear when sCr concentration was <133 $\mu\text{mol/L}$. Notably, the present study was just retrospective with a small sample size. Further well-designed large-scale studies should be necessary to validate these findings and identify the candidates with ascites who are suitable for early use of terlipressin.

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CONFLICTS OF INTEREST

The authors have none to declare.

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Yang An: Methodology, Software, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Zhaohui Bai:** Methodol-

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SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jceh.2020.05.002>.

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