

Letter to Editor**Systemic hemodynamic and renal effects of midodrine and octreotide in cirrhotic patients with ascites**

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We read with great interest the article by Minakari et al. regarding the effects of treatment with subcutaneous octreotide and oral midodrine in cirrhotic patients with ascites who continued to receive their standard diuretic treatment<sup>1</sup> and we would like to comment on their results.

First, the administration of midodrine for 3 days caused a non-significant increase in mean arterial pressure (MAP). In this respect, we have recently described a delay in the improvement of systemic hemodynamics after the initiation of midodrine in nonazotemic cirrhotic patients with ascites.<sup>2</sup> Nevertheless, midodrine caused a significant decrease in plasma renin activity (PRA), which together with the significant increase in glomerular filtration rate (GFR), strongly indicate a marked increase in systemic vascular resistance possibly due to a concomitant significant decrease in cardiac output. Moreover, it can be suggested that midodrine-induced systemic hemodynamic improvement enhanced the natriuretic response to diuretic treatment<sup>3</sup> as shown by a remarkable mean weight decrease of 3.65 kg at the end of the study.

On the other hand, octreotide induced a significant reduction in PRA, an increase in MAP and GFR, although not significant, and a mean weight decrease of 2.23 kg, which was possibly resulted from increased diuresis. Overall, these results indicate beneficial effects of octreotide on systemic hemodynamics and

renal function considering that treatment duration was only 3 days. However, we and other investigators have previously shown that multiple-dose treatment with subcutaneous octreotide alone impairs systemic hemodynamics and renal function in cirrhotic patients with ascites despite a significant decrease in circulating renin and aldosterone levels.<sup>4,7</sup> In this regard, several lines of evidence have suggested a direct inhibitory effect of both somatostatin and its analogue octreotide on renin production.<sup>8-10</sup> Given the questionable splanchnic vasoconstrictive effect of chronic treatment with octreotide alone,<sup>4,7</sup> an inappropriate suppression of renin-angiotensin axis could be harmful for systemic hemodynamics and renal perfusion. In contrast, we have shown that the addition of octreotide to diuretic treatment suppresses only the diuretic-related component of the activation of renin-angiotensin axis while its basal stimulation is maintained.<sup>4,11</sup> This leads to improvement of systemic hemodynamics,<sup>4</sup> possibly due to enhanced activity of the endogenous vasoconstrictors by the decrease in glucagon levels,<sup>12</sup> renal function and natriuresis.<sup>4</sup> Consequently, the effects of octreotide in the study by Minakari et al. are likely to be attributed to its addition to diuretic treatment and not octreotide per se.

In conclusion, the addition of octreotide or midodrine to standard diuretic treatment in cirrhotic patients with ascites deserves further attention.

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## Conflict of Interests

Authors have no conflict of interests.

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