

# CORRESPONDENCE

## Improvement of Refractory Ascites in Cirrhotic Patients on Hemodialysis After Midodrine Treatment

We read with great interest the article by Sourianarayanan and colleagues regarding the effects of the  $\alpha$ -agonist midodrine on refractory ascites in 2 patients with cirrhosis and chronic renal failure (CRF) undergoing hemodialysis.<sup>1</sup> A decrease in the volume of ascitic fluid drained and improvement in arterial pressure were noticed in both patients after the administration of midodrine. This effect of midodrine was not sufficiently explained and, according to a previous report, was attributed to a possible decrease in circulating nitric oxide (NO) levels that led to a decrease in portal pressure and reduced ascitic fluid accumulation.<sup>2</sup>

However, the potential contribution of decreasing NO levels after midodrine treatment to the control of ascites in the described patients is brought into question by the fact that plasma NO concentration has been shown to fall significantly during hemodialysis.<sup>3,4</sup> Indeed, hemodialysis has been proposed as a possible approach for removing excess NO from the circulation in pathophysiologic states such as cirrhosis.<sup>3</sup> Consequently, circulating NO levels in cirrhotic patients undergoing hemodialysis are expected to be low. Furthermore, NO depletion has been associated with increased intrahepatic portal venous resistance.<sup>5</sup> Therefore, other mechanisms—rather than changes in circulating NO levels—are likely to be involved in the beneficial effects of midodrine on ascites in the patients described by Sourianarayanan and colleagues.<sup>1</sup>

Midodrine could have ameliorated portal hypertension by causing splanchnic arterial vasoconstriction, which in turn could have reduced portal blood flow.<sup>6</sup> On the other hand, ascites in patients with CRF, termed nephrogenic ascites, can also occur shortly or several months after the onset of hemodialysis or in patients who are not undergoing hemodialysis.<sup>7</sup> The pathogenesis of nephrogenic ascites has been primarily associated with uremia-induced increased peritoneal membrane permeability and changes in lymphatic channels leading to decreased reabsorption of peritoneal fluid.<sup>7</sup> The aforementioned mechanisms have also been suggested to contribute to the pathogenesis of ascites in patients with portal hypertension due to cirrhosis.<sup>8,9</sup> In this respect,  $\alpha$ -agonists have been shown to improve endothelial barrier function and reduce peritoneal

microvascular permeability, which, combined with the reduction in portal pressure, could reduce ascites formation after midodrine treatment in cirrhotic patients with CRF.<sup>10,11</sup> Finally, modifications in hemodialysis to prevent hypotension have been reported to improve control of nephrogenic ascites.<sup>7</sup>

Regardless of the underlying mechanisms, the role of midodrine in reducing the frequency of large-volume paracentesis in cirrhotic patients with CRF and refractory ascites deserves further attention.

**Georgios N. Kalambokis, MD**  
**Epameinondas V. Tsianos, MD, PhD, AGAF, FEBG**

*1st Division of Internal Medicine and Hepato-Gastroenterology Unit, Medical School of Ioannina, Ioannina, Greece*

Address correspondence to: Dr. Epameinondas V. Tsianos, Professor of Internal Medicine, 1st Division of Internal Medicine and Hepato-Gastroenterology Unit, Medical School of Ioannina, 45110 Ioannina, Greece; Tel: +30 26510 07501; Fax: +30 26510 07016; E-mail: etsianos@uoi.gr

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