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COMMENT

Celiac ganglia: potential new targets in neuromodulation for hypertension

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The sympathetic nervous system plays a critical role in the pathophysiology of hypertension. In recent times, there is growing anticipation for the emergence of novel therapeutic strategies for hypertension through the utilization of newer device technologies in neuromodulation, including renal denervation and baroreflex activation therapy [1–3]. Of these, there is accumulating basic and clinical evidence for renal denervation. As therapeutic mechanisms of renal denervation, not only inhibition of the renin-angiotensin system and the water and sodium retention through the denervation of efferent renal nerves, but also suppression of central sympathetic activation through the denervation of afferent renal nerves has been focused [2, 4, 5]. Furthermore, among the sympathetic nervous system components contributing to cardiovascular regulation, the splanchnic nerves have also been focused as potential targets for denervation [6–8]. Celiac ganglia are mainly joined by splanchnic nerves and innervate the splanchnic organs including the stomach, liver, spleen, and intestines. Celiac ganglionectomy was shown to lower blood pressure in patients with hypertension [9], potentially through the regulation of the splanchnic vascular bed [10].

The present study by Dai et al. demonstrates that celiac ganglia neurolysis decreases blood pressure in spontaneously hypertensive rats and Dahl salt-sensitive hypertensive rats [11]. The authors validated the reduced viability of celiac ganglia by morphological changes, such as the discontinuity of the nerve fiber and the rupture of the ganglion cell nucleus, and by decreases in tyrosine hydroxylase staining. Along with blood pressure lowering, celiac ganglia neurolysis resulted in decreased circulating renin-angiotensin system components (plasma renin, angiotensin II, and aldosterone levels) and increased plasma nitric oxide levels. Previous studies also demonstrated that celiac ganglionectomy decreased blood pressure in Dahl salt-sensitive hypertensive rats [12] and genetically hypertensive Schlager (BPH/2 J) mice [13]. Foss et al. showed that, in Dahl salt-sensitive rats, blood pressure was decreased in renal denervated rats and celiac ganglionectomized rats, and further decreased in rats that underwent both renal denervation and celiac ganglionectomy [12]. Asirvatham-Jeyaraj et al. demonstrated that renal denervation but not celiac ganglionectomy normalized neurogenic pressor activity evaluated by the blood pressure lowering responses to ganglion blocker hexamethonium, whereas renal denervation and celiac ganglionectomy similarly decreased blood pressure in BPH/2 J mice [13]. These previous studies suggest that the mechanisms of blood pressure lowering are, at least in part, different between renal denervation and celiac ganglionectomy. Denervation of splenic nerve, which originates from the celiac ganglion, may be involved in a potential pressor mechanism of celiac ganglionectomy. Splenic nerve ablation prevented T-cell activation and normalized blood pressure in deoxycorticosterone acetate-salt hypertensive mice [14]. Although the parameters of sympathetic activity were not shown in the present study by Dai et al., the activity of the circulating renin-angiotensin system, mainly determined by renal sympathetic nerve activity, was decreased by celiac ganglia neurolysis; therefore, systemic and/or renal sympathetic nerve activity might be decreased by celiac ganglia neurolysis. Celiac ganglia neurolysis and celiac ganglionectomy are needed to be further investigated to clarify their mechanisms of blood pressure lowering.

The present study by Dai et al. also discusses the clinical intervention for celiac ganglia neurolysis. Endoscopic ultrasound-guided celiac ganglia neurolysis, a relatively

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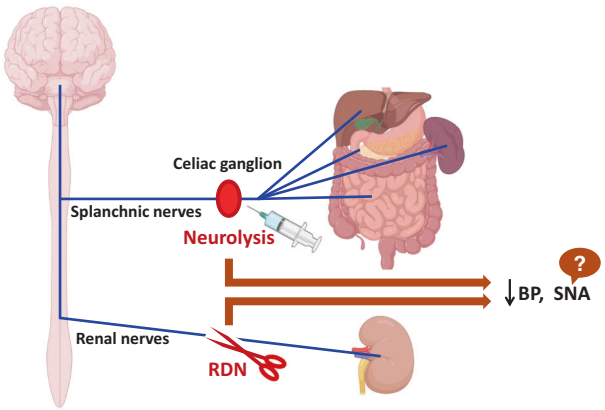

Fig. 1 Targets in neuromodulation for hypertension. Splanchnic nerves and celiac ganglia can be new targets for denervation. BP blood pressure, RDN renal denervation, SNA sympathetic nerve activity

simple endoscopic procedure, involves ablation of the celiac ganglia with real-time imaging of endoscopic ultrasound. It is a minimally invasive procedure to deliver neurolytic agents to the celiac ganglia to relieve pain in patients with pancreatic cancer or other abdominal conditions [15]. Compared to surgical celiac ganglionectomy, endoscopic ultrasound-guided celiac ganglia neurolysis is simpler, safer, and completer. In fact, some patients who underwent ultrasound-guided celiac ganglia neurolysis had a reduction in blood pressure [15]. However, pain relief from the cancer itself can lead to a decrease in blood pressure. Further clinical studies investigating celiac ganglia neurolysis in patients with hypertension are necessary. In the context of neuromodulation for hypertension and cardiovascular diseases, the inhibition of systemic sympathetic nerve activity is crucial and desirable. Therefore, there is a need for studies that specifically address the parameters related to sympathetic nerve activity, as well as blood pressure (Fig. 1).

Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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