Vasoactive Intestinal Contractor as a Genesis of Renal Hypertension

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Dear Sir,

Hypertension is a pathophysiological abnormality which results from a derangement in one or more of a variety of cardiovascular control mechanisms. Cardiac output and peripheral vascular resistance are the hemodynamic factors which determine a subject's blood pressure. A number of functional abnormalities which can influence cardiac output and peripheral vascular resistance occur in patients with renal parenchymal diseases [1]. Although the severity of hypertension during the course of chronic renal diseases varies considerably in individuals, blood pressure tends to increase with the progression of chronic renal diseases. The genesis of renal hypertension has been reported as an increased extracellular fluid volume and sodium content, enhanced vasopressor system activity, and decreased release of renal vaso-depressor substances [2].

Concerning the enhanced activities of the vasopressor system in renal hypertension, increased renin secretion, increased aldosterone secretion, accentuated sympathetic nerve activities, increased catecholamine secretion, and enhanced vascular response to vasopressor hormones have been reported [2]. We have recently suggested that a pressor substance or its precursor exists in the digestive tract of nephrectomized rats by employing oral sorbent (AST-120, developed by Kureha Chemical Industry Co. Ltd, Tokyo) [3]. It was reported that vasoactive intestinal contractor (VIC), which differs from endo-thelin in 3 amino acid residues, was cloned and sequenced from the mouse genome, and VIC induced a prolonged contraction in mouse ileum as well as porcine coronary artery in vitro [4]. We therefore examined the possibility that VIC is one of the genesis factors for renal hypertension.

VIC (Peptide Research Center, Tokyo) solution (9×10^{-8} M/kg b.w.) and vehicle were intravenously and duodenally administered in one shot to conscious male Sprague-Dawley rats with 4/5 nephrectomy. The level of blood pressure was elevated from 113 to 135 mm Hg by the intravenous administration of VIC solution and from 110 to 122 mm Hg by the duodenal administration of VIC, while the level of blood pressure was not changed by the intravenous and duodenal administration of vehicle. VIC thus has a vasopressor effect in vivo. 5 ml of VIC solution and the VIC solution with 12.5 mg of AST-120 were incubated at 37°C for 3 h with vibration of 180 min⁻¹ rpm. The supernatants were analyzed using total

organic carbon analyzer-500 (Shimazu Co., Tokyo). The supernatant of VIC solution contained 0.87 mg/dl of VIC, while the supernatant of VIC solution with AST-120 contained only 0.02 mg/dl of VIC, indicating that VIC was completely adsorbed by AST-120 in this condition.

Since the intravenous and duodenal administration of VIC elevated blood pressure, VIC was adsorbed by AST-120 in vitro and the oral administration of AST-120 reduced blood pressure in nephrectomized rats [3], it is strongly suggested that VIC is one of the genesis factors for renal hypertension.

References

Russell RP, Whelton PK: Hypertension in chronic renal failure: Clinical presentation, prognosis, pathophysiology and treatment. *Am J Nephrol* 1983;3:185-192. Cheigh JS, Stenzel KH, Rubin AL: Hypertension in kidney disease: in Cheigh JS, Stenzel KH, Rubin AL (eds): *Hypertension in Kidney Disease*. Dordrecht, Nijhoff, 1986, pp 1-18. Takahashi S, Okada K, Shimamura T: Influence of factors in the digestive tract on the progression of chronic renal failure. *Jpn J Nephrol* 1993;35:1-11.

Ishida N, Tsujioka K, Tomoi M, Saida K, Mitsui Y: Differential activities of two distinct endo-thelin family peptides on ileum and coronary artery. *FEBS Lett* 1989;247:337-340.