Sympatho-modulation by Renal Denervation in Spontaneously Hypertensive Rats

Yusuke Sata, Toru Kawada, Markus Schlaich, Murray Esler, Masaru Sugimachi, Member IEEE

Abstract—Recently, catheter-based renal sympathetic nerve ablation has been introduced as a treatment for resistant hypertension. To elucidate the mechanisms of blood pressure reduction by renal sympathetic denervation (RDN), we examined the open-loop static characteristics of the carotid sinus baroreflex in normotensive Wistar Kyoto rats (WKY) and spontaneously hypertensive rats without (SHR) and with renal denervation (RD-SHR). The operating-point arterial pressure (AP) was determined from the intersection between the baroreflex neural and peripheral arc in a baroreflex equilibrium diagram. RD-SHR showed the operating-point AP of 129.8 ± 6.9 mmHg, which was between that of WKY (111.3 ± 4.4 mmHg) and that of SHR (145.1 ± 5.7 mmHg). Renal denervation modulates the baroreflex control of sympathetic nerve activity (SNA), and decreased the operating-point AP in RD-SHR compared to SHR. However, RDN did not completely normalize SNA or AP regulation compared to WKY.

I. INTRODUCTION

The sympathetic nervous system has been a major focus in both basic and clinical studies of hypertension. The role of renal sympathetic nervous activity is particularly important in the regulation of blood pressure.[1] Recently, catheter-based radiofrequency ablation of renal sympathetic nerves has been trialed in patients with resistant hypertension and demonstrated a significant fall in blood pressure and a reduction in renal norepinephrine (NE) spillover.[2-4] While centrally mediated anti-hypertensive effects have been proposed, this has not yet been demonstrated. To elucidate the exact mechanisms of blood pressure regulation and RDN-induced modulation of sympathetic nervous system, we examined the effects of RDN on the open-loop static characteristics of carotid sinus baroreflex in SHR.

II. METHODS

Male adult SHR (n=5, 417 ± 14 g) were treated with combined surgical and chemical bilateral RDN by stripping the renal nerves around the renal artery and vein adventitia and painting with 10% phenol in absolute ethanol under isoflurane anesthesia. Open-loop baroreflex experiments were performed at 6-7 weeks after operation.[5] Under anesthesia with a mixture of urethane and α-chloralose, bilateral carotid sinus regions were isolated from the systemic circulation after vagotomy and aortic denervation. We analyzed the input-output relation between carotid sinus pressure (CSP) and splanchnic SNA [CSP-SNA, neural arc], as well as the relation between SNA and AP [SNA-AP, peripheral arc]. The data were compared with those obtained previously in WKY and SHR without RDN.

III. RESULTS

An increase in CSP decreased AP in an inverse sigmoidal fashion. In the neural arc, the increase in CSP decreased SNA in an inverse sigmoid fashion. When compared to WKY, the percent reduction of SNA was decreased and the maximum slope of percent changes in SNA to CSP was smaller in both RD-SHR and SHR. In regard to the peripheral arc, an increase in SNA linearly increased AP. The slope of AP response to percent changes in SNA was steeper in RD-SHR and SHR than in WKY. The intersection between the neural arc and the peripheral arc in a baroreflex equilibrium diagram gives the operating point AP. RDN decreased the operating point AP from 145.1 ± 5.7 mmHg in SHR to 136.6 ± 6.9 mmHg in SHR-RD, but it was not normalized completely compared to WKY (111.3 ± 4.4 mmHg). Plasma NE was significantly higher in SHR and SHR-RD than in WKY, but both AP and plasma NE were decreased to the similar levels in all three groups after the ganglionic blockade.

IV. DISCUSSION AND CONCLUSION

The baroreflex equilibrium diagram indicates that RDN reduced SNA, and, through the baroreflex regulation of SNA, decreased AP in RD-SHR compared to SHR. The neural arc, shifted leftward after RDN, indicates baroreflex-independent antihypertensive effects. However, RDN did not completely normalize either SNA or AP regulation to the levels seen in WKY.

REFERENCES


*Research supported by Japan Heart Foundation / Bayer Yakuhin Research Grant Abroad.
Y. Sata, M. Schlaich, and M. Esler are with the Baker IDI Heart and Diabetes Institute, 75 Commercial Road, Melbourne VIC 3004 Australia (Corresponding author, Y. Sata, T; +61 (03) 8532 1502 F: +61 (03) 8532 1100 E: Yusuke.Sata@bakeridi.edu.au).
T. Kawada and M. Sugimachi are with the Department of Cardiovascular Dynamics, National Cerebral and Cardiovascular Center, Osaka 565-8565, Japan.