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学位論文の題名	Angiotensin receptor blockers regulate the synchronization of circadian rhythms in heart rate and blood pressure (アンジオテンシン受容体拮抗薬は血圧と心拍に関する日内リズムを同調させる) J Hypertension, 31(6):1233-1238,2013

It has been suggested that the sympathetic nervous system may play an important role in blood pressure (BP) regulation even in the early stages of chronic kidney disease (CKD) [1,2]. In addition, variability of circulatory dynamics fluctuated less as sympathetic function is activated [3,4]. Furthermore, inhibitors of the renin-angiotensin system (RAS) are known to suppress sympathetic nerve activity [5–7]. Finally, we have reported that an angiotensin II receptor blocker (ARB) restored the circadian BP rhythm [8,9]. On the basis of these findings, we analyzed the synchronicity in circadian rhythms of both heart rate (HR) and BP, as well as HR variability (HRV, SD), in relation to renal function in CKD before and during treatment with ARB. Our hypothesis is that the ratio of [day/night ratio of HR] over [day/night ratio of MAP] was increased as renal function deteriorated at baseline, and became independent of renal function during ARB treatment.

To understand the role of the sympathetic system, we examined the relationship between day/night ratios of both HR and mean arterial pressure (MAP) as well as HR variability (HRV, SD) before and during an 8-week treatment with ARB, olmesartan, in 45 patients with CKD.

The day/night HR ratio strongly correlated with the day/night MAP ratio before and during ARB treatment. The ratio of [day/night HR ratio] over [day/night MAP ratio] was increased as renal function deteriorated at baseline (r = -0.31, P = 0.04), and it was attenuated (1.10 ± 0.10 to 1.06 ± 0.10 ; P = 0.04) and became independent of renal function during ARB treatment (r = -0.04, P = 0.8). ARB increased both the day/night HR ratio ($1.17\pm0.09 - 1.21\pm0.13$; P = 0.04) and HRV ($10.6\pm2.9 - 1.1.7\pm4.2$; P = 0.04), which were lower when baseline renal function deteriorated.

The present study indicates that there exists a close correlation in circadian rhythms between HR and MAP in CKD. Synchronization between the two rhythms was progressively lost as renal function deteriorated, and ARB partly restored the synchronization. These findings suggest that the sympathetic nervous system is activated as renal function deteriorates, and ARB may suppress its activation.

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