A Special Focus on the Role of α1D-Adrenoceptors in the Assessment of Renal Tubular Sodium Re-absorptive Responses in Spontaneously Hypertensive Rats Subjected to High Sodium Diet

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(Received May 16, 2010; Accepted October 25, 2010)

α1D-Adrenoceptors are involved in the genesis/maintenance of hypertension in spontaneously hypertensive rats (SHR). This study aims to investigate the role of α1D-adrenoceptors in the antinatriuretic and antidiuretic responses in SHR subjected to high sodium (SHRHNa) and normal sodium (SHRNNa) intake for six weeks. Renal inulin clearance study was performed in which the antinatriuretic and antidiuretic responses to phenylephrine were examined in the presence and absence of U-14,14,14-2,4-Dimethylaminoisobutyric acid analogue of α1D-adrenoceptors blocker BMV7778. Data, mean±S.E.M., were subjected to ANOVA with significance at p<0.05. Results show that feeding SHR for six weeks with high salt did not cause any change in blood pressure. SHRHNa had higher (all p<0.05) urine flow rate (UFR), fractional and absolute excretion of sodium (FE and UE) compared to SHRNNa. Phenylephrine infusion produced significant reduction in UFR, FE and UE in both SHRHNa and SHRNNa. The antidiuretic and antinatriuretic responses to phenylephrine in both groups were attenuated in the presence of BMV7778. Moreover, the antidiuretic and antinatriuretic responses to phenylephrine and BMV7778 were independent of any significant changes in renal and glomerular hemodynamics in both groups. Thus, we conclude that high sodium intake did not bring any further increase in blood pressure of SHR, however, it results in exaggerated natriuresis and diuresis in SHRNNa. Irrespective of dietary sodium changes, α1-adrenoceptors are involved in mediating the antinatriuretic and antidiuretic responses to phenylephrine in SHR. Further, high sodium intake did not significantly influence the functionality of α1D-adrenoceptors in mediating the adrenergically induced antinatriuresis and antidiuresis.

Key words—α1D-adrenoceptor; high sodium; renal function; spontaneously hypertensive rat (SHR)

INTRODUCTION

High dietary salt intake has long been associated with high blood pressure. Chronic exposure to a high-salt diet appears to be a major pathophysiological factor involved in the frequent occurrence of hypertension.1,2 Hypertension is a condition where in adrenergic responsiveness, sympathetic nervous system activity and alpha adrenoceptors remains altered.3,4 Renal α1-adrenoceptors has shown to mediate the actions of renal sympathetic nerve in the control of the various renal functions such as renal hemodynamic, glomerular ultra filtration and sodium reabsorption, thus contributing to the regulation of extracellular fluid volume and arterial blood pressure.

In addition, the release of renin from the granular cells of the juxtaglomerular apparatus is also mediated by renal α1-adrenoceptors.5 Renal α1-adrenoceptor is of primary pathogenic importance in hypertension6 and dietary sodium intake has shown to exert a role in the regulation of renal α1-adrenoceptors in the essential hypertension.7,8 α1-Adrenoceptors are subdivided into three distinct subtypes, α1A, α1B and α1D.8 Among the subtypes of α1-adrenoceptors, α1D-adrenoceptors is expressed in several vascular beds including the renal vasculature in spontaneously hypertensive rats (SHR) and are actively involved in the regulation of renal vascular resistance.9,10 α1D-Adrenoceptors is also suggested to be functionally important in the genesis and maintenance of essential hypertension thus contributing to the pathogenesis of hypertension.11-13 The fact evi-