

Category: Hypertension

Effect of inhibition of the prorenin receptor (prp) on the production of cytokines in cells of the immune system in a model of hypertension by nephrectomy 5/6

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Introduction: Hypertension is a condition where blood pressure is persistently high; this pathology affects 1.13 billion people worldwide and 95% of cases do not have an identifiable cause. Several systems are involved in blood pressure regulation. Among them, the renin-angiotensin-aldosterone system (SRAA) and the immune system (SI) stand out, which seem to participate in the onset and permanence of the disease. It has been documented that Angiotensin II (Ang II) induces cytokine production and a proinflammatory state; on the other hand, a new component of RAAS, the prorenin/renin receptor (PRR), seems to have participation in several processes where the system has relevance, such as hypertension itself, diabetes mellitus and some forms of glomerulonephritis. The presence of PRR in several SI cells has also been reported. The role of PRR in the production of cytokines, however, is unknown.

Objective: To evaluate the effect of PRR inhibition, by use of handle peptide, upon secretion of TNF α , IL-6, TGF β , and IL-10 on immune system cells in a renal-origin hypertension model.

Material and Methods: We used a 5/6 nephrectomy model and two experiment times, 7 and 15 days. The model was characterized by measuring blood pressure, quantification of urinary volume, water and food intake, proteinuria and serum and urine creatinine. At 7 and 15 days after nephrectomy and sham surgery, rats were sacrificed with an overdose of sodium pentobarbital, the spleen was removed, and the immune cells were isolated. These were incubated with or without the peptide (1 μ M) for 30 minutes, 1 hour, 6 and 12 hours, and then the mRNA quantification of TNF α , IL-6, TGF β and IL-10 was determined by RT-PCR. All procedures in animals complied with NOM-062-ZOO-1999 and institutional animal care committee.

Results: We found that 5/6 nephrectomy groups had an increase in blood pressure (169/95 mmHg), a decrease in the feed intake, an increase in water consumption and urine volume. In the biochemical parameters, an increase in serum creatinine, a decrease in urine creatinine and as a consequence a decrease creatinine clearance, compared to the Sham group. Quantification of mRNA for the mentioned cytokines, a significant decrease of their expression was observed in hypertensive groups exposed to the peptide compared with the Sham groups.

Conclusions: With 5/6 nephrectomy surgery, it is possible to induce hypertension and renal failure. Blockade of prorenin receptor (PRR), significantly decreases TNF α , IL-6, IL-10 and TGF β expression in hypertensive rats.

Keywords: Hypertension, rats, renal failure, experimental nephrectomy