Chronic kidney disease (CKD) is one of the leading sanitary problems in Argentina. Vasopressin (VP), the main regulator of Aquaporin-2 (AQP2) expression, was suggested as a contributor to the development of CKD. However, the mechanisms of VP contribution remain unknown. We characterized a model of CKD induced by adenine administration and found increased renomedullary AQP2 expression. The aim of this work is to study the effect of Tolvaptan (T; 30 mg/kg/day in the food), a V2 receptor antagonist, on renal parameters and on AQP2 expression in this model of CKD. Male Sprague-Dawley rats were divided in 4 groups: C (Control; fed with standard rat chow powder); CKD (0.25% adenine in food); CKD + T and T; n=3/4 for each group. After 2 weeks, animals were kept in metabolic cages to collect 24 h urine. Blood samples were obtained and the kidneys were processed for further determinations. Results: Media ± SEM; ANOVA followed by Bonferroni was performed. Renal (w/100 g bw): C= 0.36 ± 0.01; CKD= 0.46 ± 0.02 ***##; CKD + T= 0.43 ± 0.02; T= 0.38 ± 0.01. Plasmatic (P) Urea (g/l): C= 0.57 ± 0.08; CKD= 0.82 ± 0.12 *##; CKD + T= 0.58 ± 0.12; T= 0.39 ± 0.03 Urinary (U) urea (g/l): C= 31.67 ± 4.23; CKD= 47.44 ± 7.76*#&; CKD + T= 30.42 ± 1.36; T= 33.66 ± 1.50. P Creatinine (mg/l): C= 6.19 ± 0.31; CKD= 8.86 ± 0.35*#; CKD + T= 6.94 ± 1.11; T= 5.40 ± 0.16. Creatinine Clearance (ml/min): C= 2.01 ± 0.14; CKD= 1.50 ± 0.06*#&; CKD + T= 1.68 ± 0.24; T= 2.60 ± 0.30 AQP2 expression (WB): C= 1.00 ± 0.11; CKD= 1.54 ± 0.19*#&; CKD + T= 0.91 ± 0.12; T= 1.01 ± 0.06. cAMP renomedullary concentration (pmol/mg protein): C= 2.92 ± 0.04; CKD= 5.73 ± 1.7 *#&; CKD + T= 1.32 ± 0.44; T= 1.51 ± 0.32. *p < 0.05 vs. C; ***p<0.005 vs. C; #p < 0.05 vs. T; ##p < 0.01 vs. T; & p < 0.05 vs. CKD + T. Tolvaptan administration prevented the increase in AQP2 expression and improved some of the P and U parameters, suggesting that AQP2 increased expression could be at least one of the mechanisms by which VP is involved in the development of CKD.

0307 - FROM BRAIN TO KIDNEY: CENTRAL AT1 RECEPTORS AND SYMPATHETIC NERVOUS SYSTEM INTERACTION IN SODIUM EXCRETION MECHANISMS

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Central angiotensin II through AT1 receptors (AT1-R), closely interact with sympathetic nervous system (SNS) in the maintenance of renal sodium equilibrium under normal and pathological conditions. Our aim was to unmask the brain AT1-R role in the renal sodium excretion mechanisms and the interaction with the SNS. For these purposes, male Wistar rats with renal nervous ablation/sham and implanted with bilateral cannulae in lateral ventricle, received normosodic (0.4 %) or hypersonic (4 %) diet in metabolic cages for 5 days. The surgical procedures were performed under ketamine/xylaxine (75/5 mg/kg i.p.) anesthesia. The urine was daily collected and water intake was register along the experiment. On day 6 the animals received saline/losartan (AT1-R antagonist 4ug/1 µl) intracerebrally and sacrificed 12 hours later. The parameters analyzed were; in urine: volume, sodium, potassium, water, creatinine and osmolarity to evaluate kidney function; at brain: c-Fos expression in paraventricular (PVN), supraoptic (SON) and subfornical (SFO) nucleus and vasopressin by immunohistochemistry. The data were analyzed by factorial ANOVA. The effects of central AT1-R and the interaction with SNS were observed on water intake and sodium and water excretion. Renal sodium excretion and water intake are under central AT1-R activation depending on renal nervous integrity. AT1-R blockade blunted the increased c-Fos expression induced by hypersodic diet in vasopressinergic neurons (PVN and SON). We conclude that SNS regulates the complex interaction between central angiotensin II, through AT1-R, and vasopressinergic neurons at SON and PVN under sodium overload conditions.

0309 - POSTNATAL INHIBITION OF ENDOTHELIN SYSTEM AND SALT SENSITIVITY GENERATION IN ADULTHOOD: PARTICIPATION OF AVP PATHWAY

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Previous results from our group showed that postnatal inhibition of Endothelin (ET) system generates salt sensitivity (SS) in male adult rats. These animals have an impaired ability to eliminate water and sodium overload, with increased AQP2 and α-ENaC expression and increased blood pressure. It was shown that both transporters are regulated by vasopressin (AVP) through V2 receptors (Stockand JD. Kidney Int. 2010;78(9):849-56) and that adenylyl cyclase 6 (AC6) mediates AVP-stimulated ENaC activity in the kidney (Roos KP et al. J Am Soc Nephrol. 2013;24:218-27). The aim of this work was to investigate the participation of AVP system in the mechanism of SS in this experimental model. We evaluated: V2 receptor expression and AC6 by real time PCR and cAMP production in the renal medulla of adult male Sprague-Dawley rats fed with a normosodic (NS) or hypersodic (HS) diet (the animals had been treated during their postnatal period with a dual ET receptor antagonist [ERA]: bosentan 20 mg/kg/day). Four experimental groups were studied: control males with NS diet (CNS), control males with HS diet (CHS), ERA males with NS diet (ERANS) and ERA males with HS diet (ERAHS). Two-way ANOVA was used for statistics. V2 receptor mRNA expression was significantly lower in ERANS vs. CNS ($p<0.05$) and in ERAHS vs. CHS ($p<0.05$); AC6 mRNA expression increased in ERAHS vs. CHS group ($p<0.05$). Besides, ERANS group had a higher level of AC6 expression than CNS ($p<0.05$). There was a tendency to increase cAMP production (expressed as pmol cAMP/g protein) in ERAHS vs ERANS rats meanwhile that tendency was not seen in CHS vs CNS. The increased renomedullary expression of AQP2 and α-ENaC in ERAHS rats would not be due to a greater level of V2 receptor expression. The increased expression of both transporters in ERAHS rats could be mediated, at least in part, by increased AC6 expression and activity and cAMP production.

0320 - CHARACTERIZATION OF CHRONIC KIDNEY DISEASE IN RATS TREATED WITH LITHIUM

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Lithium (Li) is the drug of choice for long-term prophylactic treatment of bipolar disorder. Chronic kidney disease is one of the complications of prolonged use of Li, which may be more frequent than previously thought. The aim of this study was to evaluate renal damage in rats treated with Li for 3 and 6 months. Forty Wistar male rats were divided into 4 groups (G): control (C) fed ad libitum standard diet or experimental (E) fed the same diet containing 60