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Introduction: Moderate zinc deficiency during fetal and postnatal life is associated with cardiovascular and metabolic disorders in male adult rats. **Objective:** We evaluated if fetal and postnatal zinc deficiency exacerbates the extent of adiposity and metabolic dysfunction induced by high fat diet (HFD) in male adult rats. **Methods:** Female Wistar rats received low(L:8ppm) or control(C:30ppm) zinc diets from pregnancy to offspring weaning. C male offspring continued with C(C) or HFD (60% of total calories)(CH) diets. L offspring were fed L (L) or L and HFD(LH) diets. At day 81, plasma adiponectin levels, oral glucose tolerance test (OGTT)and morphology and oxidative state of retroperitoneal adipose tissue (RAT) were measured. **Results:** CH and LH had higher body weight (C:418±13;CH:505±9*;L:401±10;LH:444±5ǂǂg) and showed an increase of RAT weight, a decrease of adipose cells density and adipocytes hypertrophy (C:4958±388;CH:9621±586*;L:8130±448*; LH:11833±440ǂǂμm²). LH showed lower body weight and higher adipocyte area than CH. HFD induced a decrease of plasma adiponectin levels(C:8.3±0.6; CH:6.5±0.4*;L:8.6±0.9; LH:6.4±0.1ŧμg/ml) and functional changes in RAT like a decrease of SOD and catalase antioxidant activities and an increase of TBARS (C:0.21 ±0.02;CH:0.38±0.04*;L:0.40±0.06*;LH:0.43±0.05*pmol MDA/mg prot).L rats showed an increase in oxidative stress in RAT. LH and CH showed an increase of OGTT curve area(C:27797±504;CH:30827±971*;L:27826±809; Lh:34851±1344ŧǂmin.mg/d). L, LH and CH showed higher plasma glucose levels after 3 hours of glucose overload. Zinc deficiency exacerbated alterations induced by HDF. Two way ANOVA, Bonferroni post-test,mean±SEM,*p<0.01 Vs C ,ŧp<0.01 Vs L and ǂp<0.01 Vs Ch. N=8 per group **Conclusion:** Zinc deficiency and HFD induce alterations in glucose metabolism and RAT, increasing the predisposition for the development of metabolic diseases in adult life. Zinc deficiency during fetal and postnatal life exacerbates some of these changes.

NEFROLOGÍA

526. (118) **ANGIOTENSIN II EFFECT ON MICROTUBULE DYNAMICS IN RENAL TUBULAR CELLS**

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Tubular remodeling in response to acute kidney injury (AKI) involves the dedifferentiation and regeneration of the remaining epithelial tubular cells. Microtubules (MT) dynamic instability plays a central role in renal repair after AKI. Angiotensin II (AGII) has two main receptors, AT1R and AT2R, which mediate dissimilar effects. During ischemia reperfusion (IR), AT1R mediates a pro-fibrotic response, whereas AT2R facilitates the recovery of the kidney function (our unpublished data). The aim of this work was to investigate AT1R and AT2R participation in the regulation of factors associated with MT dynamic instability that could affect the epithelial tubular cell-response to an AKI. MDCK cells were grown in conditions that assure a well-defined epithelial polarity and treated with 0.5 μM AGII (AGII), AGII plus the AT1R antagonist losartan (5 μM) (AGII + los), or 1 μM C21, AT2R agonist (C21). EB1 is a central regulator of MT dynamic instability that participates in tubulogenesis. AGII induced an increase in EB1 levels which was mimicked by C21 (+50%*, n=3) and was not prevented by Los. α-tubulin acetylation is linked to the presence of stable MT. Our preliminary data showed that activation of AT2R, but not AT1R, decreased the fraction of acetylated α-tubulin (Control (C): 0.55 ± 0.05; AGII: 0.25 ± 0.05; AGII + Los: 0.06 ± 0.03; C21: 0.14 ± 0.03, n=2). Primary cilia are organelles of tubular cells that are down-regulated during AKI-tubular remodeling, whose length directly correlates with the levels of acetylated α-tubulin. Analysis of the primary cilia showed that through AT1R AGII increases whereas through AT2R it decreases the cilia length (in μm: C: 2.8 ± 0.1; AGII: 3.1 ± 0.1; AGII + Los: 2.4 ± 0.1 *; C21: 2.3 ± 0.1 *, n>80). Overall, our results indicate that AGII increases MT dynamic instability through AT2R, which would favor tubular remodeling. Our future studies will evaluate the relevance of these effects in the response to IR induced AKI. * p<0.05 vs C.

527. (190) **RENAL EXPRESSION OF Na-K-Cl COTRANSPORTER 2 AND AQUAPORIN 2 IN RATS WITH ACUTE OBSTRUCTIVE CHOLESTASIS**

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Na-K-Cl cotransporter 2 (NKCC2) and Aquaporin 2 (AQP2) are proteins localized in the apical membrane of the renal thick ascending limb of Henle's loop (TAL) and the collecting duct (CD), respectively. NKCC2 performs active transport of NaCl in the TAL, which contributes to create the corticomedullary concentration gradient. The interstitial hypertonicity achieved in the renal medulla leads to water absorption through the AQP2 water channel in the CD. In acute obstructive cholestasis (OC), increases in urinary flow and in the fractional excretion of osmolytes were observed. In order to evaluate the roles of NKCC2 and AQP2 in the modifications of renal handling of water and osmolytes detected, renal expression of NKCC2 and AQP2 was evaluated in rats with OC. Bile duct ligation of 21 h (BDL, n=4) was performed in Wistar rats. Sham-operated rats served as controls (S, n=4). Apical membranes were isolated from renal cortical (C_{AM}) and medullary (M_{AM}) tissue. The expression of NKCC2 and AQP2 was evaluated by immunoblotting and immunohistochemistry. %NKCC2: C_{AM}: S=100±8 BDL=71±8*; M_{AM}: S=100±4 BDL=91±4. %AQP2: C_{AM}: S=100±10 BDL=98±13; M_{AM}: S=100±3 BDL=81±4* (*p<0.05). The immunohistochemistry confirmed the data obtained by immunoblotting. In BDL rats, NKCC2 protein expression remained unchanged in M_{AM}, while it decreased in C_{AM}. AQP2 protein expression decreased in M_{AM} of BDL rats, where it is mostly localized. The decrease in the expression of NKCC2, in C_{AM} of BDL rats, could lead to a decrease of the interstitial hypertonicity by reducing the reabsorption of sodium, potassium and chloride and, consequently, avoiding the subsequent reabsorption of water. The decrease in AQP2 expression could contribute to increase the urine output, by decreasing the reabsorption of water in the CD.

528. (546) **EFFECTS OF THE ANGIOTENSIN II TYPE 2 RECEPTOR (AT2R) AGONIST, COMPOUND C21, ON THE EXPRESSION OF APELIN AND ITS RECEPTOR APJ IN THE POST-ISCHEMIC KIDNEY. POSSIBLE INTERACTION BETWEEN RENIN-ANGIOTENSIN AND APELINERGIC SYSTEMS.**

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In previous experiments we observed that pretreatment with the AT1R antagonist, losartan, or the AT2R agonist, C21, prevents glomerular filtration drop, loss of sodium reabsorption, and loss of brush border in a renal ischemia/reperfusion (I/R) model. On the other hand, we have found that I/R decreases the expression of the adipokine apelin; and in turn the pretreatment with apelin prevents the impairment of proximal tubular transport and has anti-inflammatory effects in this model. We also demonstrated that losartan prevents the decreased expression of apelin and its receptor APJ. The aim of this study was to evaluate the effects of the AT2R agonist, C21, on apelin and APJ mRNA levels in an I/R model. Male Wistar rats (5-6 per group) underwent unilateral renal ischemia for 40 min followed by 24 h of reperfusion (I/R) or sham surgery (C). C21, 0.3mg/Kg/d i.p., or its vehicle was administered for two days prior to I/R. mRNA levels were analyzed by qRT-PCR. Apelin mRNA levels decreased in I/R. This decrease was prevented with C21 pretreatment (%change fold C: C+C21=+15; I/R= -92*; I/R+C21= -12#; *p<0.05