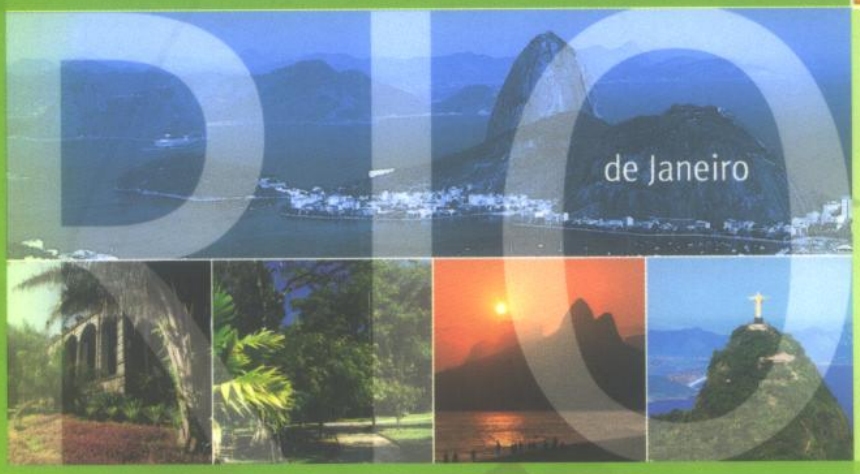
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April 21-25, 2007
Rio de Janeiro, Brazil

WCN 2007
Book of Abstracts

RIO – Renal Insights and Opportunities

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and muscle strip contractile function were assessed. Evaluation of myocardial gene expression of cytokines, growth factors, calcium-handling and myofilament proteins was also performed. Statistical analysis was performed by one-way ANOVA followed by Student's t-test for unpaired comparisons.

Results: PAN injection consistently resulted in massive proteinuria and impaired creatinine clearance. Sodium retention was observed at day 7, while a negative sodium balance was present at day 14 with no changes in blood pressure or end-diastolic pressures. Skeletal and cardiac muscle atrophy were present in PAN treated animals 14 days after injection. This was accompanied by disturbed left ventricular (LV) systolic and diastolic function, and impaired performance of LV isolated muscle strips. Increased LV mRNA levels of cytokines (IL-1B; and TNF-alpha) and decreased expression of SERCA2a, with phospholamban upregulation, were also observed.

Conclusion: PAN nephrosis associates with cardiac atrophy in the absence of altered loading conditions. This resulted in myocardial dysfunction in the presence of local cytokine activation and disturbed calcium-handling gene expression. These results suggest that, in the NS, systemic inflammatory activation and protein wasting induce cardiac remodeling and dysfunction.

M-PO-0622 Altered cytokine/chemokine (CK/CC) profiles in hemodialysis subjects (HDs) with hemodialysis catheters (HDC) and fistulae (F)

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Introduction: CV disease and sepsis account for 65-80% of the annual mortality among HDs. Malnutrition is a contributory factor. CK/CC's are implicated in CV damage, infection, and malnutrition. To test the hypothesis that HDC may induce inflammation without manifestations of infection we measured a broad array of cytokines and markers of infection in HDs with HDC or fistulae, (n=9 each).

Methods: Exclusion criteria were active malignancy, abnormal liver function, infections in the prior 6 weeks, chronic viral infections, immunosuppressive drugs and hematologic disorders. No evidence of infection (by leukocyte count, temperature, observation, etc) was observed in both groups of subjects. Blood was collected in EDTA before and after midweek HD on two consecutive weeks and plasma was frozen at -70C. CK/CC concentrations were analyzed with xMAP technology using a Beadlyte® System (Upstate:Chemicon:Millipore) with a Luminex®100™ System. Statistical comparison between the 2 groups was done by the Mann-Whitney U Test. (Predialysis concentrations, N=normal level, decimal points omitted, M±SD, * p<0.05-0.001 between F & HDC). [GM-CSF = granulocyte-macrophage colony stimulating factor, IL=interleukin, MCP=monocyte chemoattractant protein, TNF= tumor necrosis factor and RANTES = regulated on activation normal T-cell expressed and secreted].

Results: Substantial increases in CK/CC were observed in HDs, consistent with recent reports in literature. However there were statistically significant higher concentrations of CK/CC in HDC v. the fistulae group suggesting that HDC contribute to alteration of CK/CC profiles.

Table:

Cytokines and Chemokines in subjects with F and HDC

	GM-CSF (pg/ml)	IL-6 (pg/ml)	IL-8 (pg/ml)	IL-10 (pg/ml)	MCP-1 (pg/ml)	MIP-1a (pg/ml)	TNF (pg/ml)	RANTES (pg/ml)
N	<7.8	<3.12	1.75 - 7.7	<7.8	153	<46.9	1.98	849
F	28±43	24±34	40±35	2±2	118±178	250±221	16±29	165±51
HDC	102±146*	68±109*	81±100	8±10*	345±298*	533±270*	16±24	429±571*

*(Decimal points omitted, M±SD, * p<0.05-0.001 between F & HDC)*

Conclusion: Whether the difference between F and HDC is related to subclinical catheter infection or luminal biofilm is not yet clear and awaits clinical correlation. The significantly higher CK/CC in HDC could indicate a higher cardiovascular risk in HDs with HDC

M-PO-0623 Influence of annexin A5 and VCAM1 concentration on the function of the endothelium at patients with chronic kidney disease

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Introduction: The mechanisms of developing and progression of the chronic kidney disease (CKD) are diverse. The great attention among them is devoting to vascular disorders, especially to endothelial dysfunction (ED). The important role at the developing of the ED is playing factors which rise the sensitivity of the vascular wall to the different stimulus an determining apoptosis rate. The aim of the study: to investigate the influence of the leve of VCAM1 and annexin A5 (A5) on the function of the endothelium at the patients with CKD

Methods: 52 patients with CKD and without clinical signs of atherosclerosis (22 men an 32 women at the age of 46.4+2.3 years) were investigated. The glomerular filtration rat (GFR) was calculated by MDRD formula. The concentration of A5 and VCAM1 was determine by immunoenzime method. The thickness of intimamedia complex and the volume velocit at the microvessels of the skin (Qas, ml/s) was determining by dopplerography. The functio of the endothelium was inspected during the pharmacological probes with acetylcholin (Ach) and nytroglycerine (Ng).

Results: The ED was determined at all of the patients. At the same it was revealed gradu elevation of the concentration of the A5 during the progression of CKD: CKD 1 0,187+0,0 ng/ml, CKD 2 1,51+0,19 ng/ml, CKD 3 2,57+0,39 ng/ml, CKD 4 6,18+0,67 ng/ml, CKD 8,19+0,83 ng/ml, p<0,05. The concentration of VCAM1 rise at first (CKD 1 244+58 ng/m CKD 2 384+61 ng/ml, CKD 3 536+82 ng/ml, p<0,05), and then decreased (CKD 4 198+4 ng/ml, CKD 5 96+21 ng/ml, p<0,05). The interrelation between levels of A5 and VCAM1 an parameters of lipidogram and intima media complex was not revealed. At the holding multiple regression was revealed the following model for the A5 level: A5=18,9-0,08*GFI ml/min-0,24*Albumin, g/l-maximal increment Qas at the probe with Ach, %; R2=0,50 p<,05. At the holding of multiple regression was revealed the following model for the VCAM level: VCAM1=798,9-467,9*maximal increment Qas at the probe with Ng, % +5,8*puls pressure, mm Hg; R2= 0,372 F=6,51 p<0,02.

Conclusion: The decrease of the kidney function accompanies with develops of ED at fir due to disturbances of the intercellular interrelations, and then due to apoptosis acceleratio

M-PO-0624 The measurement of biophotons from the plasma of hemodialysis patients

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Introduction: Biophton is being emitted from a living object. Its number could be a few p 1 cm2 or it might be counted in thousands. These non-thermal photons are believed come from imperfections of metabolic activity in living organism. One of these metabo activities is known to be free radicals and peroxides. Therefore, the patients with pathogenesis that is known to be related to free radicals, such as longstanding old diabe patients, long-term undergoing hemodialysis, were expected to emit more biophtons th the normal population. We measured 43cases, who is undergoing hemodialysis in o hospital.

Methods: We measured spontaneous photon emission from the plasma of long ter undergoing hemodialysis patients and compared with those from normal plasma. For t detection of extremely weak photon emission from the sample we used a sensiti photomultiplier tube (PMT) attached to a dark chamber.
2cc of the plasma was separated and inserted for the measurement at the photomultipl for 10 minutes. The PMT attached to a dark chamber, responsive to the spectrum from 3 nm to 650 nm, is connected with high voltage equipment (1600 V) and the computer th analyze the data. The plasma was separated immediately and transferred to the dark roo under the cool temperature for the measure within 3 hours.

Results: 1). 43 cases we measured were composed of 24 male cases and 19 female cas The average age was 50.4 ± 16.8 years old and aged cases more than 65 years were cases. The average duration of hemodialysis was 60.8 ± 12.7 months.
2). The mean of measured biophotons of patients undergoing hemodilysis was 580.28 352.02 counts/min/cm^2.
The normal population showed 90.34 ± 45.07 counts/min/cm^2. The measured counts patients undergoing hemodialysis were significantly higher than normal population (P<0.0
3). The measured biophoton value was not correlated with the age, vital sign, the durati of hemodialysis, the amount of ultrafilteration during HD, whether combined state w diabetes, the level of hemoglobin, serum albumin and various laboratory data.

Conclusion: The counts of biophoton are increased significantly in chronic renal patie undergoing hemodialysis and this result isn't correlated with other influential clinical facto

References: Shinichi A., Toshiyuki N., Masaki K., Masashi U., Haruo W., Hiroshi S., Humic Hydroxyl Radical-induced characteristic chemiluminescent spectra from plasma hemodialysis patients.

M-PO-0625 Darbepoetin administration after ethanol toxicity: An experimental study in rats

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Introduction: Darbepoetin is used in treatment of anemia of chronic renal insufficiency. It is not known exactly its neuroprotective effects. Neuron-specific enolase (NSE) is a dimeric isoenzyme of the glycolytic enzyme enolase. S100 beta is a small, acidic, calcium binding protein which is highest in concentration in the vertebrate nervous system. S-100B is found in high concentrations in astroglial and Schwann cells. In this study, the effects of darbepoetin administration in ethanol toxicity were investigated.

Methods: 44 Wistar-albino adult rats were divided into four groups: Saline-treated group(S) (n=10), Saline-Darbepoetin-treated group (SD)(n=10), Ethanol- treated group (ET) (n=12), Ethanol-Darbepoetin-treated group (ETD) (n=12). 20% ethanol solution prepared with sterile saline was administered to rats ip at a dosage of 2.5 g/kg for two times with a 2-h interval. Darbepoetin was administered ip just after the second dose of ethanol at a dosage of 10 µg /kg. Twenty-four hours after the first dose of ethanol, the animals were decapitated under Ketamine (5-10ml/kg). Brain tissue's oxidant-antioxidant parameters which are Malonyl dialdehyde (MDA), Cu-Zn Superoxide dismutase (Cu-Zn SOD), Glutathione(GSH) and Catalase(CAT); neuronal damage markers which are S-100Beta (CanAg S100 EIA REF 708-10, Sweden) and Neuron Specific Enolase(NSE) (CanAg NSE EIA REF 420-10) was evaluated.

Results: Ethanol increases significantly S100 levels ($p<0.05$) in ET. Darbepoetin administration decreases significantly NSE levels in ETD ($p<0.01$).

Conclusion: Darbepoetin might be protecting against ethanol induced neurodegenerative effect. It might be beneficial effects in treatment of neuropathy and anemia of uremic patients

M-PO-0626 Plasma concentrations of eotaxin: Differences between hemodialysis catheter (HDC) and fistula (F) hemodialysis subjects (HDs)

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Introduction: Eotaxin stimulates chemokine receptor-3 to produce reactive oxygen species via the extracellular signal-regulated kinases (ERKs), ERK1 and ERK2. Eotaxin and CCR3 are both upregulated in human atherosclerosis. In vitro tumor necrosis factor (TNF) and IL-8 have been shown to stimulate eotaxin induced ROS, which in turn have been detected in increased concentrations in HDs. No studies have examined whether HDC differ from F in eotaxin concentrations.

Methods: We measured a broad array of cytokines and other markers of infection in HDs with HDC or F, (n=9 each). Exclusion criteria were active malignancy, abnormal liver function, infections in the prior 6 weeks, chronic viral infections, immunosuppressive drugs and hematologic disorders. No evidence of infection (by leukocyte count, temperature, observation, etc) was observed in both groups of subjects. Blood was collected in EDTA before and after midweek HD on two consecutive weeks and plasma was frozen at -70C. CK/CC concentrations were analyzed in duplicate with xMAP technology using a Beadlyte® System (Upstate:Chemicon:Millipore) with a Luminex®100™ System. Statistical comparison between the 2 groups was done by the Mann-Whitney U Test. (N=normal level, IL = interleukin, IP=interferon inducible protein-10, INFg = interferon gamma, MIP = macrophage inflammatory protein 1 alpha]

Results: In all HDs substantial increases in CK/CC were observed consistent with recent literature in HDs. Significantly higher concentrations of eotaxin were observed in HDC v. F group with no correlation to TNF or IL-8 concentrations.

Table:

Pre-Dialysis Eotaxin and other CK/CC in Subjects with F and HDC

	Eotaxin (pg/ml)	IIL-4 (pg/ml)	IL-6 (pg/ml)	IL-8 (pg/ml)	IP-10 (pg/ml)	INFg (pg/ml)	MIP1a (pg/ml)	TNF (pg/ml)
N	125	<0.25	<3.12	1.75-7.74	96	<15.6	<46.9	1.98
F	256±400	1±0.3	24±34	40±35	135±104	16±24	250±221	16±29
HDC	542±496*	5±10	68±109*	81±100	241±83*	40±58*	533±270*	16±24

*(Selected decimal points omitted, M±SD, * p<0.05-0.001 between F & HDC).*

Conclusion: These findings suggest that eotaxin concentrations may be driven by factors in addition to IL-8 and TNF. Eotaxin is of major interest in cardiomyopathy and atherosclerosis and needs further study in HDs.

2.3 Vascular Biology and Inflammation, Immunology and Pathology - Extracellular Matrix, Fibrosis, Renal Scaring

M-PO-0627 ADAM17 expression in human renal disease is associated with structural deterioration and renal function decline

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Introduction: ADAMs (A Disintegrin And Metalloproteinase) are crucially involved in shedding growth factors from the cell membrane. ADAM17 (TACE; TNF-alpha converting enzyme) is known to shed members of the EGF family, including neuregulin, HB-EGF and TGF-alpha. Recently, ADAM17 was shown to be involved in angiotensin II-induced renal damage in mice through shedding of TGF-alpha. Pharmacological ADAM17-inhibition in these mice substantially reduced renal inflammatory and fibrotic lesions, identifying ADAM17 as a promising target of intervention in human renal disease. However, no data on TACE in the human kidney exist yet.

Methods: We studied ADAM17 in 18 developing kidneys, 8 normal kidneys and 72 inflammatory and fibrotic renal diseases, using paraffin-embedded human renal tissue. RNA in situ hybridization was applied to detect ADAM17 mRNA and levels of expression were semi-quantitatively scored. Parameters of renal structural damage (mesangial matrix expansion (MME), focal glomerulosclerosis (FGS), interstitial fibrosis (IF) and macrophage infiltration) and renal function (estimated GFR) from all patients at the time of biopsy or nephrectomy were studied for associations with ADAM17 expression using the Kruskal-Wallis test. We performed double-immunofluorescence stainings to identify colocalization between ADAM17 and its possible substrates from the EGF family.

Results: ADAM17 mRNA was abundantly present in the nephrogenic blastema and nephrogenic vesicles of developing human kidneys, suggesting developmental regulation. ADAM17 was constitutively expressed in normal human kidneys, with highest expression in distal tubuli. When compared to normal human kidneys, ADAM17 was de novo expressed in proximal tubuli, peritubular capillaries and the glomerular mesangium of renal diseases and strongly upregulated in all other renal structures. Glomerular mesangial and endothelial ADAM17 was significantly associated with MME, FGS and glomerular macrophage infiltration (all $p<0.01$). Furthermore, peritubular capillary and proximal tubular ADAM17 was significantly associated with IF and interstitial macrophage infiltration (all $p<0.01$). Finally, both glomerular and interstitial ADAM17 were significantly associated with renal function decline ($p<0.05$). We additionally showed that ADAM17 was coexpressed with TGF-alpha, and also HB-EGF and neuregulin, in human renal fibrotic lesions.

Conclusion: Our data suggest a modulatory role for ADAM17 in human renal disease through shedding of ligands for the EGFR. Receptor binding and activation may then induce proinflammatory and profibrotic cascades. These data are in line with experimental data and suggest a promising position of ADAM17 as target of intervention in human renal disease.

M-PO-0628 Delipidated albumin stimulates tubular epithelial mesenchymal transformation (EMT)

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Introduction: Albuminuria is a major risk factor for the progression of chronic kidney disease (CKD). Emerging evidence indicates that mature proximal tubular epithelial cells (PTCs) can undergo EMT, a phenotypic conversion that is fundamentally linked to the pathogenesis of renal interstitial fibrosis. Evidence suggests that a large proportion of interstitial fibroblasts are originated from PTCs via EMT in diseased kidney. Selective blockade of EMT in a mouse model reduces fibrotic lesions. This study explores the intriguing hypothesis that exposure of PTCs to albumin in vitro induces EMT

Methods: Normal rat PTC line (NRK52E) was cultured on plastic or collagen type I- coated plates until they reached 70% confluency or complete confluency. The cells were then starved for 24hr and then exposed to delipidated bovine serum albumin (dBSA) for six days (dBSA: 0.5,1,5,10,15 and 20mg/ml). The media was changed after day three, at which point fresh albumin was added. EMT was assessed by Western blot, immunoflorescence and light & electron microscopy for the neo-expression of alpha-SMA and down-regulation of E-cadherin.

Results: Exposure to dBSA led to binding and uptake by PTCs in culture. Light microscopy showed changes involving hypertrophy with cells becoming elongated. Immunohistochemical staining showed that the addition of dBSA to confluent and sub-confluent cells caused a loss of the expression of the epithelial marker E-Cadherin and the de novo expression of the mesenchymal marker alpha-SMA in a dose dependent manner. In