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Can Losartan and Enalapril Prevent DNA Damage in Renal Transplant Recipients with Renin-Angiotensin System Polymorphisms?

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Introduction. Oxidative injury of DNA may be supervised by renin-angiotensin system (RAS). In the study the effect of losartan (L) and/or enalapril (E) on reduction of DNA damage was evaluated regarding to renin-angiotensin system polymorphisms.
Methods. After determination of genotypes of the angiotensin converting enzyme (ACE I/D), angiotensinogen (AGT M235T) and angiotensin II type 1 receptor (ATR1 A1166C) by polymerase chain reaction, 64 renal transplant recipients randomly allocated to one of the four groups: first (13 patients) and second (20 patients) groups were treated with E (E+: 10 mg/d) and L (L+: 50 mg/d) alone respectively. The third group (13 patients) as positive control received E+L (E+L+: 10mg/d + 50 mg/d) and the forth group (22 cases) received no medication as negative control (E-L-). The subjects were followed for 8 weeks. After 2 weeks washout period, E group changed to L and vice versa as cross-over design. They were followed for another 8 weeks. Before and after 2, 4 months treatment, we checked the serum 8-OHdG and Malondialdehyde (MDA) as biomarkers of DNA damage and lipid peroxidation respectively.
Results. Serum 8-OHdG levels were significantly decreased after 2 months of treatment in the E+L+ and L+ groups (6.07±1.1 ng/mL to 3.6±0.58 ng/mL, P = .000; 5.30 ± 0.86 ng/mL to 3.6 ± 0.47 ng/mL, P = .001 respectively). 8-OHdG level was not decreased significantly in E+ group (6 ± 1.19 ng/mL to 4.7 ± 1.39 ng/mL, P = .07) and E-L- group (5.30 ± 0.84 to 5.6 ± 0.88 ng/mL, P = .11). In the 4th month of treatment the same results was found. Patients with DD genotype of ACE and CC genotype of ATR1 had higher serum 8-OHdG levels at the baseline (P = .02, P = .002 respectively). Only TT genotype of AGT had the most antioxidative role regarding to kind of above treatment regimens (P = .01). We found a remarkable correlation between MDA and DNA damage levels before and after intervention (r = 0.48, P < .001; r = 0.35, P = .006).
Conclusions. Although serum 8-OHdG level is higher in DD and CC genotypes of ACE and ATR1 polymorphisms; the protective effects of L+ and E+L+ on DNA breaks are surprising regarding to the RAS genotypes. TT genotype of AGT had important role in prevention of DNA break regarding to kind of treatment.

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The Evaluation of Antioxidant Defense Systems in Chronic Peritoneal Dialysis Patients

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Introduction. Oxidative stress due to overproduction of reactive oxygen species and impairment in antioxidant defense has been suggested as possible factors contributing to the pathogenesis of atherosclerosis in ESRD patients. The aim of this study was to evaluate changes in markers of oxidative stress in chronic peritoneal dialysis patients.
Methods. Chronic ambulatory Peritoneal Dialysis (PD) patients who were regularly admitted to our clinics were included if chronic peritoneal dialysis was initiated for more than 2 months. Diabetic patients were excluded. Those patients who had any febrile or infectious episode or hospitalization during the last month before the beginning of the study were also excluded. As control group, healthy adults with no evidence of clinical cardiovascular disease, hypertension, hyperlipidemia, diabetes mellitus and kidney disease by means of history / physical examination and paraclinic studies were selected. Erythrocyte glutathione as a major antioxidant and plasma level of glutathione peroxidase (GPx) that catalyzes the oxidation of glutathione in exposure to oxidative stress, and glutathione reductase (GR) that catalyzes oxidized glutathione to reduced form and total antioxidant capacity were determined spectrophotometrically.
Results. Twelve PD patients and 17 healthy controls (age range: 25-60 and 22-53 years, respectively) were enrolled. Glutathione levels and GPx activity were markedly lower in patients than in controls (1.17± 0.28 vs 1.42 ± 0.25 µmol/mL, P < .05 and 57.1 ± 21.8 U/L versus 142.5 ± 33.7 U/L; P < .05, respectively). Higher levels of GR activity were noted in patients (57.5 ± 16.4 U/L versus 32 ± 9.4U/L, P < .05). Mean of total antioxidant capacity was 0.60 ± 0.09 µmol/mL in the patients group versus 0.47± 0.11 µmol/mL in controls (P < .05).
Conclusions. Decreased glutathione levels and alteration in the activities of its related enzymes may imply increased oxidative stress. Higher total antioxidant activity may be due to vitamin E supplementation in dialysis patients

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Comparison Between Light and Electron Microscopic Findings in 30 Patients With Lupus Nephritis

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Introduction. The diagnosis and clinical management of patients with lupus nephritis can be a challenge from clinicopathologic point of view. The kidney biopsy specimen is used for determination of the immunomorphologic characteristics, patterns and distribution of renal involvement, determination of activity and chronicity indices which is useful in patients management, initial diagnosis of patients with SLE who at the time of biopsy lack either diagnostic clinical manifestation and or serologic markers. Another role is evaluation of renal dysfunction in transplanted patients when lupus has occurred in renal allograft. The aim of this study is correlating the findings of light, immunofluorescent and electron microscopy in thirty patients with lupus nephritis.
Methods. The kidney biopsies of thirty patients with SLE were studied for purpose of correlating the findings of light (LM), immunofluorescent and electron microscopy (EM). We studied 30 parameters in light microscopy sections, 5 parameters in semi -thin and EM sections and IgG, IgM, IgA, C3, C4 and fibrinogen in different structures of specimens by immunofluroscent microscopy. The P value and measurement of agreement of kappa was calculated.
Results. In 25 cases LM and EM was correlated completely including lupus nephritis class, activity and chronicity indices and presence or absence of immune complex deposition. In 5 cases discrepancy between light microscopy and electron microscopy diagnosis have been found. Three cases were classified as class III according to LM and class II by EM. LM reevaluation of all three cases shows focal and segmental endocapillary cell proliferation with neutrophilic infiltration. We found that LM study is cornerstone in the focal lesions because of the limited glomeruli in EM. One case of class IV by LM, in EM shows massive (grade III) subepithelial depositions and grade I subendothelial deposition and classified it as Class V + VI. In LM findings cellular crescent in six glomeruli, severe endocapillary cell proliferation with activity index (16/24) was detected. So the correct diagnosis was Class V + VI. The last case in LM classification was classified as IV. LM revealed moderate mesangial cell proliferation with obliteration of lumens. In EM, we had three glomeruli which all of them show mesangial cell proliferation, grade II mesangial deposition, with one focus of small (grade I) subendothelial deposition. According to the above mentioned findings the EM class of patient was class II.
Conclusions. The EM study in cases with lupus nephritis has a great role in classification and management of patients with lupus nephritis and most of the time give valuable data but EM technique is expensive and a non-rapid method .We found that in our center most of the time agreement between LM and EM findings is present. We recommended taking biopsy for EM study with appropriate fixation and storage for ultra-structural evaluation and use it if it is necessary .We found that there is agreement between EM and semi-thin sections for detection of exact site of depositions as well as their grading. Study of semi-thin sections by LM can demonstrate the deposits which are observed on EM.

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Novel Mutation of SMARCAL 1 Causes Schimke Immuno Osseous Dysplasia

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Introduction. Schimke immuno- osseous dysplasia (SIOD) is a rare autosomal recessive disorder characterized by steroid resistant nephrotic syndrome, immune deficiency and osseous dysplasia. SMARCAL1 is the gene responsible for SIOD but the underlying pathophysiologic mechanism is unclear. We report two cases of SIOD from south of Iran associated with the novel mutation in SMARCAL1 gene in the second case.
Methods. DNA samples of the alive patient # 2 and his family members analyzed for SMARCAL 1 gene sequence. The coding exons of SMARCAL1 were amplified from genomic DNA. The amplification products were purified and sequenced by automatated dideoxy sequencing using fluorescent dye primers.
Results. A 6-year-old girl and f4-year-old boy presented with generalized edema. Considering proteinuria, hypoalbuminemia and hyperlipidemia nephrotic syndrome was diagnosed Kidney biopsy showed minimal change nephrotic syndrome in the first patient but was not conclusive in the second one. On physical examination, they had peculiar faces, short neck, disproportionate short stature, low growth indices, and protruded abdomen. Bone survey revealed platyspondyly of cervical spines, beaking of thoracolumbar vertebrae, epiphyseal dysgenesis of femur and shallow acetabulum and generalized osteopenia. Laboratory investigations showed T cell deficiency (low CD4), hypothyroidism, and periodic lymphopenia. The homozygous mutation C.1682G>A was detected in the second patient. Both the father and the mother and also one of his siblings were heterozygous for this mutation. Patient one expired at 10.5 years of age when she was on maintenance hemodialysis and patient two, who is on supportive therapy with Enalapril and Atorvastatin, recently experienced an

episode of transient ischemic attack (TIA).
Conclusions. It is emphasized that this disorder should be considered in children with steroid resistant nephrotic syndrome and bone dysplasia.

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Evaluation of Intravenous Iron Treatment on Oxidative Stress in Hemodialysis Patients: Role of Inflammation

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Introduction. Parenteral iron (IVIR) as a choice treatment of iron deficiency may aggregate oxidative stress already present in hemodialysis (HD) patients. Inflammation induced and IVIR-induced protein oxidation was shown in HD patients. Oxidative stress related inflammation in HD patients can induce activation of oxidative burst enzymes in phagocytes and contribute significantly to high prevalence and severity of atherosclerosis and infections and can decrease the survival rate and affect the quality of life of HD patients. This study aimed to clarify the role of IVIR therapy on protein oxidation and its relation to inflammation in these patients.
Methods. We examined the effect of IVIR administration on markers of protein oxidation and inflammatory factors as high-sensitivity (HS) CRP in 30 HD patients (16 males and 14 females; mean age, 52.37 ± 1.20 years) given IV iron (100 mg of iron sucrose for half hour immediately after HD) and 30 HD patients whom not received iron (16 males and 14 females; mean age, 48.27 ± 9.59) as control group. Blood samples were drawn Pre-HD, Pre-IVIR, and post-IVIR (30 minute after dialysis) for iron, transferin, ferritin, markers of free radical activities: thiol groups, malondialdehyde (MDA) and HS-CRP.
Results. HS-CRP in Iron group increased from7.27 ± 7.9 to 7.54 ± 7.47 immediately after HD and to 8.34 ± 8.22 after IVIR administration .Thiols level in Iron group decreased from 35.81 ± 17.29 to 27.54 ± 13.10 ($P < .001$) immediately and increased to 37.10 ± 15.60 ($P < .05$) after IVIR..MDA in Iron group decreased from 3.00 ± 1.24 to 2.10 ± 0.77 ($P < .001$) after HD and increased to 3.28 ± 0.98 ($P < .001$) after IVIR. In control group Thiols and HS-CRP and MDA decreased immediately and 30 minutes after HD. MDA levels before and end of HD and 30 minutes after HD were significantly higher in Iron group ($P < .05$).There was significant correlation between MDA and HS-CRP after HD ($P < .001$) and after IVIR therapy ($P < .001$) in Iron treated group (the regression was meaningful).
Conclusions. IVIR treatment increases oxidative stress in HD patients and it positively correlates with inflammatory factors like HS-CRP.

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Association Analysis of Autosomal Dominant Polycystic Kidney Disease in Familial Type in East-Azerbaijan

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Introduction. Familial form of Polycystic Kidney Disease which is inherited as an autosomal dominant pattern is one of the most common form of kidney disease. The main manifestation of this disease is the presence of growing cysts in kidney which results in malfunction of kidney. The frequency of disease is one in 1000 living birth. Mutation in one of the three different genes could result in developing polycystic kidney disease. Genetically analysis has been able to identify two of the genes, PKD1 and PKD2, located on chromosome 16 and chromosome 4, respectively. The location of the third gene remains unrevealed and the frequency of families affected due to the mutation on this gene is very low. By applying microsatellites tightly linked to the identified polycystic kidney disease genes, affected families referred from East Azerbaijan were genetically analyzed.
Methods. Families with at least three affected members by polycystic kidney disease were studied. Polymorphic microsatellites from the regions of PKD1 and PKD2 were selected by studying the members of these families. All members of the families were investigated by the polymorphic markers to study linkage analysis.
Results. Out of 13 families with 99 members referred by specialists, 7 families with 75 members were selected on the base of availability. Disease in three of these families showed linkage with PKD2 gene and in one family linkage was found between the disease and PKD1 gene. In another family linkage was observed with neither PKD1 nor PKD2 genes. None of the markers were informative in two of the families; therefore these families were excluded from the studies.
Conclusions. Most of the families with polycystic kidney disease from North West of Iran showed linkage with PKD2 gene. One of the families did not show linkage with any of the known genes. In this family, disease could be due to mutation in the third gene which remains to be identified.