EXTRACELLULAR VESICLES DERIVED FROM MESENCHYMAL STEM CELLS INHIBIT TUBULAR INJURY, T CELL PROLIFERATION AND PROMOTE REGULATORY T CELL DIFFERENTIATION THROUGH TRANSFER OF SPECIFIC RNAs: PROTECTIVE ROLE IN T-CELL-MEDIATED KIDNEY GRAFT REJECTION

Vincenzo Cantakuppi1, Michela De Lena1, Silvia Beltramo1, Silvia Ferrario1, Sergio Delepiane1, Federico Figolin1, Stefania Bruno1, Luigi Biancone1, Giuseppe Paolo Segoloni1, Cin Tetté2 and Giovanni Camussi1

Nephrology, Dialysis and Renal Transplantation Unit of University of Torino Turin Italy, *Freuenz Medical Care Bad Homburg Germany

Introduction and Aims: Mesenchymal stem cells (MSCs) are known to exert regenerative and immunomodulatory effects by releasing paracrine mediators including extracellular vesicles (EVs), small particles involved in cell-to-cell communication through transfer of proteins and genetic information. The aim of this study was to evaluate the protective role of MSC-derived EVs in the mechanisms of T-cell mediated rejection (TCMR) in kidney transplantation.

Methods: MSCs were isolated from bone marrow and EVs were characterized for size, protein and RNA content. The biological effects of EVs were studied on T-cells isolated from peripheral blood of kidney transplant recipients co-cultured with B cells purified by the spleen of matched deceased donors or on human kidney-derived tubular epithelial cells cultured in an inflammatory microenvironment typical of TCMR.

Results: MSC-derived EVs sized 60-150 nm and expressed on their surface molecules of the integrin family essential for their internalization within target cells. EVs carried different microRNAs and mRNAs including the immunoregulatory Foxp3, Tim-1 and thrombospondin-1 similarly to cells from which they originated. EVs were internalized in activated T cells isolated from kidney transplant recipients inhibiting their proliferation induced by phytohemagglutinin + ionomycine or by co-culture with matched-donor B cells used as antigen presenting cells. Of interest, EVs horizontally transferred to T cells Foxp3 mRNA, inducing a Treg phenotype. In addition, EVs can be internalized in human tubular epithelial cells inhibiting functional alterations and apoptosis induced by inflammatory cytokines, Fas-Ligand, perforin and granzymes. In particular, EVs expressed the preservation of different soluble carriers down-regulated by apoptosis and preservation of functional integrity of tubular cells. These protective effects are mediated by the horizontal transfer of specific RNAs from EVs to target cells.

Conclusions: MSC-derived EVs may have a protective role in TCMR by inhibition of T cell proliferation, by differentiation toward a T regulatory phenotype and by reduction of apoptosis and preservation of functional integrity of tubular cells. These protective effects are mediated by the horizontal transfer of specific RNAs from EVs to target cells.

IMBALANCE OF REGULATORY AND HELPER Th1 and Th2 CELLS WITH EXPRESSION OF PERMEABLE GLYCOPROTEIN PLAY ROLE IN STEROID RESPONSE IN NEPHROTIC SYNDROME

Narayan Prasad1, Akhilesh Jaisawal1, Brijesh Yadav1, Vikas Agarwall1 and Deeptak Tripathi1

1Nephrology SGPGIMS Lucknow Uttar Pradesh India, 2Immunology SGPGIMS Lucknow Uttar Pradesh India

Introduction and Aims: Although Th1 and Th2 cells are aerobic for coordinating immune system in Nephrotic Syndrome (NS), investigators are finding discrepancies in the hypothesis and propose that regulatory T cells (Tregs) may influence immunity in NS. The changes in Th1, Th2, and Tregs and its correlation with permeable glycoprotein (Pgp), one of the factor for resistance to steroids in NS, have never been studied in depth. We aimed to study the effects of Th1 (CD4+, IFN-γ), Th2 (CD4+, IL-4) and Tregs (CD4+, CD25+ and Foxp3+) in NS patients in remission, relapses and steroid resistant, and controls; and also to correlate the changes with expression of Pgp on lymphocytes.

Methods: A total of 81 (sustained remission 22, relapse 24, steroid resistant 21 and healthy controls 14) subjects (age 9.58±3.98 years) were included. Th1, Th2 and Tregs were analyzed with their corresponding markers and Pgp expression were studied on CD4+ lymphocyte using flow cytometry. The frequency of T cells and expression of Pgp amongst different categories were compared.

Results: The percentage/(%) of Tregs was greater in controls and NS in remission (7.84 ± 4.26) as compared to that of remission (3.03±1.18, p=0.001) and relapse (3.08±1.82, p=0.001). The % of Th2 cells in patients with remission (5.18±3.12) was lesser than that of relapse (9.89±5.23; P=0.006) or resistant patients (10.74±5.91; P=0.001); and was similar to that of control (4.91±1.24) p=1.0. The % of Th1 cells was lesser in patients with remission (10.37±3.49%) compared to that of relapsed (16.17±7.19; P=0.008) or resistant (20.24±7.01; P=0.001); and in controls (18.38±5.28; P=0.006). The Th1/Th2 ratio was similar in all groups. The Th1/Th2 ratios in patients with remission (1.69±1.00) was lesser than that of relapsed (6.69±3.79; P<0.001) and resistant (7.65±3.47; P<0.001) and similar to that of control (2.79±1.52). The greater level of Th1 in controls than that of remission and similar Th1/Th2 ratios in controls and remission suggest that imbalance of Th1 and Th2 cells may be a possible factor for relapse and resistance.

EFFECT OF CT-1 BLOCKADE WITH ANTI-CT-1 ANTIBODY ON THE SEVERITY OF ACUTE RENAL FAILURE INDUCED BY UNILATERAL RENAL ISCHEMIA

Rebeca Nuñez-Lozano1, Yaremi Quirós1, Penelope Sanchez-Gonzalez1, Maria P. Perez de Obarrio2, Juan Ruiz2, Francisco J. Lopez-Hernandez3,4,5 and Jose M. Lopez-Novoa3,4

1I+D Bio-inRen S.L. Salamanca Spain, 2Digna Biotech S.L. Madrid Spain, 3Department of Physiology and Pharmacology University of Salamanca Spain, 4Cardiovascular Biomedical Research Institute of Salamanca (IBSAL) Salamanca Spain, 5Hospital Universitario de Salamanca Instituto de Estudios de Ciencias de la Salud de Castilla y León (IECSAL) Salamanca Spain

Introduction and Aims: Ischaemia/reperfusion (I/R) injury is a major cause of acute kidney injury and an important determinant of long-term kidney dysfunction. I/R injury is now recognized as a highly complex cascade of events that includes interactions between vascular endothelium, interstitial compartments, circulating cells, and numerous biochemical entities, in which inflammation is known to be a key mediator. Cardiotrophin-1 (CT-1) is a member of the interleukin 6 (IL-6) family of cytokines, which protects cardiac myocytes and liver from ischemic insults. It has been reported that increased endogenous CT-1 production can act as a protective factor against ischemia. The purpose of this study is to assess the effect of endogenous CT-1 on the severity of acute renal injury induced in a mouse model of unilateral renal ischemia by blocking CT-1 actions with anti-CT-1 antibodies.

Methods: 60 male, C57BL/6 mice were randomized into eight groups (n=6-8) Control groups: mice underwent 30 minutes unilateral renal ischemia with 4 or 48th-reperfusion after uninephrectomy; Control IgG-treated groups: mice underwent 30 minutes unilateral renal ischemia and received goat preimmune IgG (50 μg/kg) i.v. with or 4 th-reperfusion after uninephrectomy; Anti-CT-1: treated groups: mice underwent 30 minutes unilateral renal ischemia and received anti-CT-1 antibody (50 μg/kg) i.v. with 4 and 48th-reperfusion after uninephrectomy; Sham groups: mice underwent the same anesthetic and surgical procedures except for ischemia. After reperfusion mice were sacrificed and blood samples were collected directly from the heart for determination of serum urea, CT-1 and TNF-α levels. Left kidney was excised; one piece homogenized for the analysis of different parameters (lipid peroxidation, myeloperoxidase and CT-1) and other piece was fixed in formalin for histological examination (H&E, CT-1 and ED-1 positive cells).

Results: All parameters renal dysfunction, injury and inflammation measured were elevated in I/R groups as compared with sham groups. Anti-CT-1: treated groups had higher levels of all the studied markers as compared with those of control I/R groups. Control-IgG groups showed non-significant changes in the levels of all the parameters previously mentioned as compared with those in Control groups.

Conclusions: Anti-CT-1 antibody administration exaggerated the severity of ischemic kidney injury in mice, possibly as a result of CT-1 blockade. These data reinforce the role of endogenous CT-1 in protecting the kidney from I/R damage.
THE REGULATION OF THE NITRIC OXIDE SYSTEM CAN MODULATE THE KLOTHO EXPRESSION IN KIDNEY VIA TWIST-2 AND E-CADHERIN

Jae Won Yang1, Jae Seok Kim1, Jun Young Lee1, Hyeon Cheol Park1, Byoung Geun Han1 and Seung Ok Choi1

1Internal Medicine Yonsei University Wonju College of Medicine Wonju Gangwon Republic of Korea

Introduction and Aims: The klotho was originally identified as an anti-aging protein but was subsequently discovered to have a multitude of biologic actions. Animal experiments clearly showed a transient renal klotho deficiency in acute kidney injury from a variety of causes, including ischemia–reperfusion injury. The renal klotho levels were decreased in animals treated with L-NAMe, suggesting that decreased nitric oxide (NO) bioavailability may result in the down-regulation of klotho gene expression, but the inter-relationship between these two proteins is still obscure. We investigated whether relationship existed between the NO pathway and the klotho expression in kidney, and studied the possible pathway as basic helix-loop-helix transcription factors (TWIST)-1, 2, E-cadherin.

Methods: The 10 weeks Sprague-Dawley rats (N= 24, 200g, male) were divided four groups. We supplied low salt diet to the control group (N=6), L-NAMe 1 mg/mL in drinking water to the L-NAMe group (N=6), and udenafil 5 mg/kg to the Udenafil group (N=6), L-NAMe and udenafil to the L-NAMe and Udenafil group (N=6) for 4 weeks. After the collection of blood and urine on day 28, the both kidneys were resected surgically. The serum creatinine, urine nitrate/nitrite, cGMP by ELISA, and tissues were investigated by immunohistochemical stain, and RT-PCR for klotho, TWIST 1, 2, E-cadherin.

Results: The serum creatinine and urine nitrate/nitrite level did not show the statistical difference between groups. The urine cGMP level showed $2.59 \pm 0.88, 1.79 \pm 0.99, 1.20 \pm 0.52, 0.69 \pm 0.59 \text{pmol/well (p=0.0087)}$. The klotho mRNA expression showed $0.98 \pm 0.01, 0.30 \pm 0.11, 0.68 \pm 0.15, 0.54 \pm 0.26 (p=0.0017)$. The TWIST-2 mRNA expression showed $1.90 \pm 1.63, 139.27 \pm 114.87, 10.33 \pm 8.42, 20.19 \pm 12.25 (p=0.0016)$. The E-cadherin mRNA expression showed $0.64 \pm 0.32, 1.57 \pm 0.97, 1.24 \pm 1.27, 13.82 \pm 3.04 (p=0.0029)$. The blocking of NO system decreased the klotho expression via the TWIST-2 increase. The induction of NO system increased the klotho expression via E-cadherin increase.

Conclusions: The regulation of the nitric oxide system can modulate the klotho expression in kidney via TWIST-2 and E-cadherin.

NEUTROPHIL ELASTASE INHIBITOR IS A POTENT THERAPEUTIC AGENT FOR CONTROL OF RENAL ISCHEMIA-REPERFUSION INJURY IN RENAL TRANSPLANTATION

Masahide Matsuyama1, Rikio Yoshimura1, Takuma Hiyama2, Jamei Chargui3, Jean-Louis Touraine3 and Norio Yoshimura1

1Department of Transplantation and Regenerative Surgery Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan,
2Department of Urology, Osaka City University Graduate School of Medicine, Osaka, Japan,
3Department of Transplantation and Clinical Immunology, Claude Bernard University of Lyon and Lyon Hospitals, Lyon, France

Introduction and Aims: Renal ischemia–reperfusion (I/R) injury is a major cause of transplant renal dysfunction. Activated neutrophils are reported to be closely involved in I/R injury after renal transplantation. Neutrophil elastase, a protease released from activated neutrophil, damages tubular endothelial cells. We investigated the beneficial effect of neutrophil elastase inhibitor (ONO-5046.Na) on renal I/R injury in rats.

Methods: The study was done using 10 male Lewis rats (270-320g) that received intravenously administered ONO-5046.Na (30mg/kg, before ischemia and after reperfusion) (group A) and control rats (group B) in 90-min renal warm I/R injury. Neutrophil elastase expression was analyzed using immunohistochemical staining, and the degree of renal dysfunction was evaluated using HE staining and blood biochemistry.

Results: Neutrophil elastase was detected in tubular endothelial cells. The necrotic area extended and encompassed nearly all of ischemic kidney within 12 hr after reperfusion. The necrotic area and the grade of neutrophil elastase staining were more significantly reduced in group A than in group B. Significant differences of blood urea nitrogen and serum creatinine levels were observed. Survival rates over a 14-day period were examined. No rats survived more than over 4-day period in group B. However, 2 (20%) of 10 rats survived over 14-day period in group A.

Conclusions: ONO-5046.Na inhibits neutrophil elastase and reduces acute tubular necrosis. Thus it is a potent therapeutic agent for control of renal I/R injury in renal transplantation.

PCR-BASED DETECTION FOR MICROCHIMERISM AND GRAFT OUTCOME IN KIDNEY TRANSPLANT RECIPIENTS

Maria Zanazzi1, Paolo Carta1, Leonardo Caroli1, Giulia Antognoli1, Pamela Pinzani2, Francesca Salvianti2, Donata Villari3 and Enrico Minetti1

1Nephrology Unit Careggi University Hospital Florence Italy, 2Clinical Physiopathology University of Florence, Florence Italy, 3Urology II Careggi University Hospital Florence Italy

Introduction and Aims: Microchimerism (MC) is the presence of a small amount of foreign cells or DNA within a person’s circulation or tissues. It has been identified in renal transplant. MC detection may improve the efficacy of immunosuppression therapy based on drug association (cyclosporine, steroids and Mycophenolate mofetil). They were prospectively studied by using a quantitative real time PCR method (qPCR) for male MC detection in plasma DNA based on the detection of the DTTS14 gene sequence on the donor genome, and studied the possible pathway between the MC and graft outcome.

Methods: This study included 12 female renal transplant recipients (RTR), mean age 47±8.5 years, undergoing their first cadaveric kidney transplantation. All patients were on prophylactic immunosuppressive therapy based on triple drug association (cyclosporine, steroids and Mycophenolate mofetil). The possible influence of donor MC after kidney transplantation for possible tolerance mechanism was analyzed.

Results: The possible influence of donor MC after kidney transplantation for possible tolerance mechanism was analyzed.
DETECTION OF CD-20-POSITIVE INFILTRATES IN RENAL BIOPSIES WITH ACUTE ALLOGRAFT REJECTION: INVESTIGATION OF THE PROGNOSTIC VALUE

Ashraf Genina,1 Wesam Ismail2 and Amr Soliman3

1Internal Medicine Beni Suef University Cairo Egypt, 2Pathology Beni Suef University Beni Suef Egypt, 3Internal Medicine Cairo University Cairo Egypt

Introduction and Aims: The recognition of antibody mediated rejection has led to a reappraisal of the role of B cells in acute and chronic allograft rejection. The risk of graft loss due to early antibody mediated acute rejection episodes is quite high despite aggressive immunosuppressive therapy. Treatment schemes are still variable, plasmapheresis and intravenous immunoglobulins are used frequently, whereas rituximab, an anti-CD20 monoclonal antibody is used mostly in resistant cases only. The role of CD20 positive lymphocytic infiltrates in acute cellular rejection has been reported to be associated with poorer clinical outcomes and reduced graft survival. And recently molecular gene analysis had shown that grafts with ABMR have lower expression of CD20. We set to identify CD20 positive cell infiltrates in ABMR, and if there is any relationship between their presence, and peritubular capillaries C4d expression as well as other histological parameters in order to see if there is a role of CD20 in acute antibody mediated rejection (ABMR) and if there is a subset of patients who could benefit from early treatment by anti CD20 monoclonal antibody.

Methods: We reviewed 90 renal allograft tissue biopsies from different transplant centers received between 2010 and 2011, including 13 patients who experienced acute antibody mediated rejection (ABMR). We also identified a matched group of 15 patients with acute T-cell mediated rejection (TCMR) diagnosed as Banff type I and IIa rejection to serve as controls. All the 28 cases were stained by anti CD 20 and anti CD 8 antibodies.

Results: We found no statistically significant difference in CD 20 and CD 8 cell counts between the ABMR and TCMR groups. The presence of CD 20 and CD 8 positive cells didn’t correlate with C4d expression. We noticed that the numbers of CD20 positive cells and the grade of severity of rejection, as well as with the degree of interstitial arteritis (v score) but not with other histological or clinical parameters.

Conclusions: Our findings suggest that there is a possible relation between the presence of CD20 positive lymphocytic infiltrates and a more severe histological form of rejection, but failed to establish a relationship between their actual presence in the interstitial infiltrate and the 2 distinct mechanisms behind acute graft rejection.

INFLUENCE OF APOPTOSIS AND INFLAMMATION GENE POLYMORPHISMS ON TRANSPLANTED KIDNEY FUNCTION

Maria L. Cappuccilli1, Gaetano La Manna1, Irene Capelli1, Olga Baraldi2, Vania Cuna3, Giuseppe Battaglino3, Paola Todeschini3, Giorgio Feliciangeli3, Maria P. Scialom1 and Sergio Stefoni1

1Nephrology Dialysis and Renal Transplantation Unit S. Orsola University Hospital Bologna Italy

Introduction and Aims: The progressive deterioration of kidney allograft function leads in most cases to transplant failure. In the last few years, several polymorphisms in genes encoding inflammatory and apoptosis molecules have been suggested as potential genetic markers for graft dysfunction, representing one conceivable explanation for interindividual differences in kidney transplant outcomes. The objective of our work was the identification of genetic risk profiles for transplanted kidney function by studying the impact of interleukin 6 (IL-6), transforming growth factor beta 1 (TGFβ1) and Fas gene polymorphisms.

Methods: The study recruited a total of 376 cadaveric kidney recipients transplanted at our center from January 2005 to June 2011. The follow-up period was 2.6 ± 1.4 years. A case-control study was carried out to assess potential associations between polymorphisms in inflammation- and apoptosis-related genes and the risk for chronic impairment of kidney graft function: the control group included 256 renal transplant recipients with stable graft function (SGF) group, whereas the group of the cases was composed by 120 patients with worsening graft function (WGF) group within the follow-up period, based on the observation of a constant and irreversible increase in serum creatinine at least 30% above baseline in the absence of recurrent primary nephropathy or other ascertained causes. After genomic DNA isolation from white blood cells, all the patients were genotyped for IL-6-174C, TGFβ1/R25P, Fas/670A polymorphisms using PCR-RFLP (Polymerase Chain Reaction - Restriction Fragment Length Polymorphism) and direct sequencing.

Results: Considering the single IL-6, TGFβ1 and Fas polymorphisms, we found similar allelic and genotype frequencies in the two groups (SGF vs WGF group).

To test the hypothesis of mutual effects of polymorphisms, multiple logistic regression was performed incorporating data for all the possible dual genotypic associations. The association of IL-6 high producer and Fas low producer genotype resulted in a protective effect against graft dysfunction (OR = 0.79; 95% C.I. = 0.72-0.86).

Conclusions: The study seems to indicate a significant predictive value of gene polymorphisms of molecules involved in inflammatory response and programmed cell death on kidney allograft function and suggests a protective effect of the carriage of the IL-6 high producer/Fas low producer genotype.

INDOLEAMINE 2,3-DIOXOGENASE (IDO) AS A NEW IMMUNOLOGICAL MARKER IN KIDNEY TRANSPLANT

Elisa Loxi1, Barbara Votta1, Alessandro Andreoni2, Andrea Ranghino3, Roberta Carri1, Lucia Peruzzi2, Maria Elena Donadio2, Ilaria Serroni1, Rachele Gallo1, Maria Paola Puccinelli2 and Rosanna Coppo1

1Nephrology, Dialysis, Transplantation Regina Margherita University Hospital Turin Italy, 2Clinical Biochemistry - Diagnostics Department Città della Salute e della Scienza Turin Italy, 3Nephrology, Dialysis, Transplantation University of Turin Italy

Introduction and Aims: Indoleamine 2,3 dioxygenase (IDO) is an enzyme induced by interferon-γ (IFN-γ) and toll-like receptors (TLR)-ligands in macrophages, dendritic cells and other cells. IDO degrades the essential amminoid tryptophan (Trp) to 5,6-dihydroxyindole and 5,6-dihydroxyindole-2-carboxylate (5,6-DHI/5,6-DHICA). High levels of indole metabolites have been associated with immune suppression and rejection in transplant patients. The aim of this study was to explore if IDO-2 could be used as a new immunological marker in kidney transplantation.

Methods: Of the 102 transplant recipients (73 male and 29 female, median age 47 years), 65 were tolerant and 37 were non-tolerant. On day 1, day 7, month 1 and month 3, serum IL-18 levels were measured by ELISA using a commercial kit (Bioscience Human IL-18 ELISA). Serum creatinine levels were analysed by modified Jaffe method in Cobas 8000 analyser. GFR was estimated by Modified Diet in Renal Disease (MDRD) equation. Patients were assigned to 2 groups: defined slow graft function (SGF) as a reduction in serum creatinine by ≤70% on day 7 and immediate graft function (IGF) as ≥70%. Patients were also separated depending on their history of AR episodes. Data were expressed as mean ± standard error. We compared IL-18 levels between the groups using both Mann-Whitney U and Student’s t-tests.

Results: Among 50 recipients, 6 had SGF, and 44 had IGF, no patient had delayed graft function (DDGF; required dialysis within 1 week of transplant). Twelve cases were clinically diagnosed as AR by renal biopsy. Serum IL-18 levels were statistically different between groups before transplantation (673.02 ± 75.70 ng/ml IGF vs 1047.59 ± 368.52 pg/ml SGF (p <0.05)). Serum IL-18 level on day 7 were significantly higher in SGF compared to IGF. There were no significant differences in serum IL-18 levels between the groups on the first day of transplant (640.72 ± 93.48 pg/ml vs 675.53 ± 16.56 pg/ml, p >0.05). Furthermore, serum levels of IL-18 at day 1 and 7 were significantly elevated in the AR group with compared with the no AR group.

Conclusions: Our findings suggest that serum IL-18 might be considered a useful marker in predicting graft function after renal transplantation. The sequential monitoring of serum IL-18 in kidney transplant recipients might be recommended to make early diagnosis of acute renal rejection. Future larger studies are needed to confirm our findings.

IMPORTANCE OF SEQUENTIAL MONITORING OF SERUM INTERLEUKIN-18 LEVELS IN PATIENTS WITH KIDNEY TRANSPLANTATION

Roberta Camilla1, Licia Peruzzi1, Maria Elena Donadio1, Ilaria Serriello1, Rachele Gallo1, Maria Paola Puccinelli2 and Rosanna Coppo1

1Nephrology, Dialysis, Transplantation Regina Margherita University Hospital Turin Italy, 2Clinical Biochemistry - Diagnostics Department Città della Salute e della Scienza Turin Italy

Introduction and Aims: Early diagnosis of kidney graft dysfunction is essential for the management of transplanted kidneys. Interleukin-18 is predominantly a macrophage-derived cytokine with a key role in inflammation and cell-mediated immunity.Recent studies have suggested that IL-18 may predict early graft function and acute rejection after renal transplantation. This prospective observational study aimed to assess the relevance of serial serum IL-18 measurements for predicting graft function and acute rejection.

Methods: We studied 50 kidney transplant recipients (13 female, 37 male; mean age: 38.12 ± 13.67). Blood samples were collected immediately before and after surgery at day 1, day 7, month 1 and month 3. Serum IL-18 levels were measured by ELISA using a commercial kit (Bioscience Human IL-18 ELISA). Serum creatinine levels were analysed by modified Jaffe method in Cobas 8000 analyser. GFR was estimated by Modified Diet in Renal Disease (MDRD) equation. Patients were assigned to 2 groups: defined slow graft function (SGF) as a reduction in serum creatinine by ≤70% on day 7 and immediate graft function (IGF) as ≥70%. Patients were also separated depending on their history of AR episodes. Data were expressed as mean ± standard error. We compared IL-18 levels between the groups using both Mann-Whitney U and Student’s t-tests.

Results: Among 50 recipients, 6 had SGF, and 44 had IGF, no patient had delayed graft function (DDGF; required dialysis within 1 week of transplant). Twelve cases were clinically diagnosed as AR by renal biopsy. Serum IL-18 levels were statistically different between groups before transplantation (673.02 ± 75.70 ng/ml IGF vs 1047.59 ± 368.52 pg/ml SGF (p <0.05)). Serum IL-18 level on day 7 were significantly higher in SGF compared to IGF. There were no significant differences in serum IL-18 levels between the groups on the first day of transplant (640.72 ± 93.48 pg/ml vs 675.53 ± 16.56 pg/ml, p >0.05). Furthermore, serum levels of IL-18 at day 1 and 7 were significantly elevated in the AR group with compared with the no AR group.

Conclusions: Our findings suggest that serum IL-18 might be considered a useful marker in predicting graft function after renal transplantation. The sequential monitoring of serum IL-18 in kidney transplant recipients might be recommended to make early diagnosis of acute renal rejection. Future larger studies are needed to confirm our findings.

Downloaded from https://academic.oup.com/ndt/article-abstract/28/suppl_1/i271/1838522 by guest on 14 March 2019
ASSOCIATION OF SERUM ADIPONECTIN LEVELS WITH ENDOTHELIAL AND PLATELET FUNCTION IN RENAL TRANSPLANT PATIENTS USING CALCINEURIN INHIBITORS

Gari Sahin1, Olga Mettem Akay2, Sema Uulu1, Cengiz Bul1, Ahmet Ugur Yalcin1 and Zafir Gulbas2

1Nephrology Eskisehir Osmangazi University Eskisehir Turkey, 2Hematology Eskisehir Osmangazi University Eskisehir Turkey, 3Biochemistry Eskisehir Osmangazi University Eskisehir Turkey, 4Biostatistics Eskisehir Osmangazi University Eskisehir Turkey

Introduction and Aims: Cardiovascular events is still an important problem in renal transplant patients. In addition to traditional risk factors, coagulation abnormalities, endothelial dysfunction and arteriosclerosis play a key role in cardiovascular disease state observed in transplanted patients. Adiponectin, an adipose tissue-derived hormone, has protective properties with respect to atherogenesis and inflammation. Plasma adiponectin levels are markedly elevated among patients with end-stage renal disease and are lower following kidney transplantation. However, there is still a debate about this topic in the literature. This study evaluated, adiponectin levels associated with markers of endothelial dysfunction and platelet function in renal transplant patients.

Methods: Sixty-six renal transplant patients were studied. Staging was performed according to immunosuppression regimen. Group 1(n=36) were treated with cyclosporine(CyA)/mycophenolate mofetil/ methylprednisolone and group 2 (n=30) were treated with tacrolimus/mycophenolate mofetil/ methylprednisolone. Plasma adiponectin, asymmetric dimethyl arginine (ADMA), sP-selectin levels and platelet aggregation tests were studied and were compared with those in control group(n=16, group 3).

Results: adiponectin and ADMA levels were higher in renal transplant patients and statistically significant differences were observed compared with those of control group, respectively (p=0.0001, p=0.01). sP-selectin levels were higher in renal transplant patients according to control group, but the difference did not reach statistical significance (p=0.069). Platelet aggregation values induced by all agonists (Adenosine diphosphate (ADP), epinephrine, ristocetin, collagen) were lower in patients than controls, but the difference did not reach statistical significance (p=0.05). When assessment were performed according to groups; Adiponectin, sP-selectin and ADMA levels were higher in group 1 and statistically significant differences were observed compared with those of group 2 and group 3, respectively(p=0.0001,p=0.05, p=0.05). Platelet aggregation values induced by all agonists (Adenosine diphosphate (ADP), epinephrine, ristocetin, collagen) were lower in group 1 than group 2 and group 3, but the difference did not reach statistical significance (p=0.05).

Conclusions: The results of our study suggest that, adiponectin levels are elevated in line with ADMA and sP-selectin levels. Since CyA induces higher adiponectin levels, platelet activation and endothelial dysfunction. These changes may be responsible from the increased the risk of posttransplant cardiovascular events in renal transplant patients.