

Selected Abstracts of Articles Published Elsewhere by Authors in Kuwait

Kuwait Medical Journal 2005, 37 (2): 133-136

Significance of Determining the Point of Reperfusion Failure in Experimental Torsion of Testis

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Int J Urol 2005; 12:81-89

Background: Experimental studies of the use of free radical scavengers in ischemic/reperfusion (I/R) injury following detorsion of the torsed testis have yielded conflicting results due to differences in the period of ischemia used. The authors studied I/R injury in the rabbit model, to define the point beyond which there is reperfusion failure.

Methods: Ischemia/reperfusion injury of the testis was created in 3-6-month-old male New Zealand white rabbits by cross-clamping the left spermatic cord for periods of ischemia lasting 0, 15, 30, 60, 90, 120 and 180 min. There were eight animals per experimental group. The right testis served as internal control. Both testes were harvested after 24 h of reperfusion in four animals and after 3 months in the remaining four animals for each group. Testicular malondialdehyde (MDA), a measure of free radical damage, was determined by using the thiobarbituric acid reaction on testicular homogenates. Johnsen score was used to assess morphological damage caused by the ischemia.

Results: After 24 h of reperfusion, the mean testicular MDA in the control right testes at 0, 15, 30, 60, 90, 120 and 180 min was 2.1, 2.5, 2.9, 2.4, 2.1 and 1.9 nmol/mg protein, respectively. The mean left testicular MDA at corresponding ischemic periods was 1.6, 2.0, 3.9, 10.0, 4.4, 6.1 and 1.0 nmol/mg protein, respectively. The maximum left testicular MDA was at 60 min (10.0 nmol/mg protein), following which the level dropped significantly to 1.0 nmol/mg protein at 180 min. At 3 months, the mean Johnsen scores for left testes subjected to 0, 60, 120 and 180 min ischemia were 9.4, 8.8, 2.3, 3.5, respectively.

Conclusion: The results suggest that following ischemia of up to 60 min in the rabbit testis, adequate reperfusion is possible, but ischemia lasting beyond 60 min results in inadequate reperfusion leading to irreversible damage. Thus, in experiments for assessing the effect of antioxidants on I/R injury of the testis in rabbits, periods up to 60 min of ischemia should be regarded as optimum to observe an effect.

Plasma Leptin Concentration in Patients with Type 2 Diabetes: Relationship to Cardiovascular Disease Risk Factors and Insulin Resistance

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Diabet Med 2005; 22:278-85

Aims: The aim of this study was to evaluate the relationship of obesity, leptin, insulin resistance and C-reactive protein (CRP) with coronary heart disease (CHD) risk factors in patients with Type 2 diabetes mellitus (DM) with CHD compared with those with Type 2 DM without CHD.

Methods: Leptin, CRP (high sensitivity assay), fasting plasma insulin, glucose, HbA(1c) and full lipid profile were determined in 58 Type 2 diabetic patients with CHD and 87 Type 2 DM patients without CHD. Results were compared between those with and without CHD. Univariate correlation as well as logistic regression analyses were used to relate these markers with traditional CHD risk factors.

Results: Leptin showed significant correlations with BMI ($r = 0.59$; $P < 0.0001$), waist circumference ($r = 0.45$; $P < 0.0001$), CRP ($r = 0.36$; $P < 0.0001$), and fasting insulin ($r = 0.53$; $P < 0.0001$) as well as with systolic ($r = 0.23$; $P = 0.007$) and diastolic ($r = 0.23$; $P = 0.007$) blood pressure. However, when those with and without CHD were compared only age ($P < 0.0001$), duration of diabetes ($P < 0.001$) and degree of microalbuminuria ($P = 0.02$) were significantly higher in patients with CHD. Leptin ($P = 0.49$), CRP ($P = 0.19$) and lipid parameters were not significantly different between the two groups.

Conclusion: Our study confirms a relationship between leptin and CRP with CHD risk factors. The lack of significant difference when patients with and without CHD are compared may be due to the potential confounding effects of treatment with aspirin and statins.

Methods for Measuring Agreement: Glucose Levels in Gingival Crevice Blood

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Clin Oral Investig 2005; 9:65-69. Epub 2005 Jan 6

The aim of the present study was to compare conclusions drawn by two different methods for comparison of blood glucose determination in capillary fingerstick blood (CFB) and gingival crevice blood (GCB). Glucose levels in CFB and GCB oozing from the gingiva after periodontal probing were measured in 31 patients with gingivitis or periodontitis using a novel, very sensitive self-monitoring device (Freestyle, TheraSense Inc.) developed for off-finger tip glucose testing. Correlation analysis revealed that measurements of glucose levels in CFB from left and right finger tips were highly correlated pointing to excellent performance of the device, whereas CFB and GCB measurements were moderately, but highly significantly, correlated. A thorough analysis of agreement revealed, on the other hand, questionable performance of the device for screening hypoglycaemic patients. The mean difference of measurements in CFB samples was $+3.2 \pm 12.7$ mg/dl. The 95% limits of agreement were -21.7 and +28.2. The mean difference of glucose determination in CFB and GCB samples was -22.0 ± 26.6 mg/dl, and limits of agreement were -74.4 and +30.1. By plotting differences on means of measurements and doing linear regression analysis no systematic trend of change in differences with increasing mean of measurements was ascertained. Analysis of agreement revealed that performance of the Freestyle measuring device yielded considerably large limits of agreement, and gingival crevice blood cannot be recommended for measuring blood glucose levels.

Social and Psychological Characteristics of Kuwaiti Children and Adolescents with Type 1 Diabetes

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Soc Sci Med 2005; 60:1835-1844

Type 1 diabetes mellitus is a chronic disease that may have an impact on children's psychosocial adjustment. This study aimed to investigate the psychosocial characteristics of Kuwaiti children with type 1 diabetes as compared to healthy children without diabetes, and assess the impact of glycaemic

control on psychosocial variables. A total of 349 school children aged 6-18 years with type 1 diabetes, and 409 children without diabetes having comparable age, gender, and social class were included in the study. Data were obtained by interviewing children and parents using a questionnaire. Psychological distress was measured by the Hopkins symptoms checklist-25 scale including anxiety and depression. Glycaemic control was assessed by glycosylated haemoglobin, HbA(1C) level. Glycaemic control was considered 'good to excellent' at HbA(1C)<8.0%, 'fair' at HbA(1C) 8.1 to 10.0%, and 'poor' at HbA(1C)>10.0%. Median scores of anxiety, depression, and total distress were significantly higher in children with diabetes indicating worse psychological adjustment. There was also significant difference between children with diabetes and those without diabetes in social aspects and school absence days. There was significant positive correlation between HbA(1C) concentration and scores of the psychological functioning indices. Children with poor glycaemic control had worse psychological adjustment. After controlling the variance accounted by gender and age, stepwise multiple regression analysis showed that girls, older children, children in need of emotional support, and those with higher HbA(1C) were at higher risk for psychological maladjustment. These variables explained 47.9% of the variation in total distress. In conclusion, the study supported our hypotheses. Children with diabetes had worse psychological adjustment, and distress was related to glycaemic control. Since psychological distress increases the risk for future complications due to its relation with glycaemic control, longitudinal studies are recommended to identify children with diabetes having distress at an early stage when preventive interventions are effective.

Signal Transduction Mechanisms Involved in Cardiac Preconditioning: Role of Ras-GTPase, Ca²⁺/Calmodulin-dependent Protein Kinase II and Epidermal Growth Factor Receptor

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Mol Cell Biochem 2005; 268:175-183

It is well established that brief episodes of ischemia/reperfusion (I/R) [preconditioning (PC)] protect the myocardium from the damage induced by subsequent more prolonged I/R. However, the signaling pathways activated during PC or I/R are not well characterized. In this study, the role of Ras-GTPase, tyrosine kinases (TKs), epidermal growth factor receptor (EGFR) and Ca²⁺/calmodulin-dependent protein kinase II (CaMK II) in mediating PC in a perfused rat heart model was investigated. A 40-min episode of global ischemia in perfused rat hearts produced significantly impaired cardiac function, measured as left ventricular developed pressure (P_{max}) and left ventricular end-diastolic pressure (LVEDP), and impaired coronary hemodynamics, measured as coronary flow (CF) and coronary vascular resistance (CVR). PC significantly enhanced cardiac recovery after IR. Combination of PC and FPT III (Ras-GTPase inhibitor FPT III; 232 ng/min for 6 days) treatment did not produce any additive benefits as compared to PC alone. In contrast, PC-induced improvements in cardiac function after I/R were significantly attenuated by pretreatment with genistein (1mg/kg/day for 6 days), a broad-spectrum inhibitor of TKs, or AG1478 (1mg/kg/day for 6 days), a specific inhibitor of EGFR tyrosine kinase or KN-93 (578 ng/min for 6 days), a CaMK II inhibitor, before PC. These observations suggest that PC and FPT III pretreatment may produce cardioprotection via similar mechanisms. Present results also indicate that activation of TKs and specifically activation of EGFR-mediated TKs and CaMK II-mediated regulation of calcium homeostasis are part of the PC mechanisms that improve recovery after IR.

Chronic Renal Disease in Kuwaiti Nationals: a Prospective Study During the Past 4 Years

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Ren Fail 2005; 27:227-33

Our study is a prospective one conducted at Al-Amiri Hospital and including all new cases of chronic renal disease (CRD) seen at the capital area of Kuwait between 1 January 1999 and 30 December 2003. Diagnosis of CRD was based on clinical, laboratory, and radiological features. Kidney biopsies were done when indicated. A total of 271 cases of chronic renal failure (CRF) were diagnosed, of whom 143 were women. The median age was 40 years (range, 5 to 80 years; mean +/- SD: 40 +/- 14). The most common cause of CRF was glomerulonephritis (32%), of which systemic lupus erythematosus and vasculitis constituted 5% and 4%, respectively. Diabetic glomerulosclerosis was the second leading cause of CRD (24%), followed by tubulointerstitial disease (11%) and nephroangiosclerosis (10%). Less frequent causes included renovascular/ischemic disease (6%), obstructive nephropathy (3%), and adult polycystic kidney disease (3%). One hundred and seven patients had 121 incidents of acute deterioration of underlying renal disease. This was mostly due to drugs (22%), infection (21%), and volume depletion (13%). Antiinflammatory drugs were the most common drugs (63%) responsible for the acute decline in renal function. By the end of the study, 18 (7%) patients died, 55 (20%) required maintenance dialysis, and 40 (15%) had received a kidney allograft. Diabetic patients did not differ from nondiabetic with regard mortality, although had more renal replacement therapy ($p = .002$). Using the Cox regression model, analysis of the relative risk factors likely to contribute to mortality, viz. age, gender, original kidney disease, fitness for transplantation, and mode of presentation, did not show significant factors except for less hazard to death in those diagnosed early with CRD (i.e., on routine testing; relative risk 0.06, $p = .01$). In conclusion, our study indicates that early diagnosis and management of CRD can improve the patient's quality of life and decrease the cost of frequent hospitalization, morbidity, and even mortality associated with end-stage renal disease.

The Prevalence of Human Leukocyte Antigen (HLA) DR/DQ/DP Alleles in Kuwaiti Children with Oligoarticular Juvenile Idiopathic Arthritis.

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Rheumatol Int 2005; [Epub ahead of print]

We have determined the prevalence of human leukocyte antigen (HLA)-DR, DQ and DP alleles in Kuwaiti children with oligoarticular juvenile idiopathic arthritis (OA-JIA) and healthy controls using the PCR-SSP (sequence specific primers) method. The analysis took into account the presence of antinuclear antibodies and chronic anterior uveitis. DRB1*03 (RR 2.20, $P < 0.001$), DRB1*08 (RR 5.280, $P < 0.026$), DQA1*0501 (RR 1.930, $P < 0.001$), DQB1*0304 (RR 7.920, $P < 0.002$), DQB1*0501 (RR 3.080, $P < 0.007$) and DPB1*0101 (RR 8.8, $P < 0.001$) were the main HLA alleles associated with OA-JIA in Kuwaiti Arabs in this study. DRB1*03 was detected in 71% of children with positive ANA, and in 50% of children with anterior uveitis. DQA1 alleles *0501, *0103 and *0105 ($P < 0.001$; 0.029 and 0.024 respectively) were found to be associated with OA-JIA. In contrast, DQA1*0301 and DQA1*0302 alleles appear to be protective in Kuwaiti children (RR 0.153, $P < 0.001$ and RR 0.278, $P < 0.016$ respectively). The DQB1 alleles *0304 and *0501 were associated with OA-JIA ($P < 0.002$ and $P < 0.007$ respectively). In the case of DPB1, only one allele (*0101) was associated with OA-JIA ($P < 0.001$). Most Kuwaiti Arab patients with OA-JIA who carried a DQ or DP susceptibility allele also had an accompanying DRB1*03 or *8 allele.