0080

Dietary acrylamide induces accelerated endothelial aging in murine and human cell model

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Introduction: Replicative senescence is characterized by a limited ability of cells to divide in vitro. Senescence induces an endothelial dysfunction. Many compounds in food can induce an earlier vascular senescence. Acrylamide (AAM) is a recent discovery in food, as a Maillard reaction product. Dietary acrylamide induces accelerated endothelial senescence in-vivo. The toxicity of AAM and GA on endothelial cells in vitro is characterized by decreased proliferation and induction of cell death at high doses. Chronic exposure at lower concentrations induce an accelerated senescence, potentially the cause of endothelial dysfunction in vivo.

Objective: To assess the effects of AAM on endothelium.

Methods: To evaluate endothelial dysfunction, mice have been fed with AAM-enriched diets (25, 50 or 100μg/kgBW/day) for 3, 6 or 9 months. Endothelium-dependent relaxation (EDR) of aortic rings was measured. AAM (1-50μM) and GA (1-5μM) toxicity was assessed by measuring Human Umbilical Vein Endothelial Cells (HUVEC) proliferation by MTS test and cell death induction by flow cytometry. Senescence was evaluated in HUVEC cultured over 3 months with AAM or GA (10 or 100μM) by measuring β-galactosidase activity (flow cytometry) and telomere length (qPCR).

Results: After 6 months of diet, AAM (100μg/kgBW/day) decreased aortic EDR (p<0.01). In-vitro, AAM (25μM) inhibited in dose- and time-dependent manners HUVEC proliferation (p<0.001) and induced apoptosis (p<0.05). GA exhibited higher toxicity since lower doses were needed to induce same results. The extended culture with AAM or GA demonstrated a significant cell division slowdown and increased β-galactosidase activity. AAM or GA (100μM) accelerated telomere shortening (p<0.05).

Discussion: The toxicity of AAM and GA on endothelial cells in vitro is characterized by decreased proliferation and induction of cell death at high doses. Chronic exposure at lower concentrations induce an accelerated senescence, potentially the cause of endothelial dysfunction in vivo.

0143

Serum thiolactonase activity and paraoxonase gene polymorphism in coronary artery Tunisian patients with or without diabetes

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Serum homocysteine thiolactonase activity is closely related to homocysteine and ox-LDL levels in coronary artery disease patients. Homocysteine thiolactonase activities are the result of environmental factors and genetic polymorphisms of paraoxonase. The relevance of gene polymorphism in coronary artery patients with or without diabetes was investigated in a case-control study.

Methods: The population included 140 control subjects, 47 coronary artery disease patient without diabetes and 44 patients with type 2 diabetes. Serum thiolactonase activity decreased significantly in coronary artery disease patients: 318.9±156 U/l those without diabetes and 388.8±180 in the diabetic ones compared with the controls: 568.8±250 U/l (p<0.001). These activities were associated with increased plasma homocysteine and ox-LDL levels (p<0.001). The paraoxonase allele frequency is significantly higher in controls than coronary artery patients (p<0.001). The frequency of R high activity allele was also higher in diabetic coronary patients (11.3%), than in those without diabetes (4.2%). No significant association was found between paraoxonase LN gene polymorphisms and diabetes in coronary patients.

Conclusions: The difference in allele frequency for the paraoxonase R gene polymorphism may be the cause of the high thiolactonase activity observed in coronary patients with type 2 diabetes mellitus. Further studies are needed to be conducted to elucidate the role of the enzyme in the development of vascular complications in these patients.

0161

The neuroprotective agent rasagiline mesylate attenuates cardiac remodeling after experimental myocardial infarction

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Introduction: Rasagiline, (R) mesylate (N-propargyl-1-(R)-aminomimid) is a selective, potent irreversible inhibitor of MAO-B with neuroprotective and anti-apoptotic properties.

Purpose: We investigated whether R could provide cardioprotection in a 6 month Wistar male rat model (350-400gr) undergoing experimental Myocardial Infarction (MI).

Methods: MI was induced surgically by a permanent ligation of the left anterior descending coronary artery. We included 3 experimental groups: R (n=10), Control (C) (n=10), and sham-operated (S) (n=10). R was administered daily (2mg/kg i.p.) for 4 weeks, beginning 24 hours after MI induction. Group C received normal saline 0.9%, i.p. Cardiac function was assessed by two-dimensional targeted M-mode echocardiography (Vivid 7, 13MHz), at baseline, 14 and 28 days post MI. Estimation of cardiac remodeling and cardiomyocyte damage was performed by immuno-fluorescent microscopy analysis.

Results: Baseline measurements were similar in all groups. Group R showed less FS (%) deterioration vs group C at 14 (31.4±2.1 vs 22.3±2.0, p<0.0001) and 28 days (31.6±2.3 vs 19.6±1.8, p<0.0001). Immuno-fluorescent microscopy analysis of the infract border zone indicated reduced collagen I staining in group R (n=3) rats compared to group C (n=3) and less cardiomyocyte degeneration as indicated by b-catenin and desmin staining. Also, apoptosis (TUNEL) was reduced by 65% in the border zone and 58% in the remote region of R treated animals. Importantly, scar size did not differ among the two groups.

Conclusions: Our study showed attenuation in cardiac remodelling after MI as presented by better systolic function in Rasagiline mesylate (a commonly used neurological drug) treated rats accompanied by less border zone fibrosis and cardiomyocyte degeneration indicating a beneficial effect in the post-MI period.

0496

Association between the MspI polymorphism of p53 gene and myocardial infarction in the Tunisian male population

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Background and aim: The association between polymorphisms in the p53 tumour suppressor gene and CAD has been reported. However, not all investigations have been consistent, and this hypothesized association remains controversial. The aim of this study was to investigate the possible association between the Msp1 in intron 6 polymorphism in the p53 gene and myocardial infarction (MI) in Tunisian subjects.

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