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Results: At admission, patients with heart failure showed low-level of serum and urinary sodium. They also showed high plasma levels of ANP, BNP, TNF-α, IL-1β and IL-6. After 8 days of treatment with high dose furosemide and small volume of HSS, patients with ALVD or CHF a significant increase of daily diuresis, serum and urinary sodium, a significant lowering of weight, SBP HR and of ANP, BNP, IL-1β, TNF-α, IL-6 plasma values. Until the end of treatment period was reached, after the acute saline load, patients with CHF or left ventricular dysfunction showed higher, though not statistically significant, plasma levels of ANP and significatively higher plasma levels of BNP, IL-1β and TNF-α, in comparison with values observed immediately after the treatment period in the same patients, nevertheless these plasma values remained lower in comparison with admission values. Moreover, patients with HF treated with i.v. high dose furosemide + HSS showed, after acute saline load, a lower absolute change of ANP, BNP, TNF-α, IL-1 β, IL-6 E-Selectin, P-Selectin plasma levels with respect to the values observed, in the same patients, at the end of treatment period in comparison respectively to the absolute change observed in control subjects (healthy and ALVD subjects), after a saline load, whereas no significant difference was observed between case and controls in absolute change of IL-10, ICAM-1 and V-CAM-1 plasma levels.
Conclusion: Treatment with high dose furosemide and HSS, by lowering volume overloading could be responsible for a stretching relief that could influence natriuretic peptides and immunoinflammatory marker plasma levels after treatment and after an acute saline load.

35 EFFECT OF A PEPTIDE MIMIC BASED ON THE DIMERISATION DOMAIN OF THE ID1 PROTEIN ON SMOOTH MUSCLE CELL PROLIFERATION, MIGRATION AND DIFFERENTIATION

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Proliferation and migration of smooth muscle cells (SMCs) are prominent features of atheroscleerosis. Among several mediators to be involved in these cellular events, recent evidence indicates a role for the class of transcription factors Helix-Loop-Helix (HLH). E2, E47 and MyoD belong to this family and directly regulate SMC proliferation and migration by inducing the expression of the marker for the contractile phenotype α-actin, and the cyclin-dependent kinase inhibitors, p21 and p16. Within the HLH family members, the protein Id act as inhibitors of the gene transcription leading to cell-cycle progression and cell de-differentiation. Thus, the proteins Id may represent pivotal players in the development of lesions of atherosclerosis and a potential pharmacological target. In order to modulate their activity, we have designed an interfering molecule (compound 1a and 1b having the same structure but different chirality) containing two copies of the first eleven residues of the Id1 helix-2 (Id1 91–101), which are N-terminally connected through the unnatural dicarboxylic amino acid cis-3-carboxycyclopentylglycine (Cpg). To investigate the effect of compounds 1a and 1b on cell proliferation, cultured SMCs from thoracic aorta have been synchronized at the G0 phase of the cell cycle and then stimulated for 3 days with medium containing 10% fetal calf serum (FCS) in the presence or absence of the peptides. 1a and 1b have shown a similar antiproliferative effect by reducing the number of cells to ~60% in the low-micromolar range (~2 μM). Also an equimolar mixture of 1a/b has induced a similar decrease in cell proliferation, thus excluding any relevant role of the conformation of the three chiral centres. The effect on cell migration was performed by pre-incubating the cells with 1 μM or 10 μM peptide for 72 hours and then measured with a modified Boyden chamber in response to 20 ng/ml PDGF-BB (platelet derived growth factor) as chemotactic agent. A moderate, but still significant, reduction of cell migration was observed at both 1 and 10 μM concentration (-30%). The ability of the Cpg-containing peptides to convert the dedifferentiated state of the SMCs into a differentiated one was evaluated by measuring the expression level of α-actin. A positive response on the expression levels of α-actin has been observed upon incubation of the cells with 10 μM concentration of compound 1a (180 ± 11%). In contrast, the Cpg-containing peptide 1a(scr) displaying two copies of a scrambled sequence of Id1 91–101 did not affect the α-actin expression. Finally, to determine whether the observed modulation of 1a/b on SMC proliferation, differentiation and migration was effectively correlated to the modulation of the Id1 protein activity, we evaluated its intracellular levels. Compound 1a significantly reduced the Id1 level by 65%. This effect may indicate that the conversion of the synthetic phenotype of the SMCs to a contractile phenotype upon incubation with 1a/b may be due to a reduced activity of the Id1 protein. In conclusion, the present study provides evidence on a possible pharmacological modulation of protein Id1, by compound 1a/1b, which regulates the proliferation, the migration and the differentiation of SMCs.

36 EFFECT OF CIGARETTE SMOKING ON CAROTID IMT AND FRS

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Objective: To investigate 1) whether smokers and no smokers with identical Framingham risk score (FRS) have a different subclinical vascular damage and 2) whether moderate cigarette smoking throughout the life (in terms of packyears, a measure of total exposure to cigarette smoking not considered in the FRS) may be considered harmless as compared to the effects of heavy cigarette smoking on the extent of sub-clinical atherosclerosis.
Methods: Carotid IMTs of never-, moderate- (packyears<30) and heavy-smokers (packyears≥30), matched for age, gender and FRS, were compared (n=72 per group).
Results: As a result of the FRS-matching, moderate- and heavy-smokers were fully comparable for all the vascular risk factors (VRFs) included into the algorithm. In contrast, never-smokers had, consequently to the matching, higher levels of total and LDL-cholesterol, blood glucose, systolic and diastolic blood pressure (all $p<0.05$).
The IMT_{mean} of both heavy- (1.05±0.31 mm) and moderate-smokers (1.02±0.27 mm) was significantly higher than in FRS-matched never-smokers (0.92±0.28 mm), (p=0.01 and p=0.003, respectively). Thus, regardless of a moderate or heavy smoking history, smokers show a worse carotid atherosclerotic profile than FRS-matched never smokers.
Conclusions: Cigarette smoking, whatever moderate or heavy, induces a vascular damage that exceeds that observed in never smokers matched for FRS, which reveals the particularly strong atherogenicity of this risk factor. Moderate cigarette consumption, as defined in this study, may not be considered a harmless alternative to smoking cessation.
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37 ASSOCIATION BETWEEN SMALL DENSE LDL AND CARDIOVASCULAR EVENTS IN FAMILIAL COMBINED HYPERLIPIDEMIA

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Introduction: The association between small dense LDL and cardiovascular events was evaluated in a group of patients (mean age=46.3 ± 12.5 years) with Familial Combined Hyperlipidemia (FCHL) recruited in the outpatient Lipid Clinic of the "Federico II" of Naples.
Methods and Results: Small dense LDL were determined in 102 probands with FCHL and 146 normolipidemic, normotensive, normoglycaemic healthy subjects. LDL particle separation was performed by Lipoprint System: seven LDL subfractions were obtained and LDL score (% of sd-LDL particles) calculated. In the group of FCHL patients 62.7% had cardiovascular events.
The association between sd-LDL and cardiovascular events was evaluated taking into account different adjustment models. Patients with elevated levels of LDL score (above the 90th percentile of control population), showed the following OR of having cardiovascular events:
3.58, 95% Confidence Interval= 1.19-10.76, p=0.023; unadjusted.
4.51, 95% Confidence Interval= 1.18-17.16, p=0.027; adjusted for age, gender, BMI, HOMA.
6.56, 95% Confidence Interval= 1.54-27.88, p=0.011; age, gender, presence of Metabolic Syndrome (MS).
Conclusion: This finding shows that this group of patients with LDL score above the 90th percentile of control population (score=10.09) is associated with presence of cardiovascular events. The association of cardiovascular events with small dense LDL is also independent of BMI, insulin resistance and MS status.

38 EFFECTS OF WEIGHT MODIFICATION ON HS-CRP IN A COHORT OF MEDITERRANEAN WOMEN: FINDINGS FROM PROGETTO ATENA

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Weight modification (Δ weight) in comparison to weight reported at 20 years of age and high sensitive C reactive protein (hs-CRP) were evaluated in a population-based cohort study in women, aged 30-69, living in the metropolitan area of Naples, Southern Italy (Progetto ATENA).