0616

08:45 h

EFFECT OF PROSTAGLANDIN E_1 ON "INFLAMMATORY" OR "ISCHEMIC" SKIN ULCER IN THE PATIENTS WITH PERIPHERAL VASCULAR DISEASE. T.Tohjima, N.Uehara, K.Sawada, Y.Tsuda, K.Sakai, H. Funayama, Y.Shiokawa. Department of Internal Medicine, Juntendo University School of Medicine, Tokyo 113 JAPAN.

Clinical, physiological and biochemical studies of PG E_1 treatment were done, in a series of 7 collagen disease patients with "inflammatory" skin ulcer and 5 diabetics with ischemic ulcers or apical gangrene of toes. Intravenous infusions of prostaglandin (PG)E_1 was given continuously in the dose of 1ng/kg/min for 72 hours. Blood samples were collected from cubital vein, before, during, right after, and at 7 days after PG E_1 therapy. Platelet aggregations induced by ADP collagen epinephrine were evaluated by light transmittance. Platelet iPG E(immuno-reactive PG E like material) levels were measured by radioimmunoassay. Essential fatty acid compositions of plasma, platelet, and red cell were analyzed by gas chromatography.

Results were as follows: 1. In all of cases, complete or almost complete healing of skin ulcers or abolition of the pain were noted. 2. Skin temperature was elevated during PG E_1 treatment. 3. The platelet basal iPG E levels were significantly decreased by PG E_1 treatment($p<0.025$). 4. The plasma and platelet linoleic acid levels were significantly higher than before the treatment(plasma: $p<0.05$, platelet: $p<0.025$). 5. In most cases, platelet aggregation was increased during PG E_1 treatment than before.

Conclusion: Dramatic therapeutic effects of PG E_1 were observed on "inflammatory" or "ischemic" skin ulcer in patients with peripheral vascular disease. This effect might be resulted from improvement of PG metabolism abnormality in the platelet etc. Platelet aggregation in vitro may dissociate from the results in vivo.

0617

09:00 h

SULFINPYRAZONE IMPROVES MYOCARDIAL BLOOD FLOW AND INHIBITS PLATELET RELEASE DURING EXERCISE IN CORONARY DISEASE. P. Steele, F. Gold, J. Sklar, Department of Medicine, Denver Veterans Administration Medical Center, Denver, CO

Exercise (EX) is associated with activation of the platelet release reaction (REL), and REL during EX is exaggerated in men with coronary disease (CAD). Sulfinpyrazone (SFP) and aspirin (ASA) inhibit REL at rest and during EX. Sixteen men with CAD underwent treadmill EX with measurement of β-thromboglobulin (β-Th) and thromboxane B_2 (TBX) (radioimmunoassay) at rest and just after angina-limited EX. Eight men were randomly assigned to SFP (200 mg po QID) and eight to ASA (300 mg po BID) and EX repeated 7 days later. Placebos were given for 7 days and EX repeated (double blind, cross-over). Myocardial blood flow distribution (MBFD) was measured during EX (^{201}Thallium; 7-pinhole tomographic image acquisition and analysis). β-Th was elevated at rest (40.±5. ng/ml; N=16; AVE±SEM; normal 18.±2. ng/ml; N=22; $p<0.001$) and during EX (120.±8. ng/ml; normal 28.±4. ng/ml; $p<0.001$). TBX was not detected in venous blood at rest, but was present in 14 men during EX (15.±3. pg/ml; N=16; normal 0. pg/ml; N=22). SFP decreased β-Th at rest (control 33.±4. ng/ml; SFP 17.±3. ng/ml; N=8; $p<0.001$) and during EX (control 121.±14. ng/ml; SFP 46.±7. ng/ml; $p<0.001$). ASA also decreased β-Th at rest (control 46.±3. ng/ml; ASA 28.±7. ng/ml; N=8; $p<0.001$) and during EX (control 118.±9. ng/ml; ASA 44.±7. ng/ml; $p<0.001$). TBX was not detected in any man either at rest or during EX during treatment with SFP and ASA. All men had abnormal MBFD during control EX. SFP improved MBFD (+364.±62. normalized counts; N=8; integrated count rate difference between control and EX with SFP; control vs placebo +17. normalized counts). ASA did not alter MBFD (+140.±29. normalized counts; ASA vs placebo +7 normalized counts). Neither SFP nor ASA altered heart rate, systolic blood pressure or ST segment depression during EX. Results suggest that REL is activated by EX in men with CAD and that SFP and ASA inhibit EX REL, including TBX. SFP has a greater effect on MBFD during EX than ASA.

0618

09:15 h

BETATHROMBOGLOBULIN AND FIBRINOPEPTIDE A IN EXERCISE-INDUCED MYOCARDIAL ISCHEMIA. A.G.G.Turpie, A.C. de Boer, B.J. Sealey, R. Butt, E. Genton, Department of Medicine, McMaster University, Hamilton, Ontario, Canada.

To investigate the role of platelet release and thrombin activity in exercise-induced myocardial ischemia, plasma betathromboglobulin (BTG) (mean ± SD, ng/ml) and plasma fibrinopeptide A (FpA) (pmol/ml) were measured before and after treadmill testing using the Bruce Protocol in normal subjects and 77 patients with suspected coronary artery disease (CAD). In normals, there was no difference between pre and post-exercise BTG (31 ± 9 v 27 ± 9) nor FpA (1.0 ± 0.8 v 0.8 ± 1.3). In 31 patients with a negative exercise test there was no difference in mean pre and post-exercise BTG conc (36 ± 14 v 41 ± 33; $p>0.1$), but there was an increase in mean FpA (1.5 ± 1.2 v 3.0 ± 3.4; $p<0.01$). Ten of the patients with negative exercise tests had documented CAD by coronary angiography and their FpA rose from 2.1 ± 1.8 to 4.3 ± 4.4 ($p<0.05$) after treadmill testing; 6 had a significant increase in FpA and 4 in BTG. In 46 patients with an abnormal exercise test (>1 mm ST-segment depression) there was an increase in mean BTG post-exercise (pre 42 ± 17 v post 60 ± 60; $p< 0.005$) and the increase was significant in 32%. The increase was more common in those patients who developed chest pain during the test. Plasma FpA increased from 1.6 ± 1.2 to 4.1 ± 4.6 in the patients with a positive test ($p<0.005$) with an increase in 33% of patients. These data indicate that exercise-induced myocardial ischemia is associated with platelet release and thrombin activity in patients with CAD. Increase in BTG after treadmill testing occurred mainly in patients with a positive test who developed chest pain. The FpA in patients with CAD increased in patients with either positive or negative treadmill tests. Increase in FpA post-exercise appears to be a more sensitive indicator of CAD than BTG.

0619

09:45 h

COHORT LABELLING OF RAT PLATELETS WITH ^{75}SE-METHIONINE J.F. Martin, Prudence Francis, D.G. Penington, Melbourne University Department of Medicine, St. Vincent's Hospital, Melbourne, Australia

The origin of platelet density heterogeneity is in dispute. We examined whether this heterogeneity is age-related or whether platelets of differing density are initially produced from megakaryocytes. ^{75}Se-methionine labels megakaryocyte protein and hence platelets produced after its intravenous injection. Rats were injected intravenously with 30 μCi of ^{75}Se-methionine. On each of the succeeding 5 days blood was taken from groups of 5 rats following intravenous injection of Prostaglandin E_1 (PGE_1), and platelets isolated by velocity sedimentation into gradients of polyvinylpurrolidone coated colloidal silica (Percoll).

The isolated platelets, which represented > 93% of the whole blood population and showed < .002% leukocyte contamination, were spun to equilibrium through continuous linear gradients of Percoll. Fractionation of these gradients yielded ≈15 density dependent platelet subpopulations, whose platelet count and density were measured.

After three washes with cold isotonic saline containing PGE_1, each fraction was also counted for platelet associated ^{75}Se activity.

The relationship of radioactivity to platelet count for each fraction for each day was measured by the mean index of concordance which was between 9.997 and 9.992 for days 1 to 5.

On day 2, modal radioactivity and modal platelet counts were found at mean densities of 1.0674 g/ml and 1.0682 g/ml respectively.

It is concluded that platelet density does not vary with platelet age.