0831
10:00 h

INCREASED CIRCULATING 6-OXO-PGF1α DURING ANGIOTENSIN II INFUSION IN MAN. K. Silberbauer and H. Sinzinger. 2nd Dept. Internal Medicine, University of Vienna, Austria.

Angiotensin II(A II) is able to stimulate phospholipase A_2. This enzyme initiates the arachidonic acid cascade. Previously we have shown that AII enhances the PGI_2 release from rat aortic rings and rat kidneys.

We, therefore, wondered if AII infusion in man might influence the plasma concentrations of 6-OXO-$PGF_{1\alpha}$ (RIA in unextracted plasma), the stable metabolite derived by non-enzymatic conversion from PGI_2. Fourteen patients with normal blood pressure, who were tested to assess left ventricular function by radionuclide angiography, received AII (2-1,5µg/min for 15 minutes i.v.). During the rise of blood pressure ($\bar{x}$:125/80mmHg to 157/102mmHg)6-OXO-$PGF_{1\alpha}$ increased significantly ($2p<0.01$). Fifteen minutes after AII termination the blood pressure returned to prevalues($\bar{x}$:125/82mmHg) and 6-OXO-$PGF_{1\alpha}$ dropped. In one patient saralasin, a competitive inhibitor of AII, had no direct effect on 6-OXO-$PGF_{1\alpha}$ (0.1µg,1µg and 10µg saralasin/kg b.w./min, each dosage was infused for 15 minutes).

The released vasodilator PGI_2, as measured by 6-OXO-$PGF_{1\alpha}$ generated in the vessel wall and in the kidney, might antagonize the vasoconstriction caused by AII.

0832
10:15 h

LOW AFFINITY PLATELET FACTOR 4/β-THROMBOGLOBULIN (LA-PF_4/βTG) ANTIGEN AND CIRCULATING PLATELET AGGREGATES DURING PROSTACYCLIN (PGI_2) THERAPY. J. Musiał, A. Szczeklik and R. Nižankowski. Department of Internal Medicine, Copernicus Academy of Medicine, Cracow, Poland.

We have found that continuous intraarterial infusion of PGI_2 alleviates rest pain and promotes healing of ischemic ulcers in patients with advanced arteriosclerosis obliterans. Since these effects could be related to the anti-platelet actions of prostacyclin, we studied serum levels of the platelet specific protein, a possible marker of platelet activation in vivo, named LA-PF_4/βTG, and compared it with those of serum circulating platelet aggregates. The former was assessed by radioimmunoassay, the latter by method of Wu and Hoak. Determinations were carried out in 16 patients with arteriosclerosis obliterans, initially and during the second day of intraarterial infusion of PGI_2 in a mean dose of 6 ng/kg/min. This therapy led to an almost uniform fall in circulating platelet aggregates. In contrast, levels of LA-PF_4/β-TG antigen at the beginning of second day of the infusion /mean = 19.19 ng/ml, ± S.D. = 8.97/ did not differ significantly from the initial values /mean = 23.59 ng/ml, ± S.D. = 13.12/.

In conclusion: 1/ In our patients vascular disease did not produce any apparent increase in serum LA-PF_4/β-TG antigen levels; 2/ Infusions of PGI_2 did not affect basal levels of this platelet specific protein, while it markedly depressed the percent of circulating platelet aggregates.

0833
10:30 h

INTERACTION BETWEEN HUMAN BLOOD PLATELETS AND POLYMORPHONUCLEAR LEUKOCYTES IN THE METABOLISM OF ARACHIDONIC ACID. J.J. Killackey, B.A. Killackey and R.B. Philp. Department of Pharmacology, University of Western Ontario, London, Ontario, Canada.

In a study of human polymorphonuclear leukocyte (PMN) prostaglandin (PG) biosynthesis from exogenous ^{14}C-arachidonic acid (^{14}C-AA), we found that combinations of platelets and PMN produced different TLC profiles of AA metabolites than either pure platelets or relatively pure PMN alone. Cells were separated from citrated whole blood by ficoll-sodium diatrizoate density gradient centrifugation. Washed platelets were prepared from citrated platelet-rich plasma. Cells were incubated with 30 uM ^{14}C-AA for 15 m at 37°C in phosphate buffered saline with or without 2-10 mg/ml serum-treated zymosan (STZ). AA metabolites were extracted and measured by radio-thin layer chromatography compared to known standards. Under these conditions, washed platelets ($1\text{-}5x10^7$) produced peaks of radio-activity corresponding to, in decreasing order, PGE_2, PGD_2 and thromboxane B_2 (TXB_2). 10 mg/ml STZ reduced the PGE_2 peak by 60%, inhibited the PGD_2 peak but did not alter the TXB_2 peak. Indomethacin (20 uM) inhibited all peaks under all conditions. Relatively pure PMN ($1\text{-}5x10^7$) containing platelets in a ratio of 1:10 PMN metabolized small amounts of AA but this increased dramatically upon the addition of STZ. Although peaks of activity corresponded to TXB_2 and PGD_2 they were not inhibited by ASA (500 uM) or indomethacin (50 uM) but were inhibited by 5 ug/ml nordihydroguaiaretic acid. This suggests that they are lipoxygenase products. PMN .mples containing platelets in a ratio of 1:3 PMN produced aximum activity corresponding to TXB_2 and this, in contrast .o platelets or PMN alone was augmented upon addition of 10 mg/ml STZ. This increase was inhibitable with cyclo-oxygenase inhibitors. These results suggest that platelets and PMN interact in the presence of STZ and AA and this interaction may play a role in inflammation.

0834
10:45 h

INHIBITION OF PLATELET AGGREGATION, MALONYLDIALDEHYDE AND THROMBOXANE FORMATION BY HYDROPEROXIDES OF ARACHIDONIC ACID. D. Aharony, J.B. Smith and M.J. Silver. Cardeza Foundation and Department of Pharmacology. Thomas Jefferson University, Philadelphia, PA 19107 U.S.A.

The arachidonate hydroperoxides 12-HPETE and 15-HPETE were biosynthesized from arachidonic acid using partially purified human platelet lipoxygenase or soybean lipoxidase respectively, and isolated by thin layer chromatography. Both compounds inhibited the arachidonic acid-induced aggregation of washed human platelets, suspended in calcium-free Krebs Henseleit solution, in a dose dependent fashion at concentrations between 1 and 50 uM. No inhibition was seen with up to 100 uM of these hydroperoxides when platelet-rich plasma was used. 12-HPETE (in micromolar concentrations) inhibited the formation of both thromboxane B_2 (radioimmunoassay) and malonyldialdehyde (spectrophotometric assay) when washed platelets were incubated with arachidonic acid. The 12-hydroxide, 12-HETE also inhibited platelet aggregation and thromboxane formation, but was less potent than 12-HPETE. We suggest that arachidonate hydroperoxide generated in platelets via the lipoxygenase pathway modulates platelet aggregation induced by arachidonic acid by inhibiting thromboxane formation.