

Friday, July 17, 1981

Poster Presentations

Drugs - II

11:00-12:30 h

Grand Ballroom Lobby Boards 232-236

0960

SULOCTIDIL: REVIEW OF ITS ANTIPLATELET AND ANTITHROMBOTIC PROPERTIES IN MAN. F. Van Stalle and G. Lambelin. Continental Pharma, Brussels, Belgium.

Suloctidil(S.) - 1-(4-isopropylthiophenyl)-2n octylamino-propanol - is a vaso-active compound endowed with antiplatelet and antithrombotic properties.

After administration to healthy volunteers it was found to inhibit thromboxan and collagen induced aggregation.

In a double blind cross-over set up - S. 200 mg T.I.D. vs. placebo - the induction of circulating platelet aggregates by venous occlusion was highly significantly inhibited.

Following positive results on P.S.T. in the baboon a.-v. shunt model, studies on P.S.T. were initiated in man:

23 patients with valvular prosthesis, all under coumarine therapy, were admitted to a double blind parallel study of 6 weeks duration comparing S. 200 mg T.I.D. (n=11) to placebo (n=12). P.S.T. (⁵¹Cr-labeling) measured before and during the last week of the study, was unchanged in the placebo and significantly increased in the S. treated group. Similar results were obtained measuring platelet regeneration time according to a modified Stewart method in an open study (n=6) in valvular prosthesis and in a double blind parallel study (S. n=25; placebo n=27) in valvular prosthesis, coronary artery disease and myocardial infarction.

In patients with obstructive arteriopathy (Fontaine II & III) inhibition of thrombin induced platelet M.D.A. production and reduction of increased BTG levels have been observed under S. therapy at rest and after ischemia.

In 31 patients suffering from recurr. ven. thrombosis, admitted to a double blind cross-over study comparing S. 200 mg T.I.D. to placebo-2 periods of 3 months each - a striking difference in the clinical evolution (placebo 12 events, S. none) was paralleled by consistent changes in biological parameters such as platelet aggregation, PF₄ and BTG.

The results obtained in pharmacological as well as in efficacy studies have justified the initiation of larger scale trials to evaluate the compounds antithrombotic potential.

0959

ANCROD IN THE MANAGEMENT OF RAPIDLY PROGRESSING GLOMERULONEPHRITIS. H.I. Glueck, V.E. Pollak, M.A. Weiss, A. Lebron-Berges, M.A. Miller. Department of Pathology and Laboratory Medicine and Department of Nephrology, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA

Ancrod, (Malayan pit viper venom) which produces *in vivo* defibrination, has been shown to improve renal function and decrease fibrin deposition and crescents in experimental glomerulonephritis. Ancrod was given for 14 days to six patients with glomerulonephritis, moderate to severe renal functional impairment, crescents, and/or fibrin deposition in glomeruli. Ancrod treatment resulted in fibrinogen levels <50 mg/dl without bleeding, normalization of previously elevated factor VIII and von Willebrand factor levels, and normalization of *in vitro* platelet hyperaggregation. Renal function improved in two patients and was affected little in three; in the sixth deterioration of function was arrested. Serial renal biopsies showed a relatively rapid decrease of glomerular thrombi in three patients, and no increase in glomerular sclerosis. Ancrod administration appears to be safe, and may have a role in treatment of certain types of glomerulonephritis.

0961

RANDOMIZED STUDY OF TICLOPIDINE ON CEREBRAL VASOSPASM FOLLOWING RUPTURED ANEURYSM. M. Mizukami¹⁾, H. Kikuchi¹⁾, H. Ono²⁾, M. Taneda³⁾ and Cooperative Study Group in JAPAN. 1) Neurological Surgery, Mihara Memorial Hospital, 2) National Cardiovascular Center, 3) Nagasaki University, 4) Hanwa Memorial Hospital.

Based on our hypothesis for the mechanisms of chronic cerebral vasospasm following subarachnoid hemorrhage (SAH), we have made a randomized study of Ticlopidine in preventing cerebral vasospasm in 71 patients with ruptured aneurysm.

Materials and Methods: Ticlopidine is a potent inhibitor of platelet aggregation and adhesiveness. The inhibitory nature of this drug is distinct from that of Aspirin which not only is an inhibitor of platelet aggregation but also suppresses PGI₂ generation in the vascular wall. Forty one patients were given Ticlopidine (400 mg/day) and 30 patients served as a control group. All patients underwent direct intracranial operation and 46 of them were operated upon 4 days after SAH. High density which indicates subarachnoid clot was observed on pre- and postoperative CT scans in the majority of both groups.

Results: Mortality was 12% in Ticlopidine group and 17% in control group. As for morbidity, excellent results were obtained 57% in Ticlopidine group and 42% in control group in Grade 1-3. In order to know the effects of Ticlopidine on cerebral vasospasm and ischemic neurological deficit caused by vasospasm, 32 patients who did not show preoperative neurological deficit and underwent surgery within 4 days after SAH were analyzed in relation to the presence or absence of high density on postoperative CT. The development of postoperative vasospasm was almost same (71.4-76.5%) in two groups, but permanent ischemic neurological deficit was 28.6% in Ticlopidine group and 66.7% in control group when postoperative CT scan showed high density in subarachnoid space.

This preliminary randomized study indicates that Ticlopidine may be effective on prevention of postoperative ischemic neurological deficits due to vasospasm.