Tuesday, July 14, 1981

Oral Presentations

Thrombosis, Clinical – III

Platelet Inhibitors

08:00–09:30 h

Thrombosis, Clinical – IV

Venous Thrombosis Treatment

09:45–11:00 h

Cinema 1

0270

08:00 h

ANTIPLATELET AGENTS IN DIABETIC LOWER EXTREMITY VASCULAR DISEASE. A VA COOPERATIVE STUDY. J. Colwell (Study Chairman), 10 VA Medical Centers and VAMC, Charleston, SC, USA.

Peripheral vascular disease is a devastating complication of diabetes mellitus. Post-operative vascular death rates are 10% or more following amputation for gangrene in diabetic patients, and three year mortality approaches 30%. An additional 20-30% of patients require subsequent amputation for diabetic gangrene. In view of these statistics, and because of the postulated role of the blood platelet in diabetic vascular disease, a collaborative study on antiplatelet agents was begun in 10 VA medical centers in 1977. In a double-blinded study, aspirin (325 mg tid) plus dipyridamole (75 mg tid) or placebos are given to adult diabetic males who had suffered a recent amputation for diabetic lower extremity vascular disease. End points are major vascular events after at least 3 years of follow-up.

Recruitment of 231 subjects was completed by May, 1980. Baseline characteristics are well matched in both groups. Mean age is 59.6 years, duration of diabetes 12.7 years, smoking history 33.3 pack years, and treatment with insulin 68%. Previous myocardial infarction, congestive heart failure, and/or cerebrovascular disease is present in 17-18% and retinopathy is present in 40% at entry. About 43% have more than one vascular complication at baseline.

Mean duration of follow-up is now 18 months. Major vascular events in separate patients are: 40 amputations, 31 deaths, 5 myocardial infarctions. Numerous less serious vascular events have also occurred, as have multiple events in single patients. Therapy has been stopped in 17% of patients, but rarely due to drug side effects. Compliance with therapy has been good.

We conclude that this study will provide important new information on the natural history of lower extremity vascular disease in diabetes. It will also provide definitive data about the efficacy of antiplatelet agents in diabetic vascular disease.

0271

08:15 h

CONTROLLED CLINICAL TRIAL OF AN ANTIAGGREGATING AGENT, TICLOPIDINE, IN VASCULAR ULCERS OF THE LEG. C. Bourde*, E. Eschwège**, M. Verry***, * Dept of angiology, Résidence du Parc Clinic, Marseille ** Dept of biostatistics, Villejuif, *** Laboratorie Millot Sanofi Paris, France.

A randomized double-blind clinical trial, Ticlopidine (T) vs Placebo (P), was performed to assess the effect of an antiaggregating therapy on the healing of arteriosclerotic and venous peripheral ulcers. The 26 in-patients of both sexes (12 controls and 14 treated subjects) were comparable, before treatment, in the two groups, for all the clinical and thermographic variables. Particularly, the clinical stage of ulcers, gradated from 1 to 7 according to the increasing severity, was similar in the two groups ($P = 6.3 \pm 1.2$ - $T = 6.0 \pm 1.5$). The thermographic state of the ulcers evaluated by a thermographic index (sum of thermal values of ulcer and its periphery, of thermic distribution and of thermal gradient) showed no statistical difference between the two groups ($P = 6.1 \pm 1.1$ - $T = 6.3 \pm 1.3$). The patients were administered orally P or T 1 g daily for the first week and 750 mg daily for the second week. Simultaneously, a standard local treatment was provided. After two weeks of treatment, we observed an important and significant improvement of the evolutive stage of ulcers treated by T ($P = 5.2 \pm 1.9$ - $T = 3.0 \pm 2.1$ - $p < 0.05$). These data are confirmed by telethermographic evolution of hypothermal area of the ulcers : it decreases up to healing in 9 % of controls and in 64 % of treated patients ($p < 0.05$). A good tolerance of the general treatment was observed in the two groups. The therapeutical benefit provided by the antiaggregating drug, i.e. improvement of epithelialisation and local revascularization, is related to its antithrombotic action on the platelet and red cell aggregates which contribute for occlusion of capillary and arterioloveinular vessels around the ulcers.

0272

08:30 h

THE EFFECT OF PIRACETAM IN PREVENTING RECURRENT DEEP VENOUS THROMBOSIS. R.L. Bick, M.K. Nix, and V. Skondia. San Joaquin Hematology Oncology Medical Group, California Coagulation Laboratories, Bakersfield, California, and UCB Pharmaceuticals, Brussels, Belgium.

Piracetam, 2-Oxy-1-pyrrolidine Acetamide is a cyclic derivative of gamma-aminobutyric acid. This agent has recently been shown to have activity in humans as a platelet suppressant. For the prophylaxis of recurrent deep venous thrombosis (RDVT), many clinicians are now resorting to antiplatelet agents, rather than vitamin K antagonist because of the questionable efficacy and severe bleeding associated with these latter agents. The most common antiplatelet agents used for prophylaxis of RDVT are ASA, dipyridamole, and sulfinpyrazone given alone or in various combinations. The purpose of this study was to assess the efficacy of Piracetam as an antiplatelet agent for the prophylaxis of RDVT. Twenty patients with a history of RDVT or with active DVT were entered into the trial; 10 of these were randomized to a combination of ASA (600 mg. BID) + Dipyridamole (50 mg QID) and 10 were randomized to Piracetam at 9.6 gm/day as 2.4 gm QID. Pre-ingestion evaluation included a complete history and physical and complete evaluation of hemostasis including PT, PTT, FDP, PSO_4, AT-III, platelet adhesion, platelet aggregation, PF-4, and platelet survival by sizing. Follow-up evaluation was performed at 6 weeks, 3 mo., and 6 mo. All patients demonstrated a laboratory response to antiplatelet therapy as manifest by aggregation and PF-4 studies, all patients on Piracetam and most patients in the other group demonstrated improvement in platelet survival studies. During the six month observation, no patients ingesting Piracetam developed rethrombosis; however, two patients ingesting ASA/Dipyridamole relapsed. These results suggest Piracetam to be equal to and possibly superior to ASA/Dipyridamole in preventing RDVT. In view of this efficacy together with lack of toxicity Piracetam may prove highly useful as a clinically effective antiplatelet agent in the prophylaxis of RDVT.