EXPERIMENTAL STUDY OF A PLATELET ANTIAGGREGATING AGENT - APPLICATION TO TICILOPIDINE.


The authors consider the various methods suitable for in vivo study of the anti-aggregating properties of a new drug - Ticlopidine:

- study of photometric ADP-induced aggregation and screen filtration pressure in vivo in the rabbit treated per os for 5 days with doses of 25 and 50 mg/kg/day. This gave average inhibitions of 20% and 45% respectively.
- study of circulating platelet aggregates using the method of Wu and Hoak after continuous infusion of 0.5 and 1% of heparin. The principle of the method involves definition of an aggregation index: the ratio between the platelet counts in the two specimens (EDTA + formol 1% + EDTA alone).

The average results showed: control group index 0.9 after infusion of ADP 0.57- after infusion of ADP under the influence of Ticlopidine (50 and 100 mg/kg/day) 0.65 to 0.78.

- the mechanism of action of the drug was studied using crossed aggregation experiments and by study of interference with insulin or ionizable groups of the platelet membrane (Isotope method, electrophoresis in liquid phase).

In parallel with these experiments, studies in vivo in the rabbit and in patients (obstructive arterial disease, Raynaud's syndrome) are in progress: interference with membrane groups, rheological properties (viscosity, rouleau formation, erythrocyte deformability) and biochemical properties (erythrocyte glycolysis enzymes).

NEW METHOD FOR ASSESSMENT OF PLASMA VON WILLEBRAND FACTOR. T. Sano, T. Motomiya, H. Masahiro and H. Yamashita. Asahana Tokyo Metropolitan Hospital, Tokyo Medical and Dental University and Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan.

As much interest has been focused on von Willebrand factor (vWF) in diabetes mellitus and atherosclerosis, request to determine vWF has been increasing recently. Two methods for assessment of plasma vWF level, without platelet aggregometer, were devised. 1) Platelet-rich plasma (PRP) sensitivity to ristocetin-induced platelet aggregation: PRP was separated, without centrifugation from citrated blood. Serially two-fold diluted ristocetin (16 to 16x2 mg/ml) was prepared in a Gloko Microtiter tray and PRP (25 μl each) was added to each concentration of ristocetin. Then the ristocetin-PRP mixture was agitated for 15 seconds using a Kowa Kisei Microterm and the minimum effective final concentration of ristocetin to give platelet aggregation was obtained microscopically and this was defined as PRF sensitivity to RIPA. This method is convenient for screening test. 2) vWF assay: Serially two-fold diluted plasma (2 to 16x24 times, in Tri-made (PH 7.2 containing 11 mg/ml hirudine serum albumin), fixed and washed platelet suspension (6x10^9/l, Macfarlane et al. 1975) and 3 mg/ml ristocetin were mixed (25 μl each) in a microtiter tray and agitated for 15 seconds. The maximal plasma dilution to induce platelet aggregation was obtained microscopically and defined as the titer of plasma vWF. In normal subjects, minimum effective ristocetin concentration (PRF sensitivity to RIPA) was around 1 to 0.5 mg/ml and maximal plasma dilution to give platelet aggregation (vWF titer) was around 16 to 32 times. The present methods have a good reproducibility and are performed easily without aggregometer and thought to be useful clinically.