THE EFFECTS OF TWO NEW ANTITHROMBOTIC AGENTS (HYDROXYQUINAZOLINES) ON PLATELET SHAPE AND AGGREGATION, S.S. Tang and M.H. Fregni, Department of Physiology, McGill University, Montreal, Quebec, Canada.

Recently, a new series of compounds was reported as a potent, nontoxic and long-lasting antithrombotic agent based on in vitro and in vivo animal tests (Bristol Laboratories). We report on the effects of this compound, 5-methyl-1,2,3,5-tetrahydroimidazo[2,1-b]quinazolin-2-one hydrochloride monohydrate (B-4162), on rabbit and human platelet shape change and aggregation, and compare them with other agents known to affect platelet adenosine 3':5'-cyclic monophosphate (cAMP). In aggregometer studies with citrated (6.25%) platelet-rich plasma (PRP), both BL-compounds were found to inhibit platelet shape change and aggregation induced by ADP, thrombin, serotonin and adenosine-3'-cyclic monophosphate (cAMP). Typically for human PRP, aggregation induced by 10 mM ADP was inhibited by 90% with 10 mM BL-3456 or 0.1 mM prostacyclin (PGI2) (PGE1), and by 60% with 10 mM BL-3456. In corresponding rabbit PRP test, 60% inhibition was caused equally by 1 mM BL-3456 or 0.1 mM prostacyclin (PGI2) (PGE1), and by 0.6 mM PGE1. Both BL-compounds, like methyloxanthines, were found to potentiate the inhibitory effect of PGE1 on platelet aggregation but did not potentiate the action of methyloxanthines. Moreover, they both slightly increased the basal level of rabbit cAMP (60%) and potentiated the elevation of cAMP by PGE1. These BL-compounds are potential inhibitors of human and rabbit shape change and aggregation and appear to act by a mechanism distinct from that of PGE1.

AN ACQUIRED PLATELET STORAGE POOL DEFICIENCY IN PATIENTS WITH SEVERE VALVULAR HEART DISEASE. C.B. Harbury and C.A. Calvan, Stanford University School of Medicine.

The purpose of this study was to assess whether patients with severe valvular disease damage their platelets in vivo and acquire a platelet storage pool deficiency. Forty-three preoperative valve patients, 43 coronary artery bypass patients (CABG) and 22 concurrent normal controls were studied. Platelets were counted by phase and forward light scatter photographs. Total and releasable platelet ATP and ADP were measured by the luciferase assay (Nolayman). Nucleotides were expressed in nanomoles per 10^9 platelets. Analysis is by a two-tailed t test. Releasable ATP control = 1.1 ± 0.4 µmol, ADP = 38.3 ± 3.4 µmol, cAMP = 3.3 ± 0.4 µmol, cGMP = 1.7 ± 0.4 µmol, significant difference. Releasable ATP: control = 1.1 ± 0.4 µmol, ADP = 1.2 ± 0.4 µmol, cAMP = 3.3 ± 0.4 µmol, cGMP = 1.7 ± 0.4 µmol, different in significant difference. Total ATP control = 1.7 ± 0.4 µmol, ADP = 2.6 ± 0.6 µmol, cAMP = 5.3 ± 1.1 µmol. This is not a significantly lower value: t = 1.07. CABG patients were not significantly different from controls, but were significantly different from valve patients. Twenty-six valve patients were studied postoperatively. Ten had received platelet transfusions and were excluded from quantitative assessments. Estimated blood loss (EBEL) valve = 1556 cc, CABG = 734 cc, p<0.001. Transfused red cells (ERBCs) valve = 8.5 g, CABG = 6.5 g, p<0.01. Postoperative chest tube drainage (CTD) above and below 400 cc, CABG = 400 cc, p<0.01. Ten valves and 2 CABG received platelet transfusions. If these are included and considered bleeders x^2 = 11.01, p<0.001. These patients with severe valvular heart disease appear to have a mild acquired platelet storage pool deficiency and a significantly greater bleeding tendency at surgery.


A new technique for platelet isolation from five ml of total blood on metrizamide gradient has been applied to the study of platelet coagulant activities. Assay methods have been described: contact product forming activity (CPA), collagen induced coagulant activity (CICA) and platelet factor 4 (PF4) have been measured in the metrizamide gradient platelets (MGP) and found similar to that of platelets in platelet rich plasma (PRP). Platelet coagulant activities of the MGP have been measured in patients with hemorrhagic tendencies like Bernard-Soulier (B-S) patients or those with thrombotic tendencies including diabetes with or without vascular complications or patients with transient ischemic attacks (TIA). CICA was not found in all the 3 patients with B-S syndrome. Of the 10 diabetics showed an increased CPA activity while 5 showed an increased CICA activity contrasting with the normal activities found in diabetics without vascular complications; PFT activity is increased in the two groups of diabetes. 3 patients of the 7 with TIA had an increased CPA as well CICA.

The results suggest that these activities may play some role in diabetes with vascular complications and in some cases with TIA.