Poster Board P6-088

0685 SUITABILITY OF THE FACTOR SENSITIVE THROMBOPLASTIN FS FOR THE CONTROL OF ORAL ANTICOAGULATION

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A new rabbit brain thromboplastin, Thromboplastin FS (Dade) was tested in 4 centers involving 997 patients including 806 coumarin treated patients. It was compared in each center with another rabbit brain preparation (Thromboplastin C, Dade) and with the routinely used thromboplastin (human brain thromboplastin, Thrombotest, Thromborel and Thromboplastin Stago). Tested on plasmas deficient in factor II, V, VII and X the sensitivity of Thromboplastin FS was comparable to human brain preparation and better than Thromboplastin C, Thromborel and Thromboplastin Stago. The calibration constants (cc) between the thromboplastins calculated according to WHO recommendations confirmed the outstanding sensitivity of Thromboplastin FS. It was comparable to human brain thromboplastin (cc=0.986), less sensitive than Thrombotest (cc=0.663), much more sensitive than Thromboplastin C (cc=2.115-2.377), Thromborel (cc=2.323) and Thromboplastin Stago (cc=1.896). The new Thromboplastin FS may be very promising for the control of oral anticoagulation.

P6-089

0686 AUTOMATED CONTROL OF COUMARIN THERAPY BY CHROMOGENIC FACTOR X ASSAY

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A fully automated chromogenic substrate method for measuring plasma factor X has been used to monitor patients attending an anticoagulant clinic. Thirty six patients already established on coumarin therapy were studied by taking four citrate plasma samples from each at monthly intervals. Factor X was assayed in 10 µl aliquots by an adaptation of the method of Aurell & Friberger (Kabi Diagnostica Information Sheet) in an LKB Mark II Analyser with pre-injection facility, allowing 60 s pre-incubation with RVV before addition of the substrate S2222. Activity was measured as Δ OD 405/min. Calibration curves were prepared by dilution of lyophilyzed normal plasma, and six coumarin controls were interspersed, with values of 18% (1.09 SD) & 22.2% (1.50 SD) of normal. The F X levels in the 36 patients at each of the monthly clinics were 23.6% (5.1 SD), 23.1 (4.9), 23.1 (5.0) & 23.7% (4.8) of normal, corresponding to RVV/phospholipid coagulant assays of 22.3% (6.3 SD), 22.3 (6.3), 20.7 (5.8) & 21% (6.1) of normal respectively. The prothrombin activities at each visit, expressed as prothrombin time ratios (PTR), averaged 2.64, 2.80, 2.64 & 2.56. Regression analysis of chromogenic F X values on individual PTR's gave r=0.65, which led to no change in coumarin dosage when this was repeated blind. The results suggest that rapid, automated F X assays may be suitable clinically, technically & geographically in long-term coumarin control when apparatus & reagents become competitive with established coagulant procedures.

P6-090

0687 A NOVEL CHROMOGENIC ASSAY EQUIVALENT TO THE ONE STAGE PROTHROMBIN TIME (PT)

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A chromogenic assay equivalent to the PT has been developed which, it is expected, will allow the standardization of therapeutic limits. Assays were performed by combining 0.25 ml S-2238 (2mM), 0.40 ml tissue thromboplastin, and 0.050 ml plasma in 1.40 ml TRIS buffer (pH=8.50, I=0.15). The rate of thrombin generation was obtained by automatically computing the slope of ln (A_{405nm}/min.) vs time. The results indicated that thromboplastin does not interfere with S-2238 hydrolysis. Thrombin production (A/min.) occurs just before clotting, rises rapidly to a maximum and falls. During its rise, the thrombin concentration increases as a positive exponential, exp(bt). The exponential rate, called b, is constant from the initial appearance to the maximum thrombin concentration. b is proportional to plasma concentration and to log Factor (X, VII, V) concentration for dilutions with deficient plasma. Log 1/b correlates with log PT using dicoumarolized plasmas. Thrombin appearance is quite delayed (12 min.) in diluted, deficient plasma. Thus, the assay appears sensitive to the extrinsic system and can be used to monitor dicoumarolized plasmas. Unlike the standard PT, this assay directly measures the rate of thrombin production and could be standardized by comparing the exponential rate to specific Factor concentrations.