0449 BIOCHEMICAL COMPARISON OF INTERMITTENT STREPTOKINASE AND INTERMITTENT STREPTOKINASE AND PLASMINOGEN THERAPY

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A comparison has been made of some biochemical parameters during streptokinase and streptokinase combined with lys-plasminogen intermittent therapies using a twice a day dosing regimen. Results showed that while the fibrinogen levels, fibrin(ogen) degradation products and total fibrinolytic activity appeared very similar there was a pronounced difference in the effect on anti-plasmin levels and on the amount of activator complex formed. With the combination therapy the anti-plasmin levels fell to zero and remained at zero throughout the therapy while the level returned daily to approximately 50% of normal with the streptokinase alone regimen. The amount of activator complex formed was much higher in the combination therapy and this could explain the lessened side effects observed in this type of therapy.

0450 RATES AND MECHANISMS OF CLOT LYSIS DURING VARIOUS STREPTOKINASE (SK)-PLASMINOGEN (PLGN) TREATMENTS

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Iodine labelled washed plasma clots were immersed alternately in SK solutions (7.5-4000 iu/ml) and lys-PLGN solutions (2.0 PLGN units/ml) and lysis rates were assessed by release of the ^{125}I label. The composition of the lysates obtained during the SK → PLGN and PLGN → SK regimens was studied by detergent gel electrophoresis and by two-dimensional immunoelectrophoresis. Lysis rates were also monitored in serum and plasma environments compared to buffered systems. Clots lysed completed in buffered PLGN during the SK → PLGN regimen while the PLGN → SK regimen yielded only partial lysis; the composition of the respective lysates suggested a more vigorous digestive procedure (free D dimer and fragment E present) during the SK → PLGN regimen. During the buffered PLGN → SK regimen the concentration of SK marginally affected lysis rates while a concentration of 125-250 iu/ml was found optimal during the SK → PLGN regimen. These data were confirmed when lysis was achieved in serum and plasma using an SK → PLGN regimen and suggested that the inhibitive effect of fibrin clot lysis was in the order: serum inhibitors, SK antibodies and fibrinogen. Lysis of clots in serum or plasma with either regimen always yielded only D dimer-E and its higher molecular weight complexes.

0451 A COMPARISON OF GLU- AND LYS-PLASMINOGENS : BINDING TO FIBRIN AND EFFECT ON LYSIS RATES

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Partially activated (lys-) plasminogen (plgn) exhibits a greater affinity than native (glu-) plgn for fibrin. To complement previous data obtained using radio-labelled plgn we have studied a range of plgn concentrations, used functional assays (S-2251, caseinolysis and binding to lysine sepharose), ensured that the fibrin is totally cross-linked, correlated affinities of plgn for fibrin with lysis rates when plgn was activated by SK, and compared buffer with plasma and serum systems containing native inhibitors. When fibrinogen or plasma was clotted in the presence of plgn then lys-plgn gave greater incorporation and faster lysis rates than glu-plgn. When washed fibrin was immersed in plgn lys-plgn again showed greater affinity than glu-plgn for fibrin, but on transfer to SK lysis rates were identical. In the most potent lysis system, immersion of fibrin in SK then transfer to plgn, lysis was slightly faster in glu- than lys-plgn. Incorporation of purified glu-plgn into plasma fibrin exceeded that of native plasma plgn and the former promoted lysis more effectively. Binding of lys-plgn to fibrin was the more susceptible to inhibition by plasma or serum. The pertinence of these data to *in vivo* requirements for thrombolytic therapy is speculative, but clearly it cannot be assumed that lys-plgn must be more effective than glu-plgn, in promoting fibrinolysis, because of superior affinity for purified fibrin.