

DIFFERENCE IN THROMBOLYTIC EFFECT BETWEEN HIGHER AND LOWER MOLECULAR WEIGHT FORMS OF UROKINASE. T. Suyama, M. Nishida, Y. Iga and R. Naito. The Green Cross Corporation Research Laboratories, Osaka, Japan.

Urokinase (UK) from human urine has been widely used for thrombolytic therapy in Japan. However, commercially available preparations are not identical but consist of mainly two forms of UK with higher and lower molecular weight (H-UK and L-UK). An attempt was made in this report to compare thrombolytic activity of H-UK with that of L-UK on artificial thrombi produced from human blood by a modification of Chandler's loop method, which was somehow comparable to the situation in vivo. Two active forms of UK were purified from crude preparation by gel filtration. The approximate molecular weight of the H-UK was 54,000 and of the L-UK 34,000. The potency of UK was determined by "two-stage lysis time method" and expressed by International unit(IU). Thrombolytic activity measured by Chandler's method was calculated as % lysis of the control thrombus that was formed in the absence of UK.

As a result, thrombus-dissolution time of H-UK was much shorter than that of L-UK. Furthermore, concentration of H-UK (IU/ml blood) necessary to induce 50% lysis was approximately one half lower than that of L-UK. The similar results were obtained on artificial thrombi from the blood of dog, rat and rabbit. The data suggest that H-UK seems to be more effective on treatment of thromboembolic disorders as compared to L-UK in terms of the same IU basis.

BIOLOGICAL EFFECTS OF THE ADMINISTRATION OF AN EQUIMOLAR STREPTOKINASE-PLASMINOGEN COMPLEX IN MAN. M.Verstraete, J.Vermeylen, W.Holleman and G.H.Barrow. Lab. of Blood Coagulation, Dept. of Medical Research, University of Leuven, Belgium and Experimental Biology Division, Abbott Laboratories, North Chicago.

Two different lots of a 1:1 stoichiometric streptokinase-plasminogen (SK-Plg) complex were prepared (J. of Biol. Chem. 242, 1419-1425, 1967). In vitro experiments suggested that the SK-Plg complex did not react with antisera against human plasminogen and SK indicating that the antigenicity of the complex might be different from that of the precursor molecules. These changes might result in a modified specificity and immunogenicity in man and therapeutic consequences both as far as the dose and repeatability of treatment are concerned. Therefore the SK-human plasminogen complex was administered in man. Five patients received a lot SK-Plg complex prepared with heat treated human plasminogen, 4 patients another non-lyophilized lot SK-Plg complex prepared with unheated human Plg. The administration of SK-Plg complex was associated with signs of immediate antigenicity in 3 and of immunogenicity in all patients.

TREATMENT OF THE HEMOLYTIC-UREMIC-SYNDROME WITH STREPTOKINASE AND ANTIPLATELET DRUGS. A.H. Sutor, F. Schindera, H. Wehinger, G. Eisenmann, and W. Künzer. Universitäts-Kinderklinik Freiburg, Germany FR.

In total we treated 11 patients with the hemolytic-uremic-syndrome (HUS) with streptokinase (SK) and platelet-aggregation-inhibitors (acetylsalicylic acid and/or dipyridamol). 9 of them survived. One patient died from bleeding complications which were probably due to erraneous underdosage of SK. Another patient had a relapse of HUS and died 18 months after treatment with aggregation inhibitors had been discontinued. All patients had very high levels of plasminogen-proactivator. We therefore recommend a high initial SK-dose of 6000 U/kg and a maintenance dose of 1500 U/kg/h for at least 24 h. We control SK-therapy with PP-determinations to avoid hyperplasminemia which may cause bleeding complications. Follow-up studies 2 years later showed normal renal function in 5 of the 9 survivors.