

1203 M945. A NONHEPARINIC MUCOPOLISACARID. IN VIVO STUDIES (HUMANS)

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It has been reported, in in vivo studies (dogs, rabbits), that the antithrombotic protection of heparin is clearly related to AntiXa enhanced activity, than to a particular KCCT level(1)(2)

In this work, 20 healthy individuals were studied. KCCT, TT, AntiXa (Denson-Bonnar) determinations were made. In vitro studies of M945 actions on these tests, at different plasma concentrations of the drug (0.02-0.2UI/ml) were performed. M945 was then SC administered, 100UI/kg weight, and blood samples collected each two hours, and KCCT, TT, AntiXa studied.

In vitro samples showed no differences in KCCT, TT, and Anti Xa activity, that the ones expected when using heparin. In 16 humans, in post infusion studies, it was seen that nearly no changes on KCCT or TT occurred, while AntiXa was enhanced in its activity, up to 90" (more than corresponding values for 0.2UI/ml of heparin in plasma).

Further work with similar drugs to M945, should open the possibility of safe antithrombotic treatments in patients with anticoagulant contraindications.

1. Szwarczer E, Giuliani R, VIII World Congr Cardiol, Abstr, 1, 1159, pg 381, 1978

2. Chiu HM, Hirsh J, Yung WL, Regoeczi E, Gent M, Blood, Vol 49, No2, 171, (feb), 1977

1204 THE IMPORTANCE OF ANTI Xa PLASMA CONCENTRATION FOR HEPARIN EFFECTIVENESS

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Low antiXa concentrations have been described in patients with DIC, cirrhosis, women on the contraceptive pill, and also as a familial phenomena, in some cases as low as 40%. It has been claimed that AntiXa concentrates infusions should be administered to these patients, to allow heparin action, (if heparin therapy needed) The influence of varying amounts of AntiXa on heparin potentiating effect, was studied.

A precise two step technique, for the measurement of AntiXa heparin potentiating effect was performed. It was carried on human adsorbed plasma (Barium sulfate, 100mg per ml, 3 times), using concentrations of 100% to 10%. Dilutions were made in Trizmal Buffer IS 0.15.

Added heparin potentiates the natural inhibitor to usual levels, even if AntiXa concentration is as low as 10%, if added heparin is 0.08UI/ml or more.

Only below 0.08UI/ml of heparin, 30% of the inhibitor is needed to obtain the same potentiating effect as with 100% AntiXa concentration.

It is therefore unnecessary to infuse AntiXa concentrates, previous to heparin treatment, for it will be therapeutically effective, even in patients with 10% Anti Xa concentration.

For effective heparin prophylaxis, 30% inhibitor concentration in plasma is needed.

1205 CRITICAL ASPECTS ON ANTI Xa HEPARIN ASSAYS IN PLASMA

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In vitro measurement conditions for precise determination of AntiXa potentiating effect of heparin were studied: Ionic strength, heat (56±15°) platelets, factor X concentration in test and substrate plasmas.

AntiXa-Xa reaction is enhanced using buffer with 0.15 IS. Presence of factor X in tested plasma, even in low concentrations (1.7%) produce shorter reaction readings, and curve regression lines, particularly at high heparin concentrations (more than 0.08UI/ml).

Heat doesn't destroy factor X completely. It also reduces AntiXa's reactivity, with an even more disturbing effect than factor X presence. Frozen and thawed platelets when mixed with adsorbed test plasma, do not alter final results of the reaction; but if the mixture is heated (15'-56°C), reading results of the reaction are altered.

A precise reading of AntiXa potentiating effect of heparin or other glucosaminoglycans can be obtained working on deficient in factor X plasmas, using 0.15IS, and Ph7.5, and measuring residual Xa on VII-X def. plasma