A REALITY-DRIVEN RAT HIND LIMB MODEL FOR STUDYING SKELETAL MUSCLE ISCHEMIA/ REPERFUSION INJURY

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Background: Acute limb ischemia may occur as a consequence of peripheral artery disease, but is also induced during surgery on extremities. Reperfusion can be accompanied by extensive ischemia/reperfusion (I/R) injury, which may cause considerable morbidity. An effective treatment of I/R injury in extremities is still missing.

Aim: The aim was to establish an acute hind limb model with shortened I/R times in consideration of 3R principles which would minimize the potential pain and suffering of the animals, but still representing a good model to analyze the effect of drug candidates on I/R injury. Furthermore, we wanted to characterize the effect of the cell-protective substance Dextran Sulfate (DXS) as well as the anti-coagulant Lepirudin in a rat model of hind limb I/R injury.

Model: Wistar rats were subjected to 2-4 hours of hind limb ischemia and two hours of reperfusion in order to obtain a moderate I/R injury. For the induction of ischemia the femoral artery was ligated under maintenance of the venous return. Compounds were injected via the femoral artery. At the end the rats were sacrificed and tissue samples were taken.

Results & Conclusions: Compared to a first series, where rats were subjected to 4 hours of ischemia and 24 hours of reperfusion during which they were awake, a considerable reduction of distress and discomfort can be obtained using an acute setting. Furthermore, Lepirudin as well as DXS reduce edema significantly. We conclude that Lepirudin and DxS are useful compounds for the reduction of I/R injury in extremities (see Fig.1).

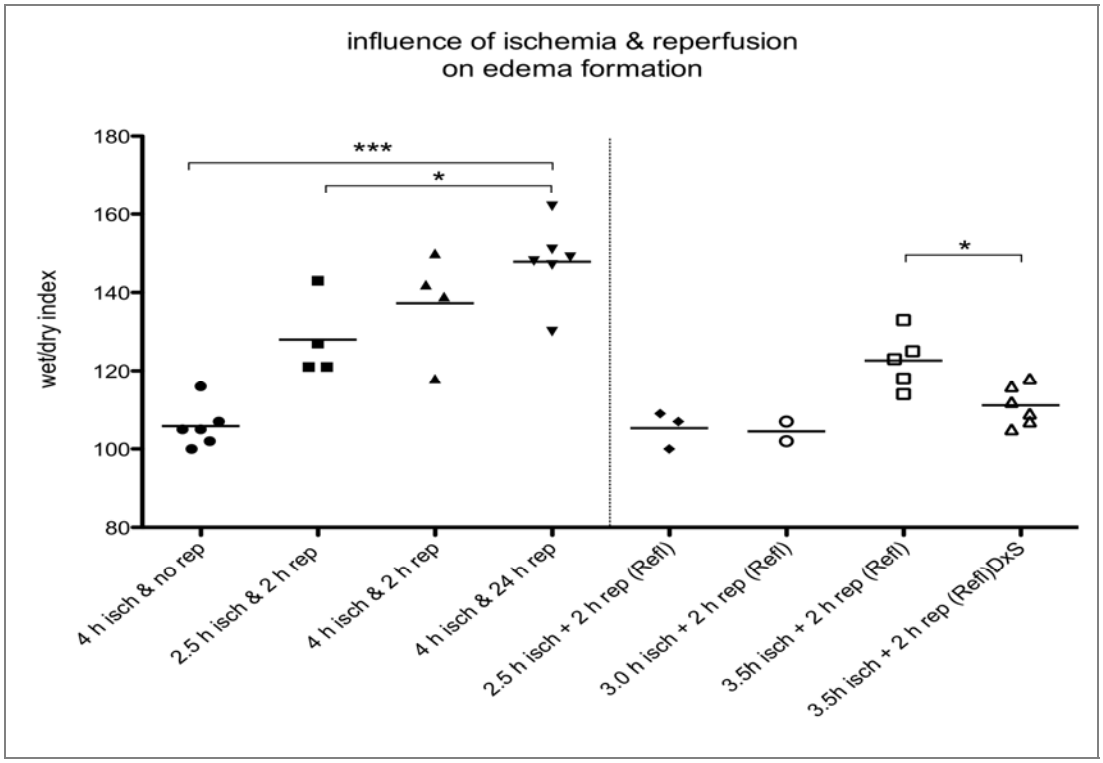

Figure 1: Significant reduction of edema by DxS & Lepirudin. *Abbreviations*: Isch. Ischemia; Rep, Reperfusion; Refl. Refludan (Lepirudin).