Comparison of pharmacokinetics of unfractionated heparin and low molecular weight heparin after subcutaneous administration in rats

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Unfractionated heparin (UFH) and its derivative, low-molecular-weight heparin (LMWH) are the main drugs in the treatment and prevention of thrombosis. However, UFH has pharmacokinetic limitations not shared by LMWHs. UFH’s chemical heterogeneity and polydispersity lead to nonspecific protein binding, yielding poor pharmacokinetics on subcutaneous (sc) injection. UFH is administered by intravascular route and therefore its therapeutic use is usually restricted to the hospital setting, where its effect can be monitored and its dosage adjusted frequently. LMWHs, in turn, may be administered subcutaneously. Moreover, LMWHs possess antithrombotic property with reduced bleeding potential. The high cost of LMWHs preparations makes their use restrictive and the sc administration of UFH has become a usual practice. This study aims to compare the efficacy and safety of sc administration of UFH and LMWH preparations using experimental models in rats. UFH and LMWH were administered at doses of 6.0 and 2.5 mg kg⁻¹ body weight, respectively, and the pharmacokinetics was assessed by anti-Xa and anti-IIa activity. Thirty minutes after injection both, LMWH and UFH were detected in plasma. For both heparins, the maximum plasma concentration was achieved at ~ 3.0 h. As expected, LMWH presents an anti-Xa activity higher than anti-IIa activity. UFH, in contrast, exhibited a potent anti-IIa activity, indicating that heparin chains with the critical length necessary for thrombin inhibition were absorbed by sc route. When administered at the same dose used for LMWH, UFH anticoagulant activity was not detected in plasma. These results demonstrate that sc administration of UFH is effective in rats.

Word Keys: unfractionated heparin, low molecular weight heparin, subcutaneous administration
Supported by: CNPq and FAPERJ