Biocomparatibility study of Enoxaparins in Current use in Brazil

Stephan-Nicollas M. C. G. Oliveira\textsuperscript{1,2}, Gabriel B. F. De Almeida\textsuperscript{1} Bianca F. Glauser\textsuperscript{1,2}, Bruno C. Vairo\textsuperscript{1,2}, Leonardo P. Cinelli\textsuperscript{3}, Mariana S. Pereira\textsuperscript{1,2} and Paulo A.S. Mourão\textsuperscript{1,2}.

\textsuperscript{1}Laboratório de Tecido Conjuntivo, Hospital Universitário Clementino Fraga Filho, \textsuperscript{2}Instituto de Bioquímica Médica, and \textsuperscript{3}Laboratório de Glicofármacos, Instituto Macaé de Metrologia e Tecnologia, Universidade Federal do Rio de Janeiro, Cidade Universitária, Ilha do Fundão, Caixa Postal 68041, Rio de Janeiro, RJ, 21941-590, Brazil.

INTRODUCTION: As a consequence biosimilar drugs are trying to obtain approval for clinical use. Five biosimilar versions of enoxaparin are now available for clinical use in Brazil. However, there still skepticism about the possibility to obtain preparations of LMWHs similar to the reference drug because of the complexity involved in the process to generate LMWHs, starting from unfractionated heparin. Here, we performed a careful analysis of biosimilar vs. Reference and we intend to assure the efficacy and safety of the biosimilar enoxaparins available for clinical use in Brazil.

MATERIAL AND METHODS: Their structures were investigated using high field nuclear magnetic resonance, including one dimensional and two dimensional spectra, the molecular size distribution was determined by gel permeation chromatography and their anticoagulant activities were established based on the anti-Xa anti-IIa assays and on direct binding to antithrombin. Approximately 100 batches of biosimilar enoxaparins were included in this initial investigation. On a second stage selected bathes were tested on animal models of experimental thrombosis and bleeding, associated with determination of their pharmacodynamic. Finally, enoxaparins were administered continuous to rats over a period of 30 days in order to investigate possible toxic effects after a long period of administrations.

DISCUSSION AND RESULTS: The biosimilar and reference batches of enoxaparin available for clinical use in Brazil have similar structures and anticoagulant activities. They also showed equivalent responses in animal models of experimental thrombosis and bleeding, achieved similar plasma concentrations, showed no toxic effect after continuous administration over a period of 30 days. CONCLUSION: Our results indicate that biosimilar enoxaparins available for clinical use in Brazil are similar to the reference drug. Each preparation requires a carefully analysis to assure their efficacy and safety. Our study may help to define a guide line for analysis of biosimilar LMWHs.

Keywords: Low-molecular-weight-heparins, generic drugs, anticoagulants, heparin, antithrombotic agents

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