Effects of Novel Oral Anticoagulants On Venous Thrombosis Model And Bleeding Time Assay

Fonseca, R.J.C.\textsuperscript{1,2}; Cortez, R.F.\textsuperscript{1}; Sucupira, I.D. \textsuperscript{1}; Mourão, P.A.S.\textsuperscript{1,2}

\textsuperscript{1}Laboratório de Tecido Conjuntivo, Hospital Universitário Clementino Fraga Filho, \textsuperscript{2}Instituto de Bioquímica Médica, UFRJ

INTRODUCTION: Heparin has been used for more than 50 years to treat and prevent thrombosis. Although heparin is the second most frequently used natural drug, its source is very limited since it is only obtained from pig intestine or bovine lung. Therefore, due to the increasing use of heparin there is an urgent need for new anticoagulants or alternative sources of heparin. In the present work, we compare the effect of novel oral anticoagulants such as dabigatran etexilate, rivaroxaban and apixaban using venous thrombosis model and bleeding time assays. Coagulation parameters were also evaluated and compared with fucosylated chondroitin sulfate, a potent anticoagulant polysaccharide extracted from sea cucumber.

MATERIAL AND METHODS: Wistar were randomly divided into several groups. Antithrombotic activity was investigated in rats with the vena cava model using thromboplastin as the thrombogenic stimulus. Bleeding tendency was evaluated using the bleeding time model.

RESULTS AND DISCUSSION: Thrombus formation was completely inhibited at 20 mg/kg of apixaban and dabigatran etexilate, while rivaroxaban had a great variation in thrombus weight at this dose. Total inhibition of thrombus formation using fucosylated chondroitin sulfate was achieved only at 50 mg/kg. All novel anticoagulants caused intense blood loss, while fucosylated chondroitin sulfate and low molecular weight heparin had no effect on bleeding time assay.

CONCLUSIONS: The approach to study novel anticoagulants involves testing compounds with well-defined structures in different assays to define the multitude of their haemostatic effects. The complexity of the regulatory mechanisms involved in the action of these compounds makes it difficult to predict the in vivo effect exclusively using in vitro assays.

Key words: sulfated polysaccharides, oral anticoagulant, fucosylated chondroitin sulfate.

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