Practical implications of the differences observed between pharmaceutical grade heparins from bovine and porcine origin

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Heparin remains the anticoagulant of choice for the treatment of thromboembolic diseases and is also required for extracorporeal circulation during cardiovascular surgery. Neutralization of heparin at the end of extracorporeal circulation requires proper doses of protamine to avoid bleeding. Recently, Roche Laboratory removed a referenced heparin preparation from the Brazilian market. Subsequently, there were increasing reports of bleeding associated with the use of heparin, mostly during cardiovascular surgeries. In a recent study, we observed that most of the heparins available in Brazil after withdrawal of the Roche product were from bovine intestinal mucosa. This is an unusual source of heparin, since worldwide pharmaceutical heparin is obtained from porcine intestinal mucosa. Depending on the source, heparin exhibit significant structural differences and therefore varies in their anticoagulant potential. Heparins with different biological properties may exhibit distinct protamine neutralization curves. In this work we compared the anticoagulant activity of porcine and bovine heparin and its neutralization by protamine. Heparin obtained from bovine intestine has a lower anticoagulant activity when compared to heparin from porcine origin. Then, we evaluated heparin neutralization in human plasma by aPTT assay and in a purified system, based on anti-Xa and anti-IIa activity. Clearly, bovine heparin requires significantly higher doses of protamine than porcine heparin to achieve neutralization. Our results demonstrated that these heparins present significant differences in specific anticoagulant activity and in the required doses for protamine neutralization and should not be considered as equivalent drugs.

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