Low-molecular-weight heparins: what is their therapeutic usefulness?

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Heparin, an anticoagulant discovered in 1916 by McLean, is still one of the main pharmacological options for venous thromboembolic prophylaxis nowadays.[1] However, its use entails some practical difficulties, due to the heterogeneity of the molecule and the considerable variability of the pharmacokinetic parameters.[2]

The anticoagulant action of heparin is mediated by its bond with at least two natural anticoagulants that exist in the circulation: antithrombin III (AT III) and heparin cofactor II. The bond with ATIII is responsible for the inhibition of thrombin (II) and factor Xa.[2] Factors XIIa, XIa and IXa are also inhibited, though with less therapeutic relevance.[2] The need for stringent control of the anticoagulant effect through the regular performance of APTT gives rise to practical problems associated with heparin therapy.

In the mid-1970's Kakkar advocated low-dose heparinization for the prevention of thromboembolism in high-risk patients submitted to surgery.[3]

The discovery of low-molecular-weight heparins (LMWH) made it possible to overcome some of the practical difficulties of conventional heparins. A highly selective inhibitory action at the level of factor Xa, associated with a reduced antagonic effect on the action of thrombin, allow a moderate anticoagulant effect, with fewer hemorrhagic effects. The small size of the molecule (around 1/3 of the molecular weight of conventional heparin) give it's a long half life, enabling longer administration intervals (sc, 1 x/day). The low molecular weight of LMWHs is also crucial for reducing the incidence of thrombocytopenia as a secondary effect of heparin use.[2] Indeed, LMWHs are the anticoagulant of choice in patients undergoing therapy with heparin and associated thrombocytopenia. The main indication of LMWHs continues to be the prophylaxis of venous thromboembolism (phlebothrombosis and pulmonary embolism in bedridden patients requiring general or orthopedic surgery, etc.). Several authors[4.7] demonstrate that its use is at least as effective as that of conventional heparin in the prophylaxis and treatment of venous thromboembolism. The importance of LMWHs in the prophylaxis and therapeutics of arterial thromboembolism (ischemic cardiopathy, thromboembolic cerebrovascular disease, etc.) has yet to be defined, given the small number of comparative studies focusing on this pathology. The long-awaited arrival at a formula for the promising anticoagulant hirudin could modify the therapeutic options of pharmacological anticoagulation in the near future. ■

References

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