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Search authors, title, keywords,...

Table of Contents

Article Archive

VETMED (63) 2018 VETMED (62) 2017

VETMED (61) 2016 VETMED (60) 2015

VETMED (59) 2014

VETMED (58) 2013

VETMED (57) 2012 VETMED (56) 2011

VETMED (55) 2010

Issue No. 1 (10-41)

Issue No. 2 (43-96)

Issue No. 3 (97-143)

Issue No. 4 (145-198)

Issue No. 5 (199-257)

Issue No. 6 (259-301)

Issue No. 7 (303-357)

Issue No. 8 (359-412)

Issue No. 9 (413-471)

Issue No. 10 (473-521)

Issue No. 11 (523-570)

Issue No. 12 (571-635)

VETMED (54) 2009

VETMED (53) 2008

VETMED (52) 2007

VETMED (51) 2006

VETMED (50) 2005

VETMED (49) 2004

VETMED (48) 2003 VETMED (47) 2002

VETMED (46) 2001

Editorial Board

Ethical Standards

Reviewers 2017

For Authors

Author Declaration

Instructions for Authors

Submission Templates

Authors' Guide

Fees

Login – submissions till 2017

Submission / Login 2018

For Reviewers

Reviewers' Guide

Heparin and its derivatives in the treatment of arterial thrombosis: a review

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Arterial occlusion due to thrombosis caused by ruptured atherosclerotic plaques (Baba et al., 1975) has been recognized as a major cause of morbidity and mortality in western populations. Thrombosis may occur in various sections of arterial circulation, peripheral arteries of the limbs, coronary arteries, brain arteries, or both major and minor vessels within the abdominal cavity. The ultimate consequence is varying degrees of organ failure, mostly of ischemic origin. Arterial thrombosis represents a continuous problem, debilitating patients and decreasing their quality of life. Moreover, along with chronic heart failure, it can significantly decrease patient life expectancy. Arterial thrombosis results in ischemia, with serious systemic consequences, such as metabolic breakdown. The major goal of treatment remains fast and efficient recanalization – surgical, interventional or thrombolytic. To be able to prevent acute reocclusion with severe consequences (rhabdomyolysis, compartment syndrome, excessive tissue necrosis leading to limb amputation, etc.), several adjunctive treatment regimens have been advocated. Among others, thrombin inhibitors and platelet inhibitors have been widely used for both prophylaxis and adjunctive treatment. Direct thrombin inhibitors and antithrombin stimulators have been recognized as typical antithrombotic drugs. Direct (antithrombin-independent) thrombin inhibitors can be divided into two main categories: monovalent, active site inhibitors (argatroban, efegatran, inovastan, melagatran) and bivalent (hirudin, hirugen, hirulog, bivalirudin), while antithrombin stimulators represent standard (unfractionated) heparin (UFH) and its depolymerizing products - low molecular weight heparins (LMWH's). Recently, a clear change in the main use of heparin, as well as low-molecular weight heparins has been advocated representing a shift from treatment and prophylaxis of deep vein thrombosis to prophylaxis of thromboembolic disease following vascular, cardiovascular or orthopedic surgery, treatment of unstable angina and prevention of acute myocardial infarction. The main effect of heparins lies in their anticoagulant activity. Heparins are involved in different pathways of the coagulation cascade with anticoagulant, antithrombotic, profibrinolytic, anti-aggregative, as well as anti-inflammatory effects. Moreover, there is a little doubt about their anti-proliferative and anti-ischemic activity (Penka and Bulikova, 2006). Unlike standard heparin, low-molecular weight heparins do not affect the patient's general coagulation profile. Obviously, the difference in molecular weight results in different pharmacokinetic and pharmacodynamic properties of the agents.

Keywords:

coagulation; arterial thrombosis; standard heparin; low-molecular weight heparins

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