Mechanisms in the inhibition of neointimal hyperplasia with triflavin in a rat model of ballon angioplasty

吳慶祥

Sheu;J.R.;Wu;C.H.;Chen;Y.C.;Hsiao;G. and Lin;C.H.

摘要

Abstract

RGD-containing peptides are able to inhibit the binding of ligands to certain β3 integrins, such as αIIbβ3 and αvβ3, both of which are involved in neointimal hyperplasia. The present study was designed to elucidate the detailed mechanisms involved in the inhibition of neointimal hyperplasia with triflavin in a rat model of balloon angioplasty. Triflavin (0.25 mg·kg − 1·d − 1), an RGD-containing disintegrin, time dependently inhibited both neointimal hyperplasia and lumen occlusion after angioplasty in carotid arteries of rats. Furthermore, electron micrographs highlighted that SMCs were phenotypically different from the typical contractile, spindle-shaped SMCs normally seen in uninjured vessel walls. PDGF-BB was strongly produced in thrombus formation and neointimal SMCs after angioplasty, and triflavin significantly reduced PDGF-BB expression in vessel lumens and neointimal SMCs after angioplasty. Balloon angioplasty caused a significant increase of nitrate and cyclic guanosine monophosphate levels compared with levels found in sham-operated rats, and these were not significantly changed with infusion of triflavin (0.25 mg·kg − 1·d − 1). Furthermore, the plasma level of TXB2 obviously increased after angioplasty, and triflavin markedly suppressed the elevation of plasma TXB2 concentration. The results indicate that triflavin effectively prevents neointimal hyperplasia, possibly through the following 2 mechanisms. First, triflavin binds to αIIbβ3 integrin on platelet membranes, resulting in inhibition of platelet adhesion, secretion, and aggregation in injured arteries, followed by inhibition of TXA2 formation and PDGF-BB release from platelets. Second, triflavin may also bind to αvβ3 integrin on SMCs, thus subsequently inhibiting cell migration and proliferation. These results provide new insights into the mechanisms of neointimal hyperplasia and have significant implications for disintegrin therapy for the treatment of restenosis and atherosclerosis. (J Lab Clin Med 2001;137:270-8)