Abstract

The main complication of aortocoronary reconstruction with vein grafts is restenosis in the course of time. The aim was to assess the effect of a periadventitial polyester system releasing sirolimus on intimal hyperplasia of autologous grafts. The controlled-release system comprises a polyester mesh coated with a sirolimus-eluting copolymer of L lactic acid and ε-caprolactone system designed to be wrapped around an autologous venous graft during its implantation. *In vitro* sirolimus release and its effects on smooth muscle and endothelial cells were assessed. *In vitro*, the copolymer-coated polyester mesh released sirolimus over a period of 6 weeks. Mesh-eluted sirolimus inhibited the growth of smooth muscle and endothelial cells in seven-day *in vitro* experiments. After seven days of sirolimus release from the mesh, smooth muscle and endothelial cell counts decreased by 29% and 75%, respectively, with the cells maintaining high viability. We implanted *v. jugularis ext*. into *a. carotis communis* in rabbits. The vein graft was either intact, or was wrapped with a pure polyester mesh, or with a sirolimus-releasing mesh. Three and six weeks after surgery, the veins were subjected to standard histological staining and the thicknesses of the *tunica intima*, the media and the intima-media complex were measured. Wrapping the vein with a mesh releasing sirolimus or with a pure mesh decreased the thickness of the intima in comparison with a vein graft by 73±11% or 73±8% after 3 weeks, and by 73±9% or 59±12% after 6 weeks, respectively. Sirolimus-releasing meshes reduced the thickness of the media by 65±9% and 20±12% after 3 and 6 weeks. The thickness of the intima-media complex in grafts with sirolimus-releasing meshes decreased by 60±6% and 30±13% in comparison with pure PES meshes, after 3 and 6 weeks, respectively. A sirolimus controlled-release system intended for periadventitial use in autologous venous grafts inhibited the growth of smooth muscle cells *in vitro* and precluded the development of neointimal hyperplasia *in vivo* in

rabbits. A periadventitial polyester mesh releasing sirolimus has the potential to become an effective device in preventing vein grafts restenosis and occlusions.

Keywords: Sirolimus, Perivascular wrap, Controlled drug release, Autologus vein, Intimal hyperplasia, Vascular smooth muscle cells, Restenosis