Vascular endothelial growth factor delivered by fibrin glue accelerating arterial endothelialization.

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Abstract:

Background: Clinical efficacy of vascular therapeutic intervention is limited by the resultant de-endothelialization, thrombogenecity and intimal hyperplasia. Objective: To evaluate the effect of fibrin glue (FG) containing vascular endothelial cell growth factor (VEGF) on re-endothelialization, cellular proliferation and intimal hyperplasia by using canine model of balloon angioplasty. Design: A randomized controlled repeated measurement design. Setting: Department of Vascular Surgery; Institute of Neurosurgery, Xijing Hospital, Fourth Military Medical University of Chinese PLA. Materials: The study was carried out in the Institute of Neurosurgery, Xijing Hospital Affiliated to Fourth Military Medical University of the Chinese PLA, between October 2002 and June 2004. Fifteen healthy adult mongrel dogs of either gender, with body mass of 12.5 to 18.9 kg, were provided by the Surgery Laboratory for Experimental Animals, Xijing Hospital. Methods: In the bilateral carotid artery, FG/VEGF/heparin of one side was set as treatment group and the other side was set as control group. The intimal injury and the treatment results were observed at three time points 10, 30 and 90 days after injury. Thickness of vascular intima and medial layer was measured with Bioquant BQ OS/2 computer morphology measuring instrument. Cell proliferation rate was quantitated by 5-bromodeoxyuridine (BrdU) incorporation by immunohistochemistry. BrdU positive cells were counted using 40 x magnification. Scanning electron microscopy (SEM) was used to evaluate the percentage of endothelial cell coverage on the luminal surface. Main outcome measures: Coverage of endothelial cells, neointimal and medial thickness, and cellular proliferation. Results: All the dogs survived till the collection of samples with no loss in the midway. 1 Coverage

rate of endothelial cells: The arterial coverage rate at the treated side at days 10 and 30 was significantly higher than that at the control side [(66.73+/-30.78)%, (40.8+/-27.74)%, P=0.04; (96.67+/-10.29)%, (82.07+/-22.82)%, P=0.048]. 2 Proliferation of each vascular layer. It reached the peak at day 10 and recovered to normal at day 90. Compared with that of control group, cellular proliferation rate of neointima and the 1/2 of inside of media as well as media was significantly increased [(7.41+/-6.75)%, (3.56+/-2.72)%; (2.81+/-2.65)%, (0.83+/-0.59)%; (2.06+/-1.81)%, (0.62+/-0.31)%, $P < 0.05$]. 3 Thickness of neointima; Compared with that of control group, the thickness of intima/thickness of medial layer in both the proximal and the middle segments was significantly increased (0.18+/-0.22, 0.10+/-0.06; 0.21+/-0.23, 0.14+/-0.14; 0.12+/-0.08, 0.09+/-0.08; 0.29+/-0.40, 0.12+/-0.12, $P < 0.05$, $P < 0.01$), but there was no change in the distal segments. Conclusion: FG can distribute cytokines into the wall of injured arteries and retain the biological function of cytokines. VEGF plus heparin delivered by FG accelerates re-endothelialization concomitant with the proliferation of smooth muscle cell and intimal hyperplasia.