

Prevention of Anastomotic Intimal Hyperplasia by a Perivascular Drug-Eluting Wrap

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A perivascular wrap is a polymeric sheet wrapped circumferentially around a vascular anastomosis by the surgeon at the time of surgery. Drug is eluted from the wrap with the intention of preventing intimal hyperplasia. Perivascular drug delivery is a logical approach to prevention of restenosis for many reasons. Drug application can occur without endoluminal manipulations; the amount of polymer that can be applied is not subject to the constraints of interference with laminar flow, and active agents that might be extremely thrombogenic if introduced into the vascular lumen might be able to theoretically be used in a periadventitial wrap.

In addition, the adventitia is an excellent site for the administration of agents for preventing restenosis. The role of the adventitia in vascular lesion formation has been largely ignored despite numerous studies that have shown its importance. Stripping of the adventitia, or periadventitial administration of appropriately irritative substances stimulate vascular lesion formation and has been used as a research model.¹⁻³ Adventitial drug delivery of multiple substances has resulted in inhibition of intimal hyperplasia in animal models.^{4,5} Using BrDU staining, Scott elegantly demonstrated that the most actively proliferating cells in the formation of intimal hyperplasia normally lie quiescent in the periadventitial region,⁶ and it is postulated that after appropriate stimulation these myofibroblasts proliferate in the adventitia, and migrate into the media and subintimal region to secrete the proteinaceous matrix that constitutes the bulk of the intimal hyperplastic lesion.

Paclitaxel has been approved by the US Food and Drug Administration as a stent coating for the prevention of coronary artery restenosis. Two-year follow-up data from two multicenter trials confirm sustained coronary stent patency and clinical efficacy.^{7,8} We have previously demonstrated that perivascular administration of paclitaxel inhibits neointimal hyperplasia without inhibition of normal vascular healing in multiple animal models.⁹

The safety and efficacy of a paclitaxel-eluting perivascular wrap is being assessed in patients treated with PTFE femoral-popliteal bypass grafts. One hundred eight patients with lifestyle-altering claudication or rest pain were randomized in 13 sites on a two-to-one basis to receive either a biodegradable polymeric wrap eluting paclitaxel (n = 72) around the distal anastomosis or no wrap (n = 36) at the time of bypass surgery with a 6 mm PTFE graft (83 above the knee, 25 below the knee). The proximal anastomosis was not wrapped in either group. Six-month clinical and duplex ultrasonography follow-up data will be presented.

Conclusions

A perivascular wrap containing paclitaxel effectively diminishes intimal hyperplasia at vascular surgical anastomoses in animal models without inhibiting vascular healing. Preliminary data from a human femoral-popliteal bypass study will be presented.

Disclosure

Dr. Machan is a consultant for Angiotech Pharmaceuticals, Inc. Dr. Avelar is an employee of Angiotech Pharmaceuticals, Inc.

References

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