Basic Science and Experimental Therapies

305 Preparation and Administration of Biodegradable Drug Delivery Microspheres into Porcine Myocardium with a Helical Injection Catheter

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Background: Intramyocardial delivery is the most effective way to deliver sensible local concentrations of angiogenic factors, genes, and drugs to heart muscle, while minimizing systemic effects. We confirmed the hypothesis that freeze-dried, biodegradable particles, for use in drug delivery, can be easily administered and dispersed into myocardial tissue using a helical injection catheter.

Methods: Biodegradable polyanhydride microspheres (1 µm) were produced by an oil-in-water emulsion technique, using polymer dissolved in methylene chloride as the oil phase and dilute blood serum as the aqueous phase. The serum proteins, which can be from the test subject species, serve as the emulsion-stabilizing agent and avoid the need for synthetic colloidal stabilizers that have the potential to produce inflammation. These preparations can be freeze-dried for storage but are easily redispersed by the addition of 0.9% saline. A fluorescent dye, coumarin-6, was added to the particles for easy visualization in the myocardial tissue by fluorescence microscopy after histologic sectioning. The injection study was performed on 4 explanted pig hearts. A Harvard Infusion Apparatus was fitted with a 1-mL syringe and the output from the apparatus was attached to a helical injection catheter. The distal (helical) end of the catheter was guided to 8 locations on 1 side of the left ventricle of each porcine heart from the endocardial surface. Eight buffer injections were done on the opposite side of the ventricle.

Results: Under fluorescence microscopy, a good dispersion of discrete spherical particles was seen in histologic slides taken around the injection sites compared with buffer-injected controls, which exhibited diffuse endogenous fluorescent structures.

Conclusion: These technologies enable the development of injectable, sustained-release therapy for the myocardium appropriate for safe and routine administration in an interventional setting. This is an attractive alternative route for the sustained delivery of agents to the coronary arteries via the lymphatics draining the myocardium, to prevent restenosis after stent implantation.

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