A Rapidly Polymerizing Polyurethane for Transcatheter Embolization

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Abstract. A polyurethane prepolymer was evaluated as a transcatheter embolizing agent. Low viscosity permits injection through small catheters. Polymerization is initiated on contact with blood and completed within 10 seconds. Downstream propagation is better than that of cyanoacrylate and comparable to that of silicone rubber. No systemic toxicity was observed in acute animal experiments. However, dissolution of arterial walls and extravasation out of the vascular bed of chronically embolized organs suggest significant local tissue toxicity and make further evaluation necessary before clinical testing.

Key words: Embolization – Polyurethane prepolymer – Plastic – Foam rubber.

The selection of an embolizing agent should be based upon the particular hemodynamic, clinical, and anatomic problem. For example, the control of arterial bleeding or the preoperative "devascularization" of a tumor can be achieved with relatively large, biodegradable embolizing "masses," such as autologous clot or Gelfoam [1, 2]. The interruption of high flow lesions (arteriovenous fistulas, inferior vena cava occlusion) requires a rapidly polymerizing and adherent plastic such as isobutyl cyanoacrylate [3, 4] or a self-retaining thrombogenic device such as a detachable balloon [5, 6], the Gianturco coil [7], or the Simon nitanol loop [8]. Embolization of a capillary bed for permanent endocrine ablation or tumor infarction requires a more slowly polymerizing material to permit adequate downstream propagation and small vessel obturation. Silicone rubber meets some of these requirements [9, 10, 11], but viscosity and the inability to control precisely polymerization times are problems.

We have been evaluating in the laboratory polyurethane prepolymer which combine many of the desirable properties of cyanoacrylate and silicone rubber. We report here our preliminary results with this potentially useful new type of embolizing agent.

Materials and Methods

Hypol® foamable hydrophilic polymer (FHP) 2000 is a polyurethane prepolymer that foams on contact with water. It is a viscous (16,000 cps@25°C), amber-colored liquid with 1-3% free toluene diisocyanate (TDI) by volume. Multiple isocyanate (NCO) sites react with water to initiate polymerization and release CO₂. The CO₂ generation expands the original polymer volume up to 15 times, and we recognize the reticulated compressible end product as "foam rubber." Amines also initiate polymerization but without CO₂ generation, so expansion in blood is not as great as in water.

A 1:2 dilution of FHP 2000 with dimethyl sulfoxide (DMSO) reduces viscosity to facilitate injection through fine catheters and at the same time decreases expansion to 40% of the initial volume, as tested in vitro with heparinized lamb's blood. Radioopacity can be achieved by adding BaSO₄, but it must be thoroughly desiccated or the small amount of contained water will initiate polymerization. Powdered tantalum is a more satisfactory opaque additive.

The use of FHP 2000 as a transcatheter embolizing agent was evaluated in five monkeys (two hepatic, three renal arteries) and four dogs (four renal arteries).

The toxicity of FHP 2000 was evaluated in five lambs. Under barbiturate anesthesia, the right kidney in each animal was embolized with 0.5-1.0 cc of the FHP 2000/DMSO mixture opacified with powdered tantalum. Serial determinations of hematocrit, white cell count (WBC), platelet count, serum electrolytes (Na, K, Ca), liver function tests (bilirubin, alkaline phosphatase, glutamic oxalacetic transaminase [SGOT], total protein, prothrombin time), and urea nitrogen (BUN) were performed preembolization,

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immediately postembolization and at one, two, seven, 28 and 112 days. The animals were then sacrificed, limited autopsies (abdomen only) were performed, and the liver and the control and embolized kidneys were examined microscopically.

The local toxicity of intraarterial DMSO was evaluated in three cats by directly infusing 2.0 ml into an axillary artery and observing the occurrence and severity of limb spasm.

An experimental polyurethane prepolymer (HypoF HFP 9911-23-1) with lower viscosity (7000 cps @ 25°C) and decreased expansion upon foaming was tested in two monkeys, three dogs, and six cats. Since DMSO seemed to have considerable local tissue toxicity when injected intraarterially and pulmonary toxicity when excreted through the lungs, saline was substituted as a diluent for the less viscous FHP 9911. Immediately prior to injection, the prepolymer was warmed to 50°C and then vigorously shaken with saline (1 part FHP 9911:2 parts saline/tantalum mixture) in a syringe for 10–15 seconds. Although the mixture was "foaming" at the time of injection, its low viscosity permitted easy injection through 100 cm 3 French catheters.

The tissue toxicity of FHP 9911 was evaluated in six cats. One kidney of each animal was embolized, the animals observed for six (three cats) to 11 (three cats) weeks, and the excised kidneys examined by microradiography and histology. Serial hematologic and chemical examinations were not performed.

Fig. 1A-C. Kidneys embolized with FHP 2000/DMSO mixture. Note bubbly appearance of cast due to CO₂ generation during polymerization. Expansion of the polymer filled the renal artery up to the aortic orifice in each case, and spill-over embolization was difficult to control.