Development of Polyurethane Artificial Vascular Graft for Hemodialysis

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INTRODUCTION

Hemodialysis is applied to more than 250,000 patients worldwide today. As the hemodialysis technique becomes more efficient and safer, patients are living much longer. For this reason, a reliable access system that will be available for many years is needed. The ideal access site should allow easy, reliable long-term entry to the circulation that is acceptable to the patient. Unfortunately, not every access method can satisfy all these criteria of all the access methods, the methods using the patient's own vessel are most successful. Especially the arterial-venous fistula (AVF) described by Cimino and Brescia [1] or variants of this type do provide the best long-term access to the circulation [2]. But the AVF operation with autologous tissue is not always successful and the frequent venipuncture for hemodialysis play a great role in AVF failure. At that time, artificial vascular graft as a second choice of treatment is needed. The expanded polytetrafluoroethylene (ePTFE) has evolved as a highly successful prosthetic material for use in the creation of secondary forms of hemoaccess. However, the ePTFE graft has critical disadvantages in performing as graft of AVF. As ePTFE graft has almost no elasticity, the venipuncture site of the graft remains open. Although the prosthetic device is given more than two weeks after implantation to stabilize the perivascular subcutaneous tissue which can help to reduce the bleeding from puncture-hole, it has great chance to give rise the perivascular hematoma and resulting perivascular infection and pseudoaneurysm. The AVF infection is known to occur up to 25% and the pseudoaneurysm up to 6% of implantation [3]. Also the ePTFE graft is known to be very unreactive to modify the surface characteristics and is reported to be more thrombogenic than PU graft. Thrombotic complication is the most common cause of failures in prosthetic graft fistulas and is reported to occur up to 40% of implantations [3].

We developed U-shaped porous PU vascular graft proper for AVF operation in chronic hemodialysis patient which is self-sealable and easily surface-modifiable. Also we performed animal experiments in 4 mongrel dogs and evaluated the patency, intravascular thrombi, tissue reactions around the graft and graft infections.

MATERIALS AND METHODS

GRAFT FABRICATION U-shaped porous PU grafts with 6 mm inner diameter were made according to the following sequence. PU pellets (Pellethane 2363 80AE, Dow Chemical Co.) were prewashed in ethanol and completely dried in vacuum oven. The PU pellets were stirred in N,N-dimethyl acetamide (1st grade, Duksan Phamaceutical Co., LTD.) to make 16%(w/v) PU solution. U-shaped clean glass mold with 6 mm diameter was dipped into the PU solution, was pulled out slowly and was rotated for 15 minutes so as for the PU solution to be evenly coated on the glass mold. The PU solution-coated glass mold was dipped into 30% ethylene glycol/ethanol solution to give porosity to PU graft. Then the PU solution layer coated on the glass mold become coagulated. At that time it become opaque and colors white. After 4 hrs, the graft was pulled off the glass mold and dipped in the pure ethanol, pure water for more than 12 hrs successively and vacuum dried.

ANIMAL EXPERIMENTS 4 mongrel dogs between 25 Kg and 30 Kg were used. The prosthetic grafts were sterilized by ethylene oxide gas before implantation. The experimental animals were anethesized with inhalation of halothane after induction with Pentothal. The prosthetic grafts were implanted in the neck of dogs by end-to-side anastomosis of graft to external jugular veins and external carotid arteries. [Figure 1] The patency of prosthetic grafts were monitored by palpation of thrills on the skin just above the grafts. The prosthetic grafts were explanted en-block when the grafts became obstructed or when the experimental animals were expired or when the implant period became 1 months. The explanted prosthetic grafts were cotton-swabbed from inside of the

lumen for microbiological study and were fixed in the 10 % formalin solution for pathological evaluation.

RESULTS AND DISCUSSIONS

Experiment 1 and 2 were terminated due to the expiration of experimental animals. Experiment 4 was terminated due to prosthetic graft tear. Experiment 3 was successfully implanted for 1 month without complication. The cause of death is not known but it is supposed to be heart failure due to too much preload by the direct bypass of blood from external carotid to jugular vein through too large diameter prosthetic graft [Table 1].

Microbiologic study reveals that grafts of Experiment 1 and 2 were infected with S. aureus and P. aeruginosa and Experiment 4 was infected with S. aureus and A. baumanii [Table 2]. We think that the environmental condition of animal operation may have greatly contributed to the increase of incidence from the point that the major organism is S. aureus, the one of the major inhabitant on the skin, and the incidence is too high.

The venous anastomosis site of Experiment 1 was teared and the lumen was obstructed with mural thrombi at the time of explantation. The lumen of prosthetic graft in Experiment 2 and 3 was free of thrombi. But no endothelialization was observed in the inner central area of prosthetic grafts. The prosthetic graft in Experiment 4 was teared near the artierial anastomosis site and the distal portion was obstructed with thrombi.

We are now planning to experiment with 4 mm diameter prosthetic graft to reduce the chance of heart failure. Also, we are planning to modify the inner surface of PU prosthetic graft with lumbrokinase to reduce the thrombogenicity.

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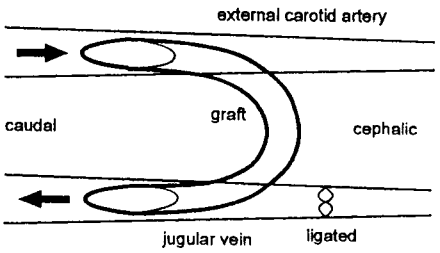

FIGURE 1. Shape of Implanted Graft

TABLE 1. Causes of experimental termination

Experiments	Cause of Termination
Exp. 1	Death due to infection
Exp. 2	Death due to heart failure
Exp. 3	Elective termination
Exp. 4	Massive hemorrhage from teared prosthetic graft

TABLE 2. Infecting Microorganisms

Experiments	Microorganisms
Exp. 1	S. aureus, P. aeruginosa
Exp. 2	S. aureus, P. aeruginosa
Exp. 3	none
Exp. 4	S. aureus, A. baumanii