A Novel Approach to Penile Augmentation Urethroplasty Using Buccal Mucosa and Amniotic Membrane: A Pilot Study in a Rabbit Model

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OBJECTIVE To evaluate and compare the success of amniotic membrane (AM) and buccal mucosa (BM) grafts and simultaneous use of both in penile augmentation urethroplasty in rabbits.

MATERIALS AND METHODS A total of 12 New Zealand rabbits were divided into 3 groups by grafting style: Group 1 (AM), Group 2 (BM), and Group 3 (simultaneous use of BM and AM). In all animals, a standardized urethral defect was created. BM and AM were obtained from the rabbits. Solely AM grafts were affixed to the defects in Group 1, solely BM grafts were affixed to the urethral defects in Group 2, and simultaneous AM + BM grafts were affixed in Group 3. At 4 and 8 weeks, the penises were subject to histological assessment of subepithelial fibrosis, epithelial transformation, and inflammatory reaction.

RESULTS Stenosis was detected in none of the groups. A dehiscence was developed in one rabbit in Group 1 and a fistula was developed in one rabbit in Group 2. After 4 weeks, minimal subepithelial fibrosis and inflammatory reaction were observed in Group 2, while subepithelial fibrosis was not in Groups 3. After 8 weeks, subepithelial connective tissue proliferation was moderate in Group 2, at both 4th and 8th weeks in Group 2. After 8 weeks, the best epithelial transformations were observed in Group 3.

CONCLUSION In an animal model, the simultaneous use of AM and BM grafts following acute urethral injury may be feasible for penile augmentation urethroplasty. Further study is needed. UROLOGY 87: 210–215, 2016. © 2015 Elsevier Inc.

Because of high failure rates and possible postoperative complications, the treatment of urethral stricture is still challenging.[1,2] Excision of stricture and primary end-to-end anastomosis are preferred for short-segment strictures, whereas for long-segment strictures, buccal mucosa (BM) onlay urethroplasty is the preferred treatment. In spite of the precautions taken with this technique, recurrence may occur following urethroplasty.[2,3] Ventral penile urethral grafts are usually unsuccessful because the covering tissue is insufficient, and lack of blood supply to this region can cause reconstruction of pendulous urethras to fail.[4]

The amniotic membrane (AM) is composed of a basement membrane and a stroma.[5] The basement membrane facilitates epithelial cell migration, strengthens adhesion of basal epithelial cells, promotes epithelial differentiation, and prevents apoptosis. The stroma includes mitogenic factors, growth factors, anti-inflammatory proteins, natural inhibitors to proteases, and anti-scarring features.[6-8]

AM has several advantages because of its biocompatible and biosoluble nature and the stable composition comprising growth factors.[9] Furthermore, amniotic cells are not characterized by immunologic reaction and scar formation. Recently, AM has been successfully used for urethral reconstruction in a limited number of clinical and experimental studies.[9,10] However, solely AM is too thin

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for anastomosis; it tends to deform and tear.[9] BM grafting has some complications and AM alone is weak for anastomosis; we hypothesized that the simultaneous use of AM and BM might be a more effective method than their usage alone.

The aim of this experimental study was to evaluate and compare the effects of AM grafts, BM grafts, and BM and AM grafts together in penile augmentation urethroplasty in rabbits. We previously hypothesized that combination of BM + AM for onlay urethroplasty may be a useful treatment option and our hypothesis has been published.[11] Therefore, we also set out to prove our previous hypothesis about the combination of the BM and AM for graft augmentation urethroplasty.[11]

MATERIALS AND METHODS

We chose rabbits for this study because the rabbit penis is similar to the human penis, rabbits are easily handled, and their histology is known. The experimental protocol was reviewed and approved by the Committee on Animal Research of Süleyman Demirel University, Isparta, Turkey. The study included 12 New Zealand white male rabbits of similar age (approximately 8 weeks) and weight (2.5-3 kg).

The rabbits were brought to the surgery unit 1 week before the study and randomly divided into three groups according to the material to be used in reconstruction: Group 1 (AM), Group 2 (BM), and Group 3 (combination of BM and AM). All animals were anesthetized intramuscularly with xylazine (5 mg/kg) and ketamine hydrochloride (30 mg/kg). The penis was blocked with 2% prilocaine. Cefazolin was administered before surgery and daily for 3 days. The procedure for all animals was performed under sterile conditions and under optical magnification (2.5×).

Amniotic Graft Preparation

The AM was obtained from a New Zealand white female rabbit's placenta after delivery and separated from the chorion under sterile conditions. It was washed with balanced saline solution that also contained 50 μg/mL of penicillin, 100 μg/mL of neomycin, 50 μg/mL of streptomycin, and 2.5 μg/mL of amphotericin B.[12] It was cut into 1 × 1.5 cm pieces, mounted on nitrocellulose backing paper, and then immediately used (Fig. 1A,B).

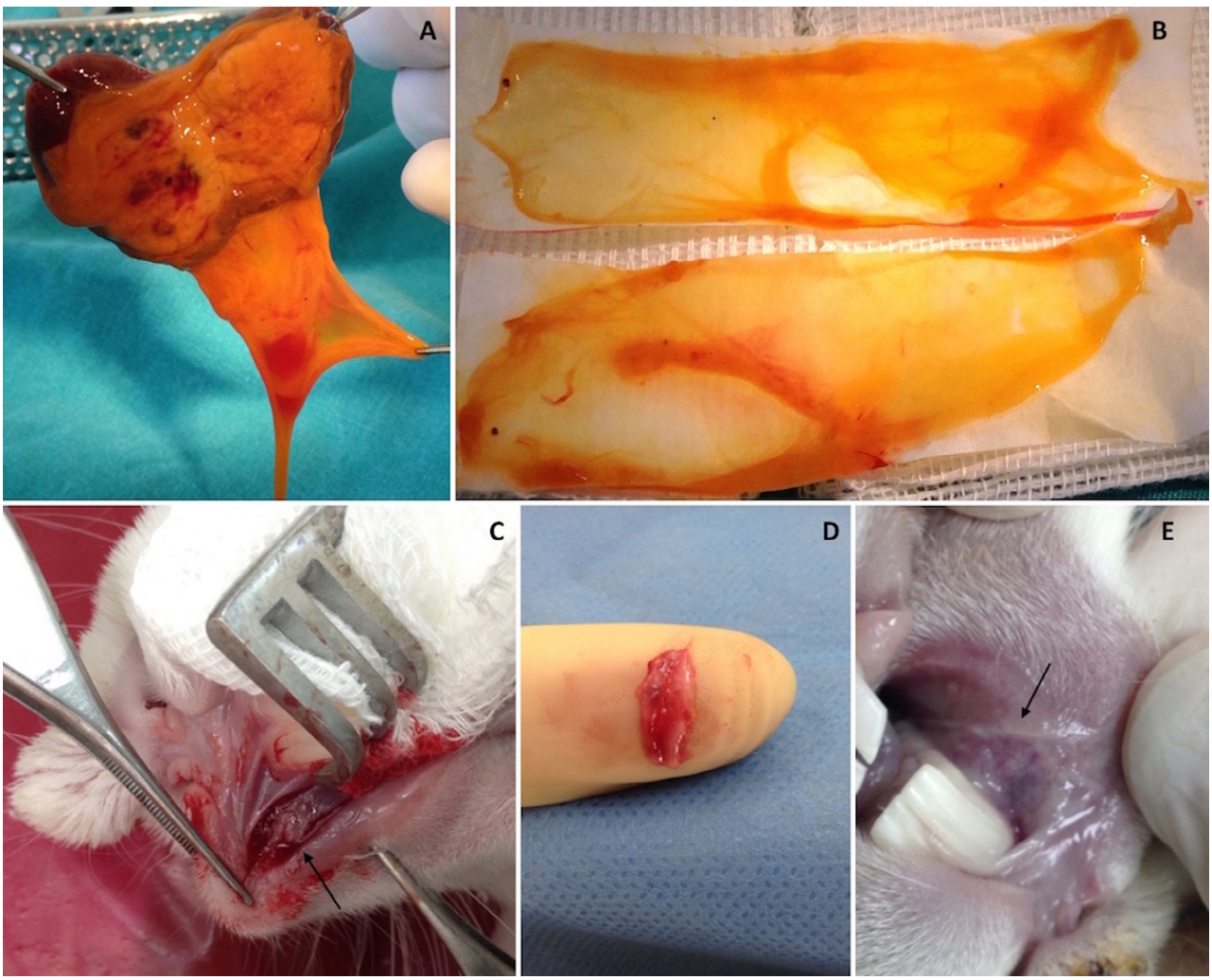

Figure 1. AM graft and BM preparations. **(A)** AM was separated from chorion. **(B)** AM pieces were mounted on nitrocellulose backing paper. **(C, D)** BM graft was harvested from rabbit's cheek. **(E)** BM graft harvest area in rabbit's cheek 4 weeks after procedure. (Color version available online.)