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Commentary

Is tissue engineering of patient-specific oral mucosa grafts the future of urethral reconstruction?

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A patient has been diagnosed with a 2 cm long urethral stricture. According to Hillary et al., 2014 urethral reconstruction or augmentation urethroplasty is suggested, rather than excision and primary anastomosis. In accordance Ram-Liebig et al., 2017 describe in their article a two-step procedure for urethral reconstruction involving some substantial logistical maneuvering. First, a biopsy 0.5 cm^2 in size is taken from the patient's mouth by the urologist (out-patient procedure); the biopsy is then transported to a well-monitored and controlled cell culture facility. In this good-manufacturing-practice (GMP) laboratory oral cells are isolated and expanded. After 3 weeks the patient specific oral mucosa graft is ready to be sent back to the urologist. The graft then needs to be implanted to the specific patient within the next 48 h.

Currently, a one-step surgical procedure for urethral reconstruction is commonly performed. However, this requires a large piece of healthy donor tissue to be used to reconstruct the urethra. This donor tissue originates mainly from penile skin or buccal mucosa and is associated with donor tissue site morbidity. It has been reported that 10% of patients undergoing one-step urethral reconstruction with oral tissue had moderate to severe oral pain 6 days post-surgery (Dublin and Stewart, 2004). The main advantage of the suggested two-step procedure is that only a small oral biopsy is needed, rather than using a large piece of donor tissue. Only in 1 of the 99 recruited patients oral adverse event has been occurring (Ram-Liebig et al., 2017). The authors agree that their proposed procedure costs more than current methods. However, they argue that the present cost-free alternative has the potential risk of developing complications to the donor site and this could lead to increase healthcare cost for the patient.

The first reports using this tissue engineered patient-specific oral mucosa graft triggered a debate among clinician specifically on the cost-effectiveness of this graft and the reliability of the study (Barbagli and Lazzeri, 2015; Osman and Chapple, 2016). Potentially, this article will raise more discussion on these topics, but also will provoke discussion on the efficacy of this two-step procedure with a reported success rate of 67.3% in the 12-month group and 58.2% in the 24-month group, when compared to the conventional one-step oral tissue replacement therapy having a success rate of 90% (Hillary et al., 2014). It can be argued a better understanding is required regarding the most-likely cause of fibrotic events observed with this tissue engineered patient-specific oral mucosa. This can be undertaken by histological examination of this patient population or even going back to pre-clinical animal models to understand the modest success rate, which was observed. Further explanation for the low success rate of this study can be attributed to the heterogeneity of the study performed in multiple centers as well as the patient group diversity: different number of previous operations, stricture location, and size.

The most ideal urethral reconstructive material for urologists and patients would be a cell-free material that does not require a donor tissue at all. This material would need to promote cellular regeneration rather than development of fibrosis, ultimately leading to natural regeneration of the reconstructed urethra. This procedure would not result in donor tissue morbidity, and there would not be a need for the high cost associated with cell culture or even waiting time for surgery. That being said to date, cell-free materials have not performed well in large urethral defect animal models (Orabi et al., 2013). It has been described however that growth factors loaded material could promote urethral regeneration in a large animal model (Jia et al., 2015).

In summary this article describes a safe tissue engineered product following good manufacturing practices, and it is one of the first tissue engineered products following the European medical agencies guidelines for advanced therapeutic medicinal products (Ram-Liebig et al., 2017). In potential future studies a need to better understand the reason behind the low efficacy results presented in this study or potentially better patient segmentation to find a specific urethral stricture patient group that could benefit with this suggested two-step therapy is needed.

Declaration

The author declares no conflicts of interest.

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