

Evaluation of Palatal Mucosa Grafts for the Treatment of Acquired Subglottic Stenosis in a Murine Model

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Introduction: Acquired subglottic stenosis (SGS) is the result of hypertrophic scar formation following injury to the laryngeal mucosa. Features of acquired SGS include excess collagen deposition and submucosal glandular hypertrophy, leading to a narrowing of the airway lumen. Inflammation following injury is believed to mediate this fibroproliferative response. The cytokines prostaglandin E2 (PGE2) and transforming growth factor beta 1 (TGF- β 1) are upregulated in acquired SGS, providing a potential target for pharmacological therapies. Skin grafting following burn injury improves recovery by mimicking wound healing by primary intention. Oral mucosal grafting has been used in airway reconstruction procedures; however a detailed histological analysis of its mechanism of treatment and efficacy has not been looked at. We aim to examine the effects of palatal mucosal grafts alone, and in conjunction with anti-inflammatory therapy, for the treatment of acquired SGS.

Methods: Twenty-four "donor" C57BL/6 mice were sacrificed, the laryngo-tracheal complexes (LTC) were excised, and transplanted to a dorsal subcutaneous pocket of 24 "recipient" mice. Six LTC's were transplanted without injury (sham procedure). Six LTC's were first injured in situ using a one mm diamond drill bit applied to the posterior subglottis for one second. Twelve LTC's were injured and received a palatal mucosal graft over the site of injury. Palatal mucosa was harvested from donor animals under microscopic guidance, pared down to a 1x3 mm strip, and laid over the site of injury at the level of the subglottis. Six of the recipient animals receiving injured LTC's with a mucosal graft also received daily intraperitoneal injections of Celebrex (celecoxib), a COX-2 selective inhibitor. Recipient animals were sacrificed on post-operative day 21 and the LTC's were harvested for histological examination.

Results: Injury of the posterior subglottis using the drill method induced a significant stenosis ($p=.02$) compared to sham injury animals. Animals receiving mucosal graft treatment following injury show no significant difference in lamina propria thickness compared to sham injured animals ($p=.45$). Animals receiving mucosal graft treatment and daily Celebrex injections had a significantly thicker lamina propria than sham injured animals ($p=.03$). The graft group had a greater percentage of graft length integrated into the lamina propria (50%) than did the graft+Celebrex group (33%), though these differences were not significant ($p=.34$). There was no clear pattern of TGF- β 1 distribution among any of the groups.

Conclusions: Mucosal grafting appears to restrict the development of acquired SGS following injury. A greater decrease in lamina propria thickness was associated with a higher degree of graft integration into the lamina propria. Reduction in PGE2 through COX-2 inhibition resulted in a lower degree of graft integration and a greater degree of stenosis. These results indicate that the inflammatory process may be an important step for graft integration and subsequent wound healing. The use of mucosal grafts is a promising source of tissue for airway reconstruction methods.