The Role of Inflammation and Prostaglandin E2 in Subglottic Stenosis Development

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Introduction: Acquired subglottis stenosis (SGS) results from aberrant wound healing following upper airway mucosal injury. Acquired SGS is characterized by hypertrophic scar formation and narrowing of the subglottic lumen, and is thought to result partly from an exaggerated or prolonged inflammatory response. Elevated levels of two inflammatory cytokines in particular, prostaglandin E_2 (PGE2) and transforming growth factor β (TGF-β), have been shown to be associated with hypertrophic scarring. In this study, pharmacological agents were used to alter PGE2 levels to examine its role in SGS development.

Methods: Twenty-four "donor" C57BL/6 mice underwent dissection and harvesting of their laryngotracheal complex (LTC). The LTCs were then transplanted into a subcutaneous pocket on the dorsum of an additional 24 genetically equivalent "recipient" mice. Before transplantation, 20 animals underwent direct subglottic injury using an electrocautery device, while 4 control LTCs were transplanted without injury. "Recipient" animals received daily intraperitoneal injections of either saline, Celebrex, or Cytotec for two weeks following surgery. After this time, the transplanted LTCs were harvested for examination.

Results: Animals administered Celebrex, a COX-2 inhibitor, following subglottic injury showed no difference in lamina propria (LP) thickness secondary to scar formation compared to uninjured animals (133.6 vs. 137.0μM, $p = .84$). A statistically significant increase in LP thickness was observed in injured animals without treatment (181.8μM, $p < .05$) and animals treated with Cytotec, a PGE2 agonist (200.2μM, $p < .02$). A significant decrease in luminal area following injury was observed only in animals treated with Cytotec ($p < .04$). Immunohistochemistry (IHC) demonstrated increased expression of TGF-β1 in animals treated with Cytotec compared to Celebrex.

Discussion: PGE2 appears to play a key role in hypertrophic scarring after subglottic mucosal injury. One mechanism by which PGE2 may contribute to hypertrophic scarring is by up-regulating TGF-β1 expression. The use of a recipient animal model for LTC transplantation limits the preservation of lumen architecture, thus hindering accurate evaluation of luminal changes following subglottic injury.