International Journal of Multiphysics
Volume 18, No. 3, 2024
ISSN: 1750-9548

Topical Corticosteroids and Graft Healing

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Abstract:

Topical corticosteroids are widely used in surgical practice due to their potent anti-inflammatory, immunosuppressive, and anti-fibrotic effects. In graft-based reconstructive procedures, particularly in urology and hypospadias repair, these agents may play a significant role in improving graft healing, reducing postoperative inflammation, and minimizing complications such as fibrosis, contraction, and stenosis. However, their effectiveness is highly dependent on proper timing, dosage, and duration of application to avoid adverse effects on graft vascularization and tissue regeneration.

Keywords: Topical corticosteroids; Graft healing; Hypospadias; Buccal mucosa graft; Fibrosis; Wound healing

Introduction:

Corticosteroids are steroid hormones with potent anti-inflammatory and immunosuppressive properties that are widely used in various medical and surgical fields. Their effects are mediated through both genomic and non-genomic mechanisms, allowing them to regulate inflammatory pathways, suppress cytokine production, and modulate immune cell activity. These properties make corticosteroids particularly valuable in controlling tissue inflammation and preventing excessive scar formation in surgical wounds and grafts **(1)**.

In reconstructive surgery, especially in urology and hypospadias repair, graft healing is a critical determinant of surgical success. Graft survival depends on adequate vascularization, controlled inflammation, and proper integration with the recipient bed. Excessive inflammation or fibrosis may lead to complications such as graft contraction, urethral stricture, fistula formation, or graft failure. Therefore, modulation of the inflammatory response using topical corticosteroids has been proposed as an effective strategy to enhance graft outcomes and improve both functional and cosmetic results **(2)**.

Topical corticosteroids are increasingly utilized in postoperative graft care due to their ability to reduce edema, suppress fibroblast activity, and limit collagen deposition. When applied appropriately after initial graft take, they can improve graft pliability, reduce scar formation, and decrease the risk of complications such as meatal stenosis and secondary contracture. However, early or excessive use may impair angiogenesis and delay wound healing, highlighting the importance of proper timing and controlled administration. This review aims to explore the role of topical corticosteroids in graft healing, their mechanisms of action, and their clinical applications in hypospadias and reconstructive surgery **(3)**.

Mechanism of Action of Corticosteroids

Corticosteroids are steroid hormones with powerful anti-inflammatory, immunosuppressive, and metabolic properties. Their effects are mediated through both genomic and non-genomic mechanisms, influencing multiple cell types and signaling pathways to regulate inflammation, immune responses, and metabolism **(4)**.

Genomic Mechanisms

The primary action of corticosteroids involves binding to intracellular glucocorticoid receptors (GRs), which then modulate gene transcription. After diffusing across the cell membrane, the corticosteroid binds to cytoplasmic GR, causing a conformational change that dissociates the receptor from chaperone proteins and

allows it to translocate into the nucleus. In the nucleus, the ligand-bound GR regulates gene expression via transactivation, upregulating anti-inflammatory proteins such as lipocortin-1, IL-10, and annexin-1, and transrepression, which inhibits pro-inflammatory transcription factors like NF-κB and AP-1, thereby suppressing cytokines (TNF-α, IL-1, IL-6), chemokines, adhesion molecules, and COX-2. These genomic actions result in reduced synthesis of inflammatory mediators, suppression of immune cell activation and recruitment, and inhibition of vascular permeability and edema formation **(5)**.

Non-Genomic Mechanisms

Non-genomic effects occur rapidly, within minutes to hours, and do not involve direct changes in gene transcription. Mechanisms include signaling via membrane-bound GRs that activate second messenger pathways, direct interactions with cytoplasmic proteins modulating kinase activity, calcium flux, and mitochondrial function, and stabilization of cellular membranes to reduce mast cell degranulation and capillary permeability. Clinically, these non-genomic effects contribute to the rapid anti-inflammatory response observed with high-dose corticosteroid therapy **(6)**.

Cellular Effects

Corticosteroids exert broad effects on various cell types. In immune cells, they suppress T-cell proliferation and differentiation, induce apoptosis of activated lymphocytes, and reduce macrophage cytokine production and antigen presentation. In endothelial cells, corticosteroids decrease adhesion molecule expression, limiting leukocyte migration. Fibroblast activity is inhibited, reducing collagen synthesis and fibrosis in chronic inflammation. Metabolically, corticosteroids enhance gluconeogenesis and lipolysis and modulate electrolyte balance through renal effects, promoting sodium retention and potassium excretion **(7)**.

Topical Corticosteroids in Graft Management

Topical corticosteroids are frequently used in postoperative graft care, including skin and mucosal grafts in hypospadias repair or burn reconstruction, to optimize graft outcomes by modulating inflammation, reducing fibrosis, and improving graft adherence and survival. Their mechanisms of action in graft healing are multifactorial. Anti-inflammatory effects reduce local cytokine production (IL-1, TNF-α, IL-6), limit leukocyte migration, and minimize edema, erythema, and tissue inflammation. Anti-fibrotic effects suppress fibroblast proliferation and collagen synthesis, thereby decreasing the risk of hypertrophic scarring, contracture, and graft distortion. Additionally, vascular stabilization lowers capillary permeability, reducing hematoma or seroma formation beneath the graft, while immunomodulatory effects limit local immune-mediated graft rejection, particularly in mucosal grafts **(8)**.

Indications for topical corticosteroid use in graft management include prevention of hypertrophic scarring and contracture, reduction of postoperative inflammation, and improvement of graft survival. In practice, corticosteroids are typically initiated after initial graft take (5–7 days postoperatively), as early application on fresh grafts may impair angiogenesis. Low- to medium-potency agents are preferred for delicate areas such as penile or mucosal grafts, while high-potency agents are reserved for thick or resistant scar tissue. Application is generally once or twice daily for 2–4 weeks using ointment formulations to maintain moisture and adherence, with creams reserved for larger areas. Evidence from burn and skin graft studies demonstrates reduced edema, improved cosmesis, and decreased incidence of secondary contraction, while limited data from hypospadias repairs support similar benefits. Potential complications—skin or mucosal atrophy, telangiectasia, delayed wound healing, and secondary infection—can be minimized by controlled potency, limited duration, proper timing, and careful monitoring of graft sites **(2)**.

Evidence from Skin Grafts in Urology and Other Surgical Fields

Topical corticosteroids have demonstrated benefits in graft management across multiple surgical disciplines, including urology, burn care, and reconstructive surgery, by reducing inflammation, minimizing scarring, and improving graft survival. In urology, particularly in hypospadias and penile reconstruction, clinical studies and case series report that postoperative application of topical corticosteroids on skin or mucosal grafts decreases edema and erythema, reduces secondary contraction, and promotes better graft take, especially in

reoperative or proximal hypospadias cases. Controlled short-term use, initiated after initial graft take (usually 5–7 days postoperatively), does not impair angiogenesis and helps prevent hypertrophic scarring, which is essential for preserving penile function and appearance. Evidence also suggests benefits in urethral and buccal mucosa grafts, where corticosteroids reduce local inflammation, enhance graft pliability, and may lower the risk of stricture formation when combined with meticulous surgical technique **(9)**.

In other surgical fields, including burn and reconstructive surgery, randomized controlled trials and systematic reviews demonstrate that topical corticosteroids improve outcomes of split-thickness skin grafts and full-thickness flaps. In burn patients, corticosteroid application reduces post-graft inflammation and hypertrophic scarring, leading to improved cosmetic results and enhanced functional range of motion when grafts cover joints. In reconstructive surgery for facial, extremity, and perineal areas, corticosteroids enhance graft adherence and survival, reduce edema and erythema, and lower fibrosis and contracture risk, particularly in delicate functional sites such as fingers or genitalia. Mechanistically, these effects are mediated through inhibition of pro-inflammatory cytokines, suppression of fibroblast proliferation and collagen deposition, and reduction of hematoma or edema beneath the graft. Key clinical principles include initiating therapy after graft revascularization, using low- to medium-potency agents, limiting duration to prevent atrophy or delayed healing, and targeting grafts in functionally critical areas to maximize both cosmetic and functional outcomes **(3)**.

Corticosteroids in Hypospadias Surgery

Several clinical studies have investigated the role of corticosteroids in improving outcomes and reducing complications following hypospadias repair, focusing on both topical and systemic administration. Topical corticosteroids have been particularly studied for the prevention and management of meatal stenosis. In a prospective study involving 83 boys with proximal hypospadias who underwent tubularized skin island-flap urethroplasty, postoperative early stenosis occurred in 19 patients. Application of 0.05% betamethasone cream daily for three months successfully restored patency in 14 patients, while only five required reoperations. This study highlighted that early calibration combined with topical corticosteroid use is effective in preventing and managing meatal stenosis without adverse effects. Similarly, studies assessing early calibration and dilatation with betamethasone application reported improved scar elasticity, facilitating urethral dilatation and minimizing stenosis formation **(10)**.

Local corticosteroid injections administered intraoperatively have also shown clinical benefits. A randomized controlled trial with 120 children undergoing hypospadias repair demonstrated that a local injection of 2 ml of long-acting corticosteroid proximal to the coronal sulcus reduced postoperative complications, including meatal stenosis, urethral fistula, superficial skin infection, and need for redo repair. Patients in the corticosteroid group also had less penile edema and improved cosmetic outcomes. In addition, a randomized, placebo-controlled trial evaluating systemic oral corticosteroids in pediatric proximal hypospadias repair observed a low overall complication rate in the prednisone group, although the results were not statistically significant. These findings suggest that corticosteroids, whether topical, local, or systemic, may play a valuable role in improving graft healing, minimizing inflammation, and reducing functional and cosmetic complications, though larger trials are needed to confirm long-term efficacy **(9)**.

Topical Corticosteroids for Meatal Stenosis Prevention: In a prospective study of 83 boys who underwent proximal hypospadias repair using tubularized skin island-flap urethroplasty, postoperative calibration was performed every 7–15 days. Patients who developed meatal stenosis were treated with daily 0.05% betamethasone cream for three months. Of the 19 patients with early stenosis, 14 achieved a patent neourethra, while five required reoperations. No adverse effects were reported. The findings indicate that early calibration combined with topical corticosteroid application is effective for preventing and managing meatal stenosis after hypospadias repair **(11)**.

Postoperative Oral Steroids: A randomized, placebo-controlled trial assessed systemic corticosteroid therapy in pediatric proximal hypospadias repair. Although the reduction in postoperative complications did not reach statistical significance, the prednisone group experienced a very low overall complication rate, with only one reported event. These results suggest that oral corticosteroids may have a role in minimizing postoperative complications, but further research with larger sample sizes is needed to confirm efficacy and safety **(12)**.

Topical Corticosteroid Use in Postoperative Graft Care

Topical corticosteroids play a crucial role in postoperative graft management by reducing inflammation, enhancing graft take, and preventing fibrosis or contracture. Correct timing, appropriate potency, and limited duration are essential to optimize outcomes while minimizing adverse effects. During the initial graft take phase (days 0–5), corticosteroids should be avoided, as early application can inhibit angiogenesis and compromise graft survival. During this period, emphasis should be placed on maintaining a moist dressing, immobilization, and infection prevention. Once initial graft adherence and revascularization are established (typically days 5–7 onward), corticosteroid therapy can be initiated to reduce inflammation, edema, and early fibrosis, facilitating improved graft remodeling and elasticity **(8)**.

Low- to medium-potency corticosteroids, such as hydrocortisone 1–2.5% or betamethasone valerate 0.05%, are preferred for delicate areas like penile skin or mucosa. High-potency agents should be reserved for resistant or hypertrophic scarring and used for short durations only. Application involves a thin layer once or twice daily, typically for 2–4 weeks, with extension up to 6 weeks in selected cases under careful monitoring. Clinicians should monitor for local side effects, including skin or mucosal atrophy, telangiectasia, delayed healing, graft necrosis, or secondary infection. Evidence from hypospadias repair and other skin graft procedures indicates that initiating corticosteroids after graft take improves pliability, reduces meatal stenosis, edema, and secondary contracture, while early use before revascularization may compromise graft survival **(13)**.

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