Postoperative Wound Modulation in Aesthetic Eyelid and Periorbital Surgery

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Key Points

- Wound modulation in the postoperative setting of aesthetic eyelid and periorbital surgery is helpful in managing scar formation and wound contracture. This is a useful adjunct in determining the surgical outcome of the procedure.
- 5-FU is a versatile anti-metabolite that can be utilized for wound modulation after aesthetic eyelid and periorbital surgery. It can be used for scar therapy, eyelid retraction, and encapsulated injected autologous fat.
- Corticosteroids can be used along with 5-FU for optimal wound modulation and scar management.
- Injectable fillers, such as hyaluronic acid gels, are a reversible tool that can be used in the postoperative period to correct contour irregularities and to act as a tissue expander to minimize tissue contracture.

27.1 Introduction

Scar formation is a highly regulated tissue response following skin or tissue injury and is anticipated after surgical manipulation. However, exuberant scar formation on conspicuous areas of the face can be aesthetically disfiguring and functionally debilitating. The modulation of scar formation in the postoperative setting is a vital component of aesthetic eyelid and facial surgery. While numerous surgical approaches have been described to revise scars, nonsurgical adjunctive treatments which target the underlying biologic process are effective and safe. A variety of nonsurgical approaches including anti-metabolites, anti-inflammatory agents, and tissue volume expansion can provide substantial improvement.

A meticulous preoperative evaluation, including a complete physical examination, discussion of functional limitations, and a realistic appraisal of patient expectations, is paramount. We cannot stress enough that realistic expectations are especially important in the setting of scar revision. Factors to consider in formulating a treatment plan include the nature, anatomic location, and extent of the scar. In addition, it is critical to assess skin type and ethnicity of the patient, etiology of the scar, history of scarring tendencies, and all prior treatments and their relative efficacy. As scar formation is an evolution, the timing of all surgical and nonsurgical interventions is critical.

27.2 Anti-metabolites

In general, antimetabolites interfere with the proliferative mechanisms of scar formation, most notably by disrupting fibroblast biology. Anti-metabolites are not cell-type specific but rather target proliferating or synthetically active cells instead of quiescent cells. Interference with fibroblast proliferation and the production of collagen and other synthetic products has proven successful in scar prevention and reduction.

27.3 5-Fluorouracil

The anti-metabolite, 5-Fluorouracil (5-FU) (Fig. 27.1), has been used widely for decades in oncology and more recently in dermatologic management of skin lesions. The drug has a long track record of efficacy, safety, and mechanistic understanding. More recently, this anti-metabolite has gained popularity in the management of exuberant scar formation as it is efficacious and has an excellent safety profile.

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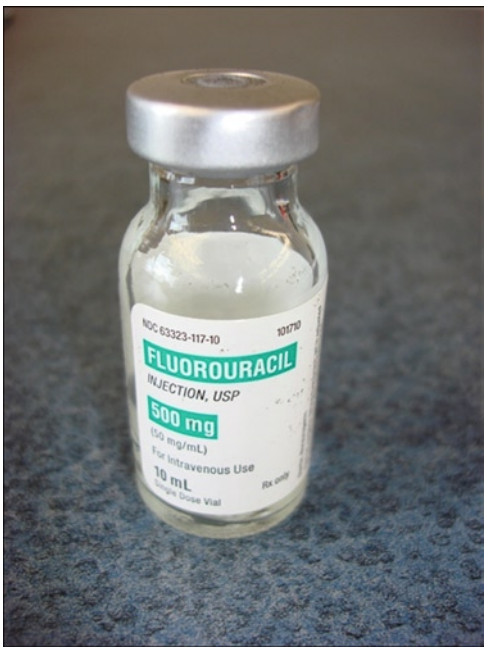

Fig. 27.1 5-Fluorouracil (5-FU) supplied in 50 mg/mL concentration

27.3.1 Mechanism of Action

5-FU minimizes scar formation by inhibiting cell proliferation through the disruption of DNA synthesis and inhibiting collagen production. As 5-FU is a fluorinated pyrimidine, it acts to inhibit DNA synthesis and cell proliferation by inhibition of thymidylate synthetase and direct misincorporation. Structurally, it is identical to uracil but with fluorine substituted for hydrogen at the C-5 position, which allows rapid cellular entry and utilization. 5-FU is converted into fluorodeoxyuridine monophosphate, which, through its interaction with thymidylate synthetase, inhibits the conversion of uracil into thymidylate. This results in a deficiency of thymidylate, a precursor of thymidine phosphate, one of the four deoxyribonucleotides needed for DNA synthesis and repair. Additionally, direct misincorporation into DNA leads to single strand breaks and aberrant incorporation into RNA, thereby interfering with normal RNA function [1–4]. 5-FU directly and specifically inhibits proliferating and synthetically active cells that cause fibrosis. The relative specificity directed to actively synthetic or proliferating cells minimizes clinical tissue toxicity.

The efficacy of 5-FU in the management of scars may also be related to its capacity to interfere with transforming growth factor-β (TGF-β) signaling and resultant type I collagen gene expression in dermal fibroblasts. Abnormally excessive accumulation of type I collagen has been found in keloids and hypertrophic scars, which is believed to play a pathological role in these exuberant scar responses [5, 6]. TGF-β is thought to be the main factor leading to tissue fibrosis secondary to its induction of collagen gene expression. 5-FU has been found to reduce intermediary cell signaling and prevent TGF-β induced gene transactivation and type I collagen production in human fibroblasts, thus providing a mechanism for the efficacy of 5-FU in the treatment of hypertrophic and keloid scars [7–10].

In glaucoma surgery, 5-FU is routinely used for its ability to inhibit and prevent scarring after trabeculectomy surgery [11]. Uppal et al. reported their results utilizing an external application of 5-FU soaked pledgets following extralesional excision of keloids. Biopsies 1 month following treatment showed a reduction in Ki-67 (a marker of cell proliferation), vascular cell adhesion molecule-1 (a marker of inflammation), and TGF-β compared to controls [12].

27.3.2 Management

Intralesional 5-FU has been described as an effective treatment modality in the management of dermal scars, particularly for the treatment of hypertrophic scars and keloids [10, 13–15]. However, as this is an off-label use for 5-FU , the indications, risks, benefits, and alternatives are explained in detail to the patient prior to treatment. For each treatment, an intradermal injection of approximately 0.2–0.3 mL (50 mg/mL, American Pharmaceutical Partners, Schaumburg, IL) is given at weekly or biweekly intervals for a course of one to three treatments based on response. Transient pain at the injection site is the main drawback. The pain of injection can be substantially reduced by mixing 5-FU and lidocaine 2% in the same syringe (2:1–5-FU:lidocaine) and using topical anesthetics. Placement of 5-FU is targeted to the areas of maximal scar density, usually the dermis and subcutaneous tissues. Placement of 0.2–0.5 cc in the skin and areas of maximal scar density using multiple passes is ideal. Given the short half-life of 5-FU, patients are discouraged from massaging the area for 8 h to allow maximal benefit. Softening and improvement in appearance can often be noted after as few as one or two treatment sessions, with continued improvement over the weeks to follow. The literature is mixed in terms of frequency of recurrence, but in the eyelid and face we have noted longstanding results with minimal regression (Fig. 27.2).

Postsurgical eyelid scarring and contracture can result after any eyelid surgery, particularly following lower eyelid reconstruction or blepharoplasty [16, 17]. It can manifest as lower eyelid retraction, ectropion, or entropion depending on the state of the anterior and posterior lamella and is usually apparent as the postoperative edema is regressing (1–2 weeks postsurgery). Resultant signs and symptoms include ocular irritation, photophobia, excessive tearing, and nocturnal

Fig. 27.2 Cicatricial left lower eyelid retraction improved after two 5-FU injections

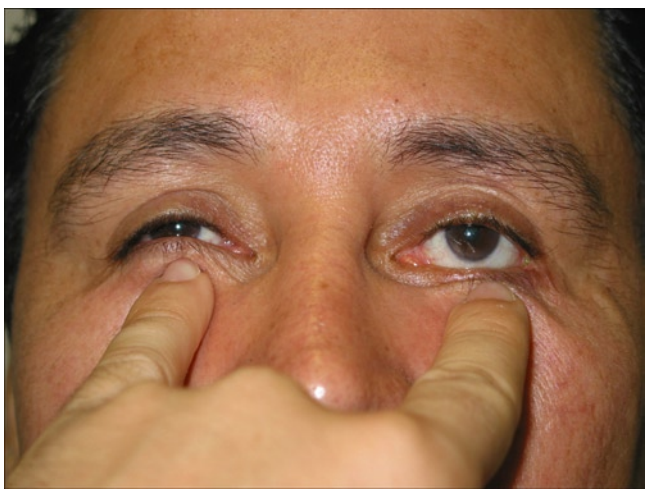

Fig. 27.3 Photograph illustrating cicatricial left lower eyelid retraction, as demonstrated by positive forced upward traction test

lagophthalmos. While aggressive lubrication of the ocular surface with artificial tears and ointments may alleviate some of these symptoms, surgical intervention is usually necessary for management.

Cicatricial wound healing of the lower eyelid can result in significant lower eyelid scarring with subsequent progressive retraction (Fig. 27.3). This can be especially problematic when combined with temporary or permanent localized facial nerve paresis (orbicularis weakness). The injection of anti-metabolites such as 5-FU at the earliest signs of contracture (typically 1–2 weeks after surgery) may minimize this process. Administration of 0.2–0.3 mL of 5-FU mixed with

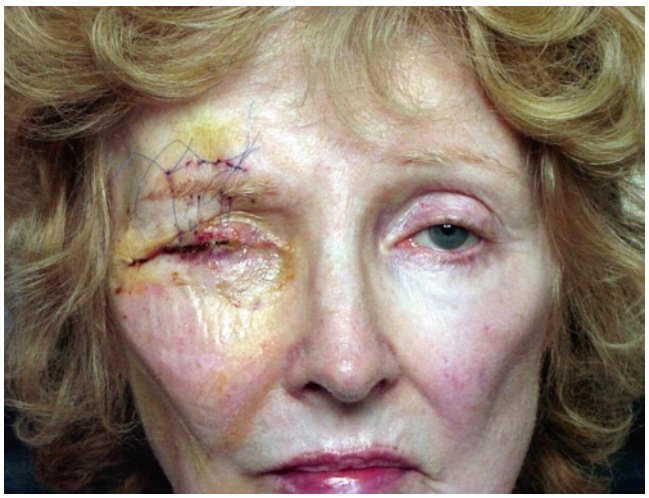

Fig. 27.4 A middle-aged woman with left eyelid Frost suture immediately after lower eyelid surgery

lidocaine in the middle eyelid lamellae surrounding maximal areas of contraction can be carried out via the transcutaneous or transconjunctival route depending upon the areas of contracture at weekly or biweekly intervals. The goal is to maximize 5-FU concentration in the scarred area so that modulation of the healing process can occur in a beneficial way, leading to less cicatrization with maintenance of normal anatomy. Patients can be carefully followed up during the postoperative period, and adjunctive treatments such as placing the eyelid on stretch (i.e., Frost suture) can be utilized (Fig. 27.4). In situations of persistent or significant scarring, we routinely treat the eyelid retraction with scar lysis and middle lamellar stenting with a tissue matrix graft (Alloderm, Lifecell, KCI, Branchburg, NJ) (Fig. 27.5) utilizing a small conjunctival incisional approach. We have found that when a tissue matrix graft is reconstituted in 5-FU, there is dramatic improvement of the cicatrix. The graft likely elutes antimetabolite over an extended time period, reducing the fibrotic process.

Autologous facial fat injections are commonly utilized for soft tissue augmentation to address contour irregularities and volume deflation associated with aging. Encapsulation of autologous injected fat with inflammatory tissue, however, is a relatively common and disfiguring complication, particularly under the thin skin of the periocular region. Attempts at surgical excision or disruption have limited success, unpredictable outcome, and can lead to irregular scars [18]. The authors routinely treat encapsulated fat with intralesional injection of 5-FU. Typically, 0.2–0.3 mL of 5-FU is injected into the fat granuloma, with repeat treatment at 2–3 week intervals. We have found improvement of these lesions with softening, and in a subset of patients, complete resolution of encapsulation of autologous injected fat.

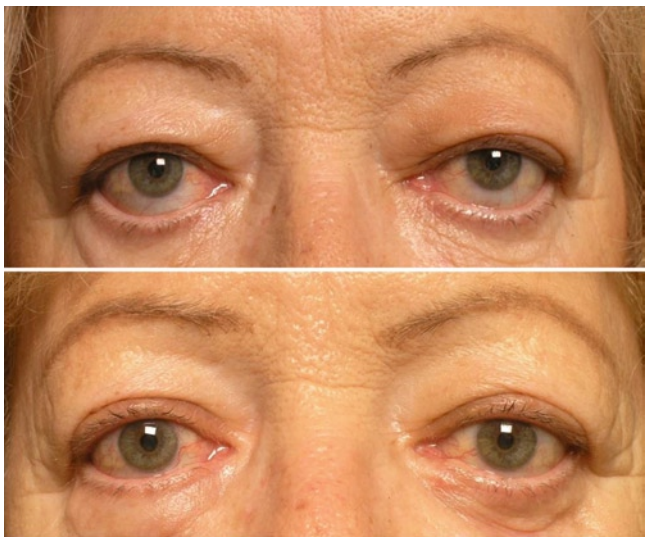

Fig. 27.5 A middle-age female patient, before (*top*) and 3 months after (*bottom*) bilateral cicatricial post-blepharoplasty lower eyelid surgery utilizing a small conjunctival incision approach with scar lysis and middle lamellar stenting with 5-FU soaked Alloderm graft

27.3.3 Safety

Intralesional injections of 5-FU are usually well tolerated, with rare adverse side effects that are typically mild to moderate and localized to the site of treatment. Adverse effects include transient pain, local erythema, edema, and erosions. Hyperpigmentation and occasional ulceration at the site of treatment have been reported, with occasional secondary infections [19, 20]. Rare cases of contact dermatitis have also been described. Serious side effects are rare and have not been experienced by the authors. They include myocardial ischemia, systemic toxicity, and bullous pemphigoid [2, 21–23]. The use of lower doses of injectable 5-FU in conjunction with combination therapy such as concurrent triamcinolone has reported higher success rates and may reduce the incidence of side effects [14, 23].

27.4 Corticosteroids

Corticosteroids have been regularly used for the treatment of pathological scars. Corticosteroid injections have resulted in reduction in scar dimensions, volume, and pliability. However, there has been significant variability in efficacy of treatment, and relatively high rates of recurrence have been reported [24].

27.4.1 Mechanism of Action

While there is a long history of intralesional corticosteroid use for the management of hypertrophic scars [25, 26] and keloids [27–30], the precise mechanism of action remains unclear. Possible mechanisms of action include inhibition of inflammatory cell migration, vasoconstriction with resultant disruption of nutrient and oxygen supply, antimitotic activity on proliferating fibroblasts and keratinocytes, and promotion of collagen degradation [25–27]. Another study showed that the mechanism of action of intralesional steroid injections may involve suppression of vascular endothelial growth factor expression and fibroblast proliferation [28].

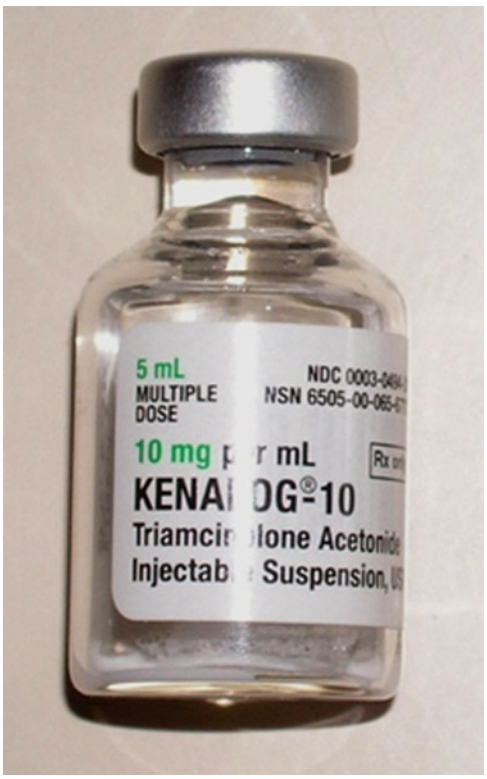

Fig. 27.6 Kenalog is supplied either in 10 mg/mL concentration as shown, or in 40 mg/mL concentration

27.4.2 Management

A variety of corticosteroid preparations have been described for the reduction of scar formation, including hydrocortisone acetate, methylprednisone, dexamethasone, and triamcinolone. A commonly utilized regimen is an intradermal injection of 0.1–0.3 mL of triamcinolone directly into the lesion every 3–4 weeks (Fig. 27.6). The lower dosage of 10 mg/mL is used for darker complexions. Prior to treatment, topical anesthetic creams are applied, and distraction techniques used.

Treatment with corticosteroids, while effective, may have relatively high recurrence rates. Some authors have described a combined approach with adjunctive agents, including 5-FU, laser, and cryotherapy, with potentially enhanced efficacy and improved long-term results [31, 32].

27.4.3 Safety

Intralesional corticosteroids are well tolerated, and adverse effects are typically localized to the site of injection. Local side effects include pain and atrophy of skin and subcutaneous tissues, which may be reversible. The potential for contour irregularities within surrounding skin and soft tissue exists, and hyper/hypopigmentation may occur. Rare, more serious complications include local skin necrosis, vascular occlusion, ulcer formation, and systemic effects, including a Cushingoid response [25, 29–31].

27.5 Fillers

Injectable tissue fillers have been increasingly utilized as a treatment modality for soft tissue augmentation to address fat deflation associated with aging. This approach is also a viable treatment option to address contour deformities associated with scar formation, while also allowing for improvement of age-related periorbital hollows.

The authors have found that cross-linked hyaluronic acid gel (Restylane, Medicis Corporation, Scottsdale, AZ) works well as a filler for the management of contour deformities in the periocular area (Fig. 27.7) related to scarring. Topical 5% lidocaine is initially applied over the eyelid skin prior to the procedure. Hyaluronic acid gel is injected in a fanning pattern, with multiple passes made to create a layered, thread-like configuration. The entire length of the needle should be directed into the scar, and gel deposited along the length of the scar. A cotton-tipped applicator is used to apply gentle pressure to the injection site to minimize bleeding/bruising.

Post-injection contour irregularities can be treated with hyaluronidase, which may reduce the effect of the filler. The effect of the filler diminishes over time (typically 6 months), although persistence may be seen for longer periods. Also, progressive tissue molding and expansion may continue after loss of filler. Maintenance treatments may be performed as needed.

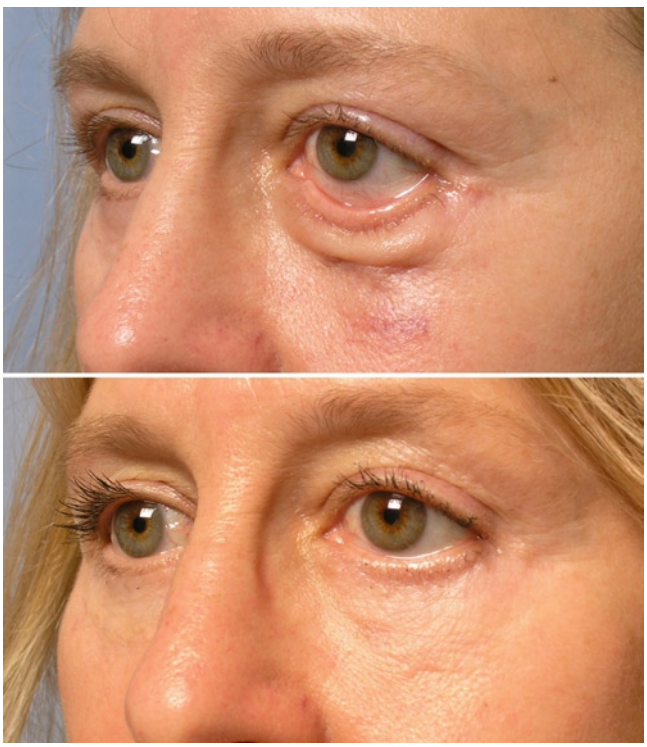

Fig. 27.7 A young female patient with left lower eye cicatricial retraction, treated with hyaluronic acid gel injection to stent the eyelid and correct the contour irregularity. Before (*top*); 3 months post-injection (*bottom*)

27.5.1 Safety

Hyaluronic acid gel filler is typically well tolerated, and adverse effects are usually limited to the injection site. Adverse effects include pain, bruising, swelling, and tenderness at the injection site. Rare but serious complications include vascular embolization with necrosis [33].

27.6 Conclusions

Wound modulation in the postoperative setting of aesthetic eyelid and periorbital surgery is critical in the final surgical outcome. While surgical advances in minimally invasive surgical techniques continue to evolve, there is a definite and necessary role for nonsurgical adjunctive methods, which address the underlying biologic process of wound healing and scar formation. These include the utilization of antimetabolites and anti-inflammatory agents (5-FU, corticosteroids) and injectable tissue fillers with tissue volume expansion. In the future, we await the production of other modulators that can target the mechanisms for scar formation more specifically.

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