Topical Mitomycin C in the Prevention of Keloid Scar Recurrence

Kenneth W. Sanders, MD; Linda Gage-White, MD, PhD; Fred J. Stucker, MD

Objective: To assess the ability of mitomycin C to prevent the recurrence of surgically excised keloid scars. Mitomycin C has been successfully used to prevent scar tissue formation at the site of subglottic stenosis in the field of pediatric otolaryngology. It appears that mitomycin C interferes with the ability of fibroblasts to produce a scar without causing changes in epithelialization.

Design: We excised keloid scars from various sites in the head and neck and then applied mitomycin C to the resected bed prior to closure of the wound at a concentration of 0.4 mg/mL for 5 minutes. All patients had multiple keloids and acted as their own control. At 1 month after the procedure both wounds were started on a regimen of triamcinolone acetonide, 40 mg/mL injections, repeated every month for 6 months. At the end of the study, photos and measurements were again taken.

Results: Fifteen patients (13 female and 2 male) ranging in age from 10 to 55 years enrolled in the study. No infections or nonhealing wounds were seen. There was no difference in postoperative pain. Eight patients completed the triamcinolone injections, 5 had fewer than 6 injections, and 2 patients had no steroid injections. Twelve patients completed follow-up and were evaluated for surgical complications and recurrence of the keloids at either site. Two patients had partial postoperative follow-up in person and then completed follow-up via telephone. One patient could not be found for follow-up. Four patients had recurrence of both excised lesions. Ten patients had no recurrence of their keloids at either site.

Conclusion: Mitomycin C made no difference in the prevention of keloid recurrence after excision when topically applied.

Arch Facial Plast Surg. 2005;7:172-175

THE MANAGEMENT OF KEOLOIDS is a well-known problem for facial plastic surgeons. These aberrations of wound healing have never been completely understood. We know that certain dark-skinned races are more prone to the development of keloids. For instance, the occurrence of keloids in black patients is between 4% and 16%.1 There are also sites of higher incidence such as the earlobe, the upper chest and back, and the shoulder area. Keloids are significantly different when compared with normal scars. The ratio of type I collagen to type III collagen is elevated.2 There is as much as a 20-fold increase in total collagen production in a keloid scar. The inciting wound may be as little as a follicular infection or it may be from significant dermal trauma such as a surgical incision or burn injury.

Mitomycin C is an antitumor antibiotic isolated from Streptomyces caespi- tus. Lee3 has shown that mitomycin C has an antifibroblastic effect without inhibiting epithelialization. Exactly how this occurs is still not understood, but there may be an inability of the fibroblast to proliferate, thus suppressing fibrosis and scar formation. Mitomycin C has been used recently in an attempt to interfere with the ability of the body to complete the scarring process. This drug has been shown to prevent scar tissue formation after glaucoma filtration surgery, canine subglottic surgery, pediatric choanal atresia repair, rabbit maxillary antrostomy surgery, and after tracheal stenosis repair.4-7 There have been no reports of adverse reactions to the mitomycin C or a lack of epithelialization. We postulated that this antifibroblastic activity is what is needed to inhibit the reformation of keloid scars after excision.

METHODS

Fifteen patients with at least 2 keloids in the head and neck region were selected for this study. The patients were enrolled in the study if they had at least 2 keloids in the head and neck region. The patients were followed for at least 12 months to determine the recurrence of keloids after excision. The patients were divided into 2 groups: group A and group B. Group A consisted of patients who received mitomycin C topically applied to the resected bed prior to closure of the wound at a concentration of 0.4 mg/mL for 5 minutes. Group B consisted of patients who received no topical mitomycin C. All patients had multiple keloids and acted as their own control. At 1 month after the procedure both wounds were started on a regimen of triamcinolone acetonide, 40 mg/mL injections, repeated every month for 6 months. At the end of the study, photos and measurements were again taken.

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study. After institutional review board approval and obtaining informed consent, 2 of the lesions were photographed and then excised with a scalpel. One of the wound beds chosen randomly was then treated with a cotton pledget soaked in mitomycin C, 0.4 mg/mL (Mutamycin; Bristol Laboratories, Princeton, NJ), for 5 minutes. In an attempt to prevent dilution from any blood on the field, meticulous hemostasis was achieved, and the wound was irrigated free of any visible clots. After the 5-minute treatment, the wound was again irrigated with 100 mL of isotonic sodium chloride solution. Closure was performed with 5-0 chromic gut suture to the skin and subcutaneous tissue. Vitamin A and D ointment was applied without any other dressing. Postoperative wound care consisted of cleansing with hydrogen peroxide and reapplying the Vitamin A and D ointment 3 times a day. Each patient was followed up at postoperative day 7 for wound check and was questioned. They were then scheduled for an intrallesional injection of 0.2- to 0.40-mL triamcinolone, 40 mg/mL to each wound at 1-month intervals for 6 months. Photographs were taken if any changes were noted in the wounds and at the 6-month point.

**RESULTS**

Fifteen patients with 2 keloids had excision of the lesions and mitomycin C applied to the wound bed during the repair. The 13 females and 2 males ranged in age from 10 to 55 years (Table). All were African American except for 1 white patient. Nine patients had bilateral earlobe keloids, 2 had bilateral auricular helix keloids, 1 had 2 distinct lesions on the same ear, 1 had 2 posterior neck lesions, 1 had 2 preauricular lesions, and 1 had multiple lesions throughout her body and had a neck and upper back lesion excised. Six patients had a history of previous excision of the keloid scars. The lesions ranged in size from 1.1 to 6 cm in diameter. All lesions were excised by the same surgeon (K.W.S.) with a scalpel. All wounds healed without incident. There were no complaints at the initial postoperative visit except for mild pain, and there was no difference in pain levels between treated and untreated wound beds. There were no complications from the mitomycin C application such as rash, burn, or wound dehiscence. Only 8 of the 15 patients completed all 6 triamcinolone injection visits. Twelve patients were able to complete follow-up visits for photography. Of the other 3 patients, 1 could not be found for follow-up and 2 were reached by telephone. Fourteen patients were either seen and photographed or interviewed by telephone at the end of the study. Four patients had recurrence of keloids at both sites (Figure 1). The other 10 patients showed no signs of recurrence (Figure 2).

Statistical analysis using the McNemar test indicates a P value greater than .99, indicating no difference in outcome between the 2 groups. Although no statistical data were measured for the size of the recurrence in relation to the primary lesion, the authors noted somewhat smaller keloids in the recurrences in about half the patients.

**COMMENT**

Good outcomes when treating keloid scars have historically been very difficult to achieve. Recurrence rates are as high as 50% to 60% after simple excision.8 There are multiple proposed methods of treatment, all of which have limited success. Previous treatment regimens have included scalpel excision, laser excision or vaporization, corticosteroid injection, calcium channel blocker and angiotensin converting enzyme inhibitor injection, cryotherapy, silicone contact therapy, pressure therapy, radiation therapy, and combinations of any of the listed modalities. Most, if not all, of these interventions have been met with a significant degree of failure. Regardless of the surgical technique, there is further injury to the dermis that leads to proliferation of fibroblasts and extreme amounts of collagen formation, and thus, keloid scar formation. There is an individual component as well; some patients have an “aggressive form” of this condition, while others seem to be easily alleviated of the lesions. The biological nature of keloids is not

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Table. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, y/Sex</th>
<th>Race</th>
<th>Site of Keloid</th>
<th>Previous Excision</th>
<th>No. of Corticosteroid Injections</th>
<th>Recurrence</th>
<th>Follow-up, mo</th>
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<tr>
<td>1</td>
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<td>Yes (9 mo)</td>
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<tr>
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<td>Helix</td>
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<td>No</td>
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</table>

Abbreviation: AA, African American; W, white; ?, could not be located for follow-up.
Mitomycin C is an alkylating antibiotic that has the ability to inhibit fibroblastic proliferation and activity. However, it has been shown that mitomycin C can affect the fibroblasts without sacrificing reepithelialization. This chemical has been used successfully in the field of ophthalmology, pediatric and adult laryngology, and pediatric and adult rhinology to avoid scarring and granulation tissue on cut mucosal surfaces. There have been no systemic adverse effects reported with topical application of mitomycin C.

We wished to extend the use of mitomycin C to the field of facial plastic surgery and specifically to inhibit keloid recurrence. After using mitomycin C-soaked pledgets on the wound beds of resected keloids in 15 patients, only 4 are known to have had a recurrence. However, all patients either had a recurrence or showed no recurrence on both lesions. One patient with recurrence is thought to have a particularly aggressive form of this condition. She has more than 40 separate keloids spread all over her body—most with no obvious traumatic inciting event. There were no complications in this series and, of note, no wound breakdown or failure to heal.

**CONCLUSIONS**

Topical mitomycin C seems to have the ability to modulate wound healing such that fibroblast activity is reduced while epithelial activity remains normal. This may hold promise for the patient with a keloid scar. Our preliminary study has shown no significant difference between the 2 treatment regimens, but we realize the limited number of participants and the lack of complete patient follow-up are limiting factors. There is need for a larger, more controlled study into the ability of mitomycin C to reduce the recurrence rates of keloid scars.
Another goal of future studies would be to determine if there is a difference between lesions in mucosal epithelium vs skin in the response to mitomycin C.

Accepted for Publication: January 17, 2004.
Correspondence: Kenneth W. Sanders, MD, Pierremont Facial Plastic Surgery, 7853 Youree Dr, Shreveport, LA 71115 (kenoto@hotmail.com).

REFERENCES


Call for Papers. The Archives of Facial Plastic Surgery plans to publish a theme issue on vascular birthmarks in late 2005. Marcelo Hochman, MD, will edit this series of articles. Please direct questions or suggestions to Dr Hochman at 843-571-4742 or hochman@facialsurgerycenter.com. Manuscripts on all aspects of the etiology, pathophysiology, diagnosis, and treatment of vascular lesions (including hemangiomas; port-wine stains; and venous, lymphatic, and arteriovenous malformations and associated syndromes) are welcome. Please submit manuscripts to the ARCHIVES editorial office with the usual requirements as detailed in the instructions for authors (available at www.archfacial.org). Include a cover letter stating that the article is to be considered for the theme issue.