EFFECT OF MITOMYCIN C APPLICATION ON HEAD AND NECK KELOIDS

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ABSTRACT: AIM: To find out the effect of mitomycin application along with surgical excision on keloid recurrence rates. **METHODS:** A prospective study of 20 study subjects treated for head and neck keloids carried out at JJM Medical College, Davangere. After removing core of Keloid by sharp dissection, Mitomycin C (0.8mg/cc) soaked cotton pledgets were applied over the wound for 5 minutes. Later wound was irrigated with normal saline. Tensionless wound closure was carried out. **RESULTS:** Weekly post-operative follow-ups were done. Patients did not report any adverse skin reactions or side effects that could be attributed to the mitomycin-C. Only 1 out of the 20 subjects had a recurrence of keloid after a 6 months followup. **CONCLUSION:** Combination of surgical excision with topical mitomycin-C application is highly effective in treating head and neck keloids.

KEYWORDS: Mitomycin C, Keloid, topical Mitomycin C, recurrent keloids.

INTRODUCTION: A keloid is an abnormal proliferation of scar tissue that forms at the site of cutaneous injury (eg, on the site of a surgical incision or trauma); it does not regress and grows beyond the original margins of the scar. Keloids of the head and neck are a relatively common entity in darker-skinned races, occurring in 5%-15% of skin wounds^[1].

Many modalities like surgical excision, compressive therapy, silicon dressings, corticosteroid injections, radiation, cryotherapy, interferon therapy, and laser therapy have all been used alone or in combination for keloid treatment with variable amounts of success. Recurrence rates typically remain in the 50%-70%^[1] range inspite of so many treatment options.

Mitomycin C is an antitumor antibiotic isolated from *Streptomyces caespitosus*.^[2] Mitomycin-C is a chemotherapeutic agent that inhibits DNA synthesis and fibroblast proliferation. Mitomycin C has also been used topically rather than intravenously in several areas. It is used in oesophageal and tracheal stenosis where application of mitomycin C onto the mucosa immediately following dilatation will decrease re-stenosis by decreasing the production of fibroblast tissue and scar tissue^[3, 4, 5].

Previous studies have demonstrated the efficacy and safety of mitomycin C topically in the treatment of airway stenosis. Mitomycin C has been used topically in the concentration ranging from 0.2mg/mL to 10mg/mL with the application time between 2 to 5 mins. Even though, Ophthalmologic literature has documented serious, vision threatening complications, there are no reports of mitomycin C toxicity in otorhinolaryngology literature^[6]. In this study, we present our results in a series of 20 patients who were treated with surgical excision of ear keloids and the application of topical mitomycin-C.

METHODS AND MATERIALS:

Subjects: A prospective study of 20 patients was carried out who were treated with surgical excision of head and neck keloids and the application of topical mitomycin-C at JJM Medical College,

Davangere. We have taken institutional ethical committee approval for this study. All procedures were performed by same Otorhinolaryngologist using same technique of excision of the keloid. All 20 cases underwent standard surgical resection of the keloids at the out- patient surgery centre under strict aseptic conditions. The details of the patients under study are shown in Table 1.

Surgery: A proper clinical examination was carried out following which related investigations were done. A written informed consent was obtained. Local infiltration at the incision site was done using 1% lignocaine with 1:1 00000 adrenaline. A 15 number surgical blade was used to make the skin incision. Part of the skin flap was left behind, and the core of the keloid was removed by sharp dissection. Cotton pledgets soaked in Mitomycin C in ratio of 0.8 mg/cc were applied to the surgical wound for 5 minutes. Wound was then irrigated with normal saline. Tensionless wound closure was done using 5-0 prolene. Entire procedure was carried out under complete aseptic conditions.

Table 1. Patient demography

Patient	Age/Sex	Location of Keloid	Size (cm)
1	22/F	Bilateral ear lobe	Lt -0.5cm Rt - 1cm
2	24/M	Left ear lobe	1.2cm
3	28/F	Left Helix	2.2cm
4	35/M	Nape of neck	2.6cm
5	23/F	Right ear lobe	1.4cm
6	26/F	Right Helix	2cm
7	22/F	Bilateral ear lobe	Lt -1.3cm Rt - 2 cm
8	20/M	Cheek(angle of mandible)	1.8cm
9	26/F	Right ear lobe	1.6cm
10	24/F	Left ear lobe	2.2cm
11	30/M	Post aural sulcus	3.2cm
12	21/F	Right Helix	1.1cm
13	25/F	Left ear lobe	0.7cm
14	27/M	Left ear lobe	1.5cm
15	32/M	Right Cheek	2cm
16	22/F	Left ear lobe	1.8cm
17	23/F	Right Helix	1cm
18	28/M	Right ear lobe	0.6cm
19	21/F	Left Helix	2.2cm
20	26/M	Right ear lobe	0.6cm

Table 2. Treatment results

Patient	Etiology	Followup	Recurrence
1	Piercing	4 months	No

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2	Piercing	6 months	No
3	Piercing	6 months	No
4	Previous surgery	6 months	No
5	Piercing	6 months	No
6	Piercing	6 months	No
7	Piercing	6 months	No
8	Trauma (razor)	6 months	No
9	Piercing	5 months	No
10	Piercing	5 months	No
11	Previous Surgery	2 months	Yes
12	Piercing	6 months	No
13	Piercing	6 months	No
14	Piercing	6 months	No
15	Trauma	6 months	No
16	Piercing	6 months	No
17	Piercing	6 months	No
18	Piercing	6 months	No
19	Piercing	3 months	No
20	Piercing	6 months	No

FOLLOWUP: All patients were instructed for a weekly follow up. 16 out of the 20 cases came on the allotted dates. 4 came on the 10th day. Sutures were removed on first follow-up visit.

RESULTS: Our Study group constituted of 8 males and 12 females ranging from age group of 20 to 35 years (mean age 28 years). Pinna was the commonest site (16 out of 20 patients) for keloids. Size of keloids ranged between 0.5 to 3.2cms (Table 1). Most (16 cases) of the keloids in our study were developed following ear piercing (Table 2). Our study, 19 out of the 20 subjects were free

Fig 1 Patient no 3 preoperative picture Patient no 3: 6 month Post-operative picture

From recurrence after a 6 months follow-up with a cure rate of 95%. Preoperative and postoperative pictures of the patients helped us document patient progress with this treatment plan. Patient with recurrence included a 30 year old male who had previously underwent ear surgery

following which he developed a post aural keloid 3.2cm in size, turned up directly after a month of surgery with recurrence at site now measuring 2.4cm size. In our study, there were no adverse skin reactions or other side effects seen.

DISCUSSION: Keloids were described by Egyptian surgeons around 1700 BC [7]. Baron Jean-Louis Alibert (1768–1837) identified the keloid as an entity in 1806. He called them cancroïde, later changing the name to chéloïde to avoid confusion with cancer. The word is derived from the Greek χηλή, chele, meaning "hoof", here in the sense of "crab pincers", and the suffix -oid, meaning "like". Persons of any age can develop a keloid. Children under 11 are less likely to develop keloids, even from ear piercing. 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% [8]. Keloids may also develop from Pseudofolliculitis barbae. The tendency to form keloids is speculated to be hereditary. Keloids can tend to appear to grow over time without even piercing the skin, almost acting out a slow tumorous growth; the reason for this is unknown. The ratio of type I collagen to type III collagen is elevated [8]. Histologically, keloids are fibrotic tumors characterized by a collection of atypical fibroblasts with excessive deposition of extracellular matrix components, especially collagen, fibronectin, elastin, and proteoglycans [9, 10]. Generally, they contain relatively acellular centers and thick, abundant collagen bundles that form nodules in the deep dermal portion of the lesion. Keloids present a therapeutic challenge that must be addressed, as these lesions can cause significant pain, pruritus (itching), and physical disfigurement [11, 12].

Table 3. Different treatment methods for keloid

Treatment Modality	Recurrence Rates
SINGLE :	
Surgical Excision	50% - 93%
Radiation therapy	15% - 94%
CO2 laser excision	39% - 92%
Pressure therapy	10% - 55%
Cryotherapy	26% - 49%
Intralesional Steroid inj	50% - 100%
Post excision intralesional IFN injections (IFN alpha, gamma)	18% - 75%
COMBINED :	
IFN / Steroid injection with CO2 laser excision	0% - 74%
Excision + Radiation	0% - 98%
Intralesional Steroid inj with Surgical excision	12% - 70%

Since many years significant number of treatment modalities has been tried for successful cure of Keloids. Prevention is key, but therapeutic treatment of keloids includes occlusive dressings, compression therapy, intralesional corticosteroid injections, cryosurgery, excision, radiation therapy, laser therapy, interferon (IFN) therapy, 5-fluorouracil (5-FU), doxorubicin, bleomycin,

verapamil, retinoic acid, imiquimod 5% cream, tamoxifen, tacrolimus, botulinum toxin, and over-the-counter treatments (eg, onion extract; combination of hydrocortisone, silicon, and vitamin E). Other promising therapies include antiangiogenic factors, including vascular endothelial growth factor (VEGF) inhibitors (eg, bevacizumab), phototherapy (photodynamic therapy [PDT], UVA-1 therapy, narrowband UVB therapy), transforming growth factor (TGF)-beta3, tumor necrosis factor (TNF)-alpha inhibitors (etanercept), and recombinant human interleukin (rhIL-10), which are directed at decreasing collagen synthesis, but none have proved to be solely effective in complete cure without recurrence^[13,14,15,16]. Table 3 shows treatment options available and their recurrence rates. Topical Mitomycin C application for keloids after surgical excision showed success rate of 95% without any toxic side effects or complications which is in line with previous study by C.E. Stewart et al^[1].

CONCLUSION: A complete treatment of Keloid is still a challenging endeavour. We conclude that combination of surgical excision with topical mitomycin-C application is highly safe and effective in treating head and neck keloids in contrast to other modalities which have either a high recurrence rate or are invasive.

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