

Role of 5% Imiquimod Cream in the Prevention of Recurrence of Keloids Post Shave Excision

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ABSTRACT

Introduction: Keloids represent an excessive connective tissue response to injury, which may be trivial. Despite numerous small case series advocating a wide range of therapies, there is no level one evidence for any single treatment. This study was done to know the role of 5% imiquimod cream in preventing recurrence of excised keloids.

Material and methods: Study was done on 30 Cases of keloids attending the Department of DVL, Osmania general hospital for a duration of 6 months from December 2017 to May 2018.

Results: It was observed that after 6 months, 7 of 8 keloids on the trunk and 4 of the 6 keloids on the extremities had evidence of recurrence while of 14 auricular keloids, only 2 had evidence of recurrence and none of the keloids in the suprapubic region had evidence of recurrence.

Conclusion: According to the present study the use of postoperative, topically applied imiquimod following shave excision is a more effective intervention compared to the standard, complete excision of keloids.

Keywords: Keloids, Imiquimod, Preventing Recurrence of Excised Keloids.

MATERIAL AND METHODS

Study was done on cases of keloids attending the department of DVL, Osmania General Hospital for the duration of 6 months from December 2017 to May 2018. Sample size was 30 patients.

Inclusion criteria: Keloids at all anatomical sites between 0.5cm to 5cm in diameter without any treatment in the previous 3 months, attending DVL OP, in Osmania General Hospital.

Exclusion criteria

- Pregnant and nursing women
- Patients with HIV seropositivity
- Patients who were unable to return for follow up visits or comply with the protocol.

Method of collection of data

After taking informed consent from all the patients were included in the study and after making a clinical diagnosis, they were examined for the location and size of keloids and the data was recorded. Biopsy of the lesions was done to confirm the diagnosis wherever required. A total of 30 keloids were shave excised tangentially along the long axis of the lesion, followed by curettage, hemostasis and a compression dressing. Patients were instructed to start nightly applications of 5% imiquimod cream for 2 months 24 hours after the procedure. Follow up visits occurred at 2 weeks after excision, and then every 4 weeks until 6 months postoperatively. 30 keloidectomy sites (14 auricular, 8 truncal, 2 suprapubic and 6 on extremities) were available for evaluation at the 6 month end point. Photographs were taken and all adverse events were recorded at each visit and

INTRODUCTION

A keloid is a benign well-demarcated overgrowth of fibrotic tissue which extends beyond the original boundaries of a defect. A scar at any site has the potential to become keloidal.¹ Keloids mostly arise at puberty with peak age of onset between 10 and 30 years of age.² There exists an equal risk between men and women. But female preponderance may be due to the number of ear lobe keloids secondary to piercing among women.^{3,4} Majority of the keloids recur at the site of keloidectomy, and currently there are no medications approved to reduce keloid recurrence after excision.⁵ Some modalities of treatment may exacerbate the condition.¹ The optimal approach may involve a combination of different modalities of treatment.¹ Imiquimod 5% cream has been found to be effective and safe in preventing recurrence of keloids on earlobes after excision.⁶ Imiquimod has its immune modulatory effect partly due to induction of production of antifibrotic IFN- α , and TNF- α , interleukins 6 and 8, as well as recruitment and activation of cytokine producing plasmacytoid dendritic cells.⁷ Surgical excision of keloids has a reported 71% average weighted recurrence rate if performed without adjuvant therapies.⁸ So this study was done to know the role of 5% imiquimod cream in preventing recurrence of excised keloids.

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How to cite this article: Gurralla Satyanarayan Reddy, Merugu Pravalika, Chelikani Vijaya Lakshmi, N. Gayathri, Fareeha Mahenaz. Role of 5% imiquimod cream in the prevention of recurrence of keloids post shave excision. International Journal of Contemporary Medical Research 2019;6(2):B1-B4.

DOI: <http://dx.doi.org/10.21276/ijcmr.2019.6.2.16>

at the end of the study.

RESULTS

A total of 30 patients with keloids at various anatomical sites attending dermatology OPD at Osmania General Hospital were recruited for the present study. After obtaining informed consent detailed history and medical examination was done. The mean age of the patients was found to be 26.06 and there were more number of females as cited in table 1. It was observed that none of the patients reported any systemic symptoms such as fever, or malaise. Majority of the patients developed keloids post trauma and other etiologies included infections and spontaneous appearance of keloids (table 2 and chart 1). Keloids in various anatomical sites such as ear, trunk, extremities and suprapubic region were included in the study (table 3). All patients sensed burning at the imiquimod application site, in addition to pain, itching, inflammation, and wound crusting (table 4 and chart 2). At 6

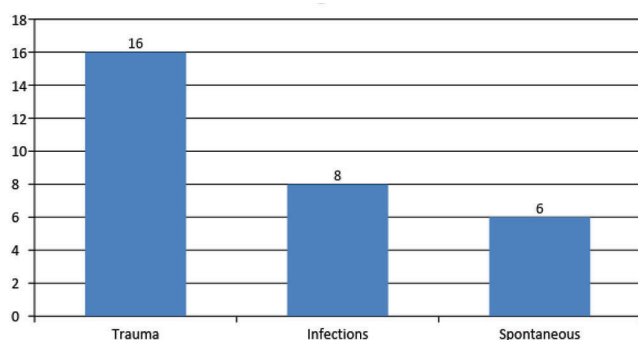


Chart-1: Etiological distribution

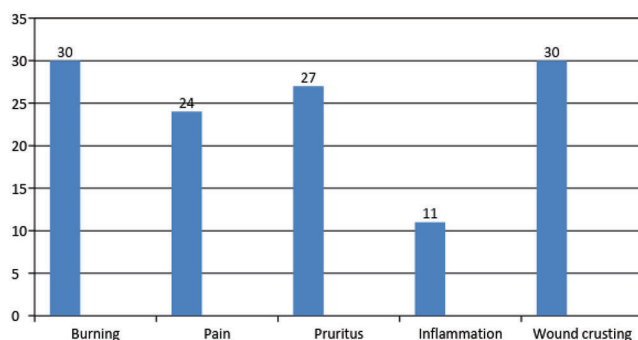


Chart-2: Adverse effect

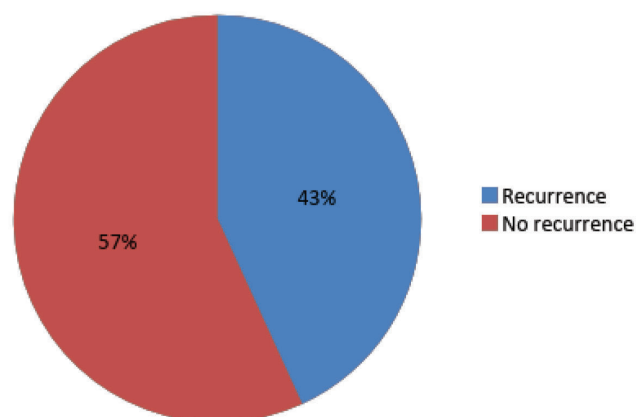


Chart-3: Percentage of recurrence of keloids

Variable	
Mean age (years)	26.06
Sex (%)	No. of cases
Female	16 (53.3%)
Male	14 (46.7%)

Table-1. Age and sex distribution

Etiology (%)	No. of cases
Trauma	16 (53.3%)
Infections	8 (26.7%)
Spontaneous	6 (20%)

Table-2: Etiological distribution

Anatomical location (%)	No. of cases
Auricular	14 (46.6%)
Trunk	8 (26.7%)
Extremities	6 (20%)
Suprapubic	2 (6.7%)

Table-3: Distribution based on anatomy

Type of side effect	No. of cases
Burning	30 (100%)
Pain	24 (80%)
Pruritus	27 (90%)
Inflammation	11 (36.7%)
Wound crusting	30 (100%)

Table-4: Adverse effects

months 7 of the 8 excised keloids on the trunk and 4 keloids excised on the extremities had evidence of recurrence while of the 14 auricular keloids only 2 had evidence of recurrence and neither of the keloids in the suprapubic region had evidence of recurrence. Therefore in the present study the recurrence rate of keloids post shave excision followed by 5% imiquimod cream application for 2 months at the end of a follow up period of 6 months was found to be 43.4% (chart 3).

DISCUSSION

The present study was conducted in the Department of DVL (Dermatology, Venereology and Leprosy), Osmania Medical College and Hospital, Hyderabad.

A total of 30 patients with keloids, attending DVL OPD at OGH were recruited for the present study. After obtaining informed consent, detailed history and medical examination was done. The keloids at various anatomical locations meeting the inclusion criteria were shave excised and 5% imiquimod cream was applied to the excised sites for a period of 2 months. All cases were followed for 6 months to evaluate the effects of 5% imiquimod cream and to study the adverse effects and recurrence of keloids.

Recurrence rates- In the present study recurrence rates were 43.3% at the end of 6 months 7 of the excised keloids on the trunk and 4 keloids excised on the extremities had evidence of recurrence while of the 14 auricular keloids only 2 had evidence of recurrence and neither keloids in the suprapubic region had evidence of recurrence.

Adverse effects- All patients sensed burning at the site of imiquimod application and most patients complained of pain, itching, inflammation, and wound crusting which gradually subsided in the due course of treatment and none of the patients reported any systemic side effects. (table 4 and chart 2).

In a study by Berman B et al⁹ at the end of 6 months, keloid recurrence rates were 37.5% and Imiquimod was well tolerated.

In a study by Malhotra A.K. et al⁶ the efficacy and safety of imiquimod 5% cream in preventing the recurrence of presternal keloids after excision (3 keloids in 2 patients) was evaluated. After excision with radiofrequency, imiquimod 5% cream was applied once daily at bedtime for 8 weeks, and the defect was left to heal by secondary intention. In all the treated keloids, the defect healed in 6–8 weeks, and no recurrence was seen while on imiquimod application; however, all keloids completely recurred within 4 weeks of stopping imiquimod. Side effects were mild and acceptable in the form of burning and pain. Imiquimod did exert an antifibrotic action but it was short-lived.

In a study by Jennifer Frias et al⁵ recurrence rates were found to be 43% which was consistent with our present study and all patients sensed burning at the imiquimod application site, in addition to pain, itching, inflammation, and wound crusting. Three patients discontinued the study early due to application site adverse effects.

Chandawarkar et al¹⁰ carried out treatment of recurrent keloid in three steps—first step was excision of keloid, application of dermal replacement materials and immobilization and dressing with a vacuum-assisted wound dressing. Second step was application of autologous split thickness skin graft and last was the local application of 5% imiquimod cream for 8 weeks. The patient was asymptomatic after 15 months of surgery. Although this

is an interesting therapeutic approach, it is of a low-level evidence since it is based on one case report.

In a study by Zainab Laftah et al¹¹, 19 keloids were excised from 16 patients and all had intraoperative triamcinolone injection into the wound edge followed by application of imiquimod. Patients were followed up for a median of 18 months Imiquimod was applied to the wound edge three times a week for a median of 2 months Side effects included pain (37%), hypopigmentation (26%), erosion (21%) and bleeding (5%), which resulted in treatment cessation in 37%. 12 keloids (10 patients) had 1-2 months of imiquimod. Compared to the original keloid, recurrence was larger in 1, half the size in 6, mild in 3, and 2 had no recurrence. 7 keloids (6 patients) had 5-6 months of imiquimod. Compared to the original, recurrence was half the size in 2, mild in 4, and 1 had no recurrence. A longer duration of imiquimod use resulted in reduced recurrence size even after lengthy follow-up. Recurrence did not depend on the site or size of the original keloid.

In a study by Fernanda Marson Cac, a^o s. et al¹² topical imiquimod 5% cream was applied postoperatively after surgical excision and primary closure and their data showed

100% recurrence in patients who returned after the treatment. Seven patients who were evaluated just after treatment showed early recurrence of the keloids (approximately 12 weeks).

Patel and Skinner¹³ reported 60 patients treated with shave excision of earlobe keloids and topical use of imiquimod 5% cream at the excision sites for 8 weeks. Only one patient experienced keloid recurrence after 24 weeks.

Stashower¹⁴ treated four patients with a total of eight pedunculate earlobe keloids with shave excision and daily application of imiquimod 5% cream for 6 weeks; 12 months afterward, there was no evidence of recurrence in any of the lesions.

Martín-García and Busquets¹⁵ treated eight earlobe keloids in six patients with shave excision and imiquimod 5% cream at the surgical site for 8 weeks and reported a 25% recurrence rate 24 weeks after surgery.

Keloids are cosmetically distressing and often painful and pruritic.¹ They occur most commonly on the chest, shoulders, upper back, back of the neck and ear lobes.¹⁶ Lesions may follow trivial trauma or inflammatory conditions such as acne. Even chemical trauma, from irritant herbal remedies, can trigger keloid formation. Sometimes keloids appear to develop spontaneously, particularly on the upper chest.¹ Despite numerous treatment options, keloids have a high recurrence rate. A combination of different treatment modalities is an optimal approach in treatment of keloids.¹⁷

CONCLUSION

5% Imiquimod cream following tangential shave excision was efficacious for the treatment of keloids. Localized adverse effects such as burning sensation at the site of application, itching, inflammation and wound crusting were reported. None of the patients had any systemic side effects. According to the present study recurrence rate of keloids was found to be less with post-operative use of 5% imiquimod cream and it was well tolerated; however more number of studies and longer periods of follow up are required to substantiate the role of 5% imiquimod in preventing the recurrence of keloids post shave excision.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 31-12-2018; **Accepted:** 10-01-2019; **Published:** 12-02-2019