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Original article

Combination of Carbon dioxide laser and Topical 5-flourouracil for Prevention of recurrence of Keloid

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ABSTRACT

Background: The treatment of keloid has been a challenge, and at times, frustrating because of the recurrence. Hence, it is essential to find treatment modality with least recurrence and good cosmetic results. This study showed the effect of topical 5-fluorouracil following carbon dioxide laser excision on recurrence of keloid. Aim: To evaluate the efficacy of combination of carbon dioxide laser and topical 5-flourouracil(5%) in prevention of recurrence of keloid. Material and methods: Total 24 patients (20 females and 4 males) of age group 12-56 years having keloid of duration 1-8 years were included in this study. Lesions were present on ear lobes, shoulder, chest, leg. CO_2 laser was used in continuous mode to excise the lesions and all patients advised topical 5-FU(5%) once daily application over the lesion in the night, once re-epithelization started, for 4 weeks. The patients were followed up initially at every week for 4 weeks then every 4 weeks for 24 weeks to evaluate the response of treatment. Result: Of the 24 patients evaluated at 24 weeks, none (0%) showed any sign of recurrence. Out of 22 patients four(18.2%) patients complained of burning sensation/irritation. Three (13.6%) patients of erythema and erosion which cleared with temporary discontinuation of topical 5-FU and completed the 4 weeks of topical therapy. Three (13.6%) patients developed hypopigmentation. Conclusion: Though response of this combination is encouraging in prevention of recurrence of keloid, recurrence on long term follow up need to be observed.

1. Introduction

A keloid is an overgrowth of dense fibrous tissue usually developing after healing of a skin injury. This tissue extends beyond the border of original wound, does not regress spontaneously and tend to recur after excision[1]. Although multiple treatment modalities exist, like intralesional corticosteroids, topical application, cryotherapy, surgery, laser therapy and silicon sheath, no single treatment has proven widely effective. In fact recurrence following treatment is generally the norm. Combination therapy is likely the optimal strategy[2].

The most recent time, treatment modality to be employed in themanagement of keloid is the carbon dioxid laser. Early studies of the effect of the laser on wound healing suggested that the carbon dioxide laser and the argon laser had favorable effects on wound healing, yielding minimal scaring[3]. Carbon dioxide (CO_2) laser has been shown to exert inhibitory effect on collagen synthesis hence recurrences have been found to be less frequent4. Though in the early studies the encouraging results were seen but in the further studies they found the recurrence following use of CO_2 laser as single therapy. So in this study we used the topical 5-fluorouracil(5%) in combination with CO_2 laser excision to prevent the recurrence of keloid.

2.Materials and Methods :

Total 24 patients (20 females, 4 males) with a clinical diagnosis of keloid were included in this study. The criterion for the clinical diagnosis of a keloid was that the lesion must have extended beyond the boundaries of the original injury. In all patients, keloids were present for at least 1 year and free from any treatment for at least last 3 months. Patient who were pregnant or nursing and those with severe pre-existing cardiac disease, uncontrolled hypertension and diabetes mellitus, extensive keloid following burn, were excluded from this study.

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A summary of patient and keloid characteristic can be found in table 1.

Table 1 : Characteristic of keloid patients

Sex	
Male	4
Female	20
Age (years)	12-55
Keloid duration (yrs)	1-8
Keloid diameter (cm)	0.8 – 6
Keloid site	
Ear lobe	20
Shoulder	2
Ankle	1
Chest	1
Keloid cause	
Ear piercing	20
Trauma or infection	4
Previous treatment	
Intralesional	11
Excision	8
No treatment	5

A written informed consent and pretreatment photographs were taken. After thorough cleaning, the lesions and the surrounding areas of the lesions were anaesthetized by injecting 2% lignocaine. The CO_2 laser was used to excise the keloid precisely at the junction of normal skin and keloid using the 1.0mm spot size and the hand held instrument in a continuous mode at a power setting of 10 to 20 watts.

Care was taken to resect the keloid in the plane just beneath the dense collagen layer. This is facilitated by firm traction at the lesion at right angles to its base. All patients were advised to apply topical antibiotic twice daily and as re-epithelization started patients advised topical 5-fluorouracil (5-FU) once daily application over the excised lesion for 4 weeks with protecting the surrounding area with help of white petroleum jelly. In most patients re-epithelization started within one week of excision.

All patients were evaluated every week for 4 weeks, then every 4 weeks for 24 weeks for burning sensation, irritation, local erythema, erosion, pigment alteration and/or recurrence of keloid. The final assessment was at 24 weeks, however several patients are still being followed up.

In all patients improvement was judged on the basis of regression in size as well as the flattening of the lesion.

The response to treatment was assessed on the basis of patient satisfaction, photographic record and observations of the lesion during the follow up.

The response was graded on a 4 point scale as follows :

Poor response	:	Upto 25% improvement
Fair response	:	26% to 50% improvement
Good response	:	51% to 75% improvement
Excellent response :	:	76% to 100% improvement

3.Results:

Of the 24 patients, 22 completed the study. A total of 22 patients were available for the final assessment. Two patients were lost during the period of follow up after 3 months, with no evidence of recurrence at the last assessment. Of the 22 patients that were evaluated at 24 weeks after laser excision, none had recurrence. All patients showed excellent response (90-100%).

Of the 22 patients, four (18.2%) patient complained of burning sensation/ irritation with application of topical 5 FU. Three (13.6%) patients experienced erosion and erythema at the application site, requiring cessation of therapy for 1 week. All patients were able to restart therapy and completed the treatment course and follow up with no further development of erythema or erosion. Three (13.6%) patients had mild hypopigmentation at the end of 24 weeks. No patient reported secondary infection.

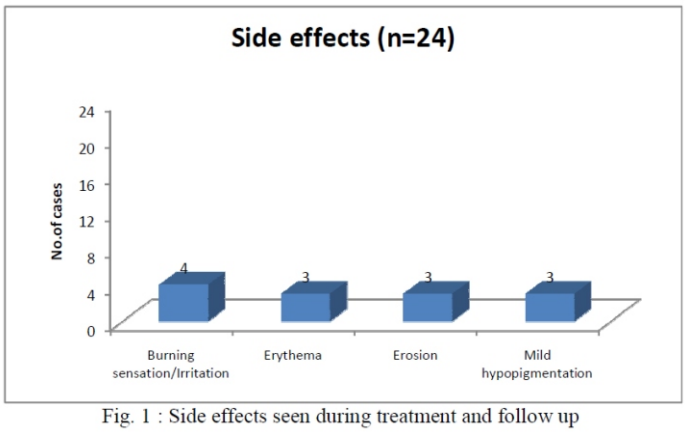

Fig. 1 : Side effects seen during treatment and follow up

4.Discussion:

The carbon dioxide laser produces an invisible high energy beam of infra-red radiation with a wavelength of 10,600 nanometers. It is absorbed by extracellular and intracellular water, which comprises 80%-90% of biological tissues. Such a non-selective photothermal transfer of energy produces instantaneous vaporization by heating target tissue to 100°C. By focusing the laser beam to a fine spot, tissue at the focal point can be removed leaving adjacent tissue unaffected. It is this precise control of the depth of tissue ablation which offers the major advantage of carbon dioxide laser over other surgical modalities by accomplishing removal of abnormal tissue with minimal loss of normal tissue3. The carbon dioxide laser has been well described for use in the treatment of keloids. Its advantage of sealing blood vessels, sealing nerve endings, and lymphatics, along with the limited thermal spread causing little peripheral tissue necrosis speaks well for its use in the excisional management of these lesions.

Bailin5, in 1982, first reported a series of patients with keloids excised by the CO_2 laser as a scalpel and left to granulate and epithelialize by secondary intention with apparent good results. This suggested that the laser's beneficial effect was the non traumatic and anti inflammatory as well as sterile excisional technique. The subsequent closure by secondary intention accomplished reduction of wound tension, aiding the low recurrence of keloid. However, Apfelberg et al6 treated 12 patients with carbon dioxide and argon laser but failed to find any improvement in their patients except one patient with an ear lobe keloid, who showed good response in a follow up of 6 months.

Norris7 evaluated the efficacy of carbon dioxide laser excision as a primary modality for the treatment of keloids in 31 patients. They found that carbon dioxide laser excision of keloids alone failed to suppress the keloid growth or recurrence. Stern and Lucente8 compared the effectiveness of laser excision with standard scalpel excision; however out of 38 patients only 4 patients with bilateral ear lobe keloids agreed to the above protocol. Authors failed to demonstrate the lower recurrence rate of keloids using CO_2 laser. To halt the problem of recurrence in keloid, Stucker and Shaw9 used a new protocol for management of large primary recalcitrant keloids by resecting the lesions by CO_2 laser followed by healing of the wound by secondary intention. Early recurrences were detected by close follow-up and were treated with injection of 40mg/ml of triamcinolone acetonide, 150 mg of hyaluronidase and 2% lidocaine using a dermajet. Patients were followed up for at least 2 years. A control rate of 84% was achieved by them. Kantor et al10 demonstrated dramatic results following carbon dioxide laser and concomitant use of corticosteroids for the treatment of keloids.

Similar way in this study we used topical 5-FU as combination therapy to prevent the recurrence of keloid following CO_2 laser excision. . Intralesional 5-FU has been investigated in combination with other treatments and as an adjuvant to operation with promising results 11,12. 5-FU is a pyrimidine analogue with antimetabolite activity, suppresses cell division and produces growth arrest at any stage of the cell cycle. It is known to affect cell membrane proteins mandatory for cell-to-cell communication and autoregulation. 5-FU has been shown in tissue culture to inhibit fibroblast proliferation13. In our study 5-FU used as topical preparation instead of intralesional because of its advantages over intralesional injection like painless and self application, lesser side effects and better patient compliance.

As a result of this combination therapy, CO_2 laser excision followed by topical 5-FU application excellent response (90-100%) are seen in all patients with decrease keloid recurrence rate with no recurrence at 24 weeks after CO_2 laser excision . Application of 5-FU was well tolerated with few side effects. Three(13.6%) patients experienced hypo-pigmentation resolved during further follow up. Patient who had erythema with erosion with irritation were able to restart application within one week without any further complication. One patient who had keloid at sternum (chest) was reported with recurrence, four months after the completion of six months study, which can be explained by its location at most tension site of the body though the exact reason needs to be found.

Fig. 1 : Side effects seen during treatment and follow up

5.Conclusion :

Encouraging results are seen at the end of 24 weeks with lower recurrence rate than the CO_2 laser excision alone, still further studies with larger number of patients and longer follow up are required to establish the superiority of this combination therapy in preventing the recurrence following CO_2 laser excision.

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