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Original Research Article

Role of intralesional bleomycin in recurrent or residual keloids and hypertrophic scars

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ABSTRACT

Background: Keloids and hypertrophic scars are difficult to treat. There are many modalities available with variable success rate. Triamcinolone is still the most commonly used drug but recurrence and partial response to this conventional treatment is still a major concern. Many studies have proved the role and efficacy of intralesional bleomycin and this study was done to assess the role of intralesional bleomycin in recurrent and residual lesions.
Methods: The patients with recurrent lesion or residual lesions after the injection of triamcinolone were enrolled in the study. Patients received local infiltration of bleomycin. The injections were scheduled at monthly intervals for three consecutive months. They were followed at 1st, 2nd, 3rd, and 12th months. Scar assessment was done by calculating its volume, Vancouver scar scale (VSS) and visual analogue score (pain and pruritis). Side effects were also recorded. Final assessment was done at 1year for any recurrence.
Results: Twenty-five patients completed the study. The most common location of scars was presternal (52%) and trauma was the most common cause in scars (20%). We observed the decrease of volume of 75.85% which was highly significant on statistical analysis (p=0.001). Similarly, statistically significant difference was noticed in VSS, VAS for pain and pruritis. No systemic side effects were noticed. No recurrence was noted at the end of 12 months.
Conclusion: Intralesional bleomycin is found to be useful in management of recurrent or residual lesions. It can be a potential option in the management of recurrent and residual hypertrophic scars and keloids.

Keywords: Recurrent keloids, Residual keloids, Recurrent hypertrophic scars, Intralesional bleomycin

INTRODUCTION

Keloids and Hypertrophic scars represent a form of abnormal pathologic wound healing affecting a substantial segment of the population. Management of keloid and hypertrophic scar is challenging with many treatment modalities available for their management. Triamcinolone is still the most commonly used drug with response rate varies from 50-100% and recurrence is noted in 9-50% of cases.[1] Hence, recurrence and partial response to this drug is still a major concern. Role of bleomycin in keloids and hypertrophic scars is well established. Many studies have proved the role, efficacy and safety profile of intralesional bleomycin.[2-6] This study was designed to assess the role of intralesional bleomycin in the management of recurrent or residual keloids and hypertrophic scars which were managed earlier with triamcinolone.

Aim and objectives of the study were to study the role of intralesional bleomycin in recurrent and residual lesions.

METHODS

The study was conducted in the department of plastic surgery of a tertiary level teaching hospital of northern

India. It is a prospective study. This study included patients in age group of 15-65 years, with recurrent or residual keloids or hypertrophic scars treated with triamcinolone in last six months. Patients with allergic reaction to bleomycin, chronic kidney disease, connective tissue disorders, pregnancy and lactation were excluded from the study. Recurrence was defined as reappearance of similar size lesion at the same site. Residual lesions were the one which showed poor response, size of lesion did not regress at least by 50% of pre-treatment value, to three or more injections of triamcinolone. A detailed history pertaining to the duration, etiologic factors, prior treatment taken, and evidence of any significant systemic disease was obtained. A well informed written informed consent was taken from all patients.

Assessment of scar: The details of the scar were noted in terms of length, breath and height measured in milli meters using Vernier calliper. The scars were scored initially before starting the treatment utilizing the Vancouver scar scale (VSS).[7,8] Symptoms of pain and pruritis were recorded using the visual analogue score (VAS).[9] The VAS includes subjective symptoms of pain and pruritus for a range of 1 to 10, 1 being minimum and 10 as maximum. Side effects like erythema, ulceration, necrosis, hypopigmentation or hyperpigmentation were also recorded.

Injection bleomycin at a concentration of 1.5 IU/mL was used. After a negative skin hypersensitivity test, the lesion anesthetized with local anaesthesia by using 2% lignocaine. Then bleomycin injected intralesional with an insulin syringe at a dose depending on lesion size (0.5 IU/cm^3). In single infiltration maximum dose given was 6 IU. Multiple injections performed to ensure that all lesion volume was entirely addressed. The injections were scheduled at monthly intervals for three consecutive months, after which the treatment was deem to have been completed, and no further injections were given.

The patients were followed up at monthly interval after the first infiltration for initial three months then at 6 months. On every visits volume of scar, VSS and VAS parameters were recorded. The final assessment was done after 12 months of therapy. Photographic documentation before institution of treatment and at scheduled follow up visits was done.

RESULTS

14 females and 11 males were enrolled in the study. Mean age was 34.8 years. Presternal (52%) was the most common site followed by face and earlobe (16%) and torso and back (16%). Trauma was the most commonly known cause which was found in 5 patients (20%) followed by infection in 4 (16%) patients. No cause could be identified in 48% of cases. The scars were assessed for the size in terms of volume (mm^3) measured pre- and post-treatment at 1, 2, 3, 6 and final assessment at 12 months in both the groups (Table 1). The table 1 shows that mean volume decreased with successive treatment. At the final assessment at one-year decrease in volume was highly significant (p=0.001).

There was improvement in VSS following first injection which was progressive throughout the course of treatment (Table 2). Statistical analysis showed that difference at 12 months was significant (p=0.001). Pain was not a major complaint but it responded well to the treatment. Progressive improvement was noticed during the course of treatment. Statistical analysis showed that difference at 12 months was significant (p=0.01). Most of the patients complained of pruritis which improved over a period of time, which was evident from the following table. Statistical analysis showed that difference at 12 months was significant (p=0.01) (Table 2). No recurrence was noted at the end of 12 months.

Most common side effect was pain and burning sensation at the injection site, complained by 7 patients (28%), which required analgesic for 3-5 days. Ulceration was observed in two patients. The ulcers were superficial and healed rapidly with topical application ointment and did not seem to cause serious problems. At the end of three session hyperpigmentation was seen in 3 patients. It improved over a period of time and at final observation only one patient had hyperpigmentation.

Table 1: Mean volume (mm^3) in follow up.

Pre-treatment volume (mm^3)	Post treatment volume (mm^3) at 1 month	Post treatment volume (mm^3) at 2 months	Post treatment volume (mm^3) at 3 months	Post treatment volume(mm^3) at 6 months	Post treatment volume(mm^3) at 12 months	Final percentage change (at 12 months) in the mean volume
3081	2372	1694	766	753	744	75.85

Table 2: Final change in mean in VSS, VAS (pain), VAS (pruritis) at 12 months.

Change in VSS (mean)			Change in VAS (pain) (mean)			Change in VAS (pruritis) (mean)		
Pre treatment	**Post treatment**	**% change**	**Pre treatment**	**Post treatment**	**% change**	**Pre treatment**	**Post treatment**	**% change**
7.28	2.44	66.48	93	33	64.51	144	41	71.52

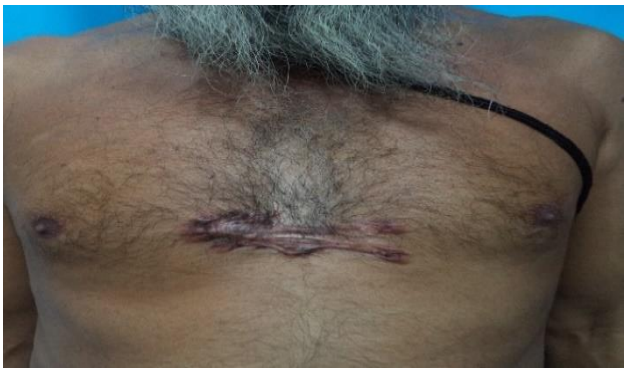

Figure 1: Pre-treatment scar.

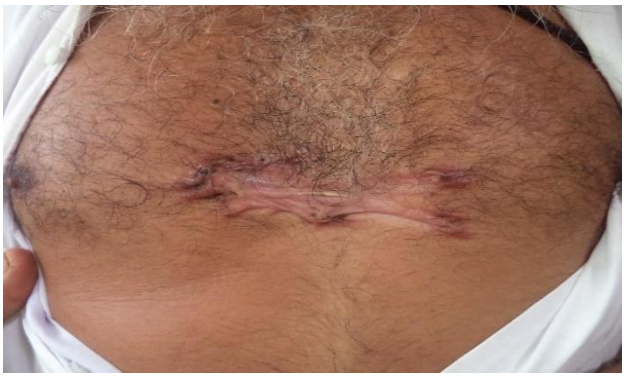

Figure 2: Post treatment at one year.

Figure 3: Pre-treatment scars.

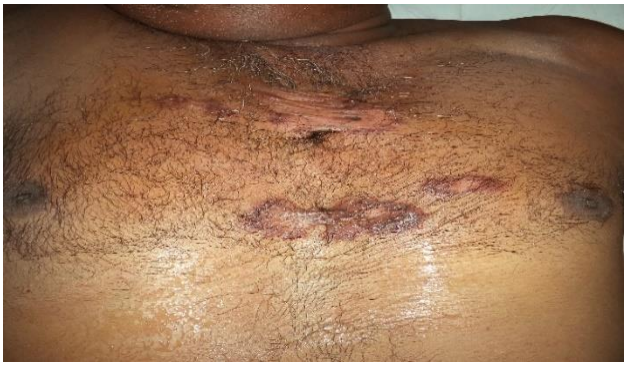

Figure 4: Post treatment at one year.

DISCUSSION

Keloids and hypertrophic scars are abnormal fibrotic conditions, have been thought to be caused by a disorder in regulation during wound healing. The exact etiology and pathophysiology of keloids and hypertrophic scars are still poorly understood. However, these lesions are hypermetabolic in nature which makes antineoplastic agents a viable treatment option.[10] Keloids are more common in darker skin types, and specific anatomic sites such as the presternal skin, upper back, shoulders, and earlobes are usual sites of predilection.[11] Several studies have investigated the role of intralesional injection of bleomycin, and there seems to be a marked improvement in rates of recurrence, patient satisfaction, and overall quality of scar.[2-6]

Bleomycin is an antineoplastic agent. It possibly acts by the inhibition of collagen synthesis by human dermal fibroblasts in keloids and hypertrophic scars.[12] The side effect profile for bleomycin strongly depends on the route of administration and dosage. No systemic toxicity has been noticed when used intralesional in various studies for these lesions.[2-6] The common reactions seen with intralesional bleomycin occur immediately after bleomycin injection and include erythema with swelling, pain, and burning sensation.

Treatment with multiple injections of bleomycin was studied by Espana et al on 13 patients, with a clinical response on all treated nodules and a complete flattening in 53 percent of lesions.[2] Saray et al reported similar results in 15 patients. The number of sessions required to successfully treat the lesions ranged from two to six.[3] Eleven lesions (73.3%) showed complete flattening. No recurrences were noted during follow up (mean duration of 19 months). Naeini et al compared bleomycin tattooing with cryotherapy and triamcinolone injections in 46 patients.[4] The therapeutic response to bleomycin was significantly better than cryotherapy combined with intralesional triamcinolone injection. Agrawal et al in their study of 50 patients complete flattening was observed in 22 cases (44%) and significant flattening in 11 cases (22%).[5] None of the patients demonstrated any pulmonary, hepatic, or other major side-effect of bleomycin per se. Seven patients showed recurrence over 18 months of follow-up. Manca et al used combination of Intralesional bleomycin and electroporation. In this study a median reduction of 87 percent (range, 49 to 100 percent) in lesion thickness and percentage of therapeutic response rate was higher (100%), with lesser number of treatment sessions (2 to 6), with lesser amount of drug.[6] No systemic side effects were noticed and local side effects were considerably low in this study.

There is a broad range of reported dosing schedules and intervals. In most of studies 2-6 injections were repeated at monthly interval. We used three doses at monthly interval to achieve standardization in treatment protocols

and eliminate bias. We observed the decrease of volume of 75.85% which was highly significant on statistical analysis (p=0.001). This observation is in accordance and comparable to the studies done by Epsana, Saray, Manca and Agrawal et al. Highly significant response was observed in VSS and VAS (pain and pruritis). No recurrence was noticed during the period of the study.

CONCLUSION

Bleomycin was effective in the management of hypertrophic scars and keloids. We observed significantly better reduction in terms of volume of scars, greater improvement in VSS, VAS (pain and pruritis) with and a markedly low side effect profile. Considering significantly better results bleomycin can be a potential option in the management of recurrent and residual hypertrophic scars and keloids. However, there is a need of studies with larger number of cases and longer follow up to conclusively ascertain these benefits.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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