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ORIGINAL ARTICLE

A CLINICAL STUDY IN MANAGEMENT OF HYPERTROPHIC SCARS AND KELOIDS WITH INTRALESIONAL INJECTION OF BLEOMYCIN

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ABSTRACT: Keloids and hypertrophic scars remain a nagging problem even with the emergence of multiple modalities in their treatment. The wide range of modalities used for their treatment also point out that no single treatment is definitively superior. **AIMS:** The aim of this study was to define the role of Bleomycin and to confirm its effectiveness in the management of keloids and hypertrophic scars. **SETTINGS AND DESIGN:** This was a prospective clinical trial involving 40 patients with hypertrophic scars and keloids. **METHODS AND MATERIAL:** Patients were followed for 1year in department of general surgery VIMS Bellary, treated with four monthly intralesional injections of Bleomycin. Assessment of the size of keloids and hypertrophic scars was done at the beginning, at the time of stopping the therapy and during the follow-up. **EXCLUSION CRITERIA:** patients under 18 years were not considered suitable for this treatment; pregnant and women likely to become pregnant women were not enrolled in the study. **STATISTICAL ANALYSIS USED:** The response to treatment was divided into the following categories: <25 percent flattening=poor response, 26–50 percent flattening=fair response, 51–75 percent flattening=good response and >75 percent flattening = excellent response. **RESULTS:** Of the forty patients, 27(67.5%) showed excellent response, 6(15%) showed good response, 4(10%) showed fair response and 3(7.5%) showed poor response. There was complete resolution of symptoms in 24 patients (60%) and improvement in the other 16(40%). **CONCLUSIONS:** In the treatment of hypertrophic scars and keloids, the intralesional injection of Bleomycin is very effective and safe.

KEYWORDS: Keloids, Bleomycin, Hypertrophic scars.

INTRODUCTION: The word keloid is derived from the Greek word chele, or crab's claw, to describe the growth of scar into neighbouring skin. The process by which keloids develop is poorly understood. There are several theories of keloid etiology, most of which are related to fibroblast dysfunction. Keloid fibroblasts, when compared with fibroblasts isolated from a normal wound, overproduce type I procollagen and express higher levels of certain growth factors including vascular endothelial growth factor, transforming growth factor β1 and β2, and platelet-derived growth factor.[1] In addition, these cells have lower rates of apoptosis and demonstrate a down regulation of apoptosis-related genes, including p53.[2,3,4] Although keloids have been documented in virtually all major ethnic groups, they are most commonly seen in individuals of African, Asian, and, to a lesser degree, Hispanic and Mediterranean descent. Dark-skinned individuals form keloids 15 times more frequently than do their lighter-skinned counterparts.[5] most cases are sporadic and do not follow any clear inheritance patterns.

Different options such as intralesional injections of bleomycin or corticosteroids either alone or combined with cryotherapy, compression therapy, silicone sheeting, radiation therapy, laser therapy, 5-fluorouracil, interferon, retinoids, imiquimod 5% cream, tacrolimus, verapamil and botulin

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toxin have been used, most of them with the aim of achieving the best functional and cosmetic solution possible.[6,7,8,9,10]

SUBJECTS AND METHODS: The study enrolled 40 patients with keloids and hypertrophic scars after obtaining clearance from institutional review board. Written informed consent was taken from all the patients before the study.

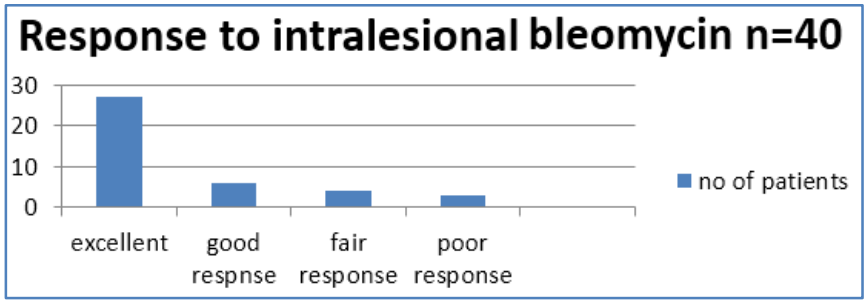
We classified hypertrophic scar as a red or dark pink, elevated scar confined to the border of the original surgical incision. A keloid is instead classified as a scar red to brown in colour, very elevated, larger than the wound margins very hard and sometimes painful or pruritic with no spontaneous regression.

In each case the maximum dose of Bleomycin used was 2mL/cm^2 of skin treated at a concentration 1.5IU/ml and a maximum of 6mL of undiluted bleomycin were given per session. The injections were given in multiple punctures with an insulin syringe. Up to a maximum of 4 doses were administered at intervals of 1 month.

The size of keloids was measured by three different observers using calipers and the mean was deduced for accurate size assessment. The response to treatment was divided into the following categories: <25 percent flattening = poor response, 26–50 percent flattening=fair response, 51–75 percent flattening=good response and >75 percent flattening=excellent response. The incidence of side effects if any was noted. Assessment of the hypertrophic scars and keloids was done at the beginning, at the time of stopping the therapy and during the follow-up. The lesions were measured and followed on monthly basis for 1 year.

RESULTS: Twenty (12 male, 8 female) patients were included in the study. The duration of keloids ranged from 3 to 14 (mean 6.6) years. The mean age of the patients was 34 years. A total of 40 keloid and hypertrophic scars were treated. The involved areas were as follows: shoulder, 6; neck, 5; ear, 9; chest, 14; upper limbs, 4 and face, 2. All the patients had itching, 28 had pain(70%).

Of the forty patients, 27(67.5%) showed excellent response, 6(15%) showed good response, 4(10%) showed fair response and 3(7.5%) showed poor response (Fig. I). There was complete resolution of symptoms in 24 patients (60%) and improvement in the other 16(40%). The drug was given undiluted and in multiple punctures. All the patients followed up for 1 year after termination of therapy. There were no signs of recurrence or reappearance of the symptoms.



DISCUSSION: Bleomycin is a cytotoxic polypeptide with antitumoral, antibacterial and antiviral properties isolated from the fungus Streptomyces verticillus. It is used as a systemic chemotherapeutical agent since its mode of action appears to inhibit DNA synthesis and DNA

destruction. RNA and protein synthesis is also inhibited to a lesser extent.[11,12] The active effect of bleomycin used in the treatment of keloids and hypertrophic scars may possibly be explained by the inhibition of collagen synthesis by human dermal fibroblasts or stimulated by the presence of TGF-β.1, a cytokine detected in scar tissues at high levels.[13]

Espana et al reported 53.8% complete response and 38.4% excellent response (more than 90% resolution) after treatment with bleomycin.[14] Bodokh and Brun treated 31 keloids and 5 hypertrophic scars with 3 to 5 intralesional infiltrations of bleomycin and obtained a total regression of 84%.[15]

The low incidence of side effects makes Bleomycin one of the safest modalities for keloid management. In similar studies, most common complication noted was minor ulceration which healed within 10 days and hyperpigmentation that resolved after 1 year of follow up.[16] none of the patients demonstrated any pulmonary, hepatic, or other major systemic side-effects of bleomycin, which may be in part due to the low dose of Bleomycin used.

CONCLUSIONS: In the treatment of hypertrophic scars and keloids, the intralesional injection of Bleomycin is very effective and safe.

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