**Original article:**

# Intralesional Bleomycin application: An effective therapeutic modality in keloids and hypertrophic scars

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**Abstract:**

**Introduction:** Keloids are described as scars that grows into neighboring skin, means extension of scars beyond the borders of original wound, while hypertrophic scars typically remain within limits of original wound.With the advancement of technology, researchers described pathophysiologic processes of wound healing and scar formation of keloid and hypertrophic scar in detail as well as more specific treatment modalities were invented.Present study was aimed to find out effectiveness of intralesional application of bleomycinin management of hypertrophic scars and keloids.

**Material & methods:** 30 patients were enrolled to participate in study. Patients present to outpatient department of surgery of TeerthankerMahaveer Medical College & Research Centre, Moradabad, INDIA.

**Results:** Out of the thirty patients, 19 (63.33%) showed excellent response, 5 (16.67%) showed good response, 4 (13.33%) showed fair response and 2 (6.67%) showed poor response. There was complete resolution of symptoms in 20 patients (66.67%) and improvement in the other 10 (33.33%) during follow up for 6 months.

**Conclusions:** Bleomycin is very effective and safe pharmacologic agent for treatment of keloid/hypertrophic scar with no significant side effects. Complete resolution of lesions can be achieved in larger extent by bleomycin therapy.

**Key words:** Bleomycin, Keloid, Hypertrophic scar.

## Introduction:

Keloids are described as scars that grows into neighboring skin, means extension of scars beyond the borders of original wound as well as these scars do not regress spontaneously and recurrence following excision is probably high, while hypertrophic scars typically remain within limits of original wound as well as they retain their shape. Both of them may arise following any injury to the deep dermis, including lacerations, abrasions, surgery, piercings, vaccinations and burns.[1]Incidence vary from40%-70% following surgery to up to 91%following burns.In pregnancy and adulthood, the keloid scar may grow to a larger size. These lesions contain neuropeptide and nerve endings; therefore, they may cause symptoms like pain and itching.[2]

Several theories has been put up by researchers in past to determine etiology of keloid, most of them links it to fibroblast dysfunction. Keloid fibroblasts overproduce type I procollagenwhen compared with

fibroblasts isolated from a normal wound. As well as keloid tissue express higher levels of certain growth factors including transforming growth factor β1 and β2, vascular endothelial growth factor and platelet-derived growth factor.[4]Keloid cells express lower apoptosis rates and demonstrate a down regulation of apoptosis-related genes, including p53.[4,5]

Individuals with darker skin phototypes like African, Asian ethnic are particularly susceptible for keloid occurrence than light skin individuals. Dark-skinned individuals form keloids 15 times more frequently than do their lighter-skinned counterparts.[6] Majority of people affected by keloid scars are in age group of 10-30 years and occurs less frequently in older individuals.[7]Hypertrophic scars most commonly occur on the extensor surfaces of joints while Keloids commonly arise on the sternum, shoulder, earlobe, and cheek.[8,9]

Patients commonly presents with symptoms of pain, burning, itching, and restrictionof motion. Scars can be extremelydisfiguring and adversely affect the patient's quality oflife by causing both physical and psychological impairment.[10]

With the advancement of technology, researchers described pathophysiologic processes of wound healing and scar formation of keloid and hypertrophic scar in detail as well as more specific treatment modalities were invented. Several treatment options were described in past for these scars. Corticosteroids administered intralesionally have been useful in keloids and hypertrophic scars. Topically applied silicones or gel sheets are sometimes a good treatment. Other treatments include cryotherapy alone or in combination with intralesional corticosteroids, intralesional 5-fluorouracil (5-FU),retinoids, imiquimod 5% cream, tacrolimus, verapamil, botulin toxin, interferons, surgery, pressure and silicone dressings and lasers. Recently some studies described the role of bleomycinin these scars.[11-15]Present study was aimed to find out effectiveness of intralesional application of bleomycinin management of hypertrophic scars and keloids.

**Material & methods:**

After obtaining approval from institutional Ethics committee, 30 patients were enrolled to participate in study. Patients present to outpatient department of surgery of TeerthankerMahaveer Medical College & Research Centre, Moradabad, INDIA. In all 30 cases the keloid/ Hypertrophic scars were accompanied by local pruritus. The lesions had been present for 1month to many years. All patients gave informed consent before we used bleomycin, and female patients were warned/ advised not to become pregnant during treatment. Methodology adopted to treat patients was similar for all 30 patients. First, the lesion was anesthetized with intralesional 2% mepivacaine injection. After that the bleomycin was dripped onto the lesion, and then multiple punctures with an insulin syringe were made on the lesions. In each case the maximum dose applied was 2 ml/$cm^2$ of skin treated, at a concentration of 1.5 IU/ml, and a maximum of 6 $cm^3$ of undiluted bleomycin was given per session. Up to a maximum of 4 doses were administered at intervals of 1 month. The response to treatment was divided into the following categories: >75 percent reduction/flattening = excellent response, 51–75 percent reduction/flattening=good response, 26–50 percent reduction/flattening=fair response and<25 percent reduction/flattening = poor response. The size of lesions was measured before, after treatment and during follow up for 6 months. Each Measurement was taken three times using vernier calipers and the mean was obtained for accurate size



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assessment. The incidence of side effects if any was noted.

**Results:**

30 patientspresenting to outpatient department of surgery of TeerthankerMahaveer Medical College & Research Centre, Moradabad, (INDIA) during April 2013 to September 2013 were enrolled to participate in study.The mean age of the patients was 29.7 years. A total of 30 keloid and hypertrophic scars were treated. The involved areas were as follows: chest-9, shoulder-5, ear-7, neck-3, upper limbs-3 and face-3. Out of the thirty patients, 19 (63.33%) showed excellent response, 5 (16.67%) showed good response, 4 (13.33%) showed fair response and 2 (6.67%) showed poor response. There was complete resolution of symptoms in 20 patients (66.67%) and improvement in the other 10 (33.33%) during follow up for 6 months. There were no signs of recurrence or reappearance of the symptoms.

**Discussion:**

Wound healing involves a carefullyorchestrated sequence of events of 3 distinct phases: inflammation,proliferation, and remodeling. Thisdepends on closeregulation of fibrin deposition, fibroblastactivity, angiogenesis and production oftissue components such as fibronectin, collagen etc. At the same time, a balance isachieved between new tissue biosynthesisand degradation and is regulated by various growth factors so that excess scar formationis avoided for normal wound healing. Inflammation or an alteration of these growth factors or any of these events may contribute to keloid or a hypertrophic scar. Hypertrophic scars and keloids are abnormal growths of the connective tissue secondary to abnormal wound healing due to trauma of the skin, the origin of which is usually apparent. While in keloid, the connective tissue spreads beyond the damaged area, in hypertrophic scars it is confined to the site of the trauma.[1,16-19]

With the advancement of technology, many treatment modalities were invented to modulate the wound-healing process. Management of keloid/hypertrophic lesionshas evolved from grossexcision and radiation to pharmacologic methods thatwork on a cellular and subcellular level.

Bleomycin sulfate is an antineoplastic agent with antibacterial and antiviral properties isolated from the fungus Streptomyces verticillusthat directly inhibit collagen synthesis in skin fibroblasts.It inhibits DNA synthesis and DNA destruction as well as RNA and protein synthesis is also inhibited to a lesser extent.[12.20] Recently, researches has shown that bleomycinled to a significant improvement in scar height and pliability as well as reduction in erythema, pruritus, and pain in the treatment of hypertrophic scars andkeloids.Occasionally,patients develop hyperpigmentationand dermal atrophy; however, systemic toxiceffects appear to be uncommon. [21,22]

Bodokh&Brun obtained a total regression of 84% scars with 3 to 5 intralesional infiltrations of bleomycin.[12]Espana et al reported more than 90% resolution (53.8% complete response and 38.4% excellent response) after treatment with bleomycin.[20] The low incidence of side effects makes Bleomycin one of the safest modalities for these lesions. In present study no significant side effects were noted in treated patients and none systemic involvement occurs.

**Conclusions:**

Bleomycin is very effective and safe pharmacologic agent for treatment of keloid/hypertrophic scar with no significant side effects. Complete resolution of lesions can be achieved in larger extent by bleomycin therapy.



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