Successful Treatment of Intrallesional Bleomycin in Keloids of Vietnamese Population

Nghi Dinh Huu¹, Sau Nguyen Huu¹, Xuan Le Thi¹, Thuong Nguyen Van¹, Phuong Pham Thi Minh¹, Trang Trinh Minh¹, Tam Hoang Van¹, Van Tran Cam¹, My Le Huyen¹, Khang Tran Hau¹, Marco Gandolfi⁴, Francesca Satolli², Claudio Feliciani⁴, Michael Tirant⁴, Aleksandra Vojvodic⁶, Torello Lotti³

¹National Hospital of Dermatology and Venereology, Hanoi, Vietnam; ²Unit of Dermatology, University of Parma, Parma, Italy; ³University of Rome G. Marconi, Rome, Italy; ⁴Psoriasis Eczema Clinic, Melbourne, Australia; ⁵Department of Dermatology and Venereology, Military Medical Academy of Belgrade, Belgrade, Serbia

Abstract

BACKGROUND: Keloid is an overactive condition of the skin tissue to early lesions characterised by proliferation of fibroblasts, excessive collagen production in the lesion. Treatment of keloids is a big challenge because of the poor response rate and high risk of recurrence after treatment. We found that bleomycin offers promise in the treatment of keloids.

AIM: To evaluate the efficacy of bleomycin injected in the injury for keloids treatment.

METHODS: The treatment was carried out in 55 patients having 120 keloids of different sizes and locations. Average treatments were 4 times.

RESULTS: Complete flattening was 70.8%, highly significant flattening was 8.3%, no patient of minimal flattening. Systemic side-effects of bleomycin were not evaluated, but local side-effects were mainly pains (100%), blisters (78.3%), ulceration (5.8%), and hyperpigmentation (56.7%).

CONCLUSION: The percentage of patients recurring 6, 12, 15, 18 months after the last treatment were 3.8, 15.4, 45.5, 50%, respectively.

Introduction

Keloid is an overactive condition of the skin tissue to early lesions characterised by proliferation of fibroblasts and excessive production of collagen in the lesion, with mechanisms not yet fully understood [1]. Areas most often affected are chest, shoulder, ear lobe. Keloid is usually itchy and painful [2]. Nowadays, therapy is a challenge although many treatments are recommended, without agreement on the effectiveness of different choice. Bleomycin-induced apoptosis with sclerosing action on endothelial cells inhibited collagen synthesis by inhibiting the lysyl-oxidase enzyme and TGF-β, and it was used in keloid treatment for the first time by Bodokh and Brun in 1996 [3].

We aimed to evaluate the efficacy of bleomycin injected in the injury for keloids treatment.

Methods

A group of 55 patients with 120 studied scars were selected (aged from 15 to 70 years). Scar duration varies from several months to years, not been treated before, not ulcerated or infected.

An injectable solution of bleomycin was prepared by diluting 15 units of bleomycin in 10 ml of sterile saline. The medication was injected into the mid-lesion in depth, 0.2-0.4 ml/cm² (maximum volume per session 3.5 ml). The interval between injections
was 4 weeks, and the total number of treatment sessions depended on the cosmetic outcome of each lesion. Patients received chest X-ray before treatment every 3 months and 6 months after the last treatment. Evaluation of the treatment response is conducted by VSS (Vancouver Scar Scale).

Results

The average number of injections was 3.9 ± 1.1. After treatment, 80.8% of patients got itchiness relief, and 73.3% of patients got pain relief. Blood vessel status, scar stiffness, and scar thickness improved at 70.6%, 89.3% and 87%, respectively, by the VSS scale. In particular: 70.8% of scars became completely flat, 8.3% fairly flat, 17.5% comparatively flat, 3.3% averagely flat and no poorly flat scars.

Regarding undesirable effects, this study showed that 100% scar tissue lasted on average of 3.6 ± 1.4, 94/120 scars accounted for 78.3% have blisters, with an average length of 4.5 ± 1.3; 5.8% of ulcer scars with an average length of 10.6 ± 1.3; Hyperpigmentation was frequently noted after therapy (56.7%) and much thicker and harder the scar was, more treatment times was needed, with stiffness improvement poorer than in the treatment of soft and thin ones. The condition of vascular, pigmentation, and scar stiffness had no relationship to some treatment as well as the level of scar thickness improvement as presented in Table 1.

Table 1: Efficacy of the treatment

| Variable               | Before treatment | After treatment | p     |
|------------------------|------------------|-----------------|-------|
| VSS scores             |                  |                 |       |
| Vascularity            | 1.7 ± 1          | 0.5 ± 0.9       |       |
| Pigmentation           | 0.2 ± 0.6        | 1.1 ± 1         | < 0.05|
| Pliability             | 2.9 ± 0.9        | 0.3 ± 0.5       |       |
| Height                 | 2.3 ± 0.6        | 0.3 ± 0.5       |       |
| Functional Symptoms    |                  |                 |       |
| Pruritus               | 80.8%            |                 |       |
| Pain                   | 73.3%            |                 |       |
| Scar thickness improvement |                |                 |       |
| The complete flattening | 70.8%           |                 |       |
| Highly significant flattening | 8.3%          |                 |       |
| Significant flattening | 17.5%            |                 |       |
| Moderate flattening    | 3.3%             |                 |       |
| Minimal flattening     | 0%               |                 |       |
| Local side-effect      |                  |                 |       |
| Pain                   | 120 (100%)       | 3.6 ± 1.4       |       |
| Swollen                | 26 (21.7%)       | 3.3 ± 1.2       |       |
| Blister                | 94 (78.3%)       | 4.5 ± 1.3       |       |
| Ulceration             | 7 (5.9%)         | 10.6 ± 1.3      |       |
| Scaled                 | 101 (84.1%)      | 13.6 ± 1.7      |       |
| Hyperpigmentation      | 68 (56.7%)       |                 |       |
| Recurrence             |                  |                 |       |
| After 3 months (n = 32) | 0                |                 |       |
| After 6 months (n = 26) | 1 (3.8%)        |                 |       |
| After 12 months (n = 13) | 2 (15.4%)       |                 |       |
| After 15 months (n = 11) | 5 (45.5%)      |                 |       |
| After 18 months (n = 6) | 3 (50%)         |                 |       |

Due to many technical and financial constraints, our study did not measure bleomycin concentrations in the blood. However, in surveying complete blood count, liver and kidney function and chest X-ray, we did not record any systemic side effect. Local side effects were noted significantly, with 100% scars with pain during treatment.

Discussion

We found that bleomycin improved vascular condition by 70.6% after treatment (mean VSS score from 1.7 ± 1 to 0.5 ± 0.6) and mean VSS of stiffness decreased by 89.3%. Some injections needed, itch and pain relief was similar to Saray et al., and S. Srivastava et al., studies [4], [5], [6].

The recurrence rate in our study was higher than in Saray (2005), with 14% of patients recurring after 18 months [4]. We found that the rate of recurrent scars in the thorax, the front of the breastbone was higher than in other surgical areas. The difference is statistically significant. In contrast, there was no relation between pre-treatment thickness and recurrence risk.

In conclusion, bleomycin is a safe and effective method for treating keloids. However, the high rate of recurrence after treatment confirms the difficulty in the correct management of keloid scars.

References

1. Kasyanju Carrero LM, Ma W-W, Liu H-F, Yin X-F, Zhou B-R. Botulinum toxin types A for the treatment and prevention of hypertrophic scars and keloids: Updated review. J Cosmet Dermatol. 2018; 00:1–6. https://doi.org/10.1111/jocd.12628
2. Gauglitz GG, Korting HC, Pavicic T, Ruzicka T, Jeschke MG. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. Molecular medicine. 2011; 17(1):113. PMid:20927486
3. Bodokh I, Brun P. Treatment of keloid with intralesional bleomycin. Annales de dermatologie et de venereologie. 1996; 123(12):791-794. PMid:9636763
4. Saray Y, Güleç AT. Treatment of keloids and hypertrophic scars with dermoeject injections of bleomycin: a preliminary study. International journal of dermatology. 2005; 44(9):777-84. https://doi.org/10.1111/j.1365-4632.2005.02633.x PMid:16135153
5. Payapvipapong K, Niumpradit N, Piriyanand C, Buranaphalin S, Nakakes A. The treatment of keloids and hypertrophic scars with intralesional bleomycin in skin of color. Journal of cosmetic dermatology. 2015; 14(1):83-90. https://doi.org/10.1111/jocd.12132 PMid:25626920
6. Aggarwal H, Saxena A, Lubana PS, Mathur RK, Jain DK. Treatment of keloids and hypertrophic scars using bleom. J Cosmet Dermatol. 2008; 7:43-9. https://doi.org/10.1111/j.1473-2165.2008.00360.x PMid:18254811