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**Original Research Article**

# Comparative efficacy and clinical outcomes of compound betamethasone and triamcinolone acetonide on IL-6 and IL-17 in keloid treatment

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## *Abstract*

***Purpose:*** *To determine the efficacy and clinical outcomes of compound betamethasone and triamcinolone acetonide on interleukin-6 (IL-6) and interleukin-17 (IL-17) in keloid management.*
***Methods:*** *This study was a retrospective analysis of 118 keloid patients treated at The First Affiliated Hospital of Hebei North University, Zhangjiakou, China from January 2020 to December 2022. Patients were randomly divided into Group A (comprising 62 patients who received compound betamethasone) and Group B (comprising 56 patients who received triamcinolone acetonide). Treatment efficacy after 6 months using the Vancouver Scar Scale (VSS), changes in IL-6 and IL-17 levels, and incidence of treatment-related adverse reactions were compared in both groups.*
***Results:*** *Group A demonstrated significantly higher overall response rate compared to Group B ($p < 0.05$). Both groups showed significant reductions in IL-6 and IL-17 levels after treatment ($p < 0.05$). However, Group A showed significantly lower IL-6 and IL-17 ($p < 0.05$) and significantly higher VSS scores t Group B ($p < 0.05$). Incidence of adverse reactions was comparable between the groups ($p > 0.05$).*
***Conclusion:*** *Compound betamethasone shows superior efficacy in reducing IL-6 and IL-17 levels and improves scar appearance in keloid patients comparable to triamcinolone acetonide. Prospective studies with larger sample sizes to evaluate the efficacy of various treatments or combination therapies should be conducted.*

***Keywords:*** *Compound betamethasone, Triamcinolone acetonide, Keloid, Interleukin-6, Interleukin-17*

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## INTRODUCTION

Keloids result from abnormal scar proliferation due to healing disorders following skin trauma, often secondary to burns, surgery, skin infections, or other injuries [1]. Unlike typical scars, keloids do not regress spontaneously, affecting aesthetic appearance and functional capacity, which leads to significant psychological distress [2]. Although the complete pathogenesis of keloids remains elusive, they are known to involve disrupted wound-healing mechanisms.

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Characteristically, keloids have a high recurrence rate, do not regress on their own, and exhibit invasive growth into surrounding tissues, mirroring the behavior of malignant tumors [3]. Histologically, keloids are marked by dense, abnormal collagen bundles and excessive fibroblast activity, producing large quantities of collagen and growth factors [4].

Currently, a variety of treatments are available for keloids, including compression therapy, surgical excision, pharmacotherapy (oral and injectable), laser therapy, immunotherapy, and gene therapy. Although these treatments are effective, they often have high recurrence rates, particularly surgical and laser interventions [5]. Glucocorticoids are among the first pharmacological treatments used for keloids due to their efficacy and minimal adverse reactions [6]. However, not all keloid cases respond to glucocorticoid treatment, and the recurrence rate remains high at approximately 50 % [7]. Thus, improving therapeutic outcomes and reducing recurrence rates remain key treatment goals in keloid management.

Triamcinolone acetonide, a commonly used glucocorticoid, exhibits anti-inflammatory and anti-allergic properties. Its local effects persist for 2 - 3 weeks, effectively inhibiting excessive proliferation of fibroblasts, inducing cellular apoptosis, and reducing scar tissue thickness [8]. Compound betamethasone injection, a long-acting corticosteroid preparation, is used for conditions such as rheumatoid arthritis, neurodermatitis, and alopecia areata [9]. This formulation includes both soluble betamethasone ester and slightly soluble betamethasone lipid, providing sustained anti-inflammatory and anti-allergic effects and proving effective in keloid treatment [10]. This retrospective study therefore investigated the efficacy of compound betamethasone and triamcinolone acetonide injections in the treatment of keloids and offers a reliable approach for clinical management.

## METHODS

### Participants

This was a retrospective study of 118 keloid patients treated at The First Affiliated Hospital of Hebei North University, Zhangjiakou, China from January 2020 to December 2022. Participants were randomly divided into Group A (62 participants receiving compound betamethasone) and Group B (56 participants administered triamcinolone acetonide). The study was approved by the Medical Ethics Committee (approval no. K2022072) and conducted in accordance with the guidelines of Declaration of Helsinki [11].

#### *Inclusion criteria*

Confirmed diagnosis of keloid, patients receiving treatment for the first time and complete medical records.

#### *Exclusion criteria*

Allergy to any of the drugs used in treatment, presence of other types of skin diseases, current infection or other inflammatory diseases, mental illness complicating normal communication, dysfunctions in heart, liver, kidney or other organs.

### Treatments

Group A received an injection composed of 1 mL compound betamethasone mixed with 1 mL of 2 % lidocaine. The mixture was injected locally into the scar tissue once every 4 weeks, for a total of 3 sessions. Group B received an injection of 1 mL of triamcinolone acetonide combined with 1 mL of 2 % lidocaine. This mixture was also injected locally into the scar tissue, following the same schedule as Group A.

### Evaluation of parameters/indices

#### *Efficacy*

Efficacy was evaluated 6 months after treatment and classified as: *Markedly effective* (ME): Over 70 % atrophy and absorption of scar tissue, softer keloid texture, pigmentation close to normal, and significant reduction or disappearance of symptoms such as pain and itching; *Effective* (E): Between 50 and 70 % atrophy and absorption of scar tissue, presence of some hard nodules, and occasional symptoms like pain and itching; *Ineffective* (I): < 30 % atrophy and absorption of scar tissue, with no alleviation of symptoms such as pain and itching. The total effective rate (TE) was calculated using Eq 1.

$$TE = ME + E \quad \ldots\ldots\ldots\ldots\ldots (1)$$

#### *Levels of interleukin-6 (IL-6) and interleukin-17 (IL-17)*

Fasting blood samples (6 mL) were collected in the morning from both groups before and after treatment. The serum was separated by centrifugation for interleukin-6 (IL-6) and interleukin-17 (IL-17) assays using enzyme-

linked immunosorbent assay kits (Abcam, UK; ab178013, ab119535).

### *Keloid severity*

Keloid severity was evaluated using the Vancouver Scar Scale (VSS) before and 6 months after treatment. The scale assesses color, thickness, vascular distribution, and hardness, with a total of 15 points. A higher score indicates more severe keloid hyperplasia.

### *Incidences of adverse reactions*

Incidences of adverse reactions during the treatment were recorded for both groups.

### Statistical analysis

Data were analyzed using Statistical Packages for Social Sciences version 20.0 (SPSS Inc., Chicago, USA) and visual representations were created with GraphPad Prism 7 (GraphPad Software Co., Ltd., San Diego, USA). Categorical data were expressed as percentages and analyzed using chi-square test ($\chi^2$). Measurement data were expressed as mean ± standard deviation (SD). Independent sample Student t-test and paired t-test were used for inter-group and intra-group comparisons respectively. $P < 0.05$ was considered statistically significant.

## RESULTS

### Baseline characteristics

There was no significant difference in baseline characteristics (gender, maximum diameter, age, number of keloids, duration of the disease, exposure to risk factors, familial history of keloids, location and causes of the scar) between both groups ($p > 0.05$; Table 1).

### Efficacy

Group A showed significantly higher efficacy compared to Group B ($p < 0.05$; Table 2).

### Inflammatory factors

There was no significant difference in levels of IL-6 and IL-17 before treatment for both groups ($p > 0.05$). However, after treatment, Group A showed significantly lower levels of IL-6 and IL-17 compared to Group B ($p < 0.05$; Figure 1).

**Table 1:** Baseline characteristics of keloid patients in this study (n, %; mean ± SD)

| Characteristic | | Group A (n=62) | Group B (n=56) | t/$\chi^2$ | *P*-value |
|---|---|---|---|---|---|
| Gender | Male | 26(41.94) | 20(35.71) | 0.479 | 0.489 |
| | Female | 36(58.06) | 36(64.29) | | |
| Age (years old) | | 33.23±9.05 | 34.02±8.72 | 0.482 | 0.631 |
| Maximum diameter (cm) | | 19.33±6.09 | 18.45±6.57 | 0.755 | 0.452 |
| Number of keloids | Single | 38(61.29) | 31(55.36) | 0.427 | 0.514 |
| | Multiple | 24(38.71) | 25(44.64) | | |
| Duration of the disease (years) | | 4.65±1.87 | 4.52±1.94 | 0.371 | 0.712 |
| Exposure to risk factors | Yes | 19(30.65) | 22(39.29) | 0.969 | 0.325 |
| | No | 43(69.35) | 34(60.71) | | |
| Family history of keloids | Yes | 17(27.42) | 19(33.93) | 0.588 | 0.443 |
| | No | 45(72.58) | 37(66.07) | | |
| Location of scar | Ears, face and neck | 17(27.42) | 18(32.14) | 0.535 | 0.766 |
| | Arms and legs | 19(30.64) | 18(32.14) | | |
| | Trunk | 26(41.94) | 20(35.72) | | |
| Causes of scar | Trauma | 21(33.87) | 21(37.50) | 1.102 | 0.894 |
| | Operation | 17(27.42) | 14(25.00) | | |
| | Acne | 7(11.29) | 8(14.28) | | |
| | Infection | 11(17.74) | 10(17.86) | | |
| | Others | 6(9.68) | 3(5.36) | | |

**Table 2:** Treatment efficacy after 6 months using the Vancouver Scar Scale (VSS)

| Parameter | Group A (n=62) | Group B (n=56) | $\chi^2$ | *P*-value |
|---|---|---|---|---|
| Markedly effective | 29(46.77) | 18(32.14) | | |
| Effective | 27(43.55) | 25(44.64) | | |
| Ineffective | 6(9.68) | 13(23.21) | | |
| Total effective | 56(90.32) | 43(76.79) | 3.991 | 0.046 |

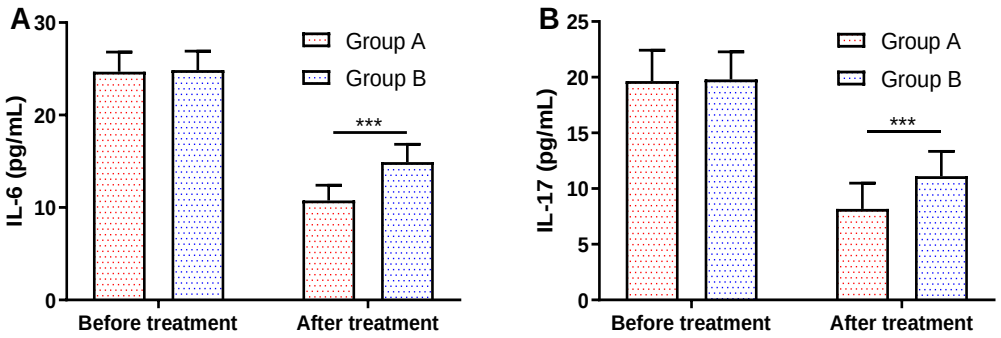


**Figure 1:** Changes in IL-6 and IL-17 levels before and after treatment. ***$P$ < 0.001, Interleukin-6 (IL-6) and interleukin-17 (IL-17)

### Changes in VSS score

There was no significant difference in VSS scores between the groups before treatment ($p$ > 0.05). However, after treatment, Group A showed significantly lower VSS scores compared to Group B ($p$ < 0.05; Figure 2).

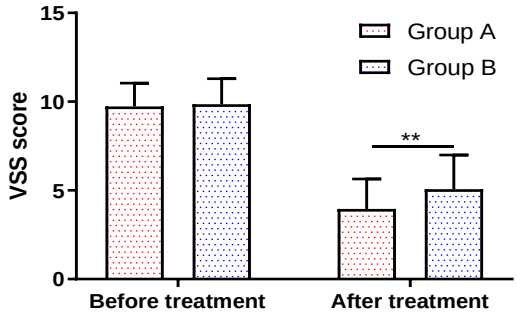


**Figure 2**: Changes in VSS score before and after treatment. **$P$ < 0.01

### Incidence of adverse reactions

Incidence of adverse reactions was higher in Group B compared to Group A, although the difference was not statistically significant ($p$ > 0.05; Table 3).

## DISCUSSION

Keloids not only compromise aesthetic appearance but also cause symptoms like itching, pain, and congestion, significantly affecting quality of life and mental health [12]. Pathogenesis of keloids is not fully understood but is generally considered a chronic inflammatory process influenced by factors such as location of growth, severity of injury, local tissue tension, race, and age [13]. Currently, numerous treatments are available for keloids, including surgery, pressure therapy, radiotherapy, laser therapy, cryotherapy, glucocorticoid injections, and cytokine therapy [14]. Each treatment option has its advantages and disadvantages, and high recurrence rates are common. However, local glucocorticoid injections remain the first-line therapy due to ease of use, safety, and efficacy. Triamcinolone acetonide, a moderate glucocorticoid, effectively inhibits fibroblast proliferation, scar overgrowth, and granulation tissue formation [15].

Compound betamethasone, comprising betamethasone dipropionate and betamethasone sodium phosphate, is a long-acting glucocorticoid that promotes scar healing by controlling fibroblast proliferation, reducing collagen fiber production, and inhibiting granulation tissue growth [16]. This study compared the therapeutic effects of compound betamethasone and triamcinolone acetonide on keloids. The results demonstrated a higher overall response rate with compound betamethasone compared to triamcinolone acetonide with no significant difference in the incidence of adverse reactions between the groups.

**Table 3:** Incidence of adverse reactions

| Parameter | Group A (n=62) | Group B (n=56) | $\chi^2$ | *P*-value |
|---|---|---|---|---|
| Itch | 2(3.23) | 3(5.36) | | |
| Erythema | 2(3.23) | 4(7.14) | | |
| Skin atrophy | 1(1.61) | 2(3.57) | | |
| Infection | 2(3.23) | 0(0.00) | | |
| Total adverse reactions | 7(11.29) | 9(16.07) | 0.574 | 0.449 |

These findings suggest that compound betamethasone injections not only provide superior therapeutic effect but also maintain safety. The dual-component nature of compound betamethasone contributes to its efficacy. Betamethasone sodium phosphate acts rapidly due to quick hydrolysis, while betamethasone dipropionate offers prolonged effectiveness due to its slow absorption and hydrolysis [17,18]. Moreover, compound betamethasone injections, administered every 3 to 4 weeks, promote prolonged drug action, reduce side effects, and improve compliance. Pathogenesis of keloids has been a significant focus in some studies, believed to be associated with various factors including inflammatory responses, genetic variations, and abnormal immune reactions, all of which are fundamental in developing clinical treatment strategies [19]. Zhang *et al* [20] reported that IL-17 induced the expression of several inflammatory mediators such as IL-6 and TNF-α, which not only contributes to inflammatory and immune responses but also promotes fibroblast activation and proliferation, and increases collagen synthesis. These processes may directly or indirectly accelerate the development and progression of keloids. Glucocorticoids, known for their strong anti-inflammatory properties, effectively reduce inflammatory exudation, reaction, and synthesis of inflammatory mediators. They also inhibit DNA synthesis in fibroblasts, curtail interstitial cell proliferation, and thus decelerate growth of granulation tissue. Elevated pre-treatment levels of IL-6 and IL-17 in this study indicated more severe inflammatory reactions in scar tissues. After treatment, these levels significantly decreased, particularly in patients treated with compound betamethasone compared to those receiving triamcinolone acetonide, demonstrating that compound betamethasone more effectively suppresses the inflammatory responses in scar tissues and ameliorates symptoms.

### Limitations of this study

The evaluation relied solely on the VSS, which lacks objective assessment indices. Also, only one treatment approach was investigated, limiting broader comparative findings. Furthermore, the small sample size of this study may have introduced statistical bias.

## CONCLUSION

Compound betamethasone injections are more effective in reducing IL-6 and IL-17 levels compared to triamcinolone acetonide treatment with good safety. Prospective studies with larger sample sizes to evaluate the clinical efficacy of various treatments or combination therapies should be conducted.

## DECLARATIONS

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None.

### *Funding*

None provided.

### *Ethical approval*

The study was approved by the Medical Ethics Committee (approval no. K2022072).

### *Availability of data and materials*

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

### *Conflict of Interest*

No conflict of interest is associated with this work.

### *Contribution of Authors*

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Leigang Chen conceived and designed the study, and drafted the manuscript. Huimin Ren, Yuanhui Wu and Guozhi An collected, analyzed and interpreted the experimental data. Xiaolei Jing and Tongxin Zhao revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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