

# Comparative study on the drug effects and adverse reactions of doxycycline and isotretinoin in the treatment of moderate to severe acne

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**Abstract:** To compare the drug effects and adverse reactions of doxycycline and isotretinoin in patients with moderate to severe acne. A retrospective analysis was conducted on 98 patients with moderate to severe acne who were treated in the Affiliated Hospital of Nanjing University of Traditional Chinese Medicine from June 2020 to June 2023. They were divided into group A and group B based on actual medication use, with 49 cases in each group. Group A was treated with doxycycline and group B was treated with isotretinoin. The drug treatment effects, skin erythema index (EI), sebum secretion, skin lesion tissue cytokines and adverse drug reactions before and after treatment were compared between the two groups. The total effective rate of treatment in group B was 89.8%, which was higher than that in group A, 75.5% ( $P < 0.05$ ). After treatment, the values of EI, sebum secretion and cytokines in skin lesions in group B were all lower than those in group A ( $P < 0.05$ ). There was no significant difference in the incidence of adverse drug reactions between the two groups. Isotretinoin is effective in treating moderate to severe acne. It can effectively reduce skin erythema, sebum secretion, and cytokines in damaged skin tissue. The drug is highly safe and worthy of drug recommendation.

**Keywords:** Doxycycline, isotretinoin, moderate to severe acne, drug effects, adverse reactions.

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## INTRODUCTION

Acne is a common skin disease that mainly affects teenagers and adults. The causes of acne are complex and mainly include factors such as abnormal sebaceous gland function, abnormal keratin hyperplasia, bacterial infection, and abnormal hormone levels (Amir *et al.*, 2023). Acne has a significant impact on patients' mental health, so symptomatic medication is very important. The cause of acne mainly involves abnormal function of sebaceous glands. Under normal circumstances, sebaceous glands secrete oil, which helps maintain skin moisture and protect the skin. However, in adolescence and adulthood, as hormone levels tend to improve, sebaceous glands tend to secrete oil, which can easily cause hair follicles to become clogged, forming acne (Raglin, 2023). In addition, abnormal hyperplasia of keratin can also easily block hair follicles and breed bacteria, causing inflammatory reactions and the formation of acne. In addition, bacterial infection is also an important factor. *Staphylococcus aureus* and *Propionibacterium acnes* are also major pathogenic bacteria. These bacteria tend to grow when hair follicles are clogged, causing an inflammatory response that worsens acne symptoms.

As for the medication for acne, it is generally based on the severity and cause of acne. In terms of clinical medication, topical medications are generally used for mild acne, such as topical ointments containing phenolic

acid, salicylic acid, benzoyl peroxide and antibiotics. For moderate and moderate acne, oral medications are mainly used, mainly retinoic acid drugs, antibiotics, estrogen, etc. Doxycycline is an antibiotic drug that inhibits bacterial protein synthesis to achieve antibacterial effects by inhibiting bacterial growth and reproduction. Isotretinoin is a retinoic acid drug. It is the active form of vitamin A. It can regulate the proliferation and differentiation of skin keratinocytes, promote melanin metabolism, thereby improving skin texture, reducing inflammation and the formation of acne and playing a role in treatment of acne. Both doxycycline and isotretinoin are common drugs used to treat moderate to severe acne. They belong to different categories. Comparative research between the two has strong reference significance.

## MATERIALS AND METHODS

### *Data sources*

A retrospective analysis of 98 patients with moderate to severe acne who were treated in the Affiliated Hospital of Nanjing University of Traditional Chinese Medicine from June 2020 to June 2023, including 49 patients taking doxycycline, were divided into group A; isotretinoin There were 49 patients taking medication and they were divided into group B. According to case data statistics, there are 21 males and 28 females in Group A, aged 18-42 years old, with an average age of  $27 \pm 2.24$  years old, a disease duration of 3-35 months, an average disease duration of  $9.48 \pm 2.26$  months and severity: Moderate 24 Examples, 25 severe cases. Group B patients included 19 males and 30 females, aged from 18 to 43 years old, with

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an average age of  $27 \pm 2.32$  years and a disease duration of 3 to 36 months, with an average disease duration of  $9.52 \pm 2.27$  months. Severity: 23 cases were moderate and 26 cases were severe. There was no significant difference in the data comparison between the two groups.

#### **Entry criteria**

**Inclusion criteria:** Guided by the “Chinese Acne Treatment Guidelines (2019 Revised Edition)” (Chinese Acne Treatment Guidelines Expert Group, 2019), meeting the diagnostic indicators of moderate to severe acne; not using other drug treatments within 1 month. **Exclusion criteria:** patients who are allergic to the drugs in this study; patients who have recently received photoelectric therapy.

#### **Medication method**

**Group A:** All patients in this group took doxycycline hydrochloride tablets, orally, 1/tablet/day for 4 consecutive weeks. The drug was procured by Jiangsu Zhengda Fenghai Pharmaceutical Co. Ltd., with national drug approval number H32020073 and product specification: 0.1g $\times$ 100 tablets/bottle.

**Group B:** All patients in this group took isotretinoin soft capsules, orally, 1 capsule/day for 4 consecutive weeks. This drug was procured by Shanghai Donghai Pharmaceutical Co., Ltd., with national drug approval number H20055201 and product specification is 10mg $\times$ 24 capsules.

#### **Drug evaluation indicators and standards**

Drug treatment effects. Mainly observe the patient's skin lesions and pigmentation after taking the medication. Based on these two items, the medication effect is formulated and divided into markedly effective, effective, and ineffective. It is judged to be effective if the skin lesions are reduced by more than 70%, there are no scars, and there is a small amount of pigmentation. It is judged to be effective if the skin lesions are reduced by 30%-70%, there is a small amount of scars and there is some pigmentation; in other cases, it is considered ineffective. Total effective rate = markedly effective + effective/49.

#### **Ethical approval**

This study was approved by the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine (No. 20240118).

### **STATISTICAL ANALYSIS**

This study uses SPSS22.0 software for data analysis. Through  $\chi^2$  or t test,  $P < 0.05$  is considered to be statistically significant.

### **RESULTS**

#### **Drug effects**

After taking the medicine, the total effective rate of group

A was 75.5, which was much lower than the 89.8% of group B ( $P < 0.05$ ) (table 1).

#### **Comparison of EI before and after medication**

EI is an index that evaluates the degree of skin erythema. It evaluates the degree of erythema by calculating the ratio of the number of red pixels on the skin surface to the number of pixels in the entire skin. Generally speaking, the normal value of EI is in the range of 0-1. If it is greater than 1, it indicates moderate erythema. Before medication in this study, the EI of both groups of patients was higher than 1, showing moderate to severe erythema. After taking the drug, the EI of both groups of patients decreased, indicating that the drug was effective. But the value of group B is lower ( $P < 0.05$ ) (table 2).

#### **Comparison of sebum secretion**

Excessive sebum production is one of the main causes of acne. The sebum secretion of both groups of patients decreased after taking the medicine, but the sebum secretion of group B was lower ( $P < 0.05$ ) (table 3).

#### **Cytokine levels in skin lesions**

There was no significant difference in the values of skin tissue factors IL-1, TNF- $\alpha$  and sIL-2R between the two groups of patients before treatment. After treatment, each value decreased, but the values in group A were lower ( $P < 0.05$ ), which illustrates that many Xicycline is better than isotretinoin in reducing inflammatory response (table 4).

#### **Comparison of adverse drug reactions**

Adverse reactions of doxycycline and isotretinoin mainly include edema, pigmentation, desquamation, dryness, itching, cheilitis, eczema, facial erythema, etc. After taking the medication, there were 7 cases of adverse reactions in group A and 9 cases in group B and no serious adverse reactions occurred. There was no significant difference between the two groups ( $P > 0.05$ ) (table 5).

### **DISCUSSION**

#### **Causes of acne and problems solved by drugs**

Acne is caused by excessive keratinization of hair follicles and sebaceous glands and obstruction of discharge of secretions. The process of acne formation includes hyperkeratosis of the hair follicle opening, excessive production of sebaceous gland secretions around the hair follicles, bacterial infection and inflammatory reaction. According to multiple studies, the formation of acne is due to excessive keratinization of hair follicles and sebaceous glands and obstruction of secretion discharge (Szybiak *et al.*, 2023). Some scholars also believe that changes in hormone levels play a very important role, especially during adolescence, where abnormal fluctuations in hormone levels can cause abnormal activity of sebaceous glands (Vladimir *et al.*,

**Table 1:** Comparison of drug effects between the two groups (n, %)

Group	N	Effective	Efficient	Invalid	Total effective rate
Group A	49	12	25	12	37 (75.5)
Group B	49	17	28	4	45 (89.8)
$\chi^2$					9.652
P					0.001

**Table 2:** Comparison of EI between two groups of patients before and after medication ( $\bar{x}\pm s$ )

Group	N	EI	
		Before medication	After medication
Group A	49	1.62±0.14	0.96±0.11
Group B	49	1.63±0.14	0.83±0.09
t		0.036	1.563
P		0.748	0.001

**Table 3:** Comparison of sebum secretion between two groups of patients before and after medication ( $\bar{x}\pm s$ )

Group	N	sebum secretion ( $\mu\text{g}/\text{cm}^2/\text{min}$ )	
		Before medication	After medication
Group A	49	2.24±0.49	1.59±0.31
Group B	49	2.23±0.51	1.18±0.21
t		0.039	1.637
P		0.716	0.001

**Table 4:** Comparison of cytokine levels in skin lesions of two groups of patients before and after treatment ( $\bar{x}\pm s$ )

Group	N	IL-1 (pg/ml)		TNF- $\alpha$ (ng/ml)		sIL-2R (pg/ml)	
		before medication	after medication	before medication	after medication	before medication	after medication
		Group A	49	96.48±8.12	87.52±7.43	1.48±0.32	1.02±0.07
Group B	49	97.14±8.23	92.36±7.96	1.48±0.31	1.28±0.09	1.71±0.43	1.58±0.38
t		0.038	1.362	0.059	1.689	0.047	1.568
P		0.724	0.001	0.865	0.001	0.796	0.001

**Table 5:** Comparison of adverse drug reactions between the two groups (n)

Adverse reactions	Group A	Group B
Edema	1	0
Pigmentation	0	1
Desquamation	1	2
dry	1	2
itching	1	2
Cheilitis	2	0
eczema	0	0
Facial erythema	1	2
Total	7	9

2023). Some scholars believe that bacterial infection is closely related to the formation of acne (Rios *et al.*, 2024). Propionibacterium species in sebaceous gland secretions are the most dominant species of bacteria on the skin of acne patients. Some studies have pointed out that inflammatory response plays a very important role in the formation of acne (Liyang *et al.*, 2013). The inflammatory reaction causes redness, swelling, pain and the formation of acne rash in the tissue surrounding the

hair follicles. In summary, the causes of acne mainly include hyperkeratosis of hair follicles and sebaceous glands, abnormal fluctuations in hormone levels, bacterial infection and inflammatory reaction. Therefore, when using acne medication, attention should be paid to solving one problem or multiple problems.

Doxycycline, an antibiotic drug used to treat acne, mainly solves the two problems of inhibiting bacterial growth and

reducing skin inflammation. Doxycycline can inhibit the growth of bacteria such as *Propionibacterium* that are common in the skin of patients with acne, reduce bacterial infection of hair follicles and sebaceous glands and reduce acne symptoms (Sadat *et al.*, 2023). Doxycycline can also inhibit the activity of sebaceous glands and reduce the secretion of sebum, thus reducing the accumulation of oil around the mouth of hair follicles and reducing hair follicle obstruction. Doxycycline can reduce skin inflammation, including redness, swelling, pain and other acne symptoms, help reduce the inflammation of acne and speed up the healing process of acne. In summary, the main effects of doxycycline are to inhibit bacteria, reduce sebum secretion and reduce inflammatory reactions.

Isotretinoin, a vitamin A acid drug, can promote skin cell renewal. Isotretinoin can promote the renewal of skin cells and the shedding of the cuticle, thereby preventing the clogging of hair follicles and reducing the accumulation of cuticles, reducing the formation of acne (Yiting *et al.*, 2023). Isotretinoin can reduce the formation of blackheads and whiteheads, remove grease and keratin accumulation at the mouth of hair follicles, and improve acne symptoms. Isotretinoin can also reduce acne inflammation in patients, primarily by reducing redness, pain, and the number of pimples. Isotretinoin can also regulate the oil secretion of the skin, improve the skin texture and prevent the recurrence of acne. To sum up, the main functions of isotretinoin are to promote skin cell renewal, reduce inflammation and reduce oil secretion.

At the molecular level of acne cells, doxycycline can reduce the number of bacteria in the sebaceous glands, thereby reducing inflammatory reactions and the occurrence of acne. In addition, doxycycline also has anti-inflammatory effects, which can reduce the infiltration of inflammatory cells and the release of inflammatory factors, thereby alleviating the symptoms of acne. Isotretinoin improves acne by regulating cell growth and differentiation. Isotretinoin can promote the shedding of keratinocytes and the excretion of sebaceous glands, preventing keratinization of hair follicles and blockage of sebaceous glands. In addition, isotretinoin can also regulate the proliferation and differentiation of keratinocytes, reduce the accumulation of keratinized substances at the opening of hair follicles and thus reduce the occurrence of acne.

#### ***Analysis of the results of this study***

In this study, the efficacy of isotretinoin was better than that of doxycycline. The reason may be that isotretinoin can promote the growth and metabolism of skin cells. By promoting the renewal of keratinocytes and increasing the discharge of keratinocytes, it can improve the hyperkeratosis and keratin blockage of the stratum corneum and reduce the obstruction of the hair follicle opening. In contrast, doxycycline is an antibiotic that treats acne by suppressing acne inflammation and killing

acne-causing bacteria. Although doxycycline can effectively control acne inflammation and reduce bacterial infection, it does not have the effect of promoting keratinocyte renewal and removing keratin accumulation. The patients in this study all had moderate to severe acne, and doxycycline may not completely solve the underlying problem of acne. There is one study that supports the results of this study. This study compared the drug effects of isotretinoin and doxycycline in the treatment of patients with moderate to severe acne, and the results pointed out that the drug effect of isotretinoin is better than doxycycline (Tingmeng *et al.*, 2023).

In this study, the EI of the isotretinoin group was lower than that of the doxycycline group. The reason for this is that the two drugs have different mechanisms of action. Isotretinoin mainly relies on regulating the skin keratinization process, promoting cell renewal and reducing keratin blockage to reduce the formation of acne lesions. As a broad-spectrum antibiotic, doxycycline's main mechanism is to inhibit the bacterial reproduction and inflammatory response caused by acne to reduce acne symptoms. The two have different mechanisms of action. Isotretinoin may be milder and less irritating to the skin, so the skin erythema index will be relatively low during the treatment process. In particular, isotretinoin can promote the growth and metabolism of skin cells and improve skin texture. Doxycycline may cause more skin irritation and erythema during use, resulting in a higher EI.

In this study, the isotretinoin group had lower sebum secretion. Isotretinoin is a derivative of vitamin A, which can promote the proliferation and differentiation of keratinocytes and accelerate the shedding of keratinocytes. Utilizing this mechanism, isotretinoin can reduce the accumulation of stratum corneum, avoid clogging of hair follicles and reduce the risk of acne lesions. In particular, isotretinoin can affect the secretory function of sebaceous gland cells and reduce sebum secretion. It reduces the activity of sebaceous glands and reduces cortical secretion by regulating the metabolism and secretion pathways of sebaceous gland cells (Adriane, 2023). The core mechanism of doxycycline is antibacterial, which has less impact on sebaceous gland secretion. It reduces acne symptoms by inhibiting bacteria and indirectly reduces sebum secretion.

In this study, the cytokine levels in the skin lesions of the doxycycline group were lower than those of the isotretinoin group. As an antibiotic, doxycycline may inhibit the activity of inflammatory cells in damaged skin tissue and reduce the degree of inflammatory response, resulting in lower cytokine levels. Doxycycline has anti-inflammatory properties and can reduce the degree of inflammation in damaged skin tissue. By inhibiting the activity of inflammatory cells and reducing the release of inflammatory mediators, the levels of cytokines in the

damaged skin tissue are reduced. Compared with doxycycline, isotretinoin may not have the effect of antibiotics. It mainly treats acne by promoting cell renewal, inhibiting sebaceous gland secretion and reducing inflammation. In particular, isotretinoin has a certain effect in promoting the release of cytokines, resulting in higher cytokine levels in the skin lesions than in the doxycycline group.

In this study, the isotretinoin group had more adverse reactions than the doxycycline group. Although there was no significant difference between the two groups, this result should be taken seriously. Isotretinoin, as a powerful vitamin A derivative, can promote keratinocyte renewal and stimulate skin regeneration. However, this effect may cause adverse reactions such as excessive dryness, scaling, redness, swelling and irritation of the skin. In contrast, antibiotics such as doxycycline do not cause significant drying or irritation to the skin. In addition, isotretinoin makes the skin more sensitive to sunlight after use and can easily cause adverse reactions such as solar dermatitis or pigmentation. Doxycycline, on the other hand, does not cause photosensitivity reactions. One study showed that the adverse reactions of isotretinoin can be treated by eating a light diet, supplementing with more water, supplementing with vitamin C and avoiding sunlight (Del Rosso 2023).

#### **Shortcomings and prospects of this study**

Acne is a relatively long-term process in adolescence and adulthood, and it is easy to recur. This study only observed indicators for 4 weeks, which has certain limitations. Later studies should observe the recurrence rate after drug withdrawal and follow up for 6 months and 12 months. In this study, no combination of drugs has been used and a combination of drugs should be used for comparison in the future.

#### **CONCLUSION**

Comparing doxycycline and isotretinoin in the treatment of moderate to severe acne, isotretinoin is more effective and can effectively reduce patients' skin erythema and sebum secretion, but is inferior to doxycycline in terms of anti-inflammatory and adverse reactions. Overall, isotretinoin should be used to treat moderate to severe acne. However, pay attention to a light diet, add more water, supplement vitamin C, avoid sunlight, etc.

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