Research Paper

Efficacy, Drug Safety and Serum Inflammatory Factors of Secukinumab in the Treatment of Plaque Psoriasis

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Our main objective is to study the efficacy, safety and influence on inflammatory factors of secukinumab in the treatment of plaque psoriasis. A total of 120 patients admitted to Tonglu People's Hospital from December 2021 to November 2022 were selected as the objects of this drug comparison and were divided into the observation group and the control group. The drugs used in the study were secukinumab and compound clobetasol propionate ointment. The treatment lasted for 4 w. The drug effects of the two groups were compared, including the total effective rate, adverse reactions, anti-inflammatory situation, etc. After treatment, the total effective rates of the observation group and the control group were 96.67 % and 86.67 %, respectively ($p<0.05$). The rates of adverse drug reactions were 1.67 % and 3.33 %, respectively ($p>0.05$). The anti-inflammatory effect of the observation group was better ($p<0.05$) than the control group. Secukinumab has good drug efficacy, high safety and good anti-inflammatory effect, which is worthy of clinical recommendation.

Key words: Secukinumab, clobetasol propionate ointment, adverse drug reactions, inflammatory factors

Secukinumab is a human Immunoglobulin G1 (IgG1) monoclonal monomer that selectively binds to cytokine Interleukin-17 (IL-17) and inhibits its binding to the receptor[1]. Secukinumab was developed for the treatment of psoriasis and is now widely used worldwide for the treatment of severe psoriasis. In recent years, we have also approved the treatment of adult moderate and severe psoriasis with secukinumab. Psoriasis is a disease of the immune system. Compound clobetasol propionate ointment is one of the common drugs for psoriasis because it is easy to use and can effectively relieves itching. Plaque psoriasis is a cutaneous disease characterized by chronic progression and inflammation, which is manifested as well-defined red plaques with silver-white scales attached to the surface, and is usually stubborn, extremely difficult to cure and easy to relapse, causing great physical and mental damage to patients[2]. As a major drug in the medication of plaque psoriasis, the study of the efficacy, safety and effects on serum inflammatory factors of secukinumab is of great significance in guiding clinical drug use. For this reason, 120 patients with plaque psoriasis treated in Tonglu First People's Hospital were chosen in this study to use secukinumab and compound clobetasol propionate ointment as research examples to explore the drug value of secukinumab.

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MATERIALS AND METHODS

A total of 120 patients with plaque psoriasis admitted to Tonglu People's Hospital from December 2021 to November 2022 were selected as the subjects of medication, comparison and were divided into the observation group and the control group, with 60 patients in each group. There was no significant difference in basic data between the two groups ($p>0.05$) as shown in Table 1.

TABLE 1: GENERAL DATA STATISTICS

Group	n	Age	Course of the disease
Observation group	60 (male-32, female-28)	41.12±12.74	3.28±1.62
Control group	60 (male-31, female-29)	42.12±12.2	3.38±1.72
p		>0.05	>0.05

Inclusion and exclusion criteria:

Inclusion criteria: Patients who meet the diagnostic criteria of plaque psoriasis and includes confirmed cases in accordance with its requirements. The patient had not received glucocorticoid or other hormonal drugs within 1 mo before treatment in our hospital. Agree to sign informed consent and willing to receive

follow up; psoriasis lesion area and Psoriasis Area and Severity Index (PASI) index≥30.

Exclusion criteria: Pregnant or lactating women; the mentally ill; patients with immune system diseases such as Acquired Immune Deficiency Syndrome (AIDS) and leukemia; patients with hepatitis such as tuberculosis and hepatitis B.

Methods:

The observation group was treated with secukinumab injection produced by Novartis Pharmaceutical Co., Ltd. The standard of medication was a single dose of 150 mg, if the body weight was less than 60 kg. If the body weight is more than 60 kg, the single dose was 300 mg. The injections were given once a week for 4 w. The production batch number of the drug is SECC6 in October 2021, the specifications are 1 ml and 150 mg each and the approval word of the Chinese Medicine (import drug registration certificate number) is S20190023. For subcutaneous injection, the lesion area should be avoided.

In the control group, compound clobetasol propionate ointment produced by Jiangsu Zhiyuan Pharmaceutical Co., Ltd. was applied to the lesion area. The standard of medication was to apply to the epidermis of the lesion area twice a day, usually once in the morning and once in the evening. The drug was given continuously for 4 w. The drug has the approval number of Chinese Medicine H20040122, 10 g each.

Before and after treatment, the lesion area and symptoms of the two groups of patients should be recorded and 3 ml of fasting venous blood should be collected, and the levels of Interleukin-17 alpha (IL-17A), Tumor Necrosis Factor alpha (TNF-α) and IL-10 should be determined by the laboratory department.

Observation indicators:

The total effect of different groups of drugs was compared. When the lesion area was reduced by 60 % or more compared with that before treatment, it was considered as significant effect. The area of lesion reduced by more than 30 % contrast with that before the medicine was taken is considered effective. The lesion area reduced by less than 30 % contrast with that before the medicine was taken is considered as ineffective. Total efficiency=Obvious efficiency+efficiency.

The lesion area and severity index were evaluated before and after treatment. The PASI score=[0.1×head W×area]+[0.2×upper limb W×area]+[0.3×Orsomucoid protein W×t area]+[0.4×Lower limbs W×area] of lower limbs. W=Erythema+infiltration+scale, each feature was evaluated by 0-4 points: 0=none; 1=mild; 2=moderate; 3=severe; 4=extremely severe. PASI scores range from 0 to 72, with higher scores indicating more severe lesions.

We evaluated the safety of the two groups after treatment including skin irritation, fever, cough, rhinitis, stomach discomfort, tuberculosis, tonsillitis and so on.

The levels of IL-17A, TNF-α and IL-10 before and after treatment were evaluated in the two groups. The lower the level of IL-17A, better the inflammatory effect; the lower the level of TNF-α, better the inflammatory effect and the higher the IL-10, better the inflammatory effect.

The life experience of the two groups of patients before and after taking the drug was evaluated. The Dermatology Life Quality Index (DLQI) assessment was used in this study and scores were given according to the DLQI assessment form. DLQI assessment of disease severity scores were as follows. Mild: 2-5 points; Moderate score: 6-10 points; Severe>10 points. The total score is 30, the lower the rating, the better the life experience.

Statistical analysis:

Statistical Package for the Social Sciences (SPSS) 16.0 statistical software was used to process the relevant data. Chi square (χ^2) test or t-test was used for the comparison between the observation group and the control group, and $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Comparison of total effective rate between the two groups was explained here. The total effective rate of the observation group and the control group were 96.67 % and 86.67 %, respectively ($p<0.05$). This suggests that secukinumab is more effective in the treatment of plaque psoriasis as shown in Table 2.

Comparison of lesion area and PASI score before and after treatment was explained here. After treatment, the PASI score of the observation group was higher than that of the control group ($p<0.05$) as shown in Table 3.

TABLE 2: COMPARISON OF THE EFFICACY OF DIFFERENT DRUGS (x̄±s)

Group	n	Effective	Get better	Invalid	Total efficiency
Observation group	60	38 (63.33 %)	20 (33.33 %)	2 (3.33 %)	96.67 %
Control group	60	28 (46.67 %)	24 (40 %)	8 (13.33 %)	86.67 %
χ^2		4.28	1.76	12.92	3.48
p		<0.05	<0.05	<0.05	<0.05

TABLE 3: COMPARISON OF PASI SCORES BETWEEN THE TWO GROUPS BEFORE AND AFTER TREATMENT (x̄±s)

Group	n	Before medication	After medication
Observation group	60	32.26±3.18	8.48±3.22
Control group	60	32.18±3.24	12.32±3.26
t		0.21	2.96
p		0.89	<0.05

Medication safety analysis of the two groups was discussed here. One case of rhinitis occurred in the observation group after medication. In the control group, 3 cases had skin irritation and 1 case had fever. Overall, the incidence of adverse events in the observation group and the control group was 1.67 % and 6.67 % ($p<0.05$) respectively as shown in Table 4.

Analysis of inflammatory factors in the two groups before and after treatment was shown here. The levels of IL-17A, TNF-α and IL-10 in the two groups were almost the same before treatment and the differences were not statistically significant. After treatment, IL-17A and TNF-α were significantly decreased and IL-10 was increased in both groups. However, after medication, the changes in the observation group were greater. In the observation group, the levels of IL-17A and TNF-α decreased more and the levels of IL-10 increased more. IL-17A and TNF-α are important indicators of inflammatory factors. After treatment, the levels of IL-17A and TNF-α decreased which indicates that the inflammatory factors are also decreased. The higher the value of IL-10 level, the better the treatment of inflammation. This indicates that secukinumab in the observation group was superior to the compound clobetasol propionate ointment in the control group in reducing inflammatory factors as shown in Table 5.

Comparison of quality of life between the two groups before and after administration of different drugs was shown here. DLQI is a quality of life rating scale for psoriasis, which mainly assesses ten questions such as pruritus, self-confidence, life impact and sexual relationship[3]. After treatment, DLQI in the observation group was lower than that in the control group. This indicates that secukinumab was superior to the control group of compound clobetasol propionate ointment in terms of quality of life improvement (Table 6).

Secukinumab is human monoclonal antibody with high cohesion force, which can selectively bind to IL-17A in human body and neutralize the biological activity of IL-17A, thus achieving anti-inflammatory effects[4]. In 2015, secukinumab was the first approved IL-17A inhibitor for the treatment of plaque psoriasis abroad. The molecular weight of secukinumab is about 151 Kilodaltons (kDa) and both heavy chains contain oligosaccharide chains. Its physical character is colorless or light yellow liquid. Compound clobetasol propionate ointment is a compound preparation composed of clobetasol propionate and retinoic acid. Its group is divided into clobetasol propionate 10 mg all-trans retinoic acid 5 mg. Compound clobetasol propionate ointment has antibacterial and anti-keratosis effect, which is one of the drug for psoriasis vulgaris. However, clobetasol compound propionate ointment contains hormones and is generally not recommended for long-term use. If used in large amounts for a long time, it may cause dry skin, hirsutism, skin softening, secondary infection, skin wrinkles, prickly heat and other conditions. If the systemic absorption is too much, some patients may have Cushing's syndrome, hyperglycemia and urine sugar and other manifestations. The drug principle of compound clobetasol propionate ointment is that it contains all-trans retinoic acid to promote the decomposition of epidermal cells, thereby accelerating the proliferation of epithelial cells, promoting the synthesis of Deoxyribonucleic Acid (DNA) in epidermal cells and achieving the regeneration of the epidermis in

TABLE 4: COMPARATIVE ANALYSIS OF THE INCIDENCE OF ADVERSE EFFECTS OF DIFFERENT DRUGS (x̄±s)

Group	n	Skin irritation	Fever	Cough	Rhinitis	Upset stomach	Tuberculosis	Tonsillitis	Overall incidence
Observation group	60	0	0	0	1	0	0	0	1.67 %
Control group	60	3	1	0	0	0	0	0	6.67 %
χ^2		0.126	0.652	9.89	0.652	9.89	9.89	9.89	0.108
p		<0.05	<0.05	>0.05	<0.05	>0.05	>0.05	>0.05	<0.05

TABLE 5: COMPARISON OF THE LEVELS OF INFLAMMATORY FACTORS BETWEEN THE TWO GROUPS BEFORE AND AFTER TREATMENT (x̄±s)

Group	n	IL-17A (pg/ml)		TNF-α (pg/ml)		IL-10 (ng/ml)	
		Before medication	After medication	Before medication	After medication	Before medication	After medication
Observation group	60	78.21±8.86	24.42±4.66	25.28±3.36	10.24±1.98	6.28±1.48	14.54±2.32
Control group	60	78.42±8.37	32.43±4.82	25.62±3.25	14.67±1.94	6.34±1.49	10.24±2.68
t		0.102	3.968	0.116	4.176	0.122	4.088
p		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

TABLE 6: COMPARISON OF DLQI SCORES AFTER DIFFERENT MEDICATIONS (x̄±s)

Group	n	DLQI	
		Before medication	After medication
Observation group	60	15.62±3.16	2.14±0.68
Control group	60	15.58±3.18	4.35±1.16
t		0.428	6.68
p		>0.05	<0.05

the lesion area.

The pathogenic mechanism of plaque psoriasis is complex and there is no conclusion at present. It is generally believed that it is closely related to the environment, genetics and personal hygiene[5]. Inflammation is closely linked to plaque psoriasis, which irritates the patient's skin and the patient itself exhibits inflammatory indicators accompanied by cutin (It refers to symptoms of horny skin caused by inflammation of the skin) symptoms. As the course of the disease progresses, a large amount of desquamation occurs and exhibits the characteristics of a rash. Studies have shown that IL-17A is a key inflammatory factor in psoriasis. Therefore, specific blockade of IL-17A signaling pathway will be the key to targeted therapy of psoriasis. IL-17A is produced by T-helper 17A (Th17A) cells. In the course of plaque psoriasis, a variety of cells such as keratinocytes and desquamation are expressed as IL-17A receptors[6]. Some data show that the level of IL-17A has a strong correlation with the area of plaque psoriasis and PASI[7]. After plaque psoriasis was improved, the serum level of inflammatory factors IL-17A was significantly decreased. TNF-α is a common inflammatory factor in psoriasis. It can induce the formation of keratinocytes and the adhesion between cells, thereby accelerating the release of various inflammatory mediators and aggravating the inflammatory response in the lesion area. Studies have shown that the opening of the IL-17A signaling pathway will attract neutrophil protease to stimulate IL-36 gamma (γ), but IL-36γ can promote the production of TNF-α and IL-17A can cooperate to aggravate the inflammatory channel response. This suggests us that the production of TNF-α may originate from IL-17A, so the core of the medication of plaque psoriasis lies in the inhibition of IL-17A[8]. Studies have shown that Th17/Regulatory T cells (Tregs) abnormality is an important factor in the pathogenic mechanism of plaque psoriasis and IL-17A is an important response factor of Th17 cells

and an important mediator of inflammation[9]. Treg can secrete IL-10 and IL-10 can inhibit inflammatory response. This indicates that increasing the level of IL-10 can reduce the inflammatory response. The key to increase the level of IL-10 is Treg. The implication of this is how to contribute to Treg levels.

Among the adverse drug reactions of secukinumab, upper respiratory tract infections (mainly rhinitis and nasopharyngitis) were the most commonly reported[10]. According to literature, adverse drug reactions caused by secukinumab are mainly divided into two categories: Infection-related and immune-related, with very few cases of serious adverse drug reactions[11]. Secukinumab is an IL-17A inhibitor, which mainly inhibits the production of IL-17A. But during this drug reaction, other cytokines change. For example, IL-17A plays a certain role in the process of granulocyte generation, neutrophil exodus and mucosal defense, such as *Candida*, which may cause other infections[12]. In general, fewer adverse reactions were reported and the drug safety was generally high. However, secukinumab has been on the market for a short time and its cases are less than other drugs, so its drug safety should be paid attention. Once adverse drug reactions occur, the drug should be stopped in time and according to the symptoms of symptomatic treatment.

In this study, the clinical efficacy of secukinumab in plaque psoriasis was superior to compound clobetasol propionate ointment. This was due to the secukinumab targeted therapy, which targeted IL-17A, the core of plaque psoriasis. The core of compound clobetasol propionate ointment is to promote the regeneration of the damaged epidermis. In this study, the administration of secukinumab resulted in lower PASI scores and better efficacy. In terms of adverse drug reactions, there was only one case of rhinitis caused by secukinumab, which induced primary rhinitis and not caused by secukinumab. Compound clobetasol propionate ointment caused skin discomfort in 3 cases and body fever in 1 case with a high incidence of adverse reactions. In terms of serum inflammatory factors, this study mainly concerns three indicators i.e., IL-17A, TNF-α, IL-10 and it act as a key indicators in research in plaque psoriasis. Especially, single resistance in the lower levels of IL-17A and TNF-α, improve the level of IL-10 better than compound clobetasol propionate ointment and its anti-inflammatory drug effect is better. In terms of improving the quality of life, the study was conducted in the form of question and answer using DLQI scale. It was found that secukinumab was more effective in improving patient's quality of life after different treatments.

In summary, although the market time of secukinumab is relatively short, it can effectively treat plaque psoriasis, its drug safety is high, it can be a good anti-inflammatory and it can improve the life experience of patients to a certain extent. It should be widely used as a clinical drug for plaque psoriasis.

Conflict of interests:

The authors declared no conflict of interest.

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