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ORIGINAL ARTICLE

Retrospective Study

Efficacy and anti-inflammatory analysis of glucocorticoid, antihistamine and leukotriene receptor antagonist in the treatment of allergic rhinitis

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Abstract

BACKGROUND

There are many adverse reactions in the treatment of allergic rhinitis (AR) mainly with conventional drugs. Leukotriene receptor antagonists, glucocorticoids and nasal antihistamines can all be used as first-line drugs for AR, but the clinical effects of the three drugs are not clear.

AIM

To examine the impact of glucocorticoids, antihistamines, and leukotriene receptor antagonists on individuals diagnosed with AR, specifically focusing on their influence on serum inflammatory indexes.

METHODS

The present retrospective study focused on the clinical data of 80 patients diagnosed and treated for AR at our hospital between May 2019 and May 2021. The participants were categorized into the control group and the observation group. The control group received leukotriene receptor antagonists, while the observation group was administered glucocorticoids and antihistamines. Conducted an observation and comparison of the symptoms, physical sign scores, adverse reactions, and effects on serum inflammatory indexes in two distinct groups of patients, both before and after treatment.

RESULTS

Subsequent to treatment, the nasal itching score, sneeze score, runny nose score, nasal congestion score, and physical signs score exhibited notable discrepancies ($P < 0.05$), with the observation group demonstrating superior outcomes compared

to the control group ($P < 0.05$). The interleukin (IL)-6, IL-10, tumor necrosis factor-alpha, Soluble Intercellular Adhesion Molecule-1, Leukotriene D4 after treatment were significantly different and the observation group It is better than the control group, which is statistically significant ($P < 0.05$). Following the intervention, the incidence of adverse reactions in the observation group, including symptoms such as nasal dryness, discomfort in the throat, bitter taste in the mouth, and minor erosion of the nasal mucosa, was found to be 7.5%. This rate was significantly lower compared to the control group, which reported an incidence of 27.5%. The difference between the two groups was statistically significant ($P < 0.05$).

CONCLUSION

Glucocorticoids and antihistamines have obvious therapeutic effects, reduce serum inflammatory index levels, relieve symptoms and signs of patients, and promote patients' recovery, which can provide a reference for clinical treatment of AR.

Key Words: Glucocorticoid; Histamine; Leukotriene receptor antagonist; Allergic rhinitis; Serum inflammatory index

Core Tip: Glucocorticoid, antihistamine and leukotriene receptor antagonist are good therapeutic agents for allergic rhinitis (AR) at present, which can avoid the adverse reactions caused by conventional drug treatment. The purpose of this paper is to explore the synergistic effect of these three drugs in the treatment of AR by combining them. The results show that glucocorticoid and antihistamine have obvious therapeutic effects and are worth popularizing widely in clinic.

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INTRODUCTION

Allergic rhinitis (AR) is a kind of allergic disease triggered by exogenous environmental factors, which leads to the immune system response, and it is one of the common diseases of respiratory system. It not only seriously endangers people's health but also easily induces a variety of diseases. AR primarily arises from the inhalation of allergens, which subsequently triggers the release of inflammatory mediators, leading to inflammation of the nasal mucosa[1]. Simultaneously, the etiology of the ailment is intricately associated with physical fitness, genetics, immunity, and additional factors. The primary clinical presentations of AR predominantly encompass nasal congestion, rhinorrhea, nasal pruritus, sneezing, and olfactory impairment[2]. In addition, it may also cause or be complicated by sinusitis, nasal polyps, pharyngitis, otitis media, tracheal and bronchitis, asthma and allergic conjunctivitis and other diseases, which seriously affect people's sleep, study, work and quality of life[3]. AR is primarily managed pharmacologically; however, the utilization of drugs is associated with safety concerns and an increased incidence of adverse reactions[4]. The current treatment methods for AR mainly include nasal glucocorticoid spray, oral antihistamine or nasal spray, intranasal anticholinergic, drug nasal spray, oral decongestant or nose drops, submucosal injection of inferior turbinate and surgery, vidian nerve surgery and nasal concussion treatment, *etc*[5]. A large number of animal experiments and clinical studies have confirmed that leukotriene receptor antagonists can inhibit the accumulation of inflammatory cells in the airway, inhibit the release of inflammatory mediators, antagonize airway inflammation, reduce airway hyperresponsiveness, and improve lung function in patients with asthma, Relieve clinical symptoms[6]. At present, it is believed that both nasal glucocorticoids and nasal antihistamines can be used as first-line drugs for AR, which can effectively alleviate nasal congestion, runny nose, sneezing and other symptoms[7]. Some scholars also believe that the combined use of nasal glucocorticoids and nasal antihistamines in the treatment of AR is expected to further improve the efficacy, but there is still a lack of sufficient evidence-based medicine[8]. Based on this, we have explored the effects of glucocorticoids, antihistamines, and leukotriene receptor antagonists on patients with AR and their effects on serum inflammatory indicators.

MATERIALS AND METHODS

General information

Before patients are included, patients are fully informed of the project, process and possible risks of the trial, and all patients are signed with informed consent forms and kept on file, and their identity records, basic information and medical records are included and kept on file. The retrospective research object of this study selected 80 patients with AR

who visited our hospital from May 2019 to May 2021. According to the experimental method, they were divided into control group (40 cases) and observation group (40 cases). There was no statistical difference in sex ratio, age distribution and other basic information between the two groups (Table 1).

Inclusion and exclusion criteria

Inclusion criteria: (1) All patients in this study met the "Expert Consensus on Allergic Rhinitis Subcutaneous Immunotherapy"[9] diagnostic criteria for AR; (2) Sneeze, clear watery mucus, nasal congestion, nasal itching and other symptoms appeared more than 2 items (including Item 2), or accompanied by conjunctival congestion and itching around the eyes, and the daily duration of symptoms exceeds 1 h or more; and (3) Pale and edema of the nasal mucosa, watery nasal discharge, positive skin prick test, positive serum specific immunoglobulin E (IgE) test, and consistent with skin prick test results are common. Exclusion criteria: (1) The subject has obvious systemic metabolic disease, or the researcher thinks that it may interfere with the evaluation of the research results or affect the safety of life. The subject has received sugar through oral, nasal or systemic routes within the past 3 mo. Corticosteroids, antihistamines, leukotriene receptor inhibitors, various decongestants or theophylline drugs; (2) Combined with serious heart, cerebrovascular, diabetes, hyperthyroidism, connective tissue diseases and hematopoietic diseases or other diseases or The disease is in the acute stage, pregnant or breast-feeding women; and (3) Thorax is obviously deformed, or has lung organic disease, or has other diseases that cannot be applied with, and has received specific immunotherapy within the past 1 year.

Method

Before the start of treatment, the doctor should introduce the uniform and correct method of nasal spray to the patient, and demonstrate on the spot: After waking up in the morning and before going to bed at night, after clearing the nasal secretions, face down, spray nozzle up or slightly outward, and hold in the left hand. Bottle, spray the right nasal cavity, hold the bottle in the right hand, spray the left nasal cavity, once a day in the morning and evening, 2 sprays on each nostril, each spray 50 g, all patients are prohibited from using other treatment drugs and methods during the treatment. Among them, the control group was given a leukotriene receptor antagonist, that is, loratadine tablets (Hainan Xinzhongzheng Pharmaceutical Co., Ltd., H20050628) were administered orally, 10 mg/time, once daily. Montelukast sodium (Hangzhou Merck Pharmaceutical Co., Ltd., J20070058) was taken orally, 10 mg/time, once/d, for 4 wk of treatment. The observation group was treated with glucocorticoids and antihistamines, that is, azelastine hydrochloride nasal spray and budesonide nasal spray were used for nasal spraying. The interval between the two nasal sprays was about 5 min. After waking up in the morning and before going to bed at night, after cleaning up nasal secretions, face down, spray nozzle upward or slightly outward, hold the bottle in the left hand to spray the right nasal cavity, and hold the bottle in the right hand to spray the left nasal cavity, once a day in the morning and evening, on each side Spray 50 g in the nostril, and the treatment time is 8 wk.

Follow-up and observation indicators

Clinical symptoms: Score the four typical symptoms of AR, namely sneezing, runny nose, nasal congestion, and nasal itching, each with a score of 1 to 3. Sneeze score 1 is divided into the number of consecutive sneezes between 3-9, score 2 is divided into the number of consecutive sneezes between 10-14, and score 3 is divided into the number of consecutive sneezes ≥ 15; the tear score is calculated based on the number of blows per day, 1 is the number of blows ≤ 4 times, 2 is the number of blows is between 5-9 times, and 3 is the number of blows ≥ 10; the nasal congestion score is 1 occasionally nasal congestion, 2 points between occasional nasal congestion and mouth breathing almost all day, 3 points almost all-day mouth breathing; nasal itching score 1 points to intermittent nasal itching, 2 points to sense of ant walking, but tolerable, 3 is divided into ant behavior, unbearable. Sign score: 3 is divided into inferior turbinate and nasal base, nasal septum only, no middle turbinate, or middle turbinate mucosal polypoid change, polyp formation; divided into inferior turbinate and nasal septum (or nasal base) only, inferior turbinate and There is still a small gap between the base of the nose (or septum); 1 is divided into mild swelling of the inferior turbinate, and the septum and middle turbinate are still visible. According to the scoring standard in the "Diagnostic Standards for Eye, Ear, Nose, and Throat Diseases"[10], the severity of symptoms of patients with AR is divided into 4 grades. 0 points: Asymptomatic; 1 point: Intermittent nasal itching, sneezing 3 to 9 times, occasional nasal congestion, the number of nose blows ≤ 4 times a day; 2 points: Obvious symptoms, nasal itching with a sense of ants, tolerable, 10 to 14 sneezes once, with obvious nasal congestion, 5 to 9 times a day to blow the nose; 3 points: Severe nasal itching and ant-like sensation, unbearable, 1 sneeze ≥ 15, severe nasal congestion, almost all day breathe through your mouth, and blow your nose ≥ 10 times a day. Calculate the curative effect according to the following formula: Integral reduction index = (pre-treatment integral-post-treatment integral)/pre-treatment integral × 100%. Significantly effective: Integral decline index ≥ 50%; effective: Integral decline index ≥ 20%; invalid: Integral decline index < 20%. Total effective rate = (marked effect + effective)/total number of cases × 100%.

Statistical analysis

The data included in this study were statistically analyzed by SPSS 23.0. Shapiro-wilk method was used to test, and the test level was $\alpha = 0.05$. The statistical method of mean standard deviation describes the data that conforms to the normal distribution, and the statistical method of M(QR) describes the data that does not conform to the normal distribution. *T*-test and χ^2 test of independent samples or paired samples are used to count the differences between groups or within groups. Integer or percentage (%) describes the counting data.

Table 1 Comparison of general information between the two groups (*n*, mean ± SD)

Group	Gender (Male/Female)	Average age (yr)	Course of disease (wk)	Body mass index (kg/m²)
Control group (40)	18/22	5.70 ± 1.32	5.6 (3.7-7.9)	27.78 ± 2.32
Observation group (40)	17/23	5.69 ± 1.66	5.5 (3.1-7.7)	27.62 ± 2.66
χ^2/t value	0.051	0.03	0.04	0.02
P value	0.822	0.976	0.965	0.984

RESULTS

Comparison of general information

There was no significant difference between the two groups in baseline data such as sex ratio, mean age, course of disease and body mass index ($P > 0.05$) (Table 1).

Comparison of symptoms and signs scores

Before treatment, there was no significant difference in symptoms and signs between the two groups ($P > 0.05$). After treatment, there were significant differences in nasal itching, sneezing, runny nose, nasal congestion and signs, and the curative effect of the observation group was better than that of the control group. In the control group, the comparison was statistically significant ($P < 0.05$) (Table 2).

Comparison of serum inflammatory indexes

The comparison of serum inflammatory indexes between the two groups before treatment was not statistically significant ($P > 0.05$). However, the levels of interleukin (IL)-6, IL-10, tumor necrosis factor-alpha (TNF-α), Soluble Intercellular Adhesion Molecule-1 (sICAM-1) and Leukotriene D4 (LTD4)-4 were significantly different after treatment, and the observation group was superior to the control group with statistical significance ($P < 0.05$) (Table 3).

Comparison of adverse reactions

After treatment, the adverse reaction rate of the observation group such as dryness of the nose, dry throat discomfort, bitter mouth, and slight erosion of the nasal mucosa was 7.5%, which was significantly lower than the control, 27.5%, which was statistically significant ($P < 0.05$) (Table 4).

DISCUSSION

AR is a series of nasal symptoms caused by lgE-mediated inflammation of the nasal mucosa after allergic individuals are exposed to allergens. The cause of the disease is believed to be the inhalation of allergens and the combination of platelets and eosinophils. The specific IgE binding on cells, mast cells and other cells causes these cells to release inflammatory mediators, which ultimately leads to the inflammatory process of the nasal mucosa[11]. Montelukast sodium is a selective leukotriene receptor antagonist, which can not only block the binding of leukotrienes and leukotriene receptors, so that it can not exert inflammatory effects, but also can inhibit copeptin growth factor Promoting maturation of basophils and eosinophils[12]. It further reduces eosinophils in the airway and surrounding blood, reduces inflammation, and the drug has no obvious adverse effects on vital organs or systems[13].

The results of this study show that after treatment, the degree of nasal itching, sneezing, runny nose, nasal congestion and signs have obviously improved, with statistical differences, and the observation group is better than the control group, indicating that the effect of glucocorticoid and antihistamine treatment is obvious, and the symptoms and signs of the patients are alleviated. The reasons are as follows: Glucocorticoids are the first-line drugs for the treatment of bronchial asthma, as well as the main treatment drugs for AR, and are currently the most effective anti-allergic inflammatory drugs[14]. From clinical observations, long-term regular inhalation of glucocorticoids can effectively control asthma symptoms, improve patients' mental state and quality of life, and reduce asthma mortality[15]. Its main mechanism of action is: Inhibit the synthesis of cytokines by lymphocytes and other immune active cells: Inhibit the chemotaxis and activation of E, reduce the synthesis of leukotrienes and prostaglandins, inhibit the metabolism of arachidonic acid, and promote the contraction of small blood vessels, Reduce blood vessel leakage, improve the responsiveness of respiratory smooth muscle 2 receptors, increase the synthesis of receptors on the cell membrane, *etc*[16]. Nasal glucocorticoids can effectively improve a series of nasal symptoms induced by AR, and the combined effect is better than antihistamines. Antihistamines are the first choice for patients with AR. They can quickly relieve the symptoms of runny nose, sneezing, nasal itching and dry eyes caused by histamine release[17]. H1 receptor blockers have a positive effect on the control of asthma. They can not only antagonize H1 receptors and reduce receptor sensitivity, but also inhibit the production of histamine stimulated I-8 and reduce the production of inflammatory mediators such as leukotrienes. And release, it has an effect on both the immediate-onset phase and the delayed-onset phase allergy in patients with asthma and AR[18].

Table 2 Comparison of the symptoms and signs scores of the two groups of patients before and after treatment (mean ± SD)

Group		Symptom score				Physical sign score
		Nasal itching score	Sneeze score	Runny nose score	Nasal congestion score	
Control group	Before therapy	2.14 ± 0.18	2.08 ± 0.32	1.84 ± 0.30	1.79 ± 0.22	2.13 ± 0.27
	After treatment	1.76 ± 0.63[a]	1.45 ± 0.26[a]	1.36 ± 0.06[a]	1.37 ± 0.31[a]	1.44 ± 0.23[a]
Observation group	Before therapy	2.04 ± 0.61	2.03 ± 0.10	1.88 ± 0.80	1.82 ± 0.39	2.25 ± 0.44
	After treatment	1.32 ± 0.31[a,b]	1.09 ± 0.26[a,b]	0.92 ± 0.24[a,b]	1.21 ± 0.31[a,b]	1.17 ± 0.37[a,b]

[a]$P < 0.05$ *vs* before treatment.
[b]$P < 0.05$ *vs* the control group.

Table 3 Comparison of serum inflammatory indexes between the two groups (mean ± SD)

Group		IL-6 (ng/L)	TNF-α (pg/L)	IL-10 (ng/L)	sICAM-1 (μg/L)	LTD4 (mg/kg)
Control group	Before therapy	11.78 ± 2.32	55.34 ± 7.40	26.51 ± 6.32	40.78 ± 7.32	517.94 ± 23.40
	After treatment	6.62 ± 1.66	22.76 ± 6.64	16.55 ± 6.11	32.62 ± 5.66	206.96 ± 19.24
Observation group	Before therapy	11.78 ± 2.32	55.28 ± 7.80	26.81 ± 4.39	40.93 ± 7.27	517.75 ± 10.44
	After treatment	4.62 ± 0.66	19.19 ± 4.74	13.41 ± 3.31	26.74 ± 3.23	158.37 ± 10.37

IL: Interleukin; TNF-α: Tumor necrosis factor-alpha; sICAM-1: Soluble Intercellular Adhesion Molecule-1; LTD4: Leukotriene D4.

Table 4 Comparison of adverse reactions between the two groups of patients (mean ± SD)

Group	Dry nose	Dry throat discomfort	Bitter	Minor erosive osmosis of nasal mucosa	Adverse reaction rate
Control group (40)	1	3	4	3	11 (27.5)
Observation group (40)	0	2	1	0	3 (7.5)
t value					5.541
P value					0.019

In this study, the comparison of serum inflammatory indexes between the two groups of patients before treatment was not statistically significant ($P > 0.05$), while the IL-6, IL-10, TNF-α, sICAM-1, and LTD4 were outstanding different after treatment. Compared with the control group, the curative effect of the observation group is better. The therapeutic effect of glucocorticoid and antihistamine is obvious, and the serum inflammatory index level is reduced. IL-6 can induce inflammatory reactions, and its source range is very wide. A large number of experimental data show that IL-6 participates in a variety of inflammatory reactions and diseases in the human body and is an important pro-inflammatory factor[19]. IL-6 can promote the proliferation and differentiation of immune cells, and improve their immune function. IL-6 can activate T lymphocytes, induce B lymphocytes to differentiate, and finally secrete immunoglobulin. Therefore, the expression level of IL-6 will show a certain downward trend with the improvement of human health level, and gradually tend to the conventional expression level. In addition, IL-10 is a multifunctional cytokine derived from multiple cells. It is an important human anti-inflammatory factor. It can regulate immune response, regulate cell growth and differentiation, and participate in anti-inflammatory reaction[20]. In addition, IL-10 is also an important immune system regulator in human body, and it is currently recognized as an immunosuppressive factor in the medical field.

As a multifunctional inflammatory cytokine, TNF-α has anti-infection and anti-tumor effects[21]. Its reaction mechanism is to stimulate eosinophils and lymphocytes to produce IL-6 and other factors by mediating the accumulation of eosinophils and lymphocytes at the inflammatory site, thus indirectly playing an anti-tumor and anti-inflammatory role. Aggregation is activated, and the vascular endothelium synthesizes fibroblasts to synthesize colony stimulating factors, thereby causing the body to produce a persistent inflammatory response[22]. TNF-α can stimulate the proliferation of B cells and promote Ig secretion. The level of TNF-α can affect the body's anti-infection ability. Macrophages release a lot of TNF-α factors, which activate neutrophils and endothelial cells to adhere to inflammatory receptors and promote the release of inflammatory factors. Therefore, in the inflammatory reaction, the more serious the virus or bacterial infection, the higher the level of TNF-α[23].

Under normal circumstances, the severity of the condition can be judged according to the TNF-level in the patient's body, which has positive significance. The main role of sICAM-1 is to mediate the interaction between cells, cells and

extracellular matrix, and play an important role in the development of physiology and pathology[24]. LTD4 is a strong active leukotriene D, which promotes the contraction of bronchial smooth muscle, increases capillary permeability and promotes mucus secretion[25]. When the body has an allergic reaction or an inflammatory reaction, phospholipase acts on the phospholipid bilayer of the cell membrane to promote the production of 5-HPETE. Leukotriene receptor antagonists inhibit the release of inflammatory mediators and cytokines by down-regulating the expression of adhesion molecules induced by sICAM-1. Down-regulating the expression of LTD4, inhibiting the release of LTD4 in the airway, and reducing the proliferation of inflammatory cells, leukotriene receptor antagonists induce apoptosis by activating the 5-HPETE tetraenoic acid pathway.

CONCLUSION

Although the idea of this study is novel, there are some shortcomings. Although this study discussed the clinical efficacy of glucocorticoid, antihistamine and leukotriene receptor antagonist in patients with AR, there was a lack of research on its specific long-term mechanism. The research object of this study comes from the same hospital, and the sample source is single and representative. In addition, the exclusion and inclusion criteria of this study are subjectively set according to the experimental direction, which may lead to biased results. In summary, glucocorticoids and antihistamines have obvious therapeutic effects, reduce serum inflammatory index levels, relieve symptoms and signs of patients, promote patient recovery, and provide a certain reference for clinical treatment of AR.

ARTICLE HIGHLIGHTS

Research background

Glucocorticoids, antihistamines and leukotriene receptor antagonists are excellent therapeutic agents for allergic rhinitis (AR) at present, but the existing research lacks the comprehensive clinical effect comparison and analysis of the three.

Research motivation

To explore the clinical and anti-inflammatory effects of glucocorticoid, antihistamine and leukotriene receptor antagonist on AR.

Research objectives

To systematically evaluate the therapeutic effect of glucocorticoid, antihistamine and leukotriene receptor antagonist on AR, and evaluate its anti-inflammatory level to guide the follow-up clinical treatment.

Research methods

To evaluate the clinical efficacy, anti-inflammatory reaction and adverse reactions before and after treatment and between groups, and to comprehensively evaluate the efficacy of leukotriene receptor antagonists, glucocorticoids and antihistamines.

Research results

All three drugs have certain therapeutic effects, and the therapeutic effect of glucocorticoid combined with antihistamine is better than that of leukotriene receptor antagonist. Glucocorticoid combined with antihistamine has better anti-inflammatory effect and lower adverse reactions.

Research conclusions

Glucocorticoids and antihistamines are more effective in the treatment of AR, and it is better to reduce the level of serum inflammatory indicators and have lower adverse reactions.

Research perspectives

Summarize the common drugs used in the treatment of AR, and comprehensively analyze the clinical efficacy, anti-inflammatory level and adverse reactions of these drugs to serve clinical treatment.

FOOTNOTES

Author contributions: Qiu C and Feng D contributed equally to this work; Feng D conceived and designed the experiments; Qiu C and Feng D selected the literature, extracted data and analyzed it; Feng D and Qiu C wrote the manuscript.

Institutional review board statement: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent statement: This study is a retrospective study, therefore informed consent forms are exempted.

Conflict-of-interest statement: The authors declare no competing financial interest.

Data sharing statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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