Review Article Effects of glucocorticoid therapy on nasal conditions and inflammatory factors in patients with allergic rhinitis

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Abstract: Objective: To investigate the effects of glucocorticoid therapy on nasal condition and inflammatory factors in patients with allergic rhinitis. Methods: A total of 200 patients with allergic rhinitis were selected, of which 90 patients were treated with glucocorticoid, budesonide through nasal spray as Group A, and 110 patients were treated with common nasal decongestant, oxymetazoline hydrochloride spray, as Group B. The total effective rate and incidence of adverse reactions in the patients were analyzed after 7 days of treatment, and their nasal pH value was detected after 14 days of treatment. The nasal symptoms and life quality of the patients were scored using the visual analog scale (VAS) and rhinoconjunctivitis quality of life questionnaire (RQLQ) after 14 days and 28 days of treatment. The expression of inflammatory factors (interleukin-4 (IL-4), interleukin-17 (IL-17), and interleukin-33 (IL-33)) was determined using the enzyme-linked immuno-sorbent assay (ELISA) before treatment and after three months of treatment. Results: The total effective rate in Group A was clearly higher than that in Group B, and the incidence of adverse reactions in Group A was significantly lower than that in Group B. Group B showed inconspicuous changes in nasal pH value before and after treatment, while Group A showed a significantly decreased nasal pH value after treatment. Moreover, after treatment, the VAS score of Group A was significantly lower than that of Group B in terms of all indexes except for ocular conditions and daily activities, and the expression of IL-4, IL-17, and IL-33 of Group A was significantly lower than that of Group B. Conclusion: Glucocorticoids are more effective than common nasal decongestants in inhibiting inflammatory factors, and they can relieve allergic rhinitis in patients more effectively and safely and strongly improve the life quality of the patients.

Keywords: Glucocorticoid, nasal decongestant, IL-4, IL-17, IL-33

Introduction

Allergic rhinitis is a mucosa inflammation driven by type 2 helper T (Th2) cells, which is induced by a reaction between allergens such as pollen, mold, and dust mites, and immune cells [1-3]. It is characterized by sneezing, rhinocnesmus, airflow obstruction and some ocular symptoms [4]. The incidence of such diseases is on the rise year by year, seriously compromising the patients' life quality and imposing heavy medical expense burdens [5, 6].

Nasal decongestants such as oxymetazoline are common drugs for allergic rhinitis [7]. These drugs can shrink nasal blood vessels and re-

duce turbinate volume, thus significantly alleviating nasal congestion. They take effect within 5-10 minutes and have a long-lasting effect, but long-term use of them will bring about huge side effects [8-10]. Some corticosteroids such as glucocorticoids are effective in treating dysosmia caused by allergic rhinitis [11]. These drugs can regulate the number of rhinitis cells (neutrophilic granulocytes and/or eosinophils) and nasal goblet cells to treat rhinitis [12]. This study aimed to investigate the effects of glucocorticoids on nasal condition, life quality, and inflammatory factors of patients with allergic rhinitis by comparing common nasal decongestants with glucocorticoids.

General data and methods

General data

A total of 200 patients with allergic rhinitis treated in our hospital from January 2015 to April 2018 were enrolled and divided into Group A and Group B. Group A (n=90) was treated with glucocorticoids, while Group B (n=110) was treated with common vasoconstrictor nasal sp-ray.

The inclusion criteria of patients were as follows: Patients diagnosed with allergic rhinitis based on the allergen skin prick test, and those whose family members understood the study. The exclusion criteria were as follows: Patients with psychological diseases and those allergic to drugs.

Methods

Patients in Group A were treated as follows: A nasal care device (Beijing Borne Tech Co., Ltd., Beijing, China) was employed to clean the nasal cavity of each patient, and then glucocorticoid budesonide spray (Shanghai Johnson & Johnson Ltd., State Food and Drug Administration (SFDA) approval number: J20180024) was adopted to spray each side of the nasal cavity at 64 μ g/time, once in the morning and once in the evening. The budesonide was sprayed in the patients for 14 continuous days, and then it was sprayed at 128 μ g/time, once in the morning, for 2 courses.

Based on the treatment for patients in Group A, patients in Group B were additionally treated with common vasoconstrictor nasal spray. The nasal decongestant oxymetazoline hydrochloride spray (Changzhou Kinyond Pharmaceutical Manufacturing Co., Ltd., SFDA: H20058017) was adopted to spray each side of the nasal cavity at 37 μ g/time, once in the morning and once in the evening. The spray was used on the patients for 14 continuous days, and then it was used as per the above standard for 2 courses after 7 days.

Patients with infection symptoms in both groups were required to be treated with antibacterial drugs and the type, dosage and treatment course of the drugs were determined according to the patients' drug allergy history and disease condition.

Detection indexes

Visual analog scale (VAS) score of nasal symptoms in patients from the two groups: The nasal symptoms of the two groups included nasal obstruction, rhinocnesmus, nasal discharge, and sneezing were analyzed using VAS after 14 days and 28 days of treatment [13]. VAS score ran between 0-10 points, with 0 points indicating no symptoms and 10 points indicating extremely severe symptoms. During subsequent visits, the nasal symptoms of the patients were evaluated again, and their changes were analyzed.

Nasal pH value of the two groups: The nasal pH value of each patient from the two groups was determined before treatment and after 14 days of treatment. The determination was carried out from 14:30 to 17:00 on the determination day at room temperature when the patients were in a stable and calm mood specifically as follows: A short range pH paper was cut into thin strips, and placed on the mucosa of inferior turbinate. After about 20 s, the strips were taken out, and immediately compared with the standard color plate, and the pH value was recorded. The interval between each measurement was about 10 min, and three measured nasal pH values were averaged as the nasal pH value of the patient.

The expression of inflammatory factors (interleukin-4 (IL-4), interleukin-17 (IL-17), and interleukin-33 (IL-33) in the two groups: Fasting venous blood (5 mL) was sampled from each patient before treatment and after three months of treatment, and let to stand for 20 min. Then the serum was separated from the sample by centrifugation at 3000 r/min for 10 min using a centrifuge manufactured by Beijing BMH Instruments Co., Ltd. The separated serum was quickly frozen in liquid nitrogen and stored at -180°C for later use. The expression of IL-4, IL-17, and IL-33 in the serum was determined using an enzyme-linked immuno-sorbent assay (ELISA) kit (Suzhou ELSBIO Co., Ltd.), and their expression between the two groups was compared.

Rhinoconjunctivitis quality of life questionnaire (RQLQ) score of the two groups: RQLQ was applied to score the two groups before treatment and after 14 days and 28 days of treat-

(70) $(X \pm 3)$				
Group	Group A (n=90)	Group B (n=110)	t/X ²	Р
Sex			0.117	0.733
Male	48 (53.33)	56 (50.91)		
Female	42 (46.67)	54 (49.09)		
Average age (Y)	35.23±5.14	34.89±5.67	0.440	0.661
Average weight (Kg)	65.54±11.03	63.95±10.57	0.104	0.301
Like smoking or not?			0.003	0.955
Yes	47 (52.22)	57 (51.82)		
No	43 (47.78)	53 (48.18)		
Drinking or not?			0.147	0.701
Yes	45 (50.00)	52 (47.27)		
No	45 (50.00)	58 (52.73)		
Hyperlipidemia			0.175	0.676
Yes	24 (26.67)	26 (56.00)		
No	66 (73.33)	82 (44.00)		
Hypertension			0.241	0.624
Yes	23 (25.56)	21 (19.09)		
No	67 (74.44)	89 (80.91)		
Diabetes mellitus			0.003	0.960
Yes	21 (23.33)	26 (23.64)		
No	69 (76.67)	84 (76.36)		

Table 1. General baseline data of Group A and Group B [n (%)] (X \pm S)

ment [14], and the score of the two groups was compared.

The total effective rate of the two groups: The total effective rate of the two groups was compared after 7 days of treatment. A patient with ruddy nasal mucosa, complete disappearance of nasal obstruction, no secretion, and no turbinate congestion and edema was judged as being cured. Treatment with the following outcomes was determined to be markedly effective: Clearly relieved nasal obstruction, significantly reduced secretion, and significantly reduced congestion and edema in nasal mucosa and turbinate. Treatment with the following outcomes was determined to be effective. Modestly relieved nasal obstruction, modestly reduced secretion, and modestly reduced congestion and edema in nasal mucosa and turbinate. Treatment without the above outcomes was determined to be ineffective.

Adverse reactions of the two groups: The two groups were evaluated after 7 days of treatment to compare their adverse reactions and incidence of adverse reactions, including mycteroxerosis, nasal cavity irritation and discomfort, nasal discharge accompanied with blood, weariness, headache, and gastrointestinal reaction.

Statistical analysis

The data were analyzed comprehensively and statistically using SPSS 19.0 (Asia Analytics Formerly SPSS, China). The enumeration data were analyzed using X², including general data about sex, personal hobbies such as smoking and drinking, diabetes, hypertension, and hyperlipidemia. The number of patients with effective treatment and the number of patients with adverse reactions were also analyzed using X². Measurement data were expressed by the $(X \pm S)$ and analyzed by t test. The measurement data included the general data about average age, weight, VAS score, RQLQ score, nasal pH, and expression of IL-4, IL-17, and IL-33 before and after surgery for three months. Post-hoc analysis was carried out using the Least Significant Difference (LSD)

method. P<0.05 indicates a significant difference.

Results

General data

It was necessary to investigate the basic conditions of the two groups, such as age, sex, weight, personal hobbies including smoking and drinking, diabetes mellitus, hypertension, and hyperlipidemia. Details are shown in **Table 1**.

VAS scores of nasal symptoms of the two groups

Inter-group comparison showed that, the VAS score of both groups significantly decreased after treatment, and the score after 28 days of treatment was significantly lower than that after 14 days of treatment (P<0.05). Comparison between the two groups showed that the difference of VAS score between the two groups before treatment was not significant (P>0.05), and the score of Group A was significantly lower than that of group B after 14 days

		Group			
Symptoms		Group A (n=90)	Group B (n=110)	t	Р
Nasal obstruction	Before treatment	5.51±3.23	5.47±3.35	0.085	0.932
	After 14 days of treatment	2.43±2.21*	3.51±2.33*	3.337	0.001
	After 28 days of treatment	1.12±1.10*,#	1.98±1.59*,#	4.349	<0.0001
Rhinocnesmus	Before treatment	4.43±3.21	4.31±3.19	0.264	0.792
	After 14 days of treatment	1.76±1.57*	2.79±1.44*	4.832	<0.0001
	After 28 days of treatment	0.88±0.79*,#	1.17±0.85*,#	2.477	0.014
Nasal discharge	Before treatment	5.87±3.36	5.93±3.17	0.130	0.897
	After 14 days of treatment	2.50±2.10*	3.48±2.44*	3.006	0.003
	After 28 days of treatment	1.84±1.41*,#	2.56±1.88*,#	3.006	0.003
Sneezing	Before treatment	6.04±3.96	5.93±3.80	0.200	0.842
	After 14 days of treatment	2.15±1.91*	4.51±2.18*	8.048	<0.0001
	After 28 days of treatment	1.08±0.93*,#	2.70±1.38*,#	9.508	<0.0001

Table 2. VAS score	of nasal symptoms	in Group A and	Group B
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Note: * indicates that in comparison with Group B, P<0.05, and # indicates that in comparison with the situation after treatment, P<0.05.



Figure 1. Nasal pH value of the two groups before and after treatment. A short range pH paper was utilized to determine the nasal pH value of the two groups before and after treatment, and the value of them before treatment was not very different (P>0.05). The change of the value in Group B before and after treatment was not significant (P>0.05). The nasal pH value in Group A after treatment was higher than that before treatment, and was lower than that in Group B (P<0.05). Note: * indicates that in comparison with Group B, P<0.05, and # indicates that in comparison with the situation after treatment, p<0.05.

and 28 days of treatment (*P*<0.05). More details are shown in **Table 2**.

Nasal pH value of the two groups

Before treatment, the nasal pH value of Group A was (7.78 \pm 0.27), and that of Group B was (7.71 \pm 0.25), so the nasal pH value difference between the two groups before treatment was

small (P>0.05). After 14 days of treatment, the nasal pH value of Group A was (7.13±0.21), and that of Group B was (7.69±0.19). It was apparent that after treatment, Group A showed significantly lower nasal pH value, but Group B showed no big difference in it, and the nasal pH value of Group A was lower than that of Group B (P<0.05). More details are shown in **Figure 1**.

The expression of IL-4, IL-17 and IL-33 in the two groups before treatment and after three months of treatment

The expression of IL-4 in the two groups: The expression of IL-4 in Group A before treatment and after three months of treatment was (87.88 ± 7.99) and (51.54 ± 5.46) , respectively, and the expression in Group B before treatment and after three months of treatment was (88.09 ± 7.68) and (60.03 ± 5.12) , respectively. It was apparent that before treatment, the IL-4 expression difference between the two groups was small (*P*>0.05), but after treatment, the expression in both groups decreased significantly, and the expression in Group B (*P*<0.05). More details are shown in **Figure 2**.

The expression of IL-17 in the two groups: The expression of IL-17 in Group A before treatment and after three months of treatment was (131.45 ± 12.33) and (87.72 ± 8.89) , respectively, and the expression in Group B before treatment and after three months of treatment was (133.22 ± 12.04) and (97.55 ± 9.55) , respective-



Figure 2. Comparison between the two groups in serum IL-4 expression. ELISA was applied to determine the serum IL-4 expression, and it turned out that after treatment, the expression of IL-4 in both groups decreased significantly (P<0.05), and the expression in Group A was lower than that in Group B (P<0.05). Note: * indicates that in comparison with Group B, P<0.05, and # indicates that in comparison with the situation after treatment, P<0.05.



Figure 3. Comparison between the two groups in serum IL-17 expression. ELISA was applied to determine the serum IL-7 expression, and it turned out that after treatment, the expression of IL-17 in both groups decreased significantly (P<0.05), and the expression in Group A was lower than that in Group B (P<0.05). Note: * indicates that in comparison with Group B, P<0.05, and # indicates that in comparison with the situation after treatment, P<0.05.

ly. It was apparent that before treatment, the IL-17 expression difference between the two groups was small (P>0.05), but after treatment, the expression in both groups decreased significantly, and the expression in Group A was clearly lower than that in Group B (P<0.05). More details are shown in **Figure 3**.

The expression of IL-33 in the two groups: The expression of IL-33 in Group A before treatment and after three months of treatment was (56.77 ± 5.49) and (32.03 ± 3.99) , respectively,



Figure 4. Comparison between the two groups in serum IL-33 expression. ELISA was applied to determine the serum IL-33 expression, and it turned out that after treatment, the expression of IL-33 in both groups decreased significantly (P<0.05), and the expression in Group A was lower than that in Group B (P<0.05). Note: * indicates that in comparison with Group B, P<0.05, and # indicates that in comparison with the situation after treatment, P<0.05.

and the expression in Group B before treatment and after three months of treatment was (57.04 \pm 6.04) and (41.00 \pm 4.88), respectively. It was apparent that before treatment, the IL-33 expression difference between the two groups was small (*P*>0.05), but after treatment, the expression of both groups decreased significantly, and the expression in Group A was clearly lower than that in Group B (*P*<0.05). More details are shown in **Figure 4**.

RQLQ score of the two groups

After treatment, both groups got significantly lower RQLQ score, and the score of the two groups after 14 days of treatment was not significantly different from that after 28 days of treatment in terms of daily activities and ocular symptoms (P>0.05), but the score after 28 days of treatment was dramatically lower than that after 14 days of treatment in other items (P>0.05). The RQLQ score of Group A was significantly higher than that of Group B in all indexes (P>0.05) (**Table 3**).

The total effective rate in the two groups

Analysis revealed that Group A showed a total effective rate of 96.67%, with 50 patients cured, 20 patients treated markedly effectively, 3 patients treated effectively, and 3 patients treated ineffectively. While Group B showed a total effective rate of 81.82%, with 48 patients cured, 23 patients treated markedly effectively,

		Gro			
Symptoms		Group A	Group B	t	Р
		(n=90)	(n=110)		
Daily activities	Before treatment	3.54±1.32	3.52±1.20	0.112	0.911
	After 14 days of treatment	1.15±1.11*	1.93±1.35*	4.398	<0.0001
	After 28 days of treatment	1.11±0.79*	1.87±0.94*	6.106	<0.0001
Sleep state	Before treatment	2.21±1.67	2.19±1.73	0.232	0.838
	After 14 days of treatment	1.11±0.82*	1.60±0.97*	4.046	<0.0001
	After 28 days of treatment	0.67±0.58*,#	1.19±0.81*,#	5.111	<0.0001
Non-nasal and ocular symptoms	Before treatment	2.86±1.31	2.81±1.60	0.238	0.812
	After 14 days of treatment	1.32±1.24*	1.96±1.48*	3.269	0.001
	After 28 days of treatment	0.89±0.40*,#	1.13±0.52*,#	3.594	0.0004
Behavioral problems	Before treatment	3.12±1.32	3.23±1.40	0.567	0.571
	After 14 days of treatment	1.50±0.21*	2.63±1.21*	8.749	<0.0001
	After 28 days of treatment	0.72±0.41*,#	1.33±0.61*,#	8.105	<0.0001
Nasal symptoms	Before treatment	3.53±1.11	3.41±1.23	0.845	0.399
	After 14 days of treatment	1.51±1.12*	2.20±1.65*	3.380	0.0009
	After 28 days of treatment	0.69±0.36*,#	1.33±0.70*,#	7.862	<0.0001
Ocular symptoms	Before treatment	1.90±1.57	1.85±1.65	0.218	0.828
	After 14 days of treatment	0.31±0.23*	0.93±0.78*	7.283	<0.0001
	After 28 days of treatment	0.32±0.15*	0.75±0.59*	6.736	<0.0001
Emotional state	Before treatment	2.11±1.23	2.02±1.40	0.477	0.634
	After 14 days of treatment	0.89±0.53*	1.45±0.79*	5.748	<0.0001
	After 28 days of treatment	0.45±0.32*,#	0.83±0.50*,#	6.239	<0.0001

Table 3. RQLQ score of Group A and Group B

Note: * indicates that in comparison with Group B, P<0.05, and # indicates that in comparison with the situation after treatment, P<0.05.

Table 4. Th	e Total	effective	rate in	Group	A and	Group
B (%)						

Group	Group A (n=90)	Group B (n=110)	X ²	Р
Cured	50 (55.56)	48 (43.64)	-	-
Markedly effective	20 (22.22)	23 (20.91)	-	-
Effective	17 (18.89)	19 (17.27)	-	-
Ineffective	3 (3.33)	20 (18.18)	-	-
Total effective rate	87 (96.67)	90 (81.82)	10.720	0.001

19 patients treated effectively, and 20 patients treated ineffectively. Therefore, the total effective rate in Group A was significantly higher than that in Group B (P<0.05) (**Table 4**).

The incidence of adverse reactions in the two groups

Group A showed an incidence of adverse reactions of 6.66%, with mycteroxerosis in 1 patient, weariness in 3 patients, headache in 1 patient, gastrointestinal reaction in 1 patient, and nasal cavity stimulation and nasal discharge accompanied with blood in 0 patients. While Group B showed an incidence of adverse reactions of 17.27%, with mycteroxerosis in 2 patients, weariness in 2 patients, headache in 2 patients, gastrointestinal reaction in 6 patients, nasal cavity stimulation in 5 patients, and nasal discharge accompanied with blood in 1 patient. Therefore, the total incidence of adverse reactions in Group A was signifi-

cantly lower than that in Group B (P<0.05). More details are shown in **Table 5**.

Discussion

Allergic rhinitis is a common respiratory tract disease, which poses a huge impact on a persons' work and life, and imposes a great economic burden on patients [15, 16]. The purpose of this study was to probe into the effects of two different drugs, glucocorticoid and common vasoconstrictor nasal spray, on the nasal

Group	Group A (n=90)	Group B (n=110)	X ²	Ρ
Mycteroxerosis	1 (1.11)	2 (1.82)	-	-
Nasal irritation and discomfort	0 (0.00)	5 (4.54)	-	-
Nasal discharge accompanied with blood	0 (0.00)	2 (1.82)	-	-
Weariness	3 (3.33)	2 (1.82)	-	-
Headache	1 (1.11)	2 (1.82)	-	-
Gastrointestinal reaction	1 (1.11)	6 (5.45)	-	-
The total incidence	6 (6.66)	19 (17.27)	5.091	0.024

Table 5. Adverse reactions in Group A and Group B

condition, life quality, and inflammatory factors in patients with allergic rhinitis.

In this study, we compared the VAS score of nasal symptoms of the two groups before and after treatment, finding that the indexes including nasal obstruction, rhinocnesmus, nasal discharge, and sneezing of the two groups gradually decreased within 14-28 days after treatment, and Group A showed dramatically lower VAS of those indexes than Group B after treatment. We also compared the expression of IL-4, IL-17, and IL-33 of the two groups before and after treatment, finding that Group A showed significantly lower expression of each of them compared to Group B three months after treatment. A study by Nabe et al. [17] uncovered that glucocorticoid drugs could effectively inhibit the expression of IL-33, and a study on eczema also revealed that glucocorticoids could effectively suppress the expression of IL-4 [18], which was similar to the results of our study. Some common nasal decongestants such as oxymetazoline take effect by stimulating vasoconstriction in the way of stimulating α -adrenoceptor, so their effect is short-term, and they are prone to cause rebound blood vessel congestion in a long period of time [19, 20]. In contrast, glucocorticoids take effect by lowering the expression of inflammatory factors through inducting apoptosis of immune cells, so their anti-inflammatory and analgesic effects are more sustained [21-24]. According to the results of this experiment, we can conclude that glucocorticoids are more effective than oxymetazoline hydrochloride in inhibiting the levels of inflammatory factors and relieving nasal symptoms.

In this study, we compared the nasal pH value of the two groups, finding that after treatment, Group B did not show a big difference in nasal pH value, while Group A showed a significant decrease in it. Nasal pH value is related to the physiological function of nasal cavity. Lysozyme in the nasal cavity can resolve bacteria only in an acidic environment, and if the nasal cavity is alkaline, the ability of lysozymes in inhibiting bacteria would be weak-

ened, and inflammation would occur [25]. An experiment by Wen et al. [26] revealed that glucocorticoids greatly lowered the nasal pH value, and relieved the disease correspondingly, which was similar to the results of our study. According to the previous study results about glucocorticoids on inflammatory factors, glucocorticoids inhibit the expression of inflammatory factors in the nasal cavity and alleviate nasal cavity inflammation, and nasal pH value decreases correspondingly. Vasoconstrictor drugs such as oxymetazoline hydrochloride are less effective than glucocorticoids in affecting inflammatory factors and rhinitis symptoms, and they are also less effective in lowering the nasal pH value. Based on the above results, we can draw a conclusion that glucocorticoids are superior to nasal decongestants in terms of nasal pH value.

Moreover, we compared the total effective rate and incidence of adverse reactions in the two groups, finding that the total effective rate in Group A was significantly higher than that in Group B, and the incidence of adverse reactions in Group A was much lower than that in Group B. It was also found that oxymetazoline exerted side effects in the nasal cavity, and it was prone to bring about headache and weariness. These drugs exert contractile effects on blood vessels, so they easily affect the central nervous system after entering the blood stream and are absorbed by the whole body [27]. Glucocorticoid drugs directly target inflammatory cells and factors [28], so they cause fewer adverse reactions than vasoconstrictor oxymetazoline. We compared the RQLQ score of the two groups after 14 days and 28 days of treatment, finding that except for some items, the score of Group A was significantly lower than that of Group B.

A study by Poletti et al. [13] found that after glucocorticoid therapy, the life quality of the patients was improved more significantly, which was in consistent with the results of this study. The above results show that glucocorticoids are more effective than vasoconstrictors in inhibiting inflammatory factors and relieving nasal symptoms, and they bring about less adverse events. Therefore, the life quality of patients after being treated with glucocorticoids would be better than that of patients after being treated with vasoconstrictors.

These experiment still have some shortcomings. For example, we have not studied the specific role of glucocorticoids on cells with inflammatory factors due to the limitation of equipment, and we have also not deeply analyzed molecular mechanisms, such as informationrelated signaling pathway proteins. In future research, we will actively purchase equipment to further analyze relevant mechanisms, and better explore the mechanism of glucocorticoids.

To sum up, glucocorticoids are more effective than common nasal decongestants in inhibiting inflammatory factors, and they can relieve allergic rhinitis in patients more effectively and safely and better improve the life quality of the patients.

Disclosure of conflict of interest

None.

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