CLINICAL EFFICACY OF TRIAMCINOLONE ACETONIDE COMBINED WITH IMMUNOTHERAPY IN THE TREATMENT OF ORAL MUCOSAL DISEASES AND ITS EFFECT ON INCIDENCE OF ADVERSE REACTIONS

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ABSTRACT

Objective: *To explore the clinical efficacy of triamcinolone acetonide combined with immunotherapy in the treatment of oral mucosal diseases and its effect on the incidence of adverse reactions.*

Methods: *The medical records of 106 patients with oral mucosal diseases treated in our hospital (January 2019-January 2021) were retrospectively analyzed. According to the treatment methods, 53 patients who received triamcinolone acetonide were set as the reference group (RG), while 53 patients who received triamcinolone acetonide combined with immunotherapy were set as the observation group (OG). The clinical efficacy of the two groups was compared and analyzed.*

Results: *No remarkable differences in the general data were observed between the two groups (P>0.05). Compared with RG, OG achieved obviously lower effective rate, higher cured rate and higher total effective rate (P<0.05), shorter pain duration and mucosal healing time (P<0.05), better hemorheology indexes (plasma viscosity, whole blood viscosity, hematocrit, fibrinogen and ESR, P<0.05), and lower immune function indexes (IgA, IgM and IgG, P<0.05). After treatment, the inflammatory factor levels in both groups decreased, with remarkably lower TNF-α, IL-6, IL-8 and CRP levels in OG (P<0.05). Symptoms such as gastrointestinal discomfort, fever, rash and muscle atrophy occurred in both groups during treatment, with a slightly higher incidence of adverse reactions in RG compared with OG (P<0.05).*

Conclusion: *Triamcinolone acetonide combined with immunotherapy can effectively improve the immune function of patients with oral mucosal diseases, with better curative effect and little adverse reactions, which is worth applying and popularizing.*

Keywords: *Oral mucosal diseases, immunotherapy, triamcinolone acetonide, clinical efficacy.*

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Introduction

Oral mucosal diseases generally refer to diseases occurring in oral mucosa and surrounding soft tissues other than tumors, with various types of diseases and different degree of damage to patients[1-3]. Due to their occurrence in the oral cavity, they are easy to trigger oral pain and eating difficulties with recurrence, causing serious adverse effects on the life and work of patients. The diseases are also once listed as major problems in oral diseases by the medical community because they are difficult to cure[4-7]. Clinical statistics show that the incidence of oral mucosal diseases is mostly related to genetic factors, immunity, and living habits, with no specific treatment at present. As a long-acting glucocorticoid, triamcinolone acetonide is a common drug the treatment of oral mucosal diseases in clinic with long-term efficacy and strong anti-inflammatory and anti-allergic effects, but it is easy to cause irreversible fibrous hyperplasia. With the deepening of immunology research and increasing

understanding of the role of immune factors in the occurrence and development of oral mucosal diseases, more attention has been paid to the immunotherapy of the diseases in clinic[8-11]. At present, no report has been found on the application of triamcinolone acetonide combined with immunotherapy in the treatment of oral mucosal diseases.

However, since the implementation of the combined treatment in our hospital, good clinical efficacy has been achieved. A retrospective study is conducted on 106 patients with oral mucosal diseases treated in our hospital, summarized as below.

Study protocol

Case screening

The medical records of 106 patients with oral mucosal diseases treated in our hospital (January 2019-January 2021) were retrospectively analyzed. According to the treatment methods, 53 patients who received triamcinolone acetonide were set as the reference group (RG), while 53 patients who received triamcinolone acetonide combined with immunotherapy were set as the observation group (OG). The protocol was approved by the ethics Committee of our hospital.

Inclusion criteria:

• The patients met the clinical diagnostic criteria of oral mucosal diseases[12];

• The patients did not receive any drugs within 1 week before treatment;

• The patients' medical records were complete;

• The patients and their families knew the study and signed the informed consent.

Exclusion criteria:

• The patients were during pregnancy or lactation;

• The patients had severe organ injury;

• The condition of the patents was extremely serious and uncontrollable;

• The patients had communication, cognitive or limb activity disorders.

Methods

All patients were given symptomatic treatment according to the severity of the disease, mainly including abstaining from alcohol, smoking, areca-nut, spicy and other irritating food, and timely vitamin supplementation[13-16]. In RG, triamcinolone acetonide injection (specification: 1ml; manufacturer: Kunming Jida Pharmaceutical Co., Ltd.; NMPA approval No. H53021604) was injected at multiple points at the base of oral mucosal lesions, with 1 ml each time and once a week. In addition to triamcinolone acetonide, OG was treated with mannatide tablets (specification: 50mg; manufacturer: Guangdong Winnerway Holdings Pharmaceutical Co., Ltd.; NMPA approval No. H20003716), with three times a day and one tablet each time. The treatment cycle of the two groups was 4 weeks (1 course of treatment).

Observation indexes

The age, disease types, gender, course of disease, BMI, oral mucosal lesion area and education level of the patients were collected at admission. The pain duration and mucosal healing time were recorded in detail during treatment. A hemorheology analyzer was adopted to detect the plasma viscosity, whole blood viscosity, hematocrit, fibrinogen and erythrocyte sedimentation rate (ESR).

The clinical efficacy was evaluated based on the criteria formulated by the Oral Mucosal Committee of the Chinese Medical Association (CMA). After one course of treatment, the patients had no pain in the oral mucosal lesion area and the ulcers disappeared completely with no recurrence in the 1 year of follow-up, which was cured; After 1 course of treatment, the pain in the oral mucosal lesion area and the ulcers basically disappeared with no recurrence within 10 months of follow-up, which was effective; After 1 course of treatment, the symptoms were not significantly improved with recurrence, which was ineffective. 5 ml of fasting peripheral blood was extracted from the patients to detect the inflammatory factor levels such as TNF-α, IL-6, IL-8 and CRP, and measure the immune function indexes such as IgA, IgG and IgM. The adverse drug reactions during treatment were recorded.

Statistical treatment

The data obtained were calculated by SPSS22.0, and graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). The study data included enumeration and measurement data, expressed as [n (%)] and ($\bar{x}\pm s$), and tested by X^2 and t test. The differences were statistically significant at $P<0.05$.

Results

General information

No remarkable differences in the general data were observed between the two groups ($P>0.05$; Table 1), which was in line with the criteria of a controlled study.

Observation indexes	RG	OG	X^2/t	P
Age(years old)	37.04±7.28	37.15±7.31	0.078	0.938
Disease types				
Oral lichen planus	24(45.28)	25(47.17)	0.038	0.846
Behcet disease	16(30.19)	18(33.96)	0.173	0.677
Recurrent aphthous ulcer	7(13.21)	4(7.55)	0.913	0.339
Leukoplakia oris	4(7.55)	3(5.66)	0.153	0.696
Lip diseases	2(3.77)	3(5.66)	0.210	0.647
Gender			0.152	0.696
Male	28(52.83)	30(56.60)		
Female	25(47.17)	23(43.40)		
Course of disease (months)	6.37±1.73	5.98±1.69	1.174	0.243
BMI(kg/m^2)	23.52±4.26	23.71±4.43	0.225	0.822
Oral mucosal lesion area(cm^2)	8.83±0.71	8.85±0.70	0.146	0.884
Education level			0.151	0.697
Junior high school and below	24(45.28)	26(49.06)		
Above junior high school	29(54.72)	27(50.94)		

Table 1: Analysis of patients' general data (n=53).

Clinical efficacy

Compared with RG, OG achieved obviously lower effective rate, higher cured rate and higher total effective rate (P<0.05; Figure 1).

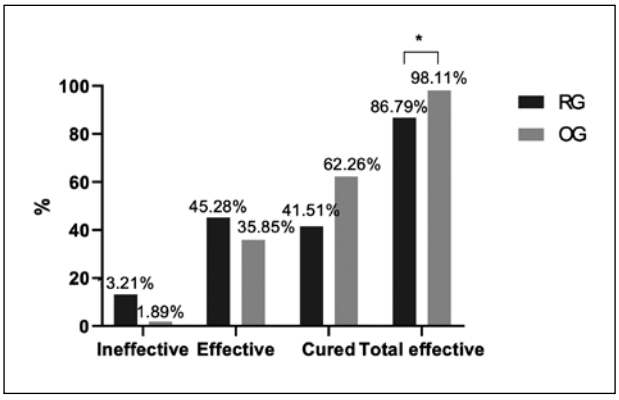

Figure 1: Analysis of patients' clinical efficacy.
*Note: The abscissa represented the evaluation dimensions, and the ordinate represented the percentage (%). In RG, 7 cases were ineffective, 24 cases were effective and 22 cases were cured, with 46 total effective cases. In OG, 1 case was ineffective, 19 cases were effective and 33 cases were cured, with 52 total effective cases. * indicated an obvious difference in the total effective rates between the two groups (X^2=4.867, P=0.027).*

Clinical observation indexes

Compared with RG, OG achieved obviously shorter pain duration and mucosal healing time (P<0.05), and better hemorheology indexes (plasma viscosity, whole blood viscosity, hematocrit, fibrinogen and ESR, P<0.05), see Table 2.

Observation indexes		RG	OG	t/P
Pain duration(d)	After treatment	8.22±1.92	5.19±1.87	8.230/<0.001
Mucosal healing time(d)	After treatment	10.09±2.20	6.47±1.21	10.496/<0.001
Plasma viscosity (mPa·a)	Before treatment	2.51±0.36	2.47±0.33	
	After treatment	2.40±0.28	1.80±0.24	11.845/<0.001
Whole blood viscosity (mPa/s)	Before treatment	14.85±2.13	14.79±2.08	
	After treatment	13.14±1.70	8.08±1.32	17.115/<0.001
Hematocrit(%)	Before treatment	45.49±4.93	45.54±5.23	
	After treatment	43.85±4.86	39.98±3.17	4.856/<0.001
Fibrinogen (g/L)	Before treatment	3.82±0.21	3.83±0.23	
	After treatment	3.61±0.18	2.15±0.14	46.011/<0.001
ESR(mm/h)	Before treatment	28.71±3.51	28.95±3.38	
	After treatment	22.58±3.24	18.28±3.22	6.853/<0.001

Table 2: Analysis of various clinical observation indexes (n=53).

Immune function indexes

The immune function indexes (IgA, IgM and IgG) were markedly lower in OG than in RG (P<0.05), as presented in in Figure 2.

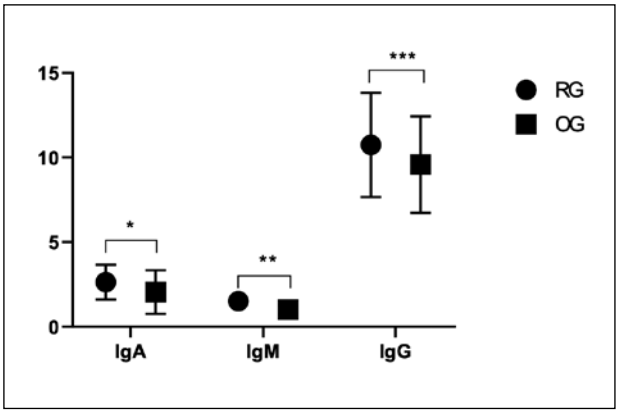

Figure 2: Analysis of patients' immune function indexes.
*Note: The abscissa represented immune function indexes, and the ordinate represented the detection level (g/L). The IgA, IgM and IgG levels after treatment were (2.63±1.02), (1.50±0.32) and (10.74±3.08) in RG, while those were (2.05±1.29), (1.01±0.28) and (9.58±2.85) in OG. * indicated an obvious difference in the IgA levels between the two groups (t=2.568, P=0.012). ** indicated an obvious difference in the IgM levels between the two groups (t=8.389, P<0.001). *** indicated an obvious difference in the IgG levels between the two groups (t=2.012, P=0.047).*

Inflammatory factor levels

After treatment, the inflammatory factor levels in both groups decreased, with remarkably lower TNF-α, IL-6, IL-8 and CRP levels in OG (P<0.05; Table 3).

Indexes		RG	OG	t/P
TNF-α (ng/L)	Before treatment	41.15±10.84	41.08±9.81	
	After treatment	28.37±8.21	19.19±9.13	5.443/<0.001
IL-6 (ng/L)	Before treatment	288.75±30.05	290.14±30.54	
	After treatment	202.17±19.16	105.37±32.66	18.611/<0.001
IL-8 (ng/L)	Before treatment	390.83±73.58	387.65±77.20	
	After treatment	249.75±40.82	110.16±58.04	14.322/<0.001
CRP (mg/L)	Before treatment	25.88±8.23	26.11±9.40	
	After treatment	17.33±9.18	12.08±5.17	3.628/<0.001

Table 3: Analysis of patients' inflammatory factor levels.

Adverse reactions

Symptoms such as gastrointestinal discomfort, fever, rash and muscle atrophy occurred in both groups during treatment, with a slightly higher incidence of adverse reactions in RG compared with OG (P<0.05; Figure 3).

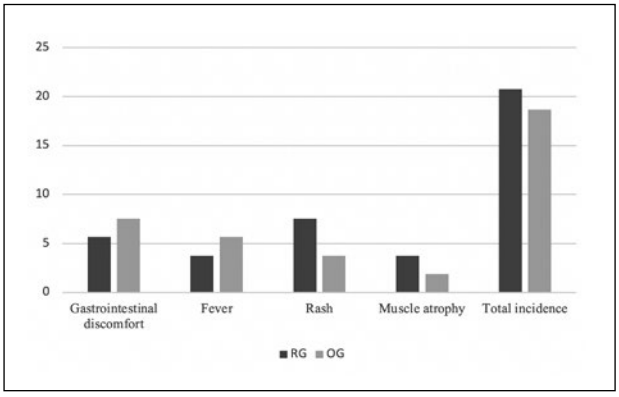

Figure 3: Analysis of patients' adverse reactions (%).
Note: The abscissa represented types of adverse reactions, and the ordinate represented the percentage (%). RG had 3 cases of gastrointestinal discomfort, 2 cases of fever, 4 cases of rash, and 2 cases of muscle atrophy, with 11 cases in total. OG had 4 cases of gastrointestinal discomfort, 3 cases of fever, 2 cases of rash, and 1 case of muscle atrophy, with 10 cases in total.

Discussion

Oral mucosal diseases are a common kind of oral disease in clinic and become difficult to treat for their recurrence, which are considered to be autoimmune diseases in a large number of studies at present. With the continuous development of immunology, the pathological changes of oral mucosal diseases have attracted the attention of scholars, and many studies have confirmed that imbalance of immune cells is their key cause[17-20]. In clinical practice, the treatment of the diseases mainly follows the principle of local symptom control, supplemented by systemic treatment, aiming to reduce local pain, enhance immunity, and promote healing of ulcer surface. Therefore, corticosteroids such as triamcinolone acetonide are commonly used in clinical practice for local treatment. However, long-term administration of these drugs results in poor tolerance of patients, increase the risk of complications and change the blood picture[21-24]. Mannatide tablets administrated in the immunotherapy of these patients in our hospital belong to an immunopotentiator that enhances the body immunity by activating the activities of T lymphocytes, phagocytes and NK cells. Their combination with triamcinolone acetonide achieved good clinical results.

In this study, the patients in OG were treated with triamcinolone acetonide combined with immunotherapy. The results showed that 1 case was ineffective, 19 cases were effective, and 33 cases were cured in OG, with the total effective rate as high as 98.11 %. Compared with the study of Sun S. et al.[25], the curative effect was remarkably better, fully illustrating that the immunotherapy based on triamcinolone acetonide can significantly improve the immune state of the patients and accelerate the tissue repair. In addition, symptoms such as gastrointestinal discomfort, fever, rash and muscle atrophy occurred in both groups during treatment, with a slightly higher incidence of adverse reactions in RG compared with OG (P<0.05), suggesting that immunotherapy will not cause obvious adverse drug reactions and can be applied to most patients with oral mucosal diseases. In addition, compared with RG, OG achieved obviously shorter pain duration and mucosal healing time (P<0.05), and better hemorheology indexes (plasma viscosity, whole blood viscosity, hematocrit, fibrinogen and ESR, P<0.05). The development of oral mucosal diseases causes blood hypercoagulability and fibrinolytic disorders in patients. The results of this study confirm that triamcinolone acetonide combined with immunotherapy can effectively reduce the content of whole blood viscosity and fibrinogen in patients. Moreover, immunotherapy can also expand the diameter of damaged mucosal blood vessels, dredge occlusion, and improve the hemorheology indexes of patients with oral mucosal diseases.

The immune function indexes (IgA, IgM and IgG) were markedly lower in OG than in RG (P<0.05). After treatment, the inflammatory factor levels in both groups decreased, with remarkably lower TNF-α, IL-6, IL-8 and CRP levels in OG (P<0.05). This demonstrates that mannatide tablets

can improve the immune function of patients, promote the synthesis and metabolism of nucleic acid, protein and mucopolysaccharide of lymphocytes, enhance the immune function of the body, and inhibit the synthesis and release of inflammatory factors, with excellent anti-inflammatory effect.

In conclusion, triamcinolone acetonide combined with immunotherapy can effectively improve the immune function of patients with oral mucosal diseases, with better curative effect and little adverse reactions, which is worth applying and popularizing. In this study, it was found that mannatide could promote immune regulation, but the specific mechanism needs to be further explored. In addition, the study also has some shortcomings such as small sample size and short follow-up time.

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