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Original Research Article

Effect of Kangfuxin liquid combined with triamcinolone acetonide in oral submucosal fibrous degeneration

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Abstract

Purpose: *To investigate the effect of Kangfuxin liquid combined with triamcinolone acetonide in the treatment of oral submucous fibrous degeneration.*

Methods: *A total of 140 patients with oral submucosal fibrous degeneration admitted to the outpatient clinic of Haiyan County Stomatological Hospital, China from June 2020 to June 2023 were divided equally into study and control groups. The study group received Kangfuxin liquid in addition to 1 mL triamcinolone acetonide (40 mg/mL) while the control group received 1 mL triamcinolone acetonide; therapeutic effects were compared after 4 weeks of treatment. Visual analogue scale (VAS) score, serum transforming growth factor (TGF-β1), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) levels were determined. Also, whole blood viscosity (WBV), plasma viscosity (PV), erythrocyte sedimentation rate (ESR), and incidence of adverse reactions were evaluated.*

Result: *The study group showed significantly reduced pain levels compared to the control group, as well as lower mucosal damage areas and improved mouth opening after 4 weeks of treatment compared to control group ($p < 0.05$). Also, the study group showed significantly lower TGF-β1, TNF-α and IL-6 compared to control group after treatment ($p < 0.05$). It showed significantly lower WBV, PV, and ESR compared to control group ($p < 0.05$). Furthermore, the study group showed significantly lower incidence of adverse reactions than the control group ($p < 0.05$).*

Conclusion: *Kangfuxin liquid, when combined with triamcinolone acetonide, lowers pain, reduces the levels of STGF-β1, improves hemorheology, and produces minimal adverse effects compared to triamcinolone alone. Future studies should focus on long-term outcomes to better assess the therapeutic potential of this combined regimen.*

Keywords: *Oral submucous fibrosis, Rehabilitation liquid, Triamcinolone acetonide, Serum transforming growth factor-β1, Interleukin-6*

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INTRODUCTION

Oral submucous fibrosis is a chronic condition that affects various parts of the oral cavity including the soft palate, gingiva, and lingual mucosa. This disease leads to tissue atrophy, deformation, and a loss of elasticity in fibrous tissues. In severe cases, it shortens the lingual frenum and restrict

the ability to open the mouth, significantly impairing oral functions and severely diminishing quality of life [1]. Etiology of oral submucous fibrosis is multifaceted, potentially triggered by genetic factors, habitual chewing of betel nut, prolonged consumption of spicy foods, weakened immunity, or vitamin deficiencies. Significantly, betel nut chewing is identified as the primary contributor to this disease, with prevalence rates as high as 30 % among users, causing a rapid increase in incidence rate [2,3].

Oral submucous fibrosis is both chronic and progressive, with potential malignant transformation if left untreated, affecting ability to eat, swallow, and speak. Currently, treatment primarily involves corticosteroids like triamcinolone acetonide, which help mitigate inflammation and reduce toxicity, thus alleviating symptoms. However, these steroids may irritate the gastrointestinal tract and prolonged usage leads to various complications. This necessitates combination with other medications to enhance efficacy and safety [4].

Traditional Chinese medicine attributes oral submucous fibrosis to damage from heat and toxins affecting Yin, as well as qi stagnation and blood stasis. Treatment strategies in this tradition focus on clearing heat, detoxifying, promoting blood circulation, and removing blood stasis. Kangfuxin, a traditional Chinese medicine derived from *Periattella americana*, is rich in amino acids and peptides. It is employed to clear heat, detoxify, promote blood circulation, nourish Yin, facilitate tissue regeneration, and is commonly used for treating burns, scalds, and various ulcerative conditions [5]. This study therefore investigated the effect of Kangfuxin solution in combination with triamcinolone acetonide in the treatment of oral submucous fibrous degeneration.

METHODS

Participants

This study was a retrospective analysis on 140 patients with oral submucous fibrosis admitted to the outpatient department from June 2020 to June 2023. The participants were randomly and equally divided into study and control groups (70 in each group). This study was approved by the Ethics Committee of Haiyan County Stomatological Hospital (approval no. MEC-1-HY-39) and was conducted in accordance with the guidelines of the Declaration of Helsinki [6]. Signed written informed consents were obtained from the patients and/or guardians prior to commencement of the study.

Inclusion criteria

Meeting the diagnostic criteria for oral submucous fibrosis, and participants who signed the informed consent form as approved by the Ethics Committee.

Exclusion criteria

Patients with other oral mucosal diseases, allergy to Kangfuxin solution or triamcinolone acetonide, presence of hepatic and renal insufficiency, immune function diseases, mental disorders, and participants who dropped out of the study.

Treatments

A total of 140 patients with oral submucous fibrosis from June 2020 to June 2023 were randomly divided into study and control group, with 70 cases in each group. The study group were administered Kangfuxin solution by gargling (10 mL) thrice daily, with no food and water intake within 30 min after gargling, in addition to intramuscular injection of 40 mg triamcinolone acetonide (1 mL, 40 mg/ml) once weekly for 4 weeks. The control group received only intramuscular injection of 40 mg triamcinolone acetonide (1 mL, 40 mg/ml) once weekly for 4 weeks.

Evaluation of parameters/indices

Degree of pain

Degree of pain was evaluated by visual analogue scale (VAS) [7], which was classified into severe pain (7-10 points), percussion pain (4 - 6 points), slight pain (1 - 3 points), and no pain (0 points); the score was proportional to the degree of pain.

Area of mucosal damage

Area of mucosal damage was measured with a sulfate paper, which was placed on the damaged mucosa, removed after discoloration, and laid on 1 × 1 mm grid paper to estimate the discolored area.

Degree of mouth opening

The distance between the incisal margins of the upper and lower central incisors of the patient was measured as the degree of mouth opening.

Inflammatory indices

Before treatment and after 4 weeks of treatment, fasting venous blood (3 mL) was collected from

the two groups, centrifuged at 3000 rpm for 10 min, and the supernatant was collected for determination of serum transforming growth factor-β1 (TGF-β1), tumor necrosis factor-α (TNF-α) by enzyme-linked immunosorbent assay (ELISA), and interleukin-6 (IL-6) by competition method.

Hemorheology

Before treatment and after 4 weeks of treatment, fasting venous blood (3 mL) was collected from the two groups, centrifuged at 3000 rpm for 10 min, and the supernatant was collected. Whole blood viscosity (WBV), plasma viscosity (PV) and erythrocyte sedimentation rate (ESR) were detected by automatic blood rheometer.

Incidence of adverse reaction

During treatment, occurrence of adverse reactions, including gastrointestinal discomfort, pruritus, and visual field changes, were recorded and compared.

Statistical analysis

The data were analyzed using Statistical Package for Social Sciences (SPSS) 25.0 software (IBM, Armonk, NY, USA). Normally distributed measurement data were expressed as mean ± standard deviation (SD), and compared using the independent sample t-test. Categorical data were expressed as frequency and percentages and compared using chi-square test (χ^2 test). $P < 0.05$ was considered statistically significant.

RESULTS

Baseline clinical data

In the control group, there were 36 males and 34 females, aged from 45 to 76 years, with an average age of 56.54 ± 5.52 years. There were 35 males and 35 females in the study group with a mean age of 55.97 ± 4.85 years (range, 45 - 75 years). There was no significant difference in general data between the two groups ($p > 0.05$).

Degree of pain, area of mucosal damage and degree of mouth opening

Before treatment, there was no significant difference in degree of pain, mucosal damage area and mouth opening between the two groups ($p > 0.05$). After 4 weeks of treatment, degree of pain, and mucosal damage area was significantly lower, while mouth opening was significantly higher in study group compared to control group ($p > 0.05$; Table 1).

Inflammatory factors

Before treatment, there was no significant difference in TGF-β1, TNF-α and IL-6 levels between the two groups ($p > 0.05$).

After treatment, the study group showed significantly lower levels of TGF-β1, TNF-α and IL-6 compared to control group ($p < 0.05$; Table 2).

Hemorheology

Before treatment, there was no significant difference in hemorheological indices (WBV, PV and ESR) between the two groups ($p > 0.05$). However, after treatment, study group showed significantly lower WBV, PV and ESR compared to control group ($p < 0.05$, Table 3).

Incidence of adverse reactions

During treatment, study group showed significantly lower incidence of adverse reactions compared to control group ($p < 0.05$, Table 4).

Table 1: Pain degree, mucosal damage area, and mouth opening (mean ± SD)

Group		Degree of pain	Area of damage (mm^2)	Mouth opening (cm)
Control	Before treatment	4.56±1.34*	152.89±48.74*	2.42±2.09*
	After treatment	1.65±0.47	68.46 ± 36.75	3.02±1.31
Study	Before treatment	4.65±1.29*	152.79±48.77*	2.49±2.03*
	After treatment	0.60±0.43#	53.61±26.02#	3.68±1.30#

***Note*: *$P < 0.05$ vs after treatment, #$p < 0.05$ vs control group**

Table 2: Inflammatory indices (N = 70 in each group, mean ± SD)

Group		TGF-β1 (μg /L)	TNF-α (ng /L)	IL-6 (pg /mL)
Control	Before treatment	27.54±7.62*	12.94±2.41*	26.98±8.47*
	After treatment	14.39±4.62	9.54±1.25	18.24±5.49
Study	Before treatment	27.62±7.59*	12.78±2.34*	26.71±8.64*
	After treatment	6.38±3.74#	7.26±1.21#	7.25±3.74#

***Note*: *$P < 0.05$ vs after treatment, #$p < 0.05$ vs control group**

Table 3: Hemorheological indices of the two groups

Group	Time	WBV (mPa·s)			PV (mPa·s)	ESR (mm/h)
		High cut	*Middle cut*	*Low cut*		
Control	Before treatment	5.69±0.41*	7.61±0.62*	12.74±3.18*	2.42±0.38*	54.56±3.47*
	After treatment	4.92±0.61	6.40±0.71	9.67±1.21	2.03±0.24	45.82±4.52
Study	Before treatment	5.62±0.92*	7.59±0.49*	13.02±2.12*	2.41±0.34*	54.69±3.59*
	After treatment	4.52±0.53#	6.12±0.51#	8.27±0.96#	1.32±0.17#	41.95±4.27#

***Note*: **P* < 0.05 vs after treatment, #*p* < 0.05 vs control group

Table 4: Incidence of adverse reactions (N, %)

Group	Gastrointestinal complaints	Pruritus	Changes in visual field	Occurrence rate
Control	4(5.71)	2(2.86)	3(4.29)	9(12.86)
Study	1(1.43)	0(0.00)	1(1.43)	2(2.86)
χ^2				4.834
P-value				0.028

DISCUSSION

Oral submucous fibrosis is commonly associated with long-term consumption of irritant foods, leading to a burning sensation in the oral mucosa, dry mouth, reduced taste sensitivity, and formation of mucosal blisters and ulcers. In severe cases, it reduces the oral mucosa's elasticity and shortens the lingual frenum, significantly affecting oral functionality and quality of life [8,9]. Currently, there are no specific medications for treating oral submucous fibrosis; however, treatments often involve corticosteroids like triamcinolone acetonide to alleviate symptoms. Prolonged use of these drugs may lead to metabolic disorders, muscle atrophy in the oral cavity, fungal infections, and other adverse effects [10].

Kangfuxin liquid, a newer traditional Chinese medicine formulation, contains a rich mix of bioactive substances such as amino acids and mucin. It is known for its effects in clearing heat, detoxifying the body, promoting blood circulation, nourishing Yin, and regenerating muscle tissue. It also enhances oral microcirculation, moderates inflammatory responses, and regulates immune function, making it increasingly popular for treating oral submucous fibrosis [11]. In this study, the control group received triamcinolone acetonide, while treatment group received Kangfuxin liquid in addition to triamcinolone acetonide. After 4 weeks, the study group showed significantly reduced pain levels, smaller areas of mucosal damage, and better mouth opening compared to control group. This suggests that the inclusion of Kangfuxin liquid, which is rich in bioactive peptides and polyol substances with anti-inflammatory and muscle-regenerating properties, enhances treatment efficacy by acting directly on the damaged oral mucosa and accelerating healing [12-14].

Serum transforming growth factor (TGF-β1), a cytokine with anti-inflammatory properties, inhibits cellular proliferation and immune responses and is a key factor in fibrosis [15]. Research has indicated that Kangfuxin liquid modulates TGF-β1 signaling pathway and suppresses fibroblast activation [16]. Also, IL-6 and TNF-α were significantly reduced in study group compared to control group, suggesting more effective inflammation control [17,18]. Also, the study highlighted significant improvement in haemorheological parameters such as WBV, PV, and ESR in study group compared to control group. These findings support using Kangfuxin liquid to promote better blood circulation, reduce blood viscosity, and enhance coagulation functions [19]. Furthermore, incidence of adverse reactions was significantly lower in study group compared to control group underscoring the safety and efficacy of combining Kangfuxin solution with triamcinolone acetonide in managing oral submucous fibrosis.

Limitations of the study

The retrospective nature and small sample size of this study may limit the generalizability of the findings. Additionally, lack of long-term follow-up may also not fully explain the long-term efficacy and potential complications associated with extended use of this combination treatment on CRF patients with dialysis-induced anemia.

CONCLUSION

Kangfuxin liquid, when combined with triamcinolone acetonide, improves the degree of pain, reduces the area of mucosa damage, improves oral functionality, reduces inflammation, and improves hemorheological indices with minimal adverse effects. Future studies should focus on long-term outcomes to

better assess the therapeutic potential of this combined regimen.

DECLARATIONS

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Ethical approval

Ethics Committee of Haiyan County Stomatological Hospital, China gave approval for this study (MEC-1-HY-39).

Availability of data and materials

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

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them. Xinyun Zhang and Shuntao Zhang contributed equally to this work.

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