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Therapeutic effects of Houttuynia eye drops combined with olopatadine hydrochloride eye drops on vernal keratoconjunctivitis

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Abstract. Therapeutic effects and safety of houttuynia eye drops combined with olopatadine hydrochloride eye drops on vernal keratoconjunctivitis (VK) were evaluated. A total of 926 patients with VK were collected in the Eye Hospital of Wenzhou Medical University from July 2011 to January 2017. Patients were divided into group A, B and C according to the use of different eye drops. Group A included 276 patients who were treated with houttuynia eye drops; group B included 305 patients who were treated with olopatadine hydrochloride eye drops; group C included 345 patients who were treated with houttuynia eye drops and olopatadine hydrochloride eye drops. Treatment was performed for 14 days. Eye symptoms before and after treatment, and at 1 h, 7 days and 14 days after drug administration were compared among groups to evaluate the therapeutic effect. At 1 h after drug administration, highest excellent rate was observed in group C, followed by group A, and good outcome rate was significantly higher in group C than in the other two groups ($P<0.05$), and effective rate was also significantly higher in group C than in the other two groups ($P<0.05$). At 7 days after treatment, excellent rate was significantly higher in group C than in the other two groups ($P<0.05$), and effective rate was higher in group C than in group B ($P<0.05$). At 14 days after treatment, excellent rate was significantly higher in group C than in the other two groups ($P<0.05$), while lowest good outcome rate and ineffective rate were found in group C, and no significant differences were found between group A and B ($P>0.05$). Houttuynia ophthalmic solution and olopatadine hydrochloride eye drops can both achieve good effect in the treatment of VK, and combined use of them can increase the efficacy and shorten treatment period. So, the combined treatment should be popularized.

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Introduction

Vernal keratoconjunctivitis (VK) is a pernicious allergic ocular surface disease with highest incidence in spring (1). As a highly infectious disease it mainly affects children and adolescents, VK incidence shows clear seasonal and regional differences (2). According to surveys, 223,000 new cases of VK are reported each year, and its incidence in spring and autumn was 62.3% higher than that in summer and winter.

VK belongs to acute conjunctival inflammation caused by bacterial infection and generally can be temporarily inhibited after simple treatment after the onset of symptoms (3). However, the recurrence rate of VK is high, and 65.3% of patients are affected by this disease after treatment (4). Radical treatment for this disease is difficult, and long-time drug treatment combined with living habit adjustment is needed to achieve satisfactory treatment outcomes (5). However, studies also reported that 2.35% of children with VK were not treated in time, inaccurately or not at all (6). This resulted in malignant retinal diseases, or even blindness (7). Clinical diagnosis of VK is relatively reliable, and inhibitory treatment with eye drops is the main treatment for this disease (8). Advances in medical technology have led to the development of various types of eye drops, while the treatment efficacy remains unclear.

In this study, houttuynia eye drops and olopatadine hydrochloride eye drops, which are commonly used eye drops, were selected to treat VK with the expectation of providing references for the clinical treatment of VK.

Patients and methods

General information. A total of 926 patients with VK were collected in the Eye Hospital of Wenzhou Medical University (Wenzhou, China) from July 2011 to January 2017. The patients were divided into groups A, B and C according to the use of different eye drops. There were 276 patients in group A (houttuynia eye drops), 305 patients in group B (olopatadine hydrochloride eye drops) and 345 patients in group C (houttuynia eye drops and olopatadine hydrochloride eye drops). The patients included 587 males and 339 females, had an age range of 5-30 years, with a mean age of 15.15±10.73 years. Monocular disease was found in 424 cases, and binocular disease in 502 cases.

Inclusion and exclusion criteria. Inclusion criteria were: patients affected by VK in spring, patients treated in Eye Hospital of Wenzhou, patients with complete clinical data, and patients willing to cooperate with the physicians. Exclusion criteria were: patients combined with other eye diseases, patients with cardiovascular and cerebrovascular diseases, patients with upper respiratory tract diseases, patients with lower gastrointestinal diseases, patients with a disability, patients transferred to another hospital halfway, and patients treated with drugs not recommended by the hospital.

All the patients signed informed consent. The study was approved by the Ethics Committee of the Eye Hospital of Wenzhou Medical University.

Methods. The patients were diagnosed as VK in the hospital, and were treated with eye drops. Patients in group A were treated with houttuynia eye drops (Sichuan Shenghe Pharmaceutical Co., Ltd., Sichuan, China), one drop each time, and 6 times daily. Patients in group B were treated with olopatadine hydrochloride eye drops (Alcon Laboratories, Inc., Fort Worth, TX, USA), one drop each time, and twice daily. Patients in group C were treated with houttuynia and olopatadine hydrochloride eye drops. The use of two eye drops was separated by >10 min. All patients were continuously treated for 14 days. Changes of eye symptoms before and after treatment, the relief of eye symptoms 30 min after drug treatment, and eye symptoms at 7th and 14th days after treatment were compared among groups to evaluate the therapeutic effect.

Evaluation criteria. Patients with no pain in the eyes, no itching, no conjunctival hyperemia, no secretions and no follicles were evaluated as excellent. Patients with press pain in eyes, relieved itching and conjunctival hyperemia, reduced secretions, and reduced number of follicles were evaluated as patients with good outcomes. Patients with eye tingling and itching, and without improvement in conjunctival hyperemia, secretions and follicular conditions were evaluated as patients with ineffective treatment outcomes. Total effective rate is the proportion of patients with excellent and good outcomes to all patients.

Statistical analysis. SPSS22.0 statistical software (IBM Corp., Armonk, NY, USA) was used. All data were expressed as rate and processed by Chi-square test. P<0.05 was considered to indicate a statistically significant difference.

Results

Comparison of clinical data among groups. There was no significant difference in the incidence of eyes, sex, age, season of onset, exercise habit, residence, ethnicity, weight and single child in the family among the three groups of patients (Table I).

Comparison of treatment outcomes at 1 h after drug administration. At 1 h after drug administration, excellent rate was highest in group C, and followed by group A, and good outcome rate of group C was significantly higher than that in the other two groups (P<0.05). Total effective rate was also significantly higher in group C than in the other two groups (P<0.05), while no significant differences were found between group A and B (P>0.05) (Table II).

Table I. Comparison of clinical data among three groups of patients (n, %).

Variables	Group A (n=276)	Group B (n=305)	Group C (n=345)	χ^2	P-value
Affected eyes				2.55	0.425
Single eye	121 (43.8)	184 (60.3)	119 (34.5)		
Both eyes	155 (56.2)	121 (39.7)	226 (65.5)		
Sex				2.25	0.316
Male	171 (62.0)	191 (62.0)	225 (65.2)		
Female	105 (38.0)	114 (38.0)	120 (34.8)		
Age (years)				3.05	0.267
<10	157 (56.9)	172 (56.4)	194 (56.2)		
≥10	119 (43.1)	133 (43.6)	151 (43.8)		
Exercise habit				3.07	0.275
Yes	166 (60.1)	183 (60.0)	198 (57.4)		
No	110 (39.9)	122 (40.0)	147 (42.6)		
Resident				3.56	0.381
Urban area	182 (65.9)	204 (66.9)	211 (61.2)		
Countryside	94 (34.1)	101 (33.1)	134 (38.8)		
Ethnicity				2.14	0.482
Han	265 (96.0)	296 (97.0)	340 (98.6)		
Minor races	11 (4.0)	9 (3.0)	5 (1.4)		
Weight (kg)				3.17	0.298
<40	143 (51.8)	161 (52.8)	187 (54.2)		
≥40	133 (48.2)	144 (47.2)	158 (45.8)		
Single child in the family				2.25	0.462
Yes	177 (64.1)	196 (64.3)	200 (58.0)		
No	99 (35.9)	109 (35.7)	145 (42.0)		

Table II. Comparison of treatment outcomes at 1 h after drug administration.

	Excellent	Good	Ineffective	Total effective rate (%)
Group A (n=276)	18 (6.52)	75 (27.17)	183 (66.31)	33.69
Group B (n=305)	10 (3.28)	79 (25.90)	216 (70.82)	29.18
Group C (n=345)	47 (13.62)	127 (36.81)	171 (49.57)	50.43
χ^2	14.51	12.54	11.01	14.68
P-value	0.028	0.041	0.045	0.025

Comparison of treatment outcomes at 7 days after drug administration. At 7 days after drug administration, excellent rate was higher in group C than in group A and B (P<0.05), and good outcome rate of group C was also significantly higher than that in the other two groups (P>0.05). In addition, total effective rate was significantly higher in group C than in

Table III Comparison of treatment outcomes at 7 days after drug administration (n, %).

	Excellent	Good	Ineffective	Total effective rate (%)
Group A (n=276)	120 (43.48)	84 (30.43)	72 (26.09)	73.91
Group B (n=305)	155 (50.82)	76 (24.92)	74 (24.26)	75.73
Group C (n=345)	218 (63.19)	115 (33.33)	12 (3.48)	96.52
χ^2	13.28	11.67	15.27	14.79
P-value	0.033	0.057	0.018	0.022

Table IV. Comparison of treatment outcomes at 14 days after drug administration.

	Excellent	Good	Ineffective	Total effective rate (%)
Group A (n=276)	181 (65.58)	77 (27.90)	18 (6.52)	93.48
Group B (n=305)	206 (67.54)	82 (26.89)	17 (5.57)	94.43
Group C (n=345)	306 (88.70)	37 (10.72)	2 (0.58)	98.18
χ^2	14.68	14.21	15.02	11.19
P-value	0.025	0.027	0.021	0.058

group A and B (P<0.05), while no significant differences were found between group A and B (P>0.05) (Table III).

Comparison of treatment outcomes at 14 days after drug administration. At 14 days after drug administration, excellent rate was significantly higher in group C than in group A and B (P<0.05), and good outcome rate and ineffective rate of group C was the lowest (P<0.05), while no significant differences were found between group A and B (P>0.05). No significant differences in total effective rate were found among three groups (P>0.05) (Table IV).

Discussion

VK is a common retinal disease in ophthalmology, and is usually caused by bacterial infections (9). Common pathogens include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Influenza bacillus* and *Haemophilus* conjunctivitis. Therefore, the main treatment is antibiotic eye drops (10). Rifampicin, tetracycline and chloramphenicol are commonly used in clinical treatment. However, due to the limited antibacterial spectrum and increased resistance in patients, traditional antimicrobial drugs fail to meet the requirements in treatment of VK (11). With strong antibacterial activities, olopatadine hydrochloride has been widely used in clinical treatment of VK (12). Olopatadine hydrochloride has a strong bactericidal activity against Gram-positive bacteria, and as the newest antibiotic drug, resistance in patients is low, so curative effect is satisfactory (13). As a traditional Chinese medicine with strong bactericidal and anti-inflammatory effects, houttuynia has been widely used in clinical treatment of various diseases (14). Houttuynia had strong inhibitory effects on yeasts and molds, and its inhibitory effects on *Staphylococcus aureus*, hemolytic *Streptococcus* and pneumococcus are satisfactory, and it can also promote tissue regeneration and wound healing (15). Houttuynia eye drops are widely used in the clinical treatment of VK (16). In this study, treatment efficacies of houttuynia eye drops, olopatadine hydrochloride eye drops and the combination of two eye drops in the treatment of VK were compared with an expectation of providing references for the treatment of VK.

Comparison of treatment efficacies at 1 h, 7 days and 14 days after treatment showed that houttuynia eye drops combined with olopatadine hydrochloride eye drops achieved better treatment outcomes than single-drug treatment. Both single treatment and combination therapy achieved satisfactory therapeutic effect at 14 days after treatment, while treatment cycle of combination therapy was shorter, and effective rate achieved 96.52% at 7 days after treatment. Effective rate of houttuynia eye drops and olopatadine hydrochloride eye drops at 7 days after treatment was only 73.91 and 75.73%, respectively. The reason for this is that binding of VK to the IgE receptor on surface of the cell conjunctiva can cause the release of the original cytochemical mediator (histamine) and the newly formed mediators (leukotrienes and prostaglandins), and intracellular H1 and H2 in this case bind to each other, resulting in increased permeability of the conjunctival blood vessels in order to trigger an inflammatory response, eventually leading to VK conjunctival vascular congestion, expansion, eye itching and eye tingling and other symptoms (17,18). Olopatadine hydrochloride has a strong inhibitory effect on selective H1 receptor, which can prevent the release of edematous medium from mast cells in blood vessels to directly prevent H1 receptor-induced inflammation phenomenon from inside the cell (19). Houttuynia yellow oil has a very strong bactericidal ability. Kim *et al* (20) reported that Houttuynin can significantly inhibit croton oil and xylene-induced mouse ear swelling and increased skin capillary permeability. Consistent results were found in this study. Excellent rate was significantly higher in patients treated with combination therapy than in other patients. In addition, treatment cycle of combination therapy was also shorter than single-drug treatment.

In this study, treatment efficacies of houttuynia eye drops, olopatadine hydrochloride eye drops and the combination thereof were compared to identify the optimal treatment program for VK. However, evaluation criteria used in this study can be refined to obtain more reliable results. In addition, all patients in this study are young Asian, and effects of ethnicity and age cannot be ignored.

In conclusion, both houttuynia and olopatadine hydrochloride eye drops achieve satisfactory efficacy in the treatment of VK. However, the combination therapy shortened treatment cycle. So, this combination therapy should be popularized in clinical treatment of VK.

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Availability of data and materials

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

Authors' contributions

XX and YC were responsible for screening and analysis of patient data. XX wrote the manuscript. Both authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Eye Hospital of Wenzhou Medical University (Wenzhou, China). Signed informed consent was obtained from the patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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