

Research progress in Chinese and Western medicine for the treatment of Vernal keratoconjunctivitis

Jingxun Guo^{1, a}, Cong Ren^{2, b} and Bin Guo^{2, c, *}

¹ School of optometry and ophthalmology, Shandong University of Traditional Chinese Medicine, Shandong 250014, China;

² Shandong University of Traditional Chinese Medicine, Shandong 250014, China.

^a excuseguo@163.com, ^b rencong2012@yeat.net, ^c guobin00002@126.com

*Correspondence Author

Abstract. Vernal keratoconjunctivitis (VKC) is a form of allergic conjunctivitis, also known as spring ophthalmia because of its recurrent and cyclical nature, which occurs in spring and summer. The main symptoms are ocular itching, photophobia and tearing, discharge, and foreign body sensation, and physical signs include flattened and thickened lid conjunctiva with pavement-like papillae, and gum-like thickening of the corneal rim of the upper lid (Horner-Trantas nodule). The pathogenesis of VKC is not yet fully understood and remains controversial. There are currently many treatment options for VKC, with the mainstream treatments being Western medicine and Chinese medicine, but with varying efficacy and individual differences. The author reviews the progress of research in the treatment of VKC with Chinese and Western medicine.

Keywords: Vernal keratoconjunctivitis; Combined Chinese and Western Medicine Treatment; Research progress.

1. Epidemiology of Vernal keratoconjunctivitis

There is a lack of uniform standards on the prevalence of VKC in China, as well as updated national VKC data with sampling considering regional representation and multi-center collaboration. An epidemiological study by Li Ying et al. [1]. on 6179 cases of allergic conjunctivitis in different regions of China showed that the prevalence of VKC was 10.5%, with the majority of the population distributed in central China. In contrast, an epidemiological study by Yuan Jiaqin et al. [2]. on VKC in the northwest of China showed that dry climate, strong sunshine, sandy winds, large temperature differences, and high altitude were important influencing factors for the high prevalence of VKC, and confirmed the idea with similar characteristics of the Mediterranean coast, Egypt and Israel. It is thus known that the prevalence of VKC varies from one geographical area to another in the country.

The prevalence of VKC has not yet been fully and accurately assessed in foreign studies. Leonardi A. et al. [3]. A study of 406 patients with VKC showed that VKC is more common in children and adolescents and less common in adults. Tesse Riccardina et al. [4]. A study of 197 children with VKC in Italy showed a prevalence of 2.4 to 27.8% and the estimated prevalence of VKC in Western Europe is 3.2 per 10,000 [5].

This may be due to differences in survey methodology, target population, customary environment, and geographical location, but it is still clear that VKC is a difficult eye disease with a high clinical incidence.

2. Modern medical understanding of Vernal keratoconjunctivitis

2.1 Etiology and pathogenesis

VKC is traditionally considered to be a form of allergic conjunctivitis in which IgE-mediated hypersensitivity reactions play a major role in the pathogenesis of VKC, and the pathogenic role of IgE-mediated allergic reactions to environmental factors in VKC is supported in the study by Sacchetti Marta et al. [6]. Bonini S. et al. [7]. Clinical evidence suggests that cellular allergic reactions

are also involved in the pathogenesis of VKC. However, approximately 50% of patients with VKC have negative allergy tests, suggesting that other pathogenic mechanisms are involved in the development and severity of VKC [8]. Furthermore, it has been shown that VKC, unlike other allergic conjunctivitis, is involved in a late inflammatory response [9]. Therefore, it has been suggested that interactions between conjunctival epithelial heat shock protein (Hsp) chaperones and the immune system may influence the progression of VKC. The demographic and geographic characteristics of VKC suggest that both genetic and environmental factors may contribute to the mechanisms of VKC pathogenesis. Few candidate atopic genes have been identified, such as Zicari, A.M. et al. [10]. An Italian study of 32 children with VKC reported an association between VKC and HLA class II alleles. In contrast, a study by Nebbioso, M. et al. [11]. on the association between sex and prevalence of VKC showed a higher prevalence of VKC in boys, with a male to female ratio of 4:1 to 2:1 and spontaneous recovery after puberty, suggesting a role for sex hormones in the development of VKC. Nebbioso, M. et al. [12]. also suggested a potential role for thyroid hormones in the pathogenesis of VKC.

Overall, the exact etiology of VKC has not been fully elucidated and includes a lymphocytic T helper type 2 response, a late allergic reaction with eosinophil infiltration, and extracellular matrix remodeling. In addition, the demographic, geographic, and clinical features of VKC suggest that other endocrine, environmental and genetic factors may play a role in the pathogenesis of this difficult eye disease.

2.2 Western medicine treatment

The current mainstream treatment for VKC is divided into pharmacological and surgical treatments. Pharmacological treatments mainly include antihistamines, mast cell stabilizers, dual-action anti-allergic drugs, glucocorticoids, non-steroidal anti-inflammatory drugs, artificial tears, and immunosuppressive drugs. Other treatments such as oral aspirin and surgical treatment are available.

2.2.1 Drug treatment

Tobramycin dexamethasone eye drops are commonly used in clinical practice for the treatment of VKC [13]., Xiang Qin et al. [14]. gave tobramycin dexamethasone eye drops to 27 patients with VKC in the control group and tacrolimus eye drops to 28 patients with VKC in the treatment group, indicating that the use of tacrolimus eye drops was more effective than tobramycin dexamethasone eye drops in the treatment of VKC. Jiang Zhidong et al. [15]. studied 92 patients with VKC and showed that the efficacy of using Orotadine hydrochloride eye drops in combination with tobramycin dexamethasone eye drops was significantly higher (89.1%) than that of the control group (67.1%) in a controlled trial study. In addition, the study by Zhang Qian et al. [16]. using Nassuta eye drops in combination with Olopatadine Hydrochloride eye drops had a more consistent treatment effect and is considered to be clinically relevant.

2.2.2 Surgical treatment

Surgical treatment of VKC is generally used in patients with VKC who have failed to respond to pharmacological treatment. Jiang Dongling et al. [17]. treated with bulbar conjunctival excision of the lesioned area of the corneal limbus combined with amniotic membrane transplantation. Belfair N et al. [18]. used CO2 laser to excise severe VKC conjunctival papillae, which can be used repeatedly for relapsing patients. Man Tanaka et al. [19]. used papillotomy and mitomycin C (MMC) wet compresses and VKC patients showed significant improvement in symptoms. In addition, papillotomy combined with autologous homologous free conjunctival grafts has also been shown to be effective [20].

3. Chinese medicine's understanding of Vernal keratoconjunctivitis

3.1 Pathogenesis

VKC is known in Chinese medicine as "Time-repeat syndrome" and is named after the book "Standards of Diagnosis and Treatment". It attacks in spring and summer, relieves in autumn and winter, and is prolonged and unrelenting, causing distress to the patient's normal life [21]. It is recorded in "Zhang's Clear View of Medicine" which is an unbearable itch, and all suffer from itchy extremes. In the book "Ophthalmic highlights", it is said that "it is self-healing without treatment, but it will occur at a later date, and then again at a later date, and if it is left untreated for a long time, it will become harmful". The "Complete Book of Eye Diseases" says: "If we say that the disease recurs at times, it will come at the end of every year. It is not to say that there will be no future problems, but it will eventually become a disaster." Both point to the clinical features of VKC. According to Bao Xi et al. [22], the onset of VKC is "often due to new sensations, as the new evil leads to the voodoo evil". According to Hong Liang et al. [23], VKC patients suffer from the disease due to the invasion of evil influence caused by the deficiency of energy and blood, and the internal ambush of evil influence in time, which causes the disease in spring and summer.

3.2 Chinese Medicine Treatment

3.2.1 Internal treatment

The treatment of VKC in TCM advocates a combination of internal and external treatment. Zhuang Zengyuan et al. [24]. used the empirical formula Qingjie mixture plus or minus, and used specific prescriptions for specific diseases with better results. Liu Futian et al. [25]. A study of 30 patients with VKC treated with Huanglian Qingxin Decoction plus and minus showed that the total effective rate was 86.67%. Feng Fei et al. [26]. gave topical 0.1% olopatadine hydrochloride eye drops to the control group, while the observation group was treated with TCM dialectic therapy, including "damp-heat with the wind" with the addition and subtraction of Dehumidification Decoction, "wind-heat from external sensation" with the addition and subtraction of Xiaofeng powder, and "blood deficiency generates wind For "Blood deficiency generates wind", Siwu Decoction was used as an addition and subtraction. Among them, the experimental observation group (95%) was significantly higher than the control group (75%), indicating that the efficacy of dialectical treatment for VKC is obvious and worth promoting.

3.2.2 External treatment methods

In the Medical origin theory, it is stated that "the method of surgery places the greatest emphasis on external treatment". Yang Ying et al. [27]. used 17 cases of VKC patients as observation subjects, and made acupuncture point patches by mixing traditional Chinese medicine into powder and ginger juice, and the total effective rate of treatment was 70.6%. Hong Liang et al. [28]. treated VKC with acupuncture points on the face using the method of moderate reinforcing and reducing, and poured the empirical formula of anti-itch decoction into an ultrasonic nebulizer to treat VKC with ultrasonic nebulization of Chinese herbs, both of which had certain efficacy.

4. Integrating Chinese and Western medicine in the management of Vernal keratoconjunctivitis

Zhang Zhongmei [29]. points out that the use of combined Chinese and Western medicine is reliable in the treatment of VKC, which can reduce recurrence and shorten the course of the disease. It is also of high clinical application and research value because of its low adverse effects and systemic conditioning. A controlled trial study by Chen Hongyan [30]. showed that VKC patients treated with a combination of Chinese and Western medicine (96.9%) were significantly more effective than those treated with Western medicine alone (75%), and the recurrence rate in the observation group (6.2%) was significantly lower than that in the control group (28.6%). Zhong Zeqin [31]. used a combination

of internal administration of Siwu Decoction with addition and reduction and external cleansing of the vast majority of Chongming Decoction (100%), which was more effective than using Segansuanna Diyanye eye drops (91.2%). In addition, a study by Wang Haiyan et al. [32]. also confirmed that the combination of Chinese and Western medicine was more effective in treating VKC than Western medicine or Chinese medicine alone, making the combination of Chinese and Western medicine an ideal treatment for VKC and a popular trend for the future mainstream treatment of VKC.

5. Summary

In summary, despite the increasing understanding of the causative mechanisms and clinical manifestations of VKC, several aspects of this challenging eye disease remain controversial and require further research. In clinical practice, both purely Western and Chinese therapies are inadequate in controlling the recurrence rate and improving the prognosis of VKC. The use of a combination of Chinese and Western medicine in the treatment of VKC has shown significant efficacy in shortening the course of the disease, reducing the incidence, decreasing discomfort, and improving the prognosis, and is worthy of clinical promotion.

Acknowledgements

Shandong University of Traditional Chinese Medicine Postdoctoral Programs, Supported by China Postdoctoral Science Foundation (No. 2020M672127).

References

- [1] LI Ying, ZHANG Xiao, LU Lan, et al. Epidemiology of allergic conjunctivitis and preliminary results of open multicenter treatment with olopatadine eye drops [J]. *Ophthalmology*, 2008(03):166-170.
- [2] YUAN Jiaqin, QI Mingxin, QU Zhankui, et al. Epidemiological study of keratoconjunctivitis in northwest China in spring[J]. *Chinese Journal of Ophthalmology*, 1986(01):43-45.
- [3] Leonardi A., Busca F., Motterle L., et al. Demographic and epidemiological study of 406 patients with springtime keratoconjunctivitis[J]. *World core medical journal abstracts. Ophthalmology*, 2006(09):57-58.
- [4] Tesse Riccardina et al. Treatment of severe vernal keratoconjunctivitis with 1% topical cyclosporine in an Italian cohort of 197 children. [J]. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology*, 2010, 21(2 Pt 1) : 330-5.
- [5] Bonini, S., Coassin, M., Aronni, S., et al. Vernal keratoconjunctivitis. *Eye* 2004, 18, 345-351.
- [6] Sacchetti Marta et al. Understanding Vernal Keratoconjunctivitis: Beyond Allergic Mechanisms[J]. *Life*, 2021, 11(10) : 1012-1012.
- [7] Bonini, S., Coassin, M., Aronni, S. et al. Vernal keratoconjunctivitis. *Eye* 2004, 18, 345-351.
- [8] Bonini, S. IgE and non-IgE mechanisms in ocular allergy. *Ann. Allergy* 1993, 71, 296-299.
- [9] Bonini, S.; Ghinelli, E. The early and late phase of the ocular allergic reaction. *Acta Ophthalmol. Scand.* 2000, 230, 41.
- [10] Zicari, A.M., Mora, B., Lollobrigida, V. et al. Immunogenetic investigation in vernal keratoconjunctivitis. *Pediatr. Allergy Immunol.* 2014, 25, 508-510.
- [11] Nebbioso, M., Zicari, A.M., Celani, C., et al. Pathogenesis of Vernal Keratoconjunctivitis and Associated Factors. *Semin. Ophthalmol.* 2015, 30, 340-344.
- [12] Zicari, A. M., Nebbioso, M., Lollobrigida, V., et al. Vernal keratoconjunctivitis: Atopy and autoimmunity. *Eur. Rev. Med. Pharmacol. Sci.* 2013, 17, 1419-1423.
- [13] Wei RZ, Li YX. Clinical treatment experience of catarrhal conjunctivitis[J]. *Chinese and foreign medical research*, 2011, 9(32):46-47. DOI:10.14033/j.cnki.cfmr.2011.32.123.

- [14] Xiang Q, Pi LIAN H, Liu X, et al. Comparison of the effect of clomox eye drops and tobramycin dexamethasone eye drops in the treatment of keratoconjunctivitis in spring[J]. Contemporary Medicine Series, 2018, 16(11): 35-37.
- [15] JIANG Zhidong, ZHANG Jing, XU Li. Comparative efficacy of olopatadine hydrochloride eye drops alone and combined with tobramycin dexamethasone eye drops in the treatment of spring keratoconjunctivitis[J]. Jilin Medicine, 2019, 40(08): 1790-1791.
- [16] Zhang Qian, Yi Yunmin, Zou Shipeng. Overview of Chinese medicine treatment of khat conjunctivitis in spring[J]. Practical Integrative Chinese and Western Medicine Clinics, 2019, 19(04): 180-182.
- [17] JIANG Dongling, ZHANG Mingchang, HU Yanhua. Clinical analysis of surgical treatment of giant papillae in keratoconjunctivitis in spring [J]. Chinese Journal of Ophthalmology, 2007(01): 14-17.
- [18] Belfair N, Monos T, Levy J, et al. Removal of giant vernal papillae by C0 2 laser. Can J Ophthalmol, 2005, 40:47
- [19] Man Tanaka, Yoji Takano, et al. Comparative evaluation of the efficacy of intraoperative mitomycin C use after the excision of cobblestone- like papillae in severe atopic and vernal keratoconjunctivitis. Cornea, 2004,23: :326-329
- [20] M. Cristina Nishiwaki-Dantas, P aulo Elias C Dantas, Simone Pezzut-t i, et al. Surgical Resection of Giant Pap illae and Autologous Con-junctival Gra ft in Patients With Severe Vernal Kerat oconjunctivitis and Giant Papillae. Oph thalmic Plastic and Reconstructive Surgery, 2000,16:438442.
- [21] Zhang Zhongmei. Observation on the effect of combining Chinese and Western medicine in the treatment of spring khat conjunctivitis[J]. Chinese community physician, 2017, 33(30): 92-93.
- [22] Bao Xie, Wen Chengping. Exploration of He Lianchen's doctrine of volatile temperature disease[J]. Zhejiang Journal of Traditional Chinese Medicine,2014,49(06): 391-393. DOI: 10.13633/j.cnki. zjtcn. 2014.06.003.
- [23] Luo JY, Hong L. Professor Hong Liang's experience in treating spring khat conjunctivitis[J]. Guangming TCM, 2019, 34(15): 2304-2306.
- [24] Zhuang Zeng Yuan, Zhang Hong. Zhuang Zeng Yuan practical ophthalmology in Chinese medicine [M]. Beijing: China Chinese Medicine Press, 2014; 115-116.
- [25] Liu F-T, Li Y-J. Treatment of 30 cases of spring conjunctivitis with Huang Lian Qing Xin Tang[J]. Chinese folk remedies,2014,22(08):47.DOI:10.19621/j.cnki.11-3555/r.2014.08.042.
- [26] Feng Fei. Clinical efficacy of Chinese medicine dialectical treatment of spring conjunctivitis[J]. Electronic Journal of Clinical Medicine Literature, 2019, 6(A1): 180-181.
- [27] Yang Ying, Chen Bing. The efficacy of acupuncture point application in the treatment of spring conjunctivitis in 17 cases[J]. Yunnan Journal of Traditional Chinese Medicine, 2011, 32(07):60. DOI: 10.16254/j.cnki.53-1120/r. 2011.07.028.
- [28] Luo JY, Hong L. Professor Hong Liang's experience in treating spring khat conjunctivitis[J]. Guangming TCM,2019,34(15):2304-2306.
- [29] Zhang Zhongmei. Observation on the effect of combining Chinese and Western medicine in the treatment of spring khat conjunctivitis[J]. Chinese community physician, 2017, 33(30): 92-93.
- [30] Chen Hongyan. Observation on the effect of combining Chinese and Western medicine in the treatment of spring khat conjunctivitis[J]. Qinghai Journal of Medicine, 2019, 49(07): 58-59.
- [31] Zhong Zeqin. Observation of 68 cases of spring khat conjunctivitis treated with combined traditional Chinese and Western medicine[J]. Journal of Practical Chinese Medicine, 2013, 29(05): 357-358.
- [32] WANG Haiyan, TANG Yangming. Clinical observation of 73 cases of spring catarrhal conjunctivitis treated with combined traditional Chinese and Western medicine[J]. Jiangsu Traditional Chinese Medicine, 2011, 43(02): 49-50.