

# To Explore the Real World Research Status of Traditional Chinese and Western Medicine in the Treatment of Dry Eye Disease

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**Abstract:** Dry eye disease (DED) is a chronic ocular surface disease caused by abnormal tear quality, quantity and dynamics, which can lead to tear film instability, ocular surface microenvironment imbalance, accompanied by inflammation, tissue damage and nerve abnormalities, causing eye discomfort and visual dysfunction [1]. The global prevalence rate is 5 % -50 %, and the incidence rate in China is 21 % -30 %, accounting for more than 30 % of ophthalmic clinics [2-3], and the disease burden is significant. Its etiology is complex, involving living habits, endocrine changes, psychological factors, environmental pollution, systemic diseases and drug effects [4]. Western medicine treatment is mainly based on symptomatic interventions such as artificial tears, anti-inflammatory drugs, and lacrimal duct embolization. Traditional Chinese medicine is based on syndrome differentiation and treatment, and multi-target regulation is achieved by oral administration of traditional Chinese medicine combined with acupuncture and other external treatments, which has the advantages of symptom relief and course delay. In recent years, real world study (RWS) has provided new ideas for the diagnosis and treatment of dry eye. The huge patient population in China has accumulated rich data for RWS, which can deeply analyze the disease mechanism, epidemiological characteristics and dynamic changes of treatment effect [5], and help to formulate individualized treatment plans. By integrating domestic and foreign research, this paper systematically reviews the real-world evidence of Chinese and Western medicine in the treatment of dry eye, aiming to provide more timely and evidence-based reference for clinical practice and promote the optimization of diagnosis and treatment strategies.

**Keywords:** Dry Eye Disease, Rreal World Study, Ophthalmic Diseases.

## 1. Research Progress of Modern Medicine on DED

DED is an ocular surface disease caused by many factors. It has been incorporated into the chronic disease management system. The core pathological features of DED are tear film instability and imbalance of ocular surface microenvironment, ranging from dry and burning eyes to impaired visual function [6]. The risk factors include gender, age, environmental exposure, ocular inflammation, drug use and ophthalmic surgery. Patients often induce anxiety and depression due to long-term discomfort, forming a vicious circle of symptom aggravation. Modern medical treatment methods include artificial tear replacement, anti-inflammatory drugs (such as cyclosporine), meibomian gland physiotherapy (massage, intense pulsed light), wet room mirror and surgical intervention (lacrimal point embolism), etc., but there are limitations: long-term use of artificial tears containing preservatives may damage the cornea; physical therapy compliance is affected by beauty or cost; the popularity of surgery is limited by the economic burden [7]. With the increasing dependence on electronic equipment, environmental pollution and changes in eye habits, the global prevalence of dry eye continues to rise and shows a younger trend, which has become the focus of attention in the field of public health [8]. Current research focuses on the development of long-term and safe tear substitutes, targeted anti-inflammatory therapy and precise diagnosis and treatment strategies to break through the bottleneck of traditional treatment.

## 2. The Understanding and Treatment of DED in Traditional Chinese Medicine

The understanding of dry eye in traditional Chinese medicine has a long history. It is believed that dry eye belongs to the category of 'white astringency', 'dry coma' and 'water will be withered'. Its common TCM disease name is 'white astringent disease', which first appeared in the ophthalmic monograph 'Examining Yaohan · white pain'. It describes its symptoms as: 'no swelling, no redness, no refreshing, no sand astringency and dimness', and points out that its pathogenesis is 'qi hidden, spleen and lung damp heat'. In the 'Plain Questions · Five-Zang Genesis Theory', there is a discussion of 'liver opening orifices in the eyes'. It is believed that the liver meridian is closely related to the eyes. If the liver blood is insufficient, the essence is lost, the eyes are lost, and the eyes are dry. The theory of 'the origin and symptoms of various diseases' discusses its pathogenesis as follows: 'There is body fluid in the five zang and six fu organs, and the tears are the eyes... If the fluid is exhausted, the eyes are apathetic. Lack of tears on the ocular surface is an important factor in the pathogenesis of DED. "Examining Yaohan · white astringent disease" is the hidden fire of qi, the spleen and lung collaterals are damp-heat, and it is more common in autumn. The black eye is located in the center of the anterior part of the eye, which is vulnerable to the invasion of wind, heat and toxin. Its surface layer is the barrier of external defense, and the invasion of external pathogens is the first. Because the lung governs the table, the black eye belongs to the liver, and the liver and kidney are homologous. Therefore, the occurrence

of this disease is related to the deficiency of essence, blood and body fluid in the lungs, liver, kidney and other organs. Yin deficiency with wind is the common cause of the disease. The liver opens to the eyes. When the liver yin is sufficient and the liver qi is adjusted, the tear secretion is normal, and the black eyes and white eyes are shiny and moist. Liver and kidney yin deficiency, liver yin deficiency, often lead to DED, less tears, is the cause of the disease, and the lung, spleen, kidney, heart dysfunction, can also affect the liver yin, induced the disease.

Summarize the etiology and pathogenesis of DED, involving qi, blood and body fluid, five zang-organs and six fu-organs, exterior and interior cold and heat, etc., but the loss of yin essence is the main basis of dry eye, and dry heat, external evil, spleen and stomach dampness and heat, liver and kidney loss are the main pathogenesis. Chinese medicine treatment is as follows:

(1) Internal treatment: Common clinical syndromes include: 1 Evil heat retention syndrome, which is treated with clearing heat and promoting lung. The prescription is modified Sangbaipi Decoction. If there is no dampness due to yin injury, Poria and Alisma can be removed from the prescription. 2 Lung and kidney yin deficiency syndrome, treated with clearing lung, nourishing yin and moistening dryness. The prescription is modified with Yangyin Qingfei Decoction. Pseudostellariae Radix and Schisandrae Chinensis Fructus can be added to the prescription to replenish qi and nourish yin. Exogenous dryness and evil plus Fangfeng, cicada slough, mint, and rhizome. Limb joint pain, flexion and extension of adverse, skin itching or erythema plus mulberry branch, cassia twig, clematis, honeysuckle vine, achyranthes. 3 Spleen and stomach damp heat syndrome, treated with heat and dampness, the application of Sanren Decoction. 4 Liver and kidney yin deficiency syndrome, treatment to tonify liver and kidney, nourishing yin and blood, to Qiju Dihuang Pill or Shihu Yeguanyang Pill addition and subtraction, if the dry mouth less Jin obvious, can add Schisandra, Scrophulariaceae, Radix Adenophorae and other nourishing yin and fluid [9].

(2) Local eye drops: Commonly used eye drops include pearl eye drops, bear bile eye drops, etc. Due to the toxic and side effects of preservatives in eye drops, there are certain limitations.

(3) Chinese medicine fumigation: some researchers have observed the clinical effect of Chinese medicine atomization in the treatment of dry eye [10], and found that after treatment, BUT, tear secretion, subjective symptom score and other aspects have obvious curative effect, and achieved good results.

(4) Acupuncture treatment: Acupuncture treatment of eye diseases has existed since ancient times. As early as in 'Lingshu · Febrile Disease Twenty-third', there was a record of 'red pain in the eyes, starting from the internal late, taking Yin burning'. Liu et al. [11] found that acupuncture at the corresponding acupoints can improve the symptoms of dryness, foreign body sensation and visual fatigue in patients with dry eye. The effect of acupuncture at the original point combined with artificial tears in the treatment of dry eye was significantly better than that of artificial tears alone [12].

(5) Acupoint injection: The drug (such as compound anisodine, methylcobalamin) is injected into the eyes of Cuanzhu, Taiyang and other acupoints, both drug penetration and acupoint stimulation effect, can promote tear secretion, repair corneal epithelial injury [13-14].

(6) Reyanbao: improve periorcular circulation by hot compress of traditional Chinese medicine, often combined with atomization or eye drops.

(7) Thunder-fire moxibustion: the use of Xin Wen efficacy and warm stimulation, dredge the eye meridians, clinical evidence can relieve symptoms and improve the quality of tear film [15-16].

### 3. Definition and Development of the Real World

The concept of RWS was first proposed by Kaplan in 1993. Its core is to evaluate the long-term effectiveness and safety of interventions based on patients' actual diagnosis and treatment choices and large sample data in a real medical environment [17-18]. Different from randomized controlled trials (RCT), RWS does not set strict inclusion and exclusion criteria, and is closer to the clinical practice scene, especially suitable for evaluating complex therapies such as syndrome differentiation and treatment of traditional Chinese medicine and individualized comprehensive intervention [19]. Since traditional Chinese medicine emphasizes the holistic view and dynamic adjustment, traditional RCT is difficult to fully reflect its therapeutic advantages, and RWS has become a key path to break through the bottleneck of research since it was introduced into the field of traditional Chinese medicine in 2010 [20]. In order to standardize RWS of traditional Chinese medicine, China has gradually established a technical standard system: the General Principles of Technical Specifications for Real World Research of Traditional Chinese Medicine was released in 2017 [21]. In 2019, China Real World Data and Research Alliance (ChinaREAL) launched a series of guidelines. In 2021, the Technical Specifications for Real World Research of Traditional Chinese Medicine further refined the five standards and promoted the standardization of research design and data processing [22-23]. However, the existing data collection still has problems such as scene limitations and insufficient objectivity. In 2023, scholars proposed to build a clinical information collection model that conforms to the characteristics of traditional Chinese medicine, and improve the quality of research by optimizing multi-source data integration [24]. The continuous development of RWS provides an important methodological support for the scientific verification and international promotion of the efficacy of traditional Chinese medicine.

### 4. The Application of the Real World in the Field of Traditional Chinese Medicine

With the development of evidence-based medicine, RCT have provided a scientific basis for the evaluation of the efficacy of traditional Chinese medicine, but its limitations have become increasingly prominent: the dynamic adjustment characteristics of individualized diagnosis and treatment of

traditional Chinese medicine, the lack of overall efficacy criteria and other issues, it is difficult to fully reflect the strict design of RCT [25]. RWS has become the key to solving this dilemma because of its inclusiveness and flexibility. The 'holistic concept' of traditional Chinese medicine focuses on the dynamic balance between the human body and the environment, and the broad clinical outcome indicators (such as quality of life, symptom improvement) concerned by RWS are highly consistent with it; the individualized scheme of 'syndrome differentiation and treatment' can be accurately evaluated by the design idea of non-random and broad inclusion criteria of RWS [26].

In recent years, RWS has shown significant application value in the field of traditional Chinese medicine. For example, in cancer treatment, RWS can dynamically evaluate the survival benefits of comprehensive therapies such as traditional Chinese medicine compound, acupuncture and moxibustion [27]; studies in the cardiovascular field have confirmed that the combination of traditional Chinese and Western medicine can improve the survival rate of patients with ischemic heart disease and reduce the risk of stroke [28]; the analysis of TCM syndromes of osteoporosis reveals the correlation between liver and kidney yin deficiency and solar terms and age [29]. In addition, traditional Chinese medicine has shown a prolonged survival effect in the adjuvant treatment of gastric cancer and liver cancer [30-31]. High colon dialysis combined with traditional Chinese medicine enema has been proved to improve the intestinal microenvironment of patients with chronic kidney disease [32]. These studies not only verify the advantages of multi-target intervention of traditional Chinese medicine, but also provide real-world evidence for the exploration of its therapeutic mechanism.

By integrating complex intervention data in clinical practice, RWS can not only objectively reflect the dynamic process of TCM syndrome differentiation and treatment, but also quantitatively evaluate its long-term efficacy and safety, and construct a scientific discourse system for the modernization and internationalization of TCM.

## 5. Application of RWS in the Field of Ophthalmology

By integrating multi-source data in real medical scenarios, RWS provides dynamic and multi-dimensional evidence support for the diagnosis and treatment of ophthalmic diseases, especially plays an important role in optimizing treatment plans, revealing disease associations, and promoting individualized medical care. The following describes its research progress in the field of major ophthalmic diseases:

1) Retinal disease: Based on RWS, the researchers observed the efficacy of different treatment regimens of ranibizumab in patients with macular edema due to branch retinal vein occlusion. It was found that the improvement of visual acuity and the decrease of central retinal thickness (CRT) after 5-needle + PRN treatment were significantly better than those after 3-needle + PRN. The thickness of CRT after 6-needle + PRN was higher than that after 5-needle + PRN [33]. Intravitreal injection of conbercept in the treatment of wet age-related macular degeneration (wAMD) RWS confirmed that it can effectively improve vision, improve macular

structure, and early intervention can delay disease progression [34]. Analysis of TCM syndromes showed that patients with proliferative diabetic retinopathy with qi and yin deficiency and collateral stasis syndrome had the best efficacy against VEGF combined with vitrectomy, highlighting the guiding value of syndrome differentiation for treatment selection [35].

2) Cataract: The study found that simple cataract surgery can reduce intraocular pressure, but the effect on patients with angle-closure glaucoma is limited [36]. The risk of cataract in patients with periodontitis is significantly increased, suggesting that systemic inflammation may affect lens metabolism through oxidative stress [37]. Chen Haiwei et al. [38] showed that AcrySof IQ PanOptix presbyopia-corrected aspheric trifocal intraocular lens can effectively improve the visual acuity, stereopsis, full-course visual acuity, reading ability and visual quality of patients after implantation of different types of cataract patients, and improve the quality of life of patients.

3) Glaucoma and ocular hypertension: Solish et al. [39] selected 55 patients with uncontrolled glaucoma or ocular hypertension for a retrospective study. One eye of these patients was dripped with bimatoprost once a day, and the contralateral eye was dripped with travoprost for 4-6 weeks, and then the patient and the doctor discussed and selected the drug of their own tendency. Both drugs can effectively reduce intraocular pressure in patients with uncontrolled glaucoma and high intraocular pressure, and there is no significant difference. However, in the trial, patients were more likely to choose than maprostanolol rather than travoprost, mainly due to the change of intraocular pressure. Tafluprost has shown stable efficacy and good tolerance in monotherapy and combination therapy, but more controlled studies are needed to verify its long-term advantages [40].

4) Some researchers have found that women are more likely to suffer from thyroid-associated ophthalmopathy (TAO) than men through RWS, and the high incidence age group is 30-50 years old. The frequency statistics of drug use show that the most commonly used drugs are *Prunella vulgaris*, *Buddleja officinalis*, *Poria cocos*, *Fritillaria thunbergii*, *Chrysanthemum morifolium*, etc. [41]. There is still a lack of recognized standards for diagnosis and treatment of traditional Chinese medicine in TAO, and there is a lack of systematic and in-depth large-sample research on clinical efficacy research. It is necessary for Chinese medicine workers to further explore and improve the understanding of thyroid-related ophthalmopathy.

5) GRM6 gene mutation was significantly associated with high myopia in Chinese Han population, while coastal and southern cities have higher rates of high myopia in adolescents due to differences in environment and eye habits. Spherical equivalent and other parameters can be used as early warning indicators [42-43].

6) Corneal diseases: Infectious keratitis is a disease that threatens vision, and may require corneal transplantation to control infection, visual rehabilitation, and maintain ocular integrity. Veugen et al. [44] found that viral keratitis was the most common transplant indication, followed by bacterial keratitis and *acanthamoeba* keratitis. There was no significant

difference in the survival rate between HLA-matched and non-HLA-matched surgery, while emergency surgery showed poor survival. The survival rate of graft size > 8.5 mm was significantly worse than that of 8.5 mm. Geerling et al. [45] found that cyclosporine A (csA) 0.1 % cationic emulsion (CE) could significantly reduce the symptoms and signs of dry eye in a prospective multicenter observational study of 44 ophthalmic clinics, which was significantly reduced in the 4th week and continued to the 12th month.

In general, RWS, such a large sample based on real world research, can not only better understand the current situation of diagnosis and treatment of common ophthalmic diseases in China, but also compare the effects and complications of various mainstream treatment schemes, so as to provide important scientific basis for improving the clinical decision-making of ophthalmology in China and improve the quality and efficiency of ophthalmic medical services [46].

## 6. Compatibility of Real-world and Clinical Studies of DED

Diquafosol (P2Y2 receptor agonist) has been shown to improve the symptoms of DED in short-term studies, but its long-term efficacy and safety need to be verified in the real world. Ohashi et al. [47] confirmed that 3 % diquafosole eye drops were well tolerated and sustained in 580 patients with long-term RWS. Pan et al. [48] found that the prevalence of dry eye in patients with polycystic ovary syndrome was high, and the amount of tear secretion decreased with the increase of age and estradiol level. However, the increase of testosterone level could prolong the tear film rupture time and relieve subjective symptoms, suggesting that there was a complex relationship between hormone level and dry eye pathology, and targeted intervention was needed. In addition, new therapies such as bio-resonant glasses are undergoing real-world studies, and their RWS for rhinitis treatment has shown significant improvement in symptoms and good safety [49], providing a potential direction for innovative treatment of DED.

## 7. Conclusion

In recent years, DED research has focused on innovative therapies and exploration of pathological mechanisms. Bioresonance glasses, ocular surface microecological regulation and gene therapy have become hot spots. RWS can accurately reveal the real incidence, course evolution and treatment response of dry eye through large-scale data in natural scenes, and provide evidence-based support for clinical decision-making. The combination of traditional Chinese and Western medicine has shown synergistic potential in RWS, such as the long-term efficacy verification of diquafosole eye drops, the correlation analysis of hormone levels and dry eye symptoms, but there are still research gaps. The current RWS faces multiple challenges: First, dry eye has a multi-dimensional pathological mechanism. Environmental exposure, genetic susceptibility, lifestyle and other factors are intertwined, and a complex causal relationship model needs to be established; secondly, the lack of international unified evaluation criteria (such as symptom scale, tear film stability test), resulting in limited comparability of research results; in addition, real-world data are often heterogeneous (such as

electronic medical records, mixed patient self-reported information), and high-quality data integration needs to be achieved with artificial intelligence and multi-omics technologies. In the future, it is necessary to promote the construction of standardized evaluation system and develop efficient data analysis tools to deepen the individualized diagnosis and treatment of dry eye and precise prevention strategies.

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