

TRADITIONAL CHINESE MEDICINE IN DRY EYE SYNDROME

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Abstract

In recent years, the prevalence of dry eye has been on the rise due to an ageing global population, increased usage of medication and environment irritants.

Current available treatments for dry eye include artificial eye drops, artificial tear ointment, vitamin A ointment, special eyewear, anti-autoimmunity drugs and lacrimal punctum occlusion. However, these treatments have limited effects. The development of dry eye treatments has been hampered by a limited understanding of the underlying pathophysiological processes.

Based on the clinical research trial data from recent years, there is strong evidence suggesting that Traditional Chinese Medicine (TCM) would provide an alternative treatment modality for the patients with dry eye syndrome and have its advantage measurements over the standard western clinical measurements when compare the treatments.

In this chapter, we aim to explore common TCM treatments available for dry eye syndrome, comprising herbal medicine, acupuncture or a combination of both methods.

Clinical trial data also strongly suggest that TCM provides an alternative mode of treatment for dry eye syndrome and is safer, more economical, and provides longer lasting effects.

Keywords: Clinical trial, Complementary medicine, Alternative medicine, Chinese medicine, dry eye, Acupuncture

1. Introduction

Dry eye syndrome is a lacrimal film abnormality caused by decreased lacrimal secretions, or hyperactive lacrimal evaporation.¹ The condition is presented with symptoms of discomfort in the eye which may accompany ocular surface diseases. If patients have isolated symptoms of dry eyes, they may recover with rest or short-term use of artificial tears.² If there is no ocular surface damage and/or any other local or systemic causes are present, it is termed 'simple dry eye'. If patients present both symptoms and clinical signs of dry eyes, it is termed 'dry eye syndrome'. With the increased usage of the computer and other IT gadgets in modern lifestyle, the incidence

of dry eyes has gradually increased while the average age of onset is much lower than before. Dry eye disease imposes a significant direct health care burden and even more so indirectly.³ Dry eye disease affects millions of people around the world with prevalence rates estimated to be as high as 35% in the general population.⁴

Traditional Chinese Medicine (TCM) is a holistic system of healthcare developed by the Chinese and has been practiced for thousands of years. The first record of TCM is dated back to 2000 years ago in the Yellow Emperor's Cannon of Internal Medicine (*Huang-di Nei Jing*). Over the years, Chinese medicine is developed from the foundations laid in the Yellow Emperor's Cannon of Internal Medicine, however the core values of TCM never deviated from it, that is, (1) holistic treatment: to look at a disease holistically and treat from the disease roots, while addressing the symptoms; (2) strengthening the body's resistance (*zheng qi* 正气) and dispelling pathogenic factors (*xie qi* 邪气), and (3) personalization of treatment based on environmental factors and individual constitution.

There are various modalities of treatment in TCM, including acupuncture, herbal remedies, massage (*tui na* 推拿), cupping, moxibustion, ear acupuncture and scraping (*guasha* 刮痧). The most commonly employed methods today are acupuncture, herbal remedies and massage, although massage is mostly used for relaxation than its healing functions today. Acupuncture is the insertion of needles into the skin or even the tongues and mucosal layer, based on the system of meridians and its connectivity to the various organs deep in the human body. A modification to the ancient technique of acupuncture is the development of electro stimulation, where needles are connected to weak pulses of electricity for increased stimulation of the acupoints. Herbal remedies are usually prescribed in the form of decoctions, although pills, pastes and baths are also available. Herbal remedies could be based on a single herb or a combination of a few or many, depending on the individual constitution, and modification of the remedies is commonly done. The principle of all modalities of treatment would be to eliminate pathogenic forces, while restoring the body's balance and strengthening it.

In Chinese medicine, the disease pertains to *bai se zheng* (白涩症, white dry eyes), or *shen shui jiang ku* (神水将枯, impending desiccation of spirit water), belonging to the category of *zao zheng* (燥症 dryness pattern).⁵ The causes are mostly attributed to lung yin insufficiency or liver and kidney yin deficiency, which lead to nutritional deficiency of the eyes.

2. Clinical Manifestation of Dry Eye Syndrome

Common ocular symptoms include asthenopia (eye strain), sensation of foreign bodies in the eyes, dryness, burning sensation, swelling, ophthalmalgia (pain in eye), photophobia, redness, etc. If these symptoms are presented, patients should be asked in detail on their history of dry eyes sensation in order to find the underlying causes. For patients who present with severe dry eyes, the clinician should check if their condition is accompanied by dry mouth or joint pain, as the dry eye symptoms could be an indication of Sjögren's Syndrome and require prompt treatment. Clinical signs of dry eye include vasodilatation, oedema, folding of bulbar conjunctiva, shortened tear meniscus height (TMH), and occasional mucopurulent discharge in the lower fornix and punctuate staining in corneal epithelium in the palpebral fissure area. When dry eye syndrome is suspected, relevant objective tests may be considered, including Schirmer's test and tear break up time (TBUT) test.⁶ Dry eyes may affect visual acuity in early stages, and further develop into filamentary keratitis. At later stages, if left untreated, dry eye syndrome may lead to corneal thinning, ulcers, and perforation, or, in some cases, a secondary bacterial infection.

3. Types of dry eye patterns in TCM

In most patients presenting with dry eye, their disease condition could be attributed to one or a combination of five main categories of 'disease pattern'. These disease patterns are identified as pathologies stemming from the 'organs', or the root of the disease, and usually present overlapping symptoms apart from dry eye. These patterns include insufficiency of lung *yin*, insufficiency of liver and kidney *yin*, and dry eye initiated by heat in various organs. These will be described in the sections below:

(1) Insufficiency of Lung Yin

Patients in this category often present with the following characteristics: Dry eyes that result in inability to see clearly over a long period, mild conjunctiva hyperemia, point lesions of the superficial corneal layer, relapses with poor recovery, dry cough with little phlegm, dry pharynx, constipation, reddish tongue with dry mouth and a thready rapid pulse.

The treatment in this case is to enrich yin and moisten the lung meridian. A representative formula is the *Yang Yin Qing Fei Tang* (Yin-Nourishing Lung-Clearing Decoction, 养阴清肺汤).⁷ Refer to Table 1 for the prescription. Please note that this prescription is often modified in 3 scenarios:

- For cases with pronounced dry throat and mouth, add *bei sha shen* (北沙参, Radix Glehniae) 15g, *shi hu* (石斛, Caulis Dendrobii) 10g to boost the *qi* and nourish the *yin*.
- For cases with constipation, add *jue ming zi* (决明子, Semen Cassiae) 15g to moisten the intestines and allow the stool to move down the rectum
- For cases with point lesions of the cornea, add *chan tui* (蝉蜕, Periostracum Cicadue) 6g, *ju hua* (菊花, Flos Chrysanthemi) 12g, *mi meng hua* (密蒙花, Flos Buddlejae) 10g to clear the heat, and brighten the eyes

牡丹皮	<i>mu dan pi</i>	10g	Cortex Moutan
白芍	<i>bai shao</i>	10g	Radix Paeoniae Alba
生甘草	<i>sheng gan cao</i>	10g	Radix et Rhizoma Glycyrrhizae
生地	<i>sheng di</i>	10g	Radix Rehmanniae
薄荷	<i>bo he</i>	6g	Herba Menthae
玄参	<i>xuan shen</i>	10g	Herba Scrophulariae
麦冬	<i>mai dong</i>	15g	Radix Ophiopogonis
贝母	<i>bei mu</i>	10g	Bulbus Fritillaria
太子参	<i>tai zi shen</i>	15g	Radix Pseudostellariae
五味子	<i>wu wei zi</i>	10g	Fructus Schisandrae Chinensis

Table 1. Prescription for *Yang Yin Qing Fei Tang*.

(2) Liver and Kidney Yin Deficiency

In this syndrome, dry eye is accompanied with symptoms of discomfort, photophobia, symptoms increased after prolonged use, dry mouth with scant saliva, lumbago, weak and/or painful knees, dizziness, tinnitus, insomnia with profuse dreams, red tongue with thin coating and a thready pulse.

The treatment principle is to nourish the liver and kidney meridians, and a representative formula is the *Modified Qi Ju Di Huang Wan* (Lycium Berry, Chrysanthemum and Rehmannia Pill, 杞菊地黄丸) (Table 2). In certain scenarios, this formulation can be modified:

- For cases with dry mouth, with scanty saliva, add *mai dong* (麦冬, Radix Ophiopogonis) 10g, *xuan shen* (玄参, Radix Scrophulariae) 10g to nourish the yin and engender the fluid.
- For cases with obvious conjunctival hyperaemia, add *sang bai pi* (桑百皮, Cortex Mori) 9g, *di gu pi* (地骨皮, Cortex Lycii) 10g to clear the heat and reduce congestion.

枸杞子	<i>gou qi zi</i>	15g	Fructus Lycii
菊花	<i>ju hua</i>	10g	Flos Chrysanthemi
熟地	<i>shu di</i>	10g	Radix Rehmanniae Praeparata
山茱萸	<i>shan zhu yu</i>	10g	Fructus Corni
山药	<i>shan yao</i>	10g	Rhizoma Dioscoreae
泽泻	<i>ze xie</i>	10g	Rhizoma Alismatis
茯苓	<i>fu ling</i>	10g	Poria
牡丹皮	<i>mu dan pi</i>	10g	Cortex Moutan

Table 2. Prescription for *Modified Qi Ju Di Huang Wan*.

(3) Dry eye initiated by wind and heat

This type of dry eye is caused by wind and heat, including xerosis conjunctiva, fulminant red eye with acute meiboma and conjunctival edema. The principle of treatment is to 'scatter' the wind and clear the heat. The representative formula is *Sang Ju Yin* 桑菊饮, or Mulberry Leaf and Chrysanthemum Beverage (Table 3).

桑叶	<i>sang ye</i>	9g	Folium Mori
菊花	<i>ju hua</i>	9g	Flos Chrysanthemi
连翘	<i>lian qiao</i>	9g	Fructus Forsythiae
桔梗	<i>jie geng</i>	9g	Rhizoma Phragmitis
杏仁	<i>xing ren</i>	9g	Semen Armeniacae Amarum
薄荷	<i>bo he</i>	6g	Herba Menthae
甘草	<i>gan cao</i>	3g	Radix et Rhizoma Glycyrrhizae
芦根	<i>lu gen</i>	15g	Rhizoma Phragmitis

Table 3. Formulation for *Mulberry Leaf and Chrysanthemum Beverage*.

(4) Dry eye initiated by heart-heat

This is dry eye initiated by overwork from prolonged use of computers, insufficient sleep or stress-induced insomnia, and usually presents with photophobia, eye strain, eye sore or pain, with red tongue tip and rapid pulse. In this scenario, the treatment principle is to clear the heart-heat from the heart meridian by promoting urination. A representative formulation to address this is *Dao Chi San* 导赤散 found in Table 4.

生地	<i>sheng di</i>	18g	Radix Rehmanniae
木通	<i>mu tong</i>	9g	Caulis Akebiae
淡竹叶	<i>dan zhu ye</i>	12g	Herba Lophatheri
山栀子	<i>zhi zi</i>	12g	Fructus Gardeniae
黄柏	<i>huang bai</i>	9g	Cortex Phellodendri Chinensis
知母	<i>zhi mu</i>	9g	Rhizoma Anemarrhenae
灯芯草	<i>deng xin cao</i>	6g	Medulla Junci
甘草	<i>gan cao</i>	6g	Herba Schizonepetae

Table 4. Treatment to reduce heat in the heart.

(5) Dry eye initiated by liver – heat

Heat can also be initiated by the liver. In this syndrome, dry eye is initiated by prolonged visual tasks, and the patients in this category are stressed and easily agitated or frustrated with dry eye with headache. He also suffers from pain in the side abdomens at times, has red tongue with white coat and a rapid thready pulse.

Here, the physician aims to clear the liver heat and dampness from the lower part of the body meridians. A formulation such as *Long Dan Xie Gan Tang* 龙胆泻肝汤 that in Table 5 can be employed.

龙胆草	<i>long dan cao</i>	12g	Radix et Rhizoma Gentianae
生地	<i>sheng di</i>	18g	Radix Rehmanniae
当归	<i>dang gui</i>	6g	Radix Angelicae Sinensis
柴胡	<i>chai hu</i>	6g	Radix Bupleuri
木通	<i>mu tong</i>	9g	Caulis Akebiae
泽泻	<i>ze xie</i>	9g	Rhizoma Alismatis
车前子	<i>che qian zi</i>	9g	Semen Plantaginis
山栀子	<i>zhi zi</i>	9g	Fructus Gardeniae
黄芩	<i>huang qin</i>	9g	Radix Scutellariae
甘草	<i>gan cao</i>	5g	Herba Schizonepetae

Table 5. Formulation for treatment of liver heat.

4. Acupuncture Treatment for dry eye

The history of using acupuncture treatment for dry eye is dated back to the Ancient Times – Northern and Southern Dynasties (581A.D). The Yellow Emperor's Inner Classic (*Huang Di Nei Jing*, 黄帝内经) had records of the anatomy and physiology of the eyes, as well as the etiology, pathology, clinical manifestation, and acupuncture strategies for eye disorders.⁷ More than 30 eye diseases were recorded in this book. In each typical treatment session, 4-6 acupoints were selected, needles retained for 20-30 minutes, and treatment was performed once every day. Ten treatments constitute one course of treatment⁷ (Table 6). Most studies conducted previously did not have proper control groups. Recently, investigators in Korea have conducted randomized controlled studies in acupuncture compared to sham acupuncture.⁸

ST1 (<i>cheng qi</i>) 承泣	太阳 (<i>tai yang</i>)	GB20 (<i>feng chi</i>) 风池
BL2 (<i>cuan zhu</i>) 攒竹	鱼腰 (<i>yu yao</i>)	SJ 23 (<i>si zhu kong</i>) 丝竹空
ST2 (<i>si bai</i>) 四白	LV3 (<i>tai chong</i>) 太冲	GB37 (<i>guang ming</i>) 光明
SP6 (<i>san yin jiao</i>) 三阴交	LI4 (<i>he gu</i>) 合谷	DU23 (<i>shang xing</i>) 上星
DU20 (<i>bai hui</i>) 百会		

Table 6. Acupuncture points for treatment of dry eye.

5. Chinese Patent Medicines

In western or clinical medicine, patients with dry eye may be given lubricants such as 1% sodium hyaluronate or carboxymethylcellulose eye drops used frequently daily. Patients with more severe or uncontrolled symptoms, may seek advice or treatment from an Ophthalmologist, who may initiate immunosuppressive, anti-inflammatory treatment, or punctum occlusion methods.

In contrast, TCM advocates the use of simple remedies comprising core herbs such as *ju hua* (菊花, Flos Chrysanthemi), *mai dong* (麦冬, Radix Ophiopogonis), *gou qi zi* (枸杞子, Fructus Lycii), *mu hu die* (木蝴蝶, Semen Oroxyli) which possess yin-nourishing properties. Depending on the condition and constitution of the patients, a selection of herbs are added (10g each) into a prescription and wrapped as a tea drink. Alternatively, they are brewed in a teapot with boiling water, and consumed 6-9 times in small amounts daily. Alternatively, Chinese physicians may choose one of these more standard therapies:

- (1) *Qi Ju Di Huang Wan* (Lycium Berry, Chrysanthemum and Rehmannia Pill, 杞菊地黄丸) 6 pills, twice daily; applicable to liver-kidney yin deficiency
- (2) *Zhi Bai Di Huang Wan* (Lycium Berry, Chrysanthemum and Redmannia Pill 知柏地黄丸) 6 pills, twice daily; applicable to liver-kidney yin deficiency or effulgent yin-deficiency

- *Yang Yin Qing Fei Kou Fu Ye* (Yin-Nourishing Lung-Clearing Oral Liquid 养阴清肺口服液) 10ml, twice daily, applicable to insufficiency of lung yin deficiency

6. Dietary Therapy and Preventive Measurements

Like in all types of medicine, Chinese medicine recognizes that environmental and dietary factors contribute to disease. Therefore, preventive measures and ways to adjust the environment that one is exposed to maybe just as helpful as therapeutic medications. Some of these measures include:

- Avoiding prolonged and excessive visual tasks. Patients are counseled that TV, computers and other IT gadgets should be placed in a position below eye level.
- Avoidance of air conditioning and dust, and measures to maintain a certain degree of humidity in the room.
- Adopting a positive attitude to life and have a happy outlook, paying particular attention to balanced and sufficient dietary components and maintaining a healthy eating habit including the consumption of fresh vegetables and fruits, while increasing vitamins A, B, C and E intake. The patients should be advised against over-consumption of spicy, greasy-fried, or fatty and processed foods.
- Regulation of the internal emotions and working on cultivating an optimistic mood; maintaining a proper balance between work and relaxation.

7. Clinical Trial in dry eye

Sometimes, Tradition Chinese Medicine physicians employ a mixture of acupuncture and oral therapies. Recently, randomized controlled studies in the use of TCM in dry eye have been published, with data that suggest TCM is useful in improving the disease condition.⁹⁻¹⁵ In a randomized placebo-controlled study, the group receiving *Chi-Ju-Di-Huang-Wan* medication had a significantly improved Rose-Bengal and fluorescein TBUT compared to placebo group at 2 and 4 weeks respectively.¹⁶ A Korean study showed that in TBUT in acupuncture group had improved TBUT (p not statistically significant) after 3 weeks.¹⁴ Finally, in one meta-analysis of 6 randomized controlled trials, the authors found that acupuncture significantly improved TBUT (p<0.0001), Schirmer test (p<0.00001) and cornea fluorescein staining (p=0.0001).¹¹

We have recently conducted clinical research involving *qi ju gan lu yin* and *qi ju gan lu yin* with acupuncture on the treatment of lung and kidney yin deficiency type of dry eye.¹⁸

In the study, we aimed to evaluate the efficacy of TCM herbal medicine "*qi ju gan lu yin*" in treating dry eye, compared to the same "*qi ju gan lu yin* with acupuncture" and a total of 89 age- and gender-matched subjects were recruited. This included 44 in Group 1, the TCM Herbal Medicine Group, and 45 in Group 2, the TCM Combined Methods Group. All participants had dry eyes as their main complaint and were aged 40-70 years old. All subjects had good general health, no ocular disease, non-smoking and were non-contact lens wearer. The inclusion criteria of dry eye subjects were a positive score in the SPEED Questionnaire (Standard Patient Evaluation for Eye Dryness Questionnaire). The study group (Group 1, TCM Herbal Medicine Group) of 44 patients were given *qi ju gan lu yin* orally and the control group (Group 2, TCM Combined Methods Group) of 45 patients were given *qi ju gan lu yin* combined with acupuncture twice a week. Both groups were treated for 30 days. Pre- and post-treatment

measurements of Schirmer's and TBUT test were obtained for the TCM Herbal Medicine Group (Group 1) and TCM Combined Methods Group (Group 2). For Schirmer's I test (mm/5 min) result in Group 1, $Z=-2.050$, $p=0.04$ (right eye); $Z=-0.030$, $p=0.976$ (left eye). In Group 2, the corresponding values in the right eye were $Z=-0.429$, $p=0.668$, and $Z=-1.526$, $p=0.127$ for left eye. For Tear Break-Up Time (TBUT), the values were $Z=-7.013$, $p<0.001$ (right eye) and $Z=-2.043$, $p<0.001$ (left eye) in Group 1 and $Z=-1.650$, $p=0.099$ (right eye), $Z=-1.985$, $p=0.047$ (left eye) in Group 2.

No significant differences were found in Schirmer's test readings between the two groups (Right eye $Z=-1.441$, $p=0.150$ and Left eye $Z=-1.072$, $p=0.284$). Significant differences were obtained for the TBUT between Group 1 and Group 2 at the post treatment visit: Right eye $Z=-4.290$, $p<0.001$ and Left eye $Z=-2.594$, $p=0.009$. Group 1 performed better than Group 2, where $Z=-7.013$, $p<0.001$ (right eye) and $Z=-2.043$, $p<0.001$ (left eye) for Group 1; was and $Z=-1.650$, $p=0.099$ (right eye) and $Z=-1.985$, $p=0.047$ (left eye) in Group 2. The total efficacy or % in improvement in SPEED was 54.4% for Group 1 and similar in Group 2 (53.3%). The SPEED improvement in group 1 was 3.58 ± 5.40 and Group 2 was 4.40 ± 7.82 . There was no significant difference between the two groups ($t=0.520$, $p=0.604$). The percentage improvement in the SANDE¹⁹ or Visual Analogue Score (VAS) in Group 1 and 2 was 61% and 55.5% respectively. VAS (Visual Analogue Score) improvement for Group 1 was 24.01 ± 23.99 and Group 2 was 22.70 ± 24.33 . The improvement between the 2 groups was not significantly different ($t=-0.252$, $p=0.802$).

In addition we found that the TCM lung and kidney yin deficiency score aggregates for Group 1 was 68.18% and for Group 2 was 71.11%. The TCM lung and kidney yin deficiency improvement in Group 1 was 3.76 ± 6.04 and Group 2 was 4.50 ± 5.81 . These were not significantly different between the two groups ($t=-0.205$, $p=0.838$).

The findings demonstrate the usefulness of TCM treatment in treating the commonly seen dry eye syndrome in Singapore. In this study, acupuncture does not demonstrate any additional therapeutic effect over and above herbal medication alone. In fact, for TBUT, Group 1 (TCM Herbal Medicine alone) has in fact shown a better result than the combined TCM methods. The result findings suggest that TCM herbal medicine may be used as an alternative medicine to treat dry eyes in Singapore.

8. General Conclusions

A previous study in Singapore has evaluated the knowledge, attitude and practice of TCM practitioners in treatment of dry eye.²⁰ This study shows that at least in institutional practice, the registered Chinese physicians were keen to participate in the treatment of dry eye. Although there has been randomized controlled studies in TCM in dry eye, the results are often controversial,¹⁷ and much larger studies are being planned and conducted.^{21, 22} Use of combined modalities of TCM may not necessarily be advantageous over a single modality, although the specific nature of the modality used may determine the outcome.

It seems that in Asian countries, the use of TCM is wide spread and prevalent. Increasingly, health care workers have realized the holistic nature of dry eye. As TCM deals holistically with patients' conditions, many dry eye patients are willing to be treated with TCM. In any case, the coordination of care of dry eye between TCM and western practitioners may be advantageous for many patients. We eagerly await the outcome of the major trials being conducted in this area.

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