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The Effect of Acupuncture and Chinese Herbal Medicine on Age-Related Macular Degeneration: Literature Review

by

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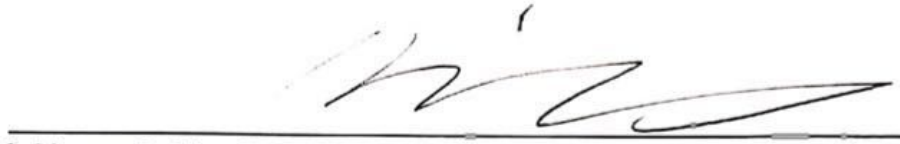

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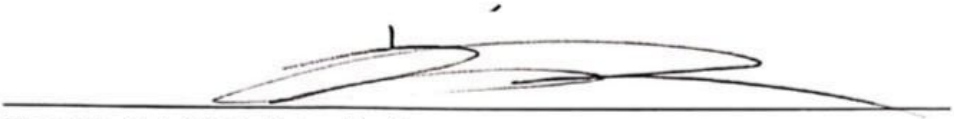

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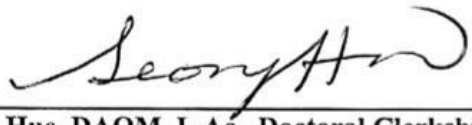

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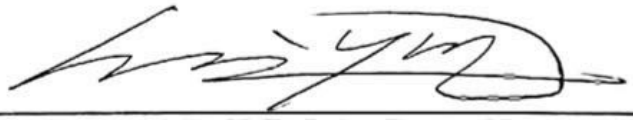

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Abstract

The purpose of this integrative literature review was to analyze the usage of acupuncture and Chinese herbal medicine on age-related macular degeneration and its effectiveness. Online published articles included with and without randomized control trials, case studies, and pilot studies. Animal tests were excluded. Electronic databases such as EBSCO, Medline, Cochrane, RISS, and Wanfang were used. A total of 13 works was selected.

For acupuncture treatment, eight articles indicated the following acupuncture points as the most prescribed locations: BL2, CV6, GB20, LI4, QIUHOU, ST1, SHANGJINGMING, and GB20. There was a consensus on the improvement of visual acuity (VA) in 7 out of 8 articles. However, only two articles had a significant change. One study had 52% of 75 subjects improve VA (P=0.012).

For Chinese herbal medicine treatment, five articles indicated the following decoctions to be effective on age-related macular degeneration: Zhujing pills, Yiqi Fuming tang, Huo Luo San Jie tang, Er Zhi tang, Huangban Fuming tang, Jia Jie Zi Yin Mingmu tang, Sanren tang, Sheng Pu Huang tang, Si Jun Zi tang, and Liu Wei Di Huang tang. Only 2 out of 5 studies had statistically significant results in the improvement of VA with the use of Zhujing pills and San Ren tang. The use of Zhujing pills improved 17 out of 20 controlled group subjects and their VA ($P<0.05$). Also, San Ren Tang had an 85% improvement rate among 40 subjects with a p-value of <0.05.

While there was an overall subjective improvement of an age-related macular degenerative condition, most cannot be substantiated and, therefore, need further comprehensive investigation with a larger sample size to determine the efficacy of acupuncture and Chinese herbal medicine on age-related macular degeneration.

TABLE OF CONTENTS

List of Figures and Tables

ACKNOWLEDGEMENT

Although my original intention was to conduct a case study on the topic, the current COVID 19 pandemic has deterred me from doing so. I would like to thank my family for the endless support and love. I would not have endured the program without their understanding. I would also like to thank my advisor, Dr. Jaejong Kim, for introducing me to the fascinating topic. Many thanks to Dr. Shanqin Cui for guiding and teaching me through MSAOM and DAOM programs. Also, I am greatful to have had Dr. Suhkyung Kim, Dr. Soo Kim, Dr. Seong Hwa Hue, and Dr. Joseph Suh for leading me through years of TCM training. Finally, a million thanks to my wife for taking every step of the way together.

In memory of my grandfather and Professor Joo.

學而不思則罔 思而不學則殆

[論語] 為政編

I. Introduction

Age-related macular degeneration (AMD) is one of the most common ocular diseases that result in partial to a full loss of central vision in older generations (Wei, 2011). There are two types of macular degeneration: dry and wet. While 90% of the patients suffering from AMD have the dry type in the US, roughly 10% of the people have a wet type. Most of the affected people are Caucasian, followed by black and Hispanic (Alfaro III et al., 2015). Women are also more prone to disease than men (Mahave et al., 2015). According to the 2019 statistics by the National Eye Institute, the population with AMD increased from 1.75 million people to 2.07 million people between the years 2000 and 2010.

AMD risk factors include age, smoking, sunlight exposure, ethnicity, sex, cholesterol level, obesity, cardiovascular diseases, diet, and genetics. The early stage is clinically indistinguishable. The late-stage will show the loss of retinal pigment epithelium, choriocapillaris density and decrease the choriocapillaris's diameter. These conditions will lead to blurry vision and loss of visual acuity (Mahave et al., 2015).

Among the many clinical characteristics of AMD, the presence of drusen is a vital sign. It is a deposit of fatty protein located below the retinal pigment epithelium (RPE) that can be classified into small, intermediate, and big sizes. Other signs include hyper and hypopigmentation, atrophy, and detachment of RPE. A combination of these signs can distinguish the condition into "early/late or dry/wet" AMD (Olivera, 2015).

The early stage of dry AMD has little impact on visual acuity. Minor drusen can be identified that can cause minor blurry vision and trouble reading. Irregular pigment dispersion is also observed. The visual field is altered slightly with less than 10 degrees of scotoma present.

Hyper-pigmentation progresses with an increasing number of drusen coalesces in the late stage (Wei, 2011).

With wet AMD, visual acuity decreases early on as "neovascularization leads to leaking fluid, hemorrhage, and scarring" in the subretinal region (Wei, 2011). Drusen coalesce early on and accumulate. The visual field is significantly affected, and abnormality is found during Amsler grid testing (Wei, 2011).

There are two approaches to the treatment that correspond to the dry and wet AMD. The dry form of AMD currently has no effective pharmaceutical treatment. Dry AMD is believed to be caused by factors such as age, exposure to sunlight, diet, comorbidities, and oxidative stress. The most effective oxidative stress intervention is anti-oxidants' oral consumption and zinc supplements (Chen & Sternberg, 2015).

There have been many techniques to treat wet AMD. The two main approaches to the treatment are non-pharmaceutical and pharmaceutical interventions. The former methods include photocoagulation, sub-retinal surgery, and sub-macular surgery. The latter will consist of intravitreal Triamcinolone, Ranibizumab, and Bevacizumab (Table 1) (Goulah., Alfaro III., & Ortiz., 2015). Unfortunately, some of the former methods are now less considered since the use of anti-VEGF. Photocoagulation destroys single blood vessels and subretinal neovascularizations. However, this procedure leads to thermal damage of the nerve fiber in the paillomacular bundle. Sub-retinal surgery has improved the vision for patients in late-stage AMD (Table 2).

Nevertheless, there were instances where the removal of RPE cause low vision. Thus, the use of pharmacologic agents proved to be a better alternative to treat wet AMD. For example, Bevacizumab is a humanized monoclonal antibody that inhibits VEGF activities that include

vascular permeability-enhancing activity (Garcia et al., 2015; Chen et al., 2015; Goulah et al., 2015). Table 1 summarizes the functions and side effects.

Table 1. Pharmaceutical Intervention to AMD

Method	Function	Side Effect
Intravitreal Triamcinolone	Steroid. Induce anti-inflammatory effects.	High-rate of cataracts, glaucoma, vitreous hemorrhage, and pseudoendophthalamitis.
Ranibizumab (Lucentis)	Antibody. Vascular endothelial growth factor A (VEGF-A) antagonists.	Conjunctival hemorrhage, eye pain, vitreous floaters, increased intraocular pressure, intraocular inflammation, endophthalmitis, retinal detachments, traumatic cataracts.
Bevacizumab (Avastin)	Antibody. Vascular endothelial growth factor A (VEGF-A) antagonists.	Same as above.

Table 2. Non-pharmaceutical Intervention to AMD

Method	Function	Side effect
Photocoagulation	Used to obliterate single blood vessels and neovascular networks.	Thermal necrosis in parts of the fovea.
Sub-retinal Surgery	Includes vitrectomy.	May result in a worsening of the vision.
Sub-macular Surgery	Includes vitrectomy	May result in a worsening of the vision.

In terms of Traditional Chinese Medicine (TCM), AMD is usually caused by one of the four patterns: blockage of phlegm-dampness, qi and blood stagnation, liver and kidney depletion, and spleen deficiency. With age, spleen qi diminishes and produces dampness, which can further

transform into phlegm. Besides AMD's common symptoms, some of the pattern characteristics are summarized in Table 3. (Wei, 2011).

Table 3. TCM Patterns for AMD

Pattern	Symptoms
Blockage of Phlegm-Dampness	● Chest distress ● Anorexia and thirst without drinking desire ● Red tongue, yellow greasy coating ● Wiry-slippery pulse
Qi and Blood Stagnation	● Decreased visual acuity ● Vertigo, dizziness ● Bitter mouth and dry throat ● Dark-purple tongue ● Wiry-unsmooth pulse
Liver-Kidney Depletion	● Low back pain ● Impotence ● Weak knees ● Vertigo ● Tinnitus ● Red thin tongue ● Thready-weak pulse

TCM has its method of treatment using acupuncture and Chinese herbal medicine. Both acupuncture points and herbal medicine differ by practitioners, and various case studies argue that TCM treatment improved visual acuity among patients, albeit subjectively most of the time. These differences in acupuncture points and medicine among practitioners have weakened treatment support and is not accepted widely in the medical community. However, the American Academy of Ophthalmology (AAO) task force has acknowledged that acupuncture may be useful as an adjunctive therapy or an acceptable alternative to conventional treatment (Taylor, 2001).

Objective

This study has conducted an integrative literature review on published works related to age-related macular degeneration found in various electronic databases to summarize treatment methods and the results with the following objectives:

Objective 1. Identify the most commonly used treatment methods for age-related macular degeneration with acupuncture and Chinese herbal medicine.

Objective 2. Analyze the treatment effects on age-related macular degeneration with acupuncture and Chinese herbal medicine.

II. Materials and Methods

Pre-selected words were used to search published works between 1980 and 2020 on electronic databases. Electronic databases used include Cochrane, Pubmed, Medline, EBSCO, and Wanfang. Key search words in a combination of two or more were used and are listed below.

- Age-related macular degeneration
- Macular degeneration
- Dry macular degeneration
- Wet macular degeneration
- Acupuncture
- Electro-acupuncture
- Chinese medicine
- Oriental medicine
- Traditional Chinese medicine
- Traditional oriental medicine
- Vascular epithelium growth factor
- VEGF
- ARMD
- AMD

Upon searching with the keywords, the total number of articles across the databases was 154. The articles were further selected based on this study's inclusion and exclusion criteria listed below. Selected articles were first divided into acupuncture and Chinese herbal medicine groups. A total of 13 articles were selected for this study.

Inclusion Criteria

1. Articles written in English, Korean, and Chinese
2. Randomized control trials
3. Pilot trials
4. Case studies
5. Articles related to ophthalmic condition also seen in AMD

Exclusion Criteria

1. Articles not written in English, Korean, and Chinese
2. Articles that are not published in journals
3. Animal trials

Data Selection

Selection was made based on the correlation to the topic of macular degeneration. Due to the lack of comprehensive work on acupuncture and macular degeneration, the range of publication years was extended to 1980. Also, animal trials were excluded. The following figure shows the selection process. 154 articles were search results only using selected keywords. Although over 100 articles were unrelated to age-related macular degeneration and Traditional Chinese Medicine, these articles must have searched because they fell under the relevant topic of ophthalmology. These were excluded during the inclusion criteria.

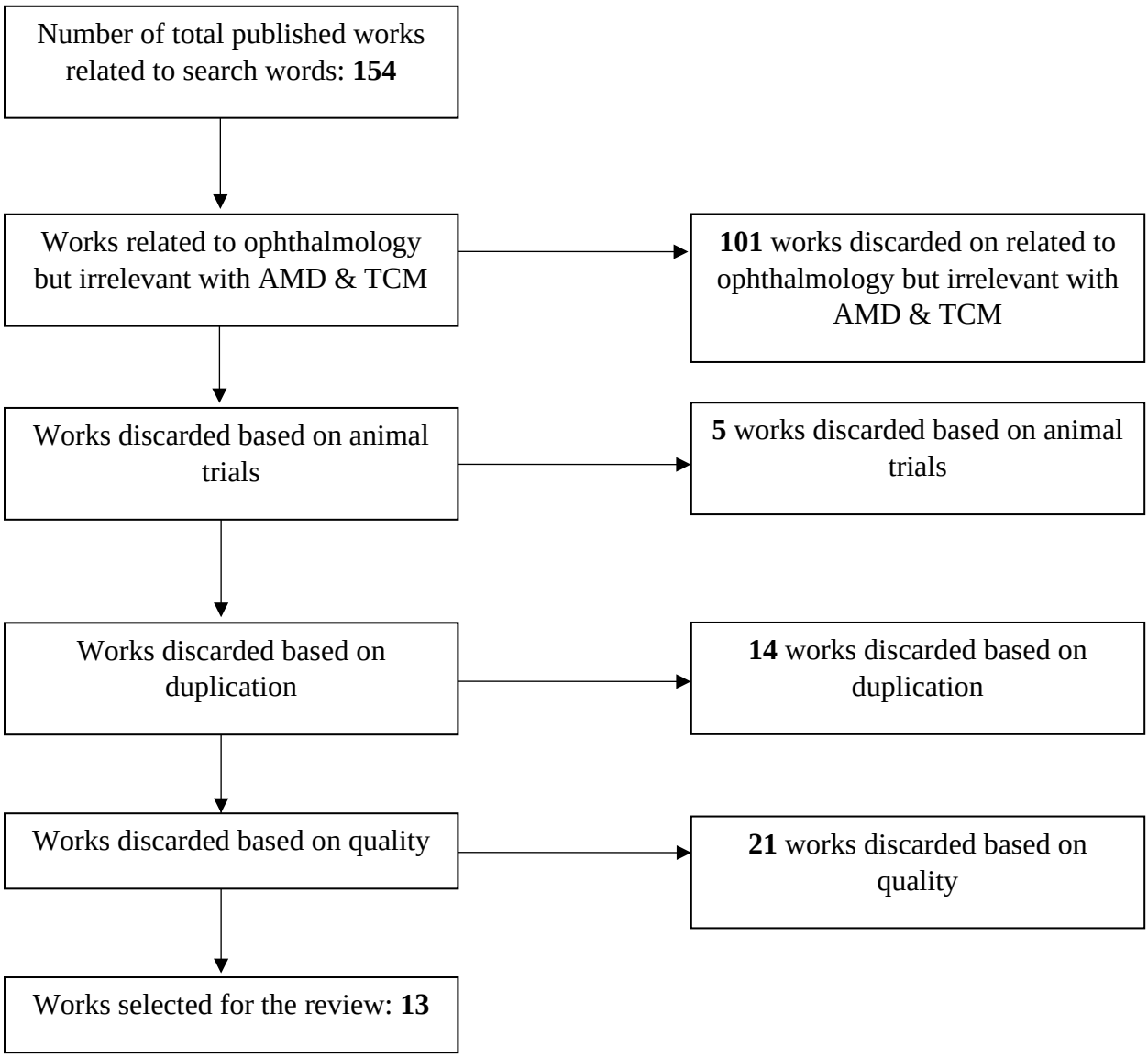

Figure 1. Data Selection Process

III. Results

Acupuncture

A total of 8 articles discussed the treatment methods of age-related macular degeneration using acupuncture.

According to Bruno (2005), the use of acupuncture in conjunction with microcurrent could have beneficial results without putting a financial burden on patients. Forty-two patients were treated over the course of one year. A visual function test (VF-14) and visual acuity tests were conducted before the treatment and every three months. Each treatment session lasted about 5 minutes, altering the current between 250 – 700 microamps. Thirty-six patients improved their visual acuity of 2 lines or more by the end of the 1-year treatment. Three patients improved visual acuity of 1 line, and two patients had no improvement. One patient lost 1 line of visual acuity (Bruno et al., 2005).

Chaikin et al., indicates that there has been a significant improvement in visual acuity with patients suffering from dry-AMD using transpalpebral microcurrent therapy. In this study, 25 patients were suffering from dry-AMD, and three patients with wet-AMD. The average age of the study group was 83. They used 150 microamps of current for 35 minutes weekly. Snellen visual acuity was measured before and after every session. The visual acuity for dry-AMD showed a significant increase in 52% of the patient (P=0.012). However, such improvement was not significant with wet-AMD, having P=0.059. There was approximately 26% of visual acuity deterioration in the study group. The rest of the 22% did not exhibit any changes (2015).

A pilot study in 2018 involved the use of electro-acupuncture around the orbis, hairline, and the scalp. Each treatment involved using needle gauge of 0.12 and 0.35 mm at acupuncture points believed to have therapeutic effects. The treatments showed a decrease in

"proinflammatory cytokines, suggesting applications for chronic inflammatory conditions" (Dhaliwal & Zhou, 2019). Ten patients enrolled in the 20-week program for ten acupuncture treatment sessions. The authors also used auricular acupuncture using semipermanent ear studs. Visual acuity, quality of life survey, color contrast sensitivity, dilated fundus examinations, and OCT were done before the treatment and throughout the 20-week sessions. However, there was no control group. Although the article is still collecting the data, no condition has worsened during the pilot study (Dhaliwal & Zhou, 2019).

In a study with 150 participants, the authors conducted acupuncture treatment with dry eye syndrome that affected visual disturbances and discomfort. Of the 150, 75 participants were allocated to the acupuncture group, and the other 75 were allocated to the artificial tear group. The selection process involved ophthalmologic tests such as tear film break-up time (TFBUT) and Schirmer I test. Those with a history of surgery, external injuries, usage of anti-inflammatory eye drops, and Stevens-Johnson syndrome were excluded. The age ranged from 19 to 65. Acupuncture points selected were BL2, GB14, SJ23, EX1, ST1, GB20, LI4, and LI11 bilaterally with GV23. The needles were inserted for 20 minutes. The 12 treatment sessions lasted four weeks, with three treatment sessions per week (Kim et al., 2018).

The results were not statistically significant in terms of general improvement with dry eye syndrome (P=0.060). However, participants from the acupuncture group had a general improvement over the artificial tear group. TFBUT had a statistically significant result (P=0.007), where both the right and left eyes had a baseline change of 0.59 and 0.46, respectively. The artificial tear group had a tear film break-up time (TFBUT) change of -0.37 on the right eye and -0.09 on the right eye. In terms of VAS, patients in the acupuncture group

experienced an improvement in the condition roughly eight weeks after the acupuncture treatment than the control group with P=0.018 (Kim et al., 2018).

According to Blechschmidt and Todorova (2016), ocular acupuncture improves ophthalmic problems and reduces symptoms experienced in Flammer syndrome (FS). People suffering from an inherited retinal disease (IRD) often suffer from symptoms related to FS. In a case study without a control group, Blechschmidt and Todorova conducted a pilot study with 17 participants over five weeks with ten acupuncture sessions lasting 30 minutes each. Twelve participants had rod/rod-cone dystrophy, 3 had cone/cone-dystrophy, and two had inherited maculopathy. These participants also had a history of FS and went through an ophthalmic examination that includes "refraction, best-corrected visual acuity, contrast vision, intraocular pressure, slit-lamp examination, biomicroscopy, and fundoscopy." Acupuncture points selected were GV20, CV6, UB18, UB20, UB23, GB20, LI4, SJ5, SI3, LV3, GB37, KD3, SP6, ST36, UB1, ST1, and EX7.

Although the test results on visual acuity, contrast vision, and visual fields were not all statistically significant, most of the group had improvement. Of the improvements, contrast vision on both the left and right eye and visual field, temporal radius of the right eye had improved statistically (Contrast vision right eye P=0.015, left eye P=0.042, visual field right eye P=0.013). Two patients showed significant improvement of macular edema with partial resorption of the right eye's vitelliform lesion in one of the cases (Blechschmidt & Todorova, 2016).

One randomized controlled trial was done in collaboration between Shanghai University of Traditional Chinese Medicine and the Eye and ENT of Fudan University. A total of 47 participants were diagnosed with dry macular degeneration for at least three months. Twenty-two

participants were in the acupuncture group, 15 in the western medicine group, and 10 in the control group. Acupuncture points selected for orbital acupuncture were jingming, shangming, medial tongziliao, jianming, chenqi, qiuhou, and taichong. Acupuncture treatments were given twice a week for two months. The western medicine group received vitamin C (0.2g) and vitamin E (0.1g) 3 times a day, orally. The control group received nothing. Pre- and post-examination were done that included the best-corrected vision test and fundus fluorescein angiography (Xia et al., 2014).

The improvement of visual acuity was not statically significant between groups ($P>0.05$). However, the acupuncture treatment group was the only group with VA improvement from 4.6 ± 0.2 to 4.7 ± 0.2. Both the western medicine and control groups showed declined visual acuity, 4.6 ± 0.2 to 4.3 ± 0.1 and 4.7 ± 0.2 to 4.3 ± 0.2, respectively. The differences within the group, however, were statistically significant ($P<0.05$). Sixteen patients from the acupuncture group showed a reduction in the retinal pigment epithelium and retinal edema. Furthermore, no bleeding or exudation was observed. The western and control group had no improvement under the fundus fluorescein angiography (Xia et al., 2014).

Case studies compiled by Xu et al. at Longhua Hospital of Shanghai University of TCM have employed acupuncture around the orbital area, electro-acupuncture, scalp, micro bleeding, and Chinese medicine drug injection. Common points used for acupuncture are qiuhou, taiyang, shenshu, ganshu, guamgming, sizhukong, shangjingming. These points were also used for electro-acupuncture. Auricular acupuncture points included liver, kidney, eyes, and shen. Pharmacologic injections included either methylcobalamin, danshen, or compound anisodine. Four cases were presented with varying degrees of abnormal macular conditions. Three of the

four cases reported improvement of visual acuity and decreased macular edema. Table 4 is a summary of the cases (Xu et al., 2013).

Table 4. Summary of the case studied from Xu et al., (2013)

	Diagnosis	Syndrome Differentiation	Treatment					Result (pre/post visual acuity)
			Acupuncture points	Electro-acupuncture	Auricular acupuncture	Scalp acupuncture	Injection	
Case 1	Stargardt disease	Liver-kidney def.	Xinming I, shinzhu, qiuhou, guamgming, shangjingming	N/A	N/A	N/A	N/A	RE[1]: 0.07/0.3 LE[2]: 0.07/0.3
Case 2	AMD	Spleen and kidney def.	Xinming I, shangjingming, shenshu, pishu, xinshu, qihaishu, baihuanshu	Xinming II	N/A	N/A	-Danshen at xinming, II, xinshu, weishu -Mecobal at qiuhou	RE: 0.4/1.0 LE: 0.5/1.0 Macular thickness: 545 μm/290 μm
Case 3	Cystoid macular edema (RE)	Vessel Stasis obstruction	Shangjingming, xinming	N/A	N/A	N/A	Methylcobalamin and danshen at qiuhou	N/A
Case 4	AMD (LE)	Liver depression and kidney def.	Xinming, qiuhou, jingming, cuanzhu, fengchi, ganshu, shenshu	N/A	N/A	N/A	Compound anisodine	LE: 0.7/0.8

[1]RE: Right eye
[2]LE: Left eye

According to a pilot study done by Bittner et al., 12 participants suffering from retinitis pigmentosa underwent acupuncture treatment to slow the condition (2014). These participants underwent pre- and post-examinations that include full-field stimulus threshold, dark-adaptometry, kinetic perimetry, visual acuity, and contrast sensitivity. Also, all of them underwent optical coherence tomography (SD-OCT) before and after the pilot study. For two weeks, ten acupuncture treatments were administered, each lasting 30 minutes. They used electro-acupuncture and regular acupuncture on the following points: GV20, GV24, YINTANG, TAIYANG, BL2, YUYAO, QIUHOU, YIMING, ST2, GB20 CV12, CV6, ST25, LI12, LI3, HT8, and GB67. Some point combinations were also selected according to palpation's sensitivity, and these were LV8/KD10, SP6/KD7, and LV2/LV3. Nine participants used an IR lamp (Bittner et al., 2014).

5 out of 12 participants produced a significant improvement in either scotopic sensitivity measures, visual acuity, or contrast sensitivity between April and December of 2012 at John Hopkins University, Wilmer Eye Institute (Bittner et al., 2014). Three of nine subjects showed significant improvement in dark-adapted full-filled stimulus threshold (FST) of 10.3 to 17.5 dB, which is greater than the previously noted improvement of 3.0 to 3.6 dB. Two of the three participants improved 43% and 54% in FST scotopic sensitivity (SST) after one week of treatment. Two subjects were exhibited in the reduction of cystoid macular edema after treatment under SD-OCT. However, the study could not conclusively state whether this reduction in edema happened spontaneously or resulted from the acupuncture treatment (Bittner et al., 2014).

Chinese Medicine

Chen and Peng (2012) conducted a randomized controlled trial at a clinic with Chinese traditional medicine on 62 participants diagnosed with age-related AMD. With an average age of

58.4, the average diagnosed period of AMD was 7.63 months. Sixty-two patients were divided into two groups of 31, where one group received western medicine comprised of Vit E (0.1g once daily), Vit C (0.2g 3 times daily), and inosine tablet (0.4g 3 times daily). The Chinese medicine group received a standardized medicine of Zhujing pill with modification according to Chinese differential diagnosis. With edema or exudation symptoms, zhu ling, fu ling, and yi yi ren were added. For diuresis and dampness, including hemorrhage, bai mao gen, pao jiang, and xian he cao were added. Finally, patients in the late-stage added dan shen, tao ren, chuanxiong, and hong hua. On average, visual acuity improved by 0.2-0.4, with slowing of macular disease development ($P<0.05$). Some cases with drusen and edema gradually decreased or disappeared. The selection of herbal medicines was to “invigorate the liver and kidney, promote blood circulation and remove blood stasis" (Chen & Peng, 2012)

Another study done by Shao and Xu (2013) indicates various Chinese medicines according to AMD's differential diagnosis. When patients exhibit spleen deficiency with dampness, Yiqi Fuming tang was used, which had an overall 68.62% visual improvement. The second decoction is for patients diagnosed with phlegm dampness stasis. According to Guo et al., (2011), Huoluo Sanjie tang can disperse phlegm and drain dampness. There was an improvement of 57.1% of visual acuity when compared to the control group. Finally, for patients with liver and kidney yin deficiency, essence and blood deficiency, and qi and blood loss were treated with Erzhi tang with modification to meet individual conditions (Ren et al., 2010). It further promoted the absorption of AMD fundus bleeding. In particular, for exudative condition, the Zhujing pill showed macula absorption of bleeding with improved eyesight (Wang et al., 2011).

Wang compiled a list of Chinese medicine that is used for dry and wet AMD. To resolve phlegm and remove stasis, Tao used Huangban Fuming tang, which is comprised of nu zhen zi

(15g), danshen (15g), gou qi zi (15g), jue ming zi (15g), dan gui (15g), huang qi (12g), mu dan pi (10g), tu si zi (10g), bai zhu (10g), fu ling (10g), mu zei (10g), shi chang pu (10g), gancao (6g), san qi(3g). Nu zhen zi and gou qi zi, in particular, has an anti-aging effect and improve the body's biochemical index. All of the ingredients have anti-oxidant properties that are considered crucial in treating AMD. Xiao et al. used Jia Jie Ziyin Mingmu tang to treat patients with liver and kidney deficiency. This decoction includes baizhu, nu zhenzi, shu di huang, dan shen, gou qi zi, dang gui, xia ku cao, che qian, and wu wei zi. Patients from these studies have combine western medical treatment with modification of zhejian for extensive wet AMD (Wang, 2020; Tao, 2016; Xiao et al., 2017)

According to Wang (2016), 40 participants were divided into a treatment group and a control group. With the experiment lasting for 17 months, the treatment group consisted of 20 people using Sanren decoction for macular edema. There were 12 males and 8 females with an average age of 45.6 years old. Sanren decoction consisted of xing ren, hua shi, zhu ye, hou po, yi yi ren, ban xia. The control group underwent laser treatment and consisted of 8 males and 12 females with an average age of 42.3. They went through a standard laser treatment using a Nidek 532 nm fundus laser instrument to cauterize obstructed blood vessels 2 to 3 papillar diameter away to the upper and lower part from the macular fovea. The treatments were conducted for eight weeks. Both visual acuity and macular thickness were measured before, after the fourth week, and at the end of the eighth week since the initial treatment (Wang et al., 2016)

Both the improvement of visual acuity and macular thickness had significant statistical results for Sanren decoction. The treatment group's total effective rate was 85% ($P<0.05$), whereas the control group was 60%. The macular thickness before the treatment for the sanren decoction group was 490 ± 23.9 μm. Four weeks into the treatment was 367.0 ± 29.6 μm.

Finally, it was 296.4 ± 24.3 μm after the 8th week. The laser treatment group had 489.7 ± 24.8 μm before treatment, 433.1 ± 39.3 μm during treatment, and 353.2 ± 46.2 μm after treatment.

Zeng et al. conducted a clinical trial with 8 participants diagnosed with senile wet-AMD without a control group. Inclusion criteria were >45 years of age with rapid vision loss, drusen fusion, and depigmentation. The trial took place between June 2003 and October of 2005. The youngest was 54 years old, and the oldest one was 82. Recovery criteria included improved visual acuity, absorption of fundus bleeding and exudation, and neovascular occlusion. They divided eight people into three groups according to syndrome and disease differentiation. Shengpuhuang decoction was used for the early stage participants who were showing wet-AMD symptoms of extensive bleeding and bright red fundus. Mid-stage wet-AMD consisted of gradual absorption of bleeding but worsening of exudation. The choice of Chinese medicine is modified Si Jun Zi tang. Blood must be absorbed entirely, but exudation continues to be absorbed during the late stage. Scars are also formed. Liu Wei Di Huang tang was used for the late-stage (Zeng et al., 2006).

Of the 8 cases, 1 participant was cured entirely, 4 participants improved their condition, and 3 had no improvement. These participants showed changes within a month of starting the treatment, whereas the other 3 participants continued their treatment for longer than six months without any improvement. One participant, in particular, returned to the hospital in 2004 with a loss of visual acuity. Upon examination through fundus fluorescein angiography, the patient exhibited round hemorrhage in the right eye's macular area where visual acuity was 0.2. Optical coherence tomography showed a macular thickness of 186 μm. Shengpuhuang tang consisting of sheng di huang, mu dan pi, xuan shen, qian cao, han lian cao, zhi zi tan, bai mao gen, che qian zi, chao pu huang, and san qi reduced the thickness to 177 μm. 7 months after the second visit,

treatment protocol changed to mid-stage wet-AMD and taking modified Si Jun Zi tang. The macular thickness was reduced to 153 μm. Visual acuity improved to 0.6. On the final visit, two months after the modification, the patient exhibited a further reduction of macular thickness to 153 μm and increased visual acuity to 1.0 (Zeng et al., 2006).

Studies selected show an overall improvement in AMD. However, most lack randomized trials, control groups, and statistical analysis. Furthermore, the variety of Chinese herbal medicines still need more investigation with a larger sample size to standardize medicine treatment.

Table 5a. Summary of the Literature: Acupuncture (8)

Author (Sample size)	Disease	Differential Diagnosis-Chinese Medicine	Tests & Evaluations	Treatment Methods	Control Group	Results
Bruno, 2005 (42)	AMD: wet and dry type	N/A	-VF-14	Microcurrent stimulation with acupuncture	N/A	-Improve VA > 2 lines = 85.7% -Improve VA 1 line = 7.1% -No improvement = 4.8% -Loss of VA 1 line = 2.4% -Overall VA improvement = +2.88 lines
Chaikin et al., 2015 (17)	AMD: wet and dry type	N/A	-BCVA[3] -FA[4] -Fundus photography	Transpalpebral Microcurrent stimulation	N/A	-VA increase in DAMD[5]: P=0.012; 52% improved VA, 25% deteriorated VA -VA increase in WMAD[6]: P=0.059; 83% improved VA, 0% deterioration VA
Dhaliwal & Zhou, 2019 (10)	AMD: dry type	N/A	-VA -Color/contrast sensitivity -Fundus Exam -OCT	-Acupuncture -Electro-acupuncture -Auricular acupuncture	N/A	N/A

[3] BCVA: best-corrected visual acuity
[4] FA: Fluorescein Angiography
[5] DAMD: Dry age-related macular degeneration
[6] WAMD: Wet age-related macular degeneration

Kim et al., 2012 (150)	Dry Eye Syndrome	N/A	-TFBUT[7] -OSDI[8] -VAS	Acupuncture: BL2, GB14, TE23, EX1, ST1, GB20, LI3, LI11, GV23	Artificial tear group	-TFBUT: significantly increased compared to the control group (P=0.007) -OSDI: No significant difference between the two groups (P=0.058) -VAS: statistically significant only after eight weeks of acupuncture treatment (P=0.018)
Blechschmidt & Todorova, 2016 (17)	-Flammer Syndrome related to Inherited Retinal Disease -Inherited Retinal Disease	N/A	-BCVA -Intraocular pressure -Fundoscopy	-Acupuncture: GV20, CV6, UB18, UB20, UB23, GB20, LI4, TE5, SI3, LV3, GB37, KD3, SP6, ST36, UB1, ST1, EX7 -Auricular acupuncture: eye, liver, kidney, heart, thalamus	N/A	-General improvement in VA -A few cases of reduced ocular pressure
Xu et al., 2013 (4)	AMD: wet and dry type	-Liver and kidney deficiency -Spleen and kidney yang deficiency -Vessel stasis -Live depression and kidney deficiency	-OCT -VA	-Acupuncture: qiuhou, taiyang, shenshu, ganshu, guamgming, sizhukong, shangjingming -Electro-acupuncture	N/A	4 out of 4 cases showed improvement in VA, and 1 case had reduced macular thickness

[7] TFBUT: Tear film break-up time
[8] OSDI: Ocular surface disease index

Bittner et al., 2013 (12)	Retinitis Pigmentosa	N/A	-FST[9] -VA -Contrast sensitivity -OCT	-Acupuncture: ST2, GB20, CV12, CV6, ST25, LI12, LI3, HT8, BL67 -Electro-acupuncture (15Hz continuous): GV20, GV24, yintang, taiyang, BL2, yuyao quihou, yiming	N/A	-5 out of 6 subjects had significant improvement FST but were not statistically significant (P=0.49) -VA improvement was not statistically significant (P=0.55)
Xia et al., 2014 (47)	AMD: dry type	N/A	-BCVA -Fundus photography -FR[10]	-Acupuncture: ming, shangming, inner tongzixiao, jianming, chenqi, qiuhou, taichong	-Western drug group: Vit C, Vit E -No treatment group	-Visual acuity improvement in the acupuncture group was statistically significant (P<0.05) -Visual acuity improvement between groups was not statistically significant (P>0.05)

[9] FST: Full-field stimulus threshold
[10] FR: Fluorescein Radiography

Table 5b. Summary of the Literature: Chinese Medicine (5)

Author (Sample size)	Disease	Differential Diagnosis - Chinese Medicine	Tests & Evaluations	Treatment Methods- Decoction	Control Group	Results
Chen & Peng, 2012 (62)	AMD: wet and dry type	-Liver and kidney deficiency -Liver qi stagnation -Qi and blood stagnation	-VA	-Zhujing pills + modifications	Vit E & C	-Statistically significant improvement of VA by 0.2-0.4 ($P<0.05$)
Shao & Xu, 2013 (N/A)	AMD: wet and dry type	-Spleen deficiency with dampness -Phlegm and dampness stasis	N/A	-Yiqi fuming tang+ modification -huoluo sanjie tang+ modification -Erzhi tang -Zhujing pills	N/A	-General improvement rate of >50% in VA
Wang, 2020 (N/A)	AMD: wet and dry type	-Spleen qi deficiency -liver and kidney deficiency -Phlegm stasis	N/A	-Huangban fuming tang+ modification -Jiajie ziyin mingmu tang+ modification	N/A	N/A
Wang et al., 2016 (40)	Macular edema	-Spleen qi deficiency -Phlegm and dampness obstruction	-VA -OCT	-Sanren decoction+ modification	Laser treatment	-Total effective rate in VA of the experimental group: 85% ($P<0.05$)

Zeng et al., 2006 (8)	AMD: wet type	-Spleen and kidney deficiency -Phlegm and blood stasis	-VA	-Shengpuhuang decoction -Sijunzi tang -Liu wei di huang tang	N/A	-5 out of 8 cases improved the wet condition

IV Discussion

Most of the articles reviewed in this study attempted to improve visual acuity using acupuncture and Chinese herbal medicine. They used a combination of examination methods to observe the macular changes during and after the treatment. These include a visual function test (VF-14), fundus fluorescein angiography (FFA), optical coherence tomography (OCT), and visual acuity test.

There were five types of articles selected for the literature review: pilot studies (3), RCT (4), case studies (2), clinical trials (2), and academic reviews (2). Nine out of thirteen articles indicated that visual acuity has improved. However, only four had statistical significance. One case measured VAS with improvements in the quality of life, and one case had a reduction of ocular pressure. The most used test was visual acuity as observed from 10 cases. Both the OCT and fundus photography were used equally in 4 separate cases. Other examination methods involved fluorescein angiography and color/contrast sensitivity.

Acupuncture treatments observed a uniformed pattern of diagnosis and point selection. The period of experiments varied between 4 weeks to 52 weeks, with a median of 12 weeks. Point selections were divided into five regions: orbital, local, distal, auricular, and scalp regions. There were a total of 44 acupuncture points used throughout AMD treatment. However, the most used points from the 8 articles were BL2, CV6, GB20, LI4, QIUHOU, ST1, SHANGJINGMING, and GB20. These points were used regardless of wet or dry type of AMD. Furthermore, the same points were also used for dry eye syndrome and Flammer syndrome.

Two articles utilized electro-stimulation as the treatment method for AMD. Only one of them had statistically significant VA improvement, where 52% of 75 controlled group subjects had better VA after microcurrent stimulation (P=0.012). The other article had an overall

improvement of VA in 42 participants without significance. One Chinese article had 4 case studies where all 4 participants had improved VA using regular acupuncture and electro-acupuncture. Unfortunately, only two articles had control groups that were compared against artificial tear and Vit C/Vit E.

The overall improvement of visual acuity was more significant in Chinese herbal medicine. Four out of five articles showed general subjective and objective improvement. Differential diagnosis from the five articles varied, but there were 4 spleen qi deficiency, 4 phlegm and dampness, 2 liver and kidney deficiency, and 1 blood and qi stagnation. Decoctions used varied as well, without any congruity. It ranged from invigorating blood decoctions to nourishing yin and tonifying qi decoctions such as Si Gun Ji tang. The most commonly used decoction was Zhujing pills modified according to individual needs. In both cases of using Zhujing pills, participants in experimental groups experienced significant VA improvement where it improved by 0.2-0.4. Sanren tang was another decoction where the effective rate of VA improvement was 85% ($P<0.05$) against the control group going through laser treatment for participants suffering from macular edema.

Despite the improvements articles shared in terms of visual acuity, macular edema, and neovascularization, 9 out of 13 articles only had generalized improvement in both wet and dry age-related macular degeneration without statistical significance.

Risks and Biases

Two articles related to treating AMD with either acupuncture, Chinese medicine, or both are examined for risks and biases.

Bruno (2005) conducted a clinical trial at a private clinic without a control group. The treatment sessions involved self-treatment, where the patients were given an orientation during

the first visit to the clinic. The orientation comprised of explaining how to use a microcurrent device, potential side effects, and possible discomfort during a treatment session. The patients were trained with a family member who will 'keep an eye' on the patient during the self-treatment. Without clinician supervision, each treatment was not controlled for factors that could affect the visit's outcome. The study has not been reproduced since, and each trial remains variable without strict guidance. Furthermore, tests conducted at a private clinic has a conflict of interest.

Xu et al. (2013) presented four successful cases of AMD. The attending doctor has utilized regular acupuncture, pharmaceutical agent injection, including methylcobalamin and danshen extract, and electro acupuncture. The work failed to justify the selection of pharmaceutical agents used for the 4 cases. The article repeatedly states the selection option between "methylcobalamin or danshen" among different patients, giving an impression that either can be substituted for one another. Also, this practice has not been replicated by someone other than the attending doctor. Despite indicating the doctor's extensive practice, the article failed to mention the estimate of AMD patients and their pre-/post- results.

Although this study indicated two works that could potentially have significant risks and biases, most of the published work lacks consistent measurement standards and large sample sizes. Only 4 out of 13 selected works were randomized control trials. There were no blinding experiments. Articles with acupuncture treatment have shared common treatment points, but Chinese medicine has not. The overall syndrome differentiation for both acupuncture and Chinese medicine agreed to spleen qi deficiency, kidney and liver deficiency, qi and blood stagnation, and phlegm/dampness obstruction. Two out of five articles regarding the use of

Chinese medicine shared the zhujing pill for deficient conditions (Chen & Peng, 2012; Shao & Xu, 2013). However, all other works used different decoction.

V. Conclusion

This study analyzed the usage of acupuncture and Chinese herbal medicine and its effectiveness on age-related macular degeneration. Based on the integrative literature review, the overall outcome of the usage of both treatment methods improved visual acuity across the spectrum. Although statistical significance lacked in the majority of the articles selected, the subjective improvement was seen in 9 out of 13 articles. Other improvements were also seen, such as a reduction in macular edema and macular thickness, though there was no statistical significance. Despite the lack of statistical evidence, the use of these methods has increased in the past two decades. The selection of acupuncture points is relatively safe, except for the orbital region. The use of various decoctions does not seem to pose a threat or contraindicate Western medicine, as the decoctions were carefully selected after long discussions between the MDs and TCM doctors as seen in Chinese articles.

The holistic approach to treat AMD has been gaining attention in the past few decades. Especially in TCM, acupuncture has not only improved visual acuity in AMD, but it also improved other ophthalmic conditions that arise from the different classification of diseases. These include Flammer Syndrome and retinitis pigmentosa. Also, Chinese herbal medicine also seemed to improve both dry and wet AMDs significantly. Gou qi zi, for example, contains lycium barbarum polysaccharides and beta-carotene that can protect keratinocytes and become the precursor for Vitamin A, respectively. However, the research is still at an infant stage to standardize the prescription of Chinese herbal medicine.

As the potential for being an alternative treatment method for AMD, acupuncture, and Chinese herbal medicine research must continue on larger scales. A prospective cohort study on a large scale would help identify and track macular degeneration that is taking place with the

younger generation. This type of longitudinal study will also help participants keep track of their conditions and benefit the scientific community. Furthermore, having a standardized Chinese herbal medicine for AMD would benefit both the patients and healthcare providers. It would eliminate many uncertainties in Chinese medicine and let researchers concentrate on factors other than variations in decoctions.

Despite these shortcomings, the subjective data from AMD patients show a promising future for acupuncture treatment. Patients from different continents have experienced improved conditions and have changed their lifestyle to maintain the improved condition. Further investigation will have a potential for acupuncture to keep its competitive edge in macular degeneration and other ophthalmic conditions.

References

Age-Related Macular Degeneration (AMD) Data and Statistics. *National Eye Institute*. (2019, July 17). https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/age-related-macular-degeneration-amd-data-and-statistics.

Arevalo, F. J., & Fernandez, C. F. (2015). Normal Anatomy of the Macula. In V. Alfaro III (Ed.), *Age-Related Macular Degeneration* (2nd ed., pp. 1-14). Philadelphia, PA: Wolter Kluwer.

Bittner, A. K., Gould, J. M., Rosenfarb, A., Rozanski, C., & Dagnelie, G. (2013). A pilot study of an acupuncture protocol to improve visual function in retinitis pigmentosa patients. *Clinical and Experimental Optometry*, *97*(3):240–247. https://doi.org/10.1111/cxo.12117

Blechschmidt T., Krumsiek M., & Todorova M. G. (2016). Acupuncture Benefits for Flammer Syndrome in Individuals with Inherited Disease of the Retina. *EPMA Journal. 8*(2):177-185. doi:10.1007/s13167-017-0096-4.

Blechschmidt, T., Krumsiek, M., & Todorova, M. (2016). Improvement in Visual Function in Patients with Inherited Diseases of the Retina Following Acupuncture Treatment. *Klinische Monatsblätter Für Augenheilkunde*, *233*(04):416–423. https://doi.org/10.1055/s-0041-111819

Bruno, G. (2005). Treatment of Macular Degeneration with Microcurrent Stimulation. *American Acupuncturist, 32*: 12–32.

Chaikin, L., Kashiwa, K., Bennett, M., Papastergiou, G., & Gregory, W. (2015). Microcurrent stimulation in the treatment of dry and wet macular degeneration. *Clinical Ophthalmology*, *9*, 2345–2353. https://doi.org/10.2147/opth.s92296

Chen, J., & Peng, G. (2012). Clinical Application Value of Traditional Chinese Medicine in Treating Age-Related Macular Degeneration. *Chinese Journal of Clinical Health*, *15*, 296–297.

Chen, Y., & Sternberg Jr, Paul. (2015). Anti-oxidants and Age-Related Macular Degeneration: Clinical Associations and Basic Mechanisms. In V. Alfaro III (Ed.), *Age-Related Macular Degeneration* (2nd ed., pp. 156-168). Philadelphia, PA: Wolter Kluwer.

Czerwonko, M. E., Ingolotti, M., Nelson, A., Brown, J., & Alfaro III, V. (2015). Animal Models for Age-Related Macular Degeneration. In D. V. Alfaro, E. P. Jablon, J. B. Kerrison, K.

A. Sharpe, & M. Rodriguez-Fontal (Authors), *Age-related macular degeneration* (2nd ed., pp. 43-54). Philadelphia, PA: Wolters Kluwer.

Dhaliwal, D. K., & Zhou, S. (2019). Acupuncture for Dry AMD. *Retina Today*, 53–55.

Du MB, Liu SZ, Xu K, Liang LN, He AP, Yao Y, Liu YM. (2017). Summarize Drug Dosage Forms in Treatment of Age-Related Macular Degeneration Disease. *China Journal of Chinese Materia Medica. 42*(4): 628-633. doi:10.19540/j.cnki.cjcmm.20170121.007.

G Li., Y Shao. (2017). Early Age-Related Macular Degeneration Treated with Emayaoling Acupuncture Technique: A Randomized Controlled Trial. *Chinese Acupuncture & Moxibustion. 37*(12): 1294-1298.

Garcia, R. A., Oria, V., Suarez Tata, L. M., & Mata-Plathy, M. (2015). Pre-Anti-VEGF Era. In V. Alfaro III (Ed.), Age-Related Macular Degeneration (2nd ed., pp. 169-179). Philadelphia, PA: Wolter Kluwer.

Goulah, J. L., Alfaro III, D. V., & Ortiz, C. E. (2015). Lucentis: Ranibizumab. In V. Alfaro III (Ed.), *Age Related Macular Degeneration* (2nd ed., pp. 189-204). Philadelphia, PA: Wolter Kluwer.

Gu, Z., Zhu, J., & Xie, Y. (2016). Case of Macular Degeneration. *Chinese Acupuncture & Moxibustion. 36*(5):504.

Guo, H. (2011). Clinical Observation on Treating 28 Cases of Phlegm and Blood Stasis type Age-Related Macular Degeneration with Huoluo Sanjie Decoction. *Clinical Journal of Chinese Medicine. 3*(3):32,34. doi:10.3969/j.issn.1674-7860.2011.03.018

Huang BL, Ding SH, Hang L, Zheng SZ, Li W, Xu XR. (2013). Prevention and Treatment of Age-Related Macular Degeneration by Extract of Fructus Lycii and its Constituents Lutein/Zeaxanthin: An in vivo and in vitro Experimental Research. *China Journal of Chinese Materia Medica. 33*(4): 531-7. PMID:23841278.

Jiao NJ. (2011). Observation on Therapeutic Effect of Age-Related Macular Degeneration Treated with Acupuncture. *Chinese acupuncture & Moxibustion. 31*(1): 43-45. PMID: 21355157.

Jin M, Dai H, Zhang X, Wang Y, Han M, Zhang H, Liu Y, Wang Z, Gao X, Li L, Wen X, Liu Y, Wei L, Chen Y. (2018). A Traditional Chinese Patent Medicine ZQMT for Neovascular Age-Related Macular Degeneration: A Multicenter Randomized Clinical Trial. *Current Molecular Medicine. 18*(9): 622-629. doi:10.2174/1566524019666190107155311.

Jin, M., Zhang, Y., Pan, L., Dou, R., Nussenblatt, R. B., & Wei, L. (2012). The Chinese medicine formula HB01 reduces choroidal neovascularization by regulating the expression of vascular endothelial growth factor. *Journal of Translational Medicine, 10*(1), 1–8. https://doi.org/10.1186/1479-5876-10-118

Kim, B. H., Kim, M. H., Kang, S. H., & Nam, H. J. (2018). Optimizing Acupuncture Treatment for Dry Eye Syndrome: A Systematic Review. *BMC Complementary and Alternative Medicine, 18*(1). doi:10.1186/s12906-018-2202-0

Kim, T.-H., Kang, J. W., Kim, K. H., Kang, K.-W., Shin, M.-S., Jung, S.-Y., … Choi, S.-M. (2012). Acupuncture for the Treatment of Dry Eye: A Multicenter Randomised Controlled Trial with Active Comparison Intervention (Artificial Teardrops). *PLoS ONE, 7*(5). doi.org/10.1371/journal.pone.0036638

Lai TY, Chen LJ, Yam GH, Tham CC, Pang CP. (2010) Development of Novel Drugs for Ocular Diseases: Possibilities for Individualized Therapy. *Personalized Medicine. 7*(4): 371-386. doi: 10.2217/pme.10.25.

Lee YM, Kim CS, Jo K, Sohn EJ, Kim JS, Kim J. (2015). Inhibitory Effect of Samul-tang on Retinal Neovascularization in Oxygen-Induced Retinopathy. *BMC Complement Alternative Medicine. 15*. doi:10.1186/s12906-015-0800-7.

Li G, Shao Y, Yin J. (2017). Early Age-Related Macular Degeneration Treated with Emayaoling Acupuncture Technique: A Randomized Controlled Trial. *Chinese acupuncture & moxibustion. 37*(12): 1294-1298. doi:10.13703/j.0255-2930.2017.12.011.

Luo D, Deng T, Yuan W, Deng H, Meng H, Jin M. (2019). Effects of Huangban Bianxing One Decoction Combined with Ranibizumab on Treating Exudative Age-Related Macular Degeneration. *Journal of Traditional Chinese Medicine. 39*(6): 892-901.

Mahave, A. M., Redondo, E. R., & Kerrison, J. B. (2015). Pathogenesis and Pathophysiology of Age-related Macular Degeneration. In V. Alfaro III (Ed.), *Age-Related Macular Degeneration* (2nd ed., pp. 36-42). Philadelphia, PA: Wolter Kluwer.

Mo Y, Wang MF, Zhou LL. (2010). Risk Factor Analysis of 167 Patients with High Myopia. International Journal of Ophthalmology. 3(1):80-2. doi:10.3980/j.issn.2222-3959.2010.01.19.

Moore, J. (2018). A Narrative Review of the Effectiveness of Acupuncture for Macular Degeneration (dissertation). South Baylo University, Anaheim, CA.

Nepp, J., Jandrasits, K., Schauersberger, J., Schild, G., Wedrich, A., Sabine, G. L., & Spacek, A. (2002). Is Acupuncture a Useful Tool for Pain-Treatment in Ophthalmology? *Acupuncture & Electro-Therapeutics Research, 27*(3/4), 171. doi.org/10.3727/036012902816025988

Olivera, M. (2015). Etiology of Late Age-Related Macular Degeneration. In D. V. Alfaro, E. P. Jablon, J. B. Kerrison, K. A. Sharpe, & M. Rodriguez-Fontal (Authors), *Age-related macular degeneration* (2nd ed., pp. 43-54). Philadelphia, PA: Wolters Kluwer.

Ren, Y., & Tang, Y. (2010). The Modern Research of Erzhiwan and Application on the Age-Related Macular Degeneration. *Liaoning Journal of Traditional Chinese Medicine. 37*(3):431-433.

Rosenfarb, A. (2017). Treating Macular Degeneration with Chinese Medicine. *Juniper Online Journal of Case Studies, 1*(4), 1-3. doi:10.19080/jojcs.2017.01.555568

Shao, Y., & Xu, X. (2013). Advances in Study of Traditional Chinese Medicine on Age-Related Macular Degeneration. *Journal of Otolaryngology and Ophthalmology of Shandong University, 27*(5), 91-94. doi:10.6040/j.issn.1673-3770.0.2013.059

Tao, L. (2018). Curative Effect of Using Huangban Fuming Decoction Combined with Acupuncture in the Treatment of AMD and the Influence on Macular Edema, Subjective Symptoms, Serum VEGF, PDGF, and ES Levels. *Journal of Sichuan Traditional Chinese Medicine. 36*(12):174-177.

Taylor, D. (2001). Alternative Eye Care. *British Journal of Ophthalmology, 85*(7), 767-768. doi:10.1136/bjo.85.7.767

Wang X, Hu S. (2001). A Review of Research Actuality on Age-Related Macular Degeneration. *Eye Science. 17*(4):245-51. PMID: 12567516.

Wang, C. (2016). Clinical Observation of Sanren Decoction in Treating Macular Edema, *Everyone's Health. 10*(4):48. doi: 10.3969/j.issn.1009-6019.2016.04.060

Wang, F. (2020). Research progress of traditional Chinese medicine treatment of age-related macular degeneration. *Chinese Journal of Gerontology, 40*(10), 2233-2236. doi:10.3969/j.issn.1005-9202.2020.10.063

Wang, S., & Cunnusamy, K. (2013). Traditional Chinese Medicine (TCM) for the Treatment of Age-Related Macular Degeneration-Evaluation of WO2012079419. *Expert Opinion on Therapeutic Patents, 23*(2), 269–272. https://doi.org/doi:10.1517/13543776.2013.751972.

Wang, Z., & Lei, Z. (2011). Clinical Observation of Jiajian Zhujing Pills to Treat on Age-Related Macular Degeneration. *Hubei Journal of Traditional Chinese Medicine. 33*(5):18-19. doi:10.3969/j.issn.1000-0704.2011.05.010

Wei, Q., Rosenfarb, A., & Ling, L. (2011). Ophthalmology in Chinese Medicine. Beijing, China: *People's Medical Publishing Company*.

Welte AK, Hahn U, Büssing A, Krummenauer F. (2017). Systematic Review of the Application of Complementary and Alternative Medicine and Their Potential Therapeutic Benefits in the Treatment of Ophthalmology Patients. *Klin Monbl Augenheilkd. 234*(5):686-696. doi: 10.1055/s-0042-106901.

Wu B, Guan G, Li J, Huang Z, Zhan Y. (1991). Statistical Analysis of Age-Related Macular Degeneration (AMD) in the Differentiation of Symptoms and Signs. *Eye Science. 7*(4):199-204. PMID: 1844077.

Xia, Y. (2016). A Survey of Research on Traditional Chinese Medicine for the Treatment of Age-Related Macular Degeneration. *Journal of Guiyang College of Traditional Chinese Medicine. 38*(6):96-99.

Xia, Y., Liu, R., Sun, J., Xin, S., Cui, H., & Liu, S. (2014). Clinical Study of Deep Needling at Orbital Points as Main Treatment for Age-Related Macular Degeneration. *Shanghai Journal of Acupuncture and Moxibustion, 33*(5): 421-423. doi:10.13460/j.issn.1005-0957.2014.05.0421

Xiao, J., & Zhu, C. (2017). Clinical Study on Zi Yin Ming Mu Tang Treating Age-Related Macular Degeneration with Liver and Kidney Deficiency. *Journal of Sichuan Traditional Chinese Medicine 35*(4):126-128.

Xu X, Hang L, Huang B, Wei Y, Zheng S, Li W. (2013). Efficacy of Ethanol Extract of Fructus Lycii and Its Constituents Lutein/Zeaxanthin in Protecting Retinal Pigment Epithelium Cells against Oxidative Stress: In Vivo and In Vitro Models of Age-Related Macular Degeneration. *Journal of Ophthalmology*. doi:10.1155/2013/862806.

Xu XR, Zhong L, Huang BL, Wei YH, Zhou X, Wang L, Wang FQ. (2014). Comparative Proteomic Analysis of Plasma Proteins in Patients with Age-Related Macular Degeneration. *International Journal of Ophthalmology. 18;7*(2):256-63.

doi:10.3980/j.issn.2222-3959.2014.02.12.

Xu Y, Lu B, Zhou Y, Ren S, Pang G, Deng A. (2020). Is dietary fat associated with the risk of age-related macular degeneration? Protocol for a systematic review and meta-analysis. *Medicine. 99*(17). doi:10.1097/MD.0000000000019081.

Xu, H., Liu, J., Wang, S., & Zhang, R. (2013). Acupuncture Application of "Different Disease, Same Treatment" in Macular Maculopathy. *Chinese Journal of Chinese Ophthalmology, 23*(3), 188-191.

Xu, H., Liu, J., Xu, S.-W., Zong, L., & Zhang, R. (2008). Analysis of Literature of Acupuncture and Moxibustion Treatment of Intractable Eye Diseases. *Acupuncture & Moxibustion. 28*(8): 625–628.

Zeng, P., Ouyang, F., & Li, X. (2006). Treatment of Wet Age-Related Macular Degeneration with Traditional Chinese Medicine. *Chinese Journal of Traditional Chinese Ophthalmology. 16*(2):112-113. doi:10.3969/j.issn.1002-4379.2006.02.020

Zhang, J. (2005). Essentials in the Treatment of Ophthalmology (III). *New England Journal of Traditional Chinese Medicine. 4*(1):22–24.