· Original article ·

Effect of joint photocoagulation and traditional Chinese medicine for the treatment of diabetic retinopathy

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Abstract

• AIM: To explore the potentially beneficial clinical effects of traditional Chinese medicine (TCM) combined with photocoagulation for diabetic retinopathy(DR).

• METHODS: Chinese patients with DR were divided into two groups. A joint treatment group received both the TCM ziyinliangxuesanyutang and photocoagulation, while a control group received only photocoagulation laser treatment. Visual acuity tests, visual field retinal sensitivity tests, and fundus fluorescein angiography (to measure neovascular regression) were performed. Vision was compared between the two groups 1 month, 6, and 12 months after treatment.

• RESULTS: Twelve months after treatment, the recovery of visual acuity (62.3% *vs* 43.1%, $P=0.037$) and retinal sensitivity [17.0±3.7 decibels (dB) *vs* 14.9±3.7dB, $P=0.002$] as well as neovascular regression (67.2% *vs* 48.3%, $P=0.036$) in the joint treatment group were all significantly greater than that of the control group.

• CONCLUSION: Compared with laser treatment alone, the joint application of TCM and photocoagulation is shown to be more effective than DR treatment method.

• KEYWORDS: photocoagulation; traditional Chinese medicine; diabetic retinopathy
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INTRODUCTION

Diabetic retinopathy (DR) is one of the serious complications of diabetes[1-3]. In American adults aged 40 years and older were known to have DM, the prevalence of retinopathy was 40.3%[3]. While in Asian developing countries, the prevalence of DR was 17.6% in India[4], 23.5% in Qatar[5] and 27.9% in China[6]. It is estimated that about 9.1 million rural adults over 30 years old suffering from DR in China[7].

Laser photocoagulation surgery is currently the main treatment for DR. However, photocoagulation cannot be used to treat macular regions, and there are some DR patients who are not sensitive to photocoagulation[8] to reduce the effectiveness. Recently studies have shown that treatment with traditional Chinese medicines (TCM) can suppress the progression of DR in rats[9]. However, there is a dearth of well-designed longitudinal clinical trial to investigate the joint effect of TCM and laser photocoagulation on the treatment of DR. Compared to DR treatment with photocoagulation alone, clinical outcomes of joint DR treatment were examined longitudinally to evaluate a potentially more effective therapeutic alternative for DR.

MATERIALS AND METHODS

Subjects Patients meeting the following criteria were enrolled in the study: (1) Patients diagnosed with diabetic by an endocrinologist, with stable diabetes and a fasting blood glucose maintained under 7.0mmol/L after treatment; (2) Diagnosed with DR stage IV by fundus fluorescein angiography (FFA); (3) No history of serious hypertension, kidney disease, ocular trauma, vitreous and retinal diseases, or intraocular surgery; (4) Provided informed consent for this study. All DR participants were collected in the 1st Hospital of Shijiazhuang from January 2007 to January 2008. 64 cases 119 DR eyes were randomly classified into two groups: a joint treatment group, which received the joint TCM-photocoagulation treatment, and a control group, which received only photocoagulation.

Methods All patients from the two groups received the same course of laser treatment from the same clinical doctor. Each eye received photocoagulation once a week for four consecutive weeks. Photocoagulation laser surgery was performed with argon green (514nm) and krypton yellow (568nm) lasers. Laser spot size was between 200 and 500μm, and exposure time was between 0.1 and 0.3 seconds. Laser output was adjusted between 150 and 300mW to create a gray-white

Table 1 Comparison of visual acuity at different therapeutic time points

Duration of DR treatment	Joint treatment group ($n=61$)		Control group ($n=58$)		χ^2	P
	Effective(%)	Ineffective(%)	Effective(%)	Ineffective(%)		
1 month	20(32.8)	41(67.2)	19(32.8)	39(67.2)	0.00	0.997
6 months	28(45.9)	33(54.1)	23(39.7)	35(60.3)	0.47	0.491
12 months	38(62.3)[a]	23(37.7)	25(43.1)	33(56.9)	4.40	0.037

[a]$P<0.05$ *vs*1 month among joint treatment group.

retinal burn. Another clinical doctor specialized in TCM formulated the TCM zīyīnliángxuèsǎnyūtāng specifically for this study. Zīyīnliángxuèsǎnyūtāng was composed of 15g Rehmannia root (shēngdìhuáng), 10g figwort root (xuánshēn), 10g tree peony root bark (mǔdānpí), 10g fragrant solomonseal (yùzhǔ), 10g wind weed root (zhīmǔ), 10g Baikal skullcap root (huángqín), 30g cogon grass root (báimáogēn), 12g Indian madder root (qiàncǎo), 10g sophora flower (huáihuā), 15g chrysanthemum (júhuā), 12g Atractylis ovata root (báishù), 12g yam (shānyào), 10g orange peel (chénpí), and 10g balloon flower (jiégěng). Patients in the joint treatment group were individually prepared the TCM by simmering ingredients in hot water and they consumed the formulation at the beginning of the first day of photocoagulation treatment twice daily for twelve months. All participants' fasting blood glucose levels were maintained below 7.0mmol/L during the course of the experiment (for twelve months starting from the date of the first photocoagulation procedure) by endocrine therapy as needed [10].

Each participant's visual acuity, visual field, retinal sensitivity and neurovascular regression were measured before and 1 month, 6 and 12 months after the first photocoagulation procedure to quantify the extent of vision loss and recovery. Vision was measured according to the following criteria: (1) For visual acuity, an increase of at least two lines over pre-surgery level on a visual acuity test chart was defined as effective treatment. The result of treatment in a vision increase of less than two lines was deemed ineffective. (2) Participants' retinal sensitivity values were quantified by campimeter (Switzerland, Octopus101) through a standard protocol assessing sensitivity within a 30-degree visual field. (3) Each patients received FFA to measure neovascular regression. Photoshop 7.0 was used to crop the neovascularization and macular edema in each angiogram, and a ultrasound B picture-capturing workstation was used to calculate the cropped image area. Effective therapy was defined as treatment decreasing the neovascularized area by more than 20% compared with the pre-surgery neovascularization. Treatment was deemed ineffective if it decreased the area less than 20% compared with pre-surgery neovascularization.

Statistical Analysis Continuous data were described as mean ± standard deviation and were analyzed by independent *t*-tests. Category data were described by rate and proportion and were analyzed by Chi-square tests (χ^2 tests). $P<0.05$ was considered statistically significant. All data were analyzed by SPSS 11.0 statistical software.

Table 2 Comparison of average retinal sensitivity at different therapeutic time points ($\bar{x}\pm s$, dB)

Duration of DR treatment	Joint treatment group($n=61$)	Control group ($n=58$)	t	P
1 month	18.3±4.4	19.3±3.5	1.45	0.150
6 months	17.7±3.6	15.9±4.1[b]	2.46	0.015
12 months	17.0±3.7	14.9±3.7[b]	3.17	0.002

[b]$P<0.01$ *vs*1 month among control group.

RESULTS

Baseline Characteristics of DR To avoid selection bias, baseline characteristics of patients in the two groups were compared before DR treatment. 33 participants 61 DR eyes were in joint treatment group, including 18 males 32 DR eyes and 15 females 29 DR eyes. The control group had 31 patients 58 DR eyes, including 16 males 31 DR eyes and 15 females 27 DR eyes. The male-to-female ratios ($\chi^2=0.055$, $P=0.814$), average age (60.1±18.3 years *vs*63.8±20.1 years, $P=0.444$), average DR duration (4.8±4.2 years *vs* 12.5±7.2 years, $P=0.121$), and average retinal sensitivity (23.2±4.4 dB *vs*22.3±4.3dB, $P=0.265$) were all not statistically differenct between the two groups.

Visual Acuity The frequency of effective visual acuity treatment were not statistically differenct between the two groups 1 month (32.8% *vs*32.8%) or 6 months (45.9% *vs*39.7%) after treatment (χ^2 tests, each $P>0.05$). However, 12 months after treatment, the effective rate of visual acuity treatment in joint treatment group were significantly higher than that of control group (62.3% *vs*43.1%, $P<0.05$, Table 1). In joint treatment group, there was no statistical significance in visual acuity 6 months after treatment, compared to 1 month ($\chi^2=2.198$, $P=0.138$). After 12 months of treatment, however, joint treatment patients had experienced a statistically significant increase ($\chi^2=10.649$, $P=0.001$) in visual acuity. Among control group patients, measurements of visual acuity at 6 months ($\chi^2=0.597$, $P=0.440$) and 12 months ($\chi^2=1.318$, $P=0.251$) showed no statistically significant increase compared with 1 month after treatment.

Visual Field After 1 month of DR treatment, the average retinal sensitivity of participants in two groups (18.3±4.4 dB *vs*19.3±3.5 dB) were not statistically different (independent *t*-tests, $P>0.05$). But after 6 months (17.7±3.6 dB *vs*15.9±4.1 dB) and 12 months (17.0±3.7 dB *vs*14.9±3.7 dB) of DR treatment, the average retinal sensitivity values were significantly higher among the joint treatment group than that of control group (each $P<0.05$, Table 2).

Table 3 Comparison of neovascular regression at different therapeutic time points

Duration of DR treatment	Joint treatment group ($n=61$)		Control group ($n=58$)		χ^2	P
	Effective(%)	Ineffective(%)	Effective(%)	Ineffective(%)		
1 month	29(47.5)	32(52.5)	24(41.4)	34(58.6)	0.457	0.499
6 months	36(59.0)	25(41.0)	26(44.8)	32(55.2)	2.399	0.121
12 months	41(67.2)[a]	20(32.8)	28(48.3)	30(51.7)	4.376	0.036

[a]$P<0.05$ *vs*1 month among joint treatment group.

In joint treatment group, visual fields after 1 month was not different from that of 6 months ($t=0.806, P=0.422$) or 12 months ($t=1.701$, $P=0.091$). However, the control group retinal sensitivity values continually decreased; compared with 1 month after treatment, sensitivity values at 6 months ($t=4.781, P<0.01$) and 12 months ($t=6.637, P<0.01$) both had statistically significance differences.

Neovascular Regression After 1 month, 6 and 12 months of DR treatment, the effective rate of neovascular regression was 47.5%, 59.0% and 67.2%, respectively, among the joint treatment group. In control group, the effective rate of neovascular regression was 41.4%, 44.8% and 48.3%, respectively. The effective rates of neovascular regression after 1 month and 6 months were not statistically different between the two groups (χ^2 tests, each $P>0.05$). However, after 12 months treatment, the effective rate of neovascular regression was significantly higher among joint treatment group patients than that of among control group patients ($P<0.05$).

Among joint treatment group patients, the effective rate of neovascular regression after 1 month was not significantly increased compared with 6 months ($\chi^2=1.614, P=0.204$), but after 12 months of treatment the rate did significantly increase ($\chi^2=4.826$, $P=0.028$). For control group patients, the effective rate of neovascular regression was not statistically different after 6 months ($\chi^2=0.141, P=0.708$) or 12 months ($\chi^2=0.558, P=0.455$) compared with 1 month, Table 3.

DISCUSSION

In this study, visual acuity and neovascularization continued to improve over pre-procedure levels in both treatment groups 1 month, 6 and 12 months after photocoagulation treatment. This confirmed photocoagulation treatment had the positive therapeutic effect for DR[8].

Visual field and retinal sensitivity values had significantly decreased between 1 month and 12 months after treatment in the photocoagulation-alone treatment group, while sensitivity values in the joint treatment group experienced no significant change at the same time. The control group result showed that the treatment of simple photocoagulation did not prevent a deterioration of visual field. By comparison, the TCM which was taken by joint treatment group patients diminished neovascularization, reversing the effects of macular edema and more effectively protecting against visual field loss[11,12].

Properties of ingredients in the TCM administered to joint treatment patients may explain its benefits for DR treatment. Cogon grass root can shorten clotting time[12]. Baikal skullcap root can inhibit aldose reductase, which has been shown to contribute to macular and retinal edema[13]. The sophora flower, chrysanthemum flower, and tree peony root bark can all reduce capillary permeability and brittleness, maintain normal capillary resistance, resist allergic and inflammatory edema, and limit the occurrence of macular and retinal edema[11,12]. Glycosides in orange peels can reduce capillary permeability, prevent microvascular bleeding, enhance fibrinolysis, and reduce thrombus formation[14]. Finally, figwort root, Atractylis ovata root, wind weed root, yam, and balloon flower all possess hypoglycemic effects useful for managing diabetes[12].

In summary, compared with the use of photocoagulation alone to treat stage IV DR, the joint use of photocoagulation and traditional Chinese medicine can more effectively improve and protect participants' vision. Further investigation into the TCM zīyīnliángxuèsǎnyūtāng or its individual ingredients may reveal useful therapies for preventing vision loss or combating neovascularization and thus may ease macular edema in diseases like DR. Provided that the benefits shown in this study support wider use of the joint treatment strategy for DR patients.

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视网膜光凝术联合中药治疗糖尿病性视网膜病变

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摘要

目的:探讨口服滋阴凉血散瘀汤联合激光治疗糖尿病性视网膜病变的临床疗效。

方法:采用口服滋阴凉血散瘀汤联合视网膜光凝治疗糖尿病性视网膜病变患者,以单纯视网膜光凝为对照组,对比两组患者在治疗后 1,6,12mo 的视力、视野及新生血管的变化情况。

结果:口服滋阴凉血散瘀汤联合光凝治疗组患者 12mo 时视力提高(62.3% *vs*43.1%, $P=0.037$),视野改变(17.0±3.7 *vs*14.9±3.7, $P=0.002$)及新生血管退缩情况(67.2% *vs*48.3%, $P=0.036$)均优于对照组患者。

结论:滋阴凉血散瘀汤联合激光治疗糖尿病性视网膜病变较单纯激光治疗更有效。

关键词:激光光凝;滋阴凉血散瘀汤;糖尿病性视网膜病变