

Protective effect of Chinese drug huoxuehuayu decoction on macula after phacoemulsification

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Abstract

• **AIM:** To investigate the protective effect of huoxuehuayu decoction on macula after phacoemulsification.

• **METHODS:** Simple age-related cataract patients (130 cases 140 eyes) were divided into A, B groups. The 80 eyes of A group were treated by conventional phacoemulsification; the patients (60 eyes) of B group were given huoxuehuayu decoction orally for two courses after phacoemulsification. Best-corrected visual acuity (BCVA), corneal and aqueous conditions, thickness of macular central fovea and changes of macular retinal tissue in A, B groups were observed before surgery, 1 day; 1 week, 2, 4, 6, 8 weeks and 3 months after surgery.

• **RESULTS:** Three months after surgery, the ratio of visual acuity ≥ 1.0 in group B was significantly higher than that of group A. One week after surgery the ratio of mild aqueous flare in group B was significantly lower than that of group A. The thickness of central fixation was significantly increased in both groups 1 week, 2, 4, 6, 8 weeks and 3 months after phacoemulsification; the difference between 2 to 8 weeks after surgery and pre-operation showed statistical significance in both groups. 11 eyes in A group had macular edema during 2 to 6 weeks after surgery, including 9 eyes with fovea thickened and 2 eyes with cystoid macular edema, and seven eyes' edema disappeared in 3 months. 2 eyes in B group had macular edema, including 1 eye fovea thickened and 1 eye cystoid macular edema, during 4 to 6 weeks after surgery, and the two eyes' edema disappeared 3 months after surgery. The fovea thickness in group B during 2 to 8 weeks after surgery was statistically lower than group A.

• **CONCLUSION:** Huoxuehuayu decoction orally has protective effect on macula after phacoemulsification.

• **KEYWORDS:** huoxuehuayu decoction; phacoemulsification; macular edema; optical coherence tomography

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INTRODUCTION

With the improvement of the technique of phacoemulsification, the incidence of postoperative complications decreases gradually and macular edema becomes a common cause affecting the improvement of postoperative visual acuity. There is no effective method to control postoperative macular edema at present, while traditional Chinese medicine is effective in the treatment of age-related macular degeneration (AMD)^[1]. Therefore, we give huoxuehuayu decoction orally for two courses after phacoemulsification and use optical coherence tomography (OCT) to observe the change of macula, in order to probe the protective effect of traditional Chinese medicine to the macular area, and to provide clinical basis for the prevention and treatment of macular edema after phacoemulsification.

MATERIALS AND METHODS

Subjects Simple cataract patients (130 cases 140 eyes) from January 2009 to March 2010 who underwent phacoemulsification and intraocular lens (IOL) implantation surgery in our hospital were collected. These patients were divided into A group with 72 patients 80 eyes and B group with 58 patients 60 eyes. The patients of A group were treated by conventional phacoemulsification; the patients in B group were given huoxuehuayu decoction orally for two courses after phacoemulsification. No diabetic retinopathy, no high myopia and their lens' opacity affected the measurements of OCT.

Methods All patients had smooth operation. These patients' blood pressure, blood sugar, routine blood, routine urine and blood coagulation were normal. Mydriatic tropicamide amide were instilled 30 minutes before operation (2 times) and oxybuprocaine hydrochloride were instilled 5 minutes before operation (3 times). Conjunctival sac was cleaned before operation. All operations were done by a highly qualified doctor successfully. After operation, cravit eye drops were instilled 4 times a day, continued until 4 weeks after surgery; dexamethasone kanamycin eye drops were instilled 4 times a day, continued until 2 weeks after surgery. Huoxuehuayu decoction 125mL were taken by oral twice a day until 10 days after operation, 5 days as a treatment course. Huoxuehuayu

Table 1 The situation of slit lamp examination 1 day and 7 days post-operation n (%)

t/d	Group	Corneal edema		Aqueous flare		Descemet folds
		Slight	Moderate	Slight	Moderate	
1:	A 80	22(27.5)	4(5)	71(88.8)	9(11.2)	9(11.3)
	B 60	15(25)	3(5)	56(93.3)	4(6.7)	6(10)
7:	A 80	5(6.2)	0	43(53.6) ^b	4(5)	0
	B 60	1(1.7)	0	19(31.7)	0	0

^bP < 0.01 vs group B.

decoction was provided by hospital pharmacy of Chinese medicine. The formula mainly included Radix Bupleuri 10g, Radix Angelica 10g, Radix Paeoniae Rubra 10g, Radix Rehmanniae Exsiccata 20g, Radix Salvia Miltiorrhizae 10g, Semen Persicae 10g, Flos Carthami 10g, Rhizoma Chuanxiong 10g, Herba Hippochaetes Hiemalis 10g, Flos Eriocanli 10g. The situation of anterior segment was observed by slit-lamp before surgery, 1 day, 1 week after surgery separately. The thickness of foveal and changes of macular retinal tissue were checked by OCT before surgery, 1, 2, 4, 6, 8 weeks and 3 months after surgery. The best-corrected visual acuity (BCVA) was measured by autorefractometer. The thickness of macula was measured by Topcon-3D OCT (resolution 5 μm).

Statistical Analysis SPSS 17.0 statistical software package was used to analyze these data. Results were compared by the Student's *t*-test and χ^2 -test. *P* < 0.05 was considered statistically significant.

RESULTS

Clinical Condition The situation of corneal edema, aqueous flare and descemet folds in both groups were similar at 1 day and 1 week postoperation (Table 1). Three months after operation, the BCVA was more than 1.0 in 56 eyes of group A, and 19 eyes was 0.6 to 0.9, 5 eyes was less than 0.15 and no eye had significant corneal edema and opacity aqueous. The BCVA was more than 1.0 in 52 eyes of group B, and 7 eyes were 0.6 to 0.9, 1 eye was less than 0.15 and no eye had significant corneal edema and opacity aqueous (Table 2).

Fovea Retina Morphology The morphology of fovea retina was normal preoperatively in group A and B, the thickness of central fixation was significantly increased in both groups 1 week, 2, 4, 6, 8 weeks and 3 months after phacoemulsification; the difference between 2 to 8 weeks after surgery and pre-operation showed statistical significance in both groups. The fovea thickness in group B during 2 to 8 weeks after surgery was lower than group A, the difference was statistically significant (Table 3).

We called the obvious lower reflection cavity in the OCT image cystoid macular edema (CME). If the thickness of fovea retina increased 2 standard deviations than the average thickness of the pre-operation at any time and there was no obvious lower reflection cavity on OCT, we considered that it was the thickness abnormality. 11 eyes in A group had macular edema during 2 to 6 weeks after surgery, including 9 eyes with fovea thickened (Figure 1) and 2 eyes with cystoid macular edema, and seven eyes' edema disappeared in 3 months. OCT showed the macular edema disappeared and the visual acuity

Table 2 BCVA 3 months post-operation n (%)

Group	≥1.0	0.9-0.6	<0.1
A	56(70.0) ^a	19(23.8)	5(6.2)
B	52(86.7)	7(11.7)	1(1.7)

^aP < 0.05 vs group B.

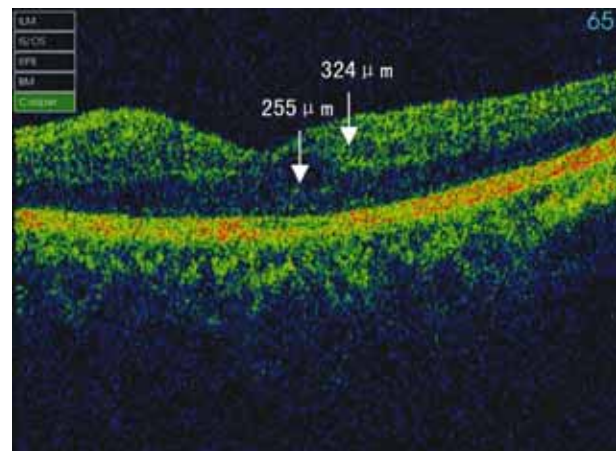


Figure 1 Cystoid macular edema after operation: The thickness of central fixation 255 μm. The thickness of edema 324 μm.

of 2 eyes was greater than 0.5 in B group and had macular edema, including 1 eye fovea thickened and 1 eye cystoid macular edema, during 4 to 6 weeks after surgery, and the two eyes' edema disappeared 3 months after surgery. The occurrence of macular edema was statistically significant in group A and B (13.7% vs 3.3%, *P* < 0.05); the occurrence rates of cystoid macular edema between group A and B showed no significant difference (2.5% vs 1.7%, *P* > 0.05).

DISCUSSION

Macular edema as one of the complications of phacoemulsification, was reported 50 years ago. Because there is no really effective method to control it, it becomes a common complication after phacoemulsification. The incidence of macular edema occurrence in clinic after cataract surgery is between 0.1% and 12.0% [2]. It has been reported that the incidence of simple cataract macular edema postoperatively checked by OCT is up to 20% [3]. We found that the incidence of simple cataract macular edema postoperatively is 13.75% and the differences may be related to the time of the surgery, the level of ultrasound energy and the surgical techniques. It is found that there is negative correlation between fovea macular thickness and visual acuity (*r* = -0.61 ~ -0.79) [4]. It had been reported that the most common

Table 3 The thickness of central fixation

($\bar{x} \pm s, \mu\text{m}$)

Group	Preoperation	Postoperation					
		1 week	2 weeks	4 weeks	6 weeks	8 weeks	3 months
A	216.8 ± 26.7	217.8 ± 16.8	228.5 ± 17.5 ^a	235.8 ± 39.2 ^a	247.4 ± 16.7 ^b	233.4 ± 22.5 ^b	222.4 ± 31.5
B	216.3 ± 23.4	216.9 ± 25.4	219.5 ± 27.1	221.5 ± 41.0	236.7 ± 18.9	224.5 ± 11.9	218.3 ± 21.8

^a $P < 0.05$, ^b $P < 0.01$ vs group B.

pathogenesis of macular edema after phacoemulsification was mechanical injury caused by surgery, which causing uveal inflammation and make plasma proteins and inflammatory cells moved into intraocular cavity that filled with liquid^[5]. The release of inflammatory mediators such as cyclooxygenase, which made an increase of prostaglandin is also a main reason. Prostaglandins, especially prostaglandin F2a made the telangiectasia around the fovea, increased the permeability of vessel, and decreased the drainage function of retinal pigment epithelial cells, which cannot remove excessive inflammatory substances and led to blood-ocular barrier damaged^[6]. The studies of Lobo *et al*^[7] showed that macular edema occurred in the central area of macula, which was related to the location of leakage points mainly located in the central macular blood vessels region, indicated the occurrence of the abnormalities of the blood-retinal barrier. In our study, the majority of macular edema patients would take this factor into account. Because the abnormal leakage of the blood-retinal barrier would create better conditions to promote vascular endothelial growth factor accumulation, and cause abnormal retinal neovascularization. When the speed of the liquid in blood vessels flowing into the retina is faster than the rate of the liquid out through the retinal vascular space, the liquid would accumulate among the retina outer plexiform layer and inner nuclear layer, then CME emerge. In addition, surgical accidents caused the barrier losing of posterior capsular and vitreous prolapse. The traction between forward vitreous body and macula damaged the blood-retinal barrier and Müller cells, which also can lead to macular edema. Two patients in group A occurred posterior capsule rupture, the diameter of one patient with resection of posterior capsule opacification was 4mm; one patient's posterior capsule rupture was less than 1/5. Both of the two patients underwent the anterior vitrectomy and their intraocular lens was implanted in their capsular bags. One patient had cystoid macular edema, while another did not. One patient's posterior capsule rupture was less than 1/5 in group B. We also did the anterior vitrectomy and made the intraocular lens implanted in the capsular bag. The patient appeared macular edema 4 weeks after surgery, then it disappeared 2 months later. The visual acuity of the patient was 1.0. Light damage resulted from long time of operation leads to the damage of blood-retina barrier, which also causes macular edema. The studies of Yan *et al*^[8] showed that under the microscope light, the more the surgery prolonged, the stronger the light was, the smaller the increase of the F-ERG responses would be, which suggested that continued operation under the microscope's light can cause light toxicity damage of retina. The time of our surgery was 10

to 20 minutes, no more than 30 minutes, so the light damage effect was little.

Because of the spontaneous remission trend of macular edema after cataract surgery, some cases of mild symptoms usually do not need to be treated. In these cases OCT showed that fovea retina thickened at the early stage of postoperation, but it returned to normal soon. So the studies of drug treatment were relatively fewer. With the continual improvement of phacoemulsification technology and surgical instruments, the incidence of serious postoperative complications decreased gradually, and the demand of postoperative vision increased. So it is more important to reduce and treat macular edema after cataract surgery. The urgent problem is how to choose effective methods to intervene at the right time and obtain the exact effect. In recent years, many researchers explored on Chinese medicine treatment of macular degeneration, these researches investigated the mechanism of the active ingredients of traditional Chinese medicine and found that many Chinese Herbal Medicine significantly inhibits retinal neovascularization. Li *et al*^[9] found that Radix Salvia Miltiorrhizae can reduce the number of vascular endothelial growth factor in vascular proliferative retinopathy mice, and prevent retinal neovascularization by improving the local oxygen poor environment, or affect various growth factors and new blood vessels. Ferulic acid, one of the active ingredients of Radix Angelica and Rhizoma Chuanxiong, can improve blood circulation, anti-coagulation and inhibit platelet aggregation, inhibit macrophage activation and arachidonic acid (AA) metabolism, histamine antagonist, reduce vascular permeability, antioxidant and scavenge free radical and other broad pharmacological effects. Ferulic acid significantly inhibited angiotensin II-induced VSMC proliferation of endothelial cells by inhibiting extracellular regulated protein kinase (ERK1/2) and stress-activating protein kinase (JNK)^[10]. The study of the mechanism of the effective components of Chinese medicine provided a strong theoretical basis for the treatment of macular degeneration and the reduction of macular edema post-operation with Chinese medicine.

Therefore, we used huoxuehuayu decoction to prevent or control the macular edema after phacoemulsification. In the study, we found that the ratio of aqueous flare of the patients between Group B and A did not have statistically significant difference 1 day after the surgery. 1 week postoperatively, the ratio of mild aqueous flare of group B was significantly lower than that of group A, and the difference was statistically significant. So we consider that huoxuehuayu decoction could reduce inflammation after cataract surgery, but the effect was

not obvious in the early postoperative period. By dilating the blood vessel, improving microcirculation, promoting the absorption of exudate and congestion, the huoxuehuayu decoction played the role of anti-inflammatory. 2 to 8 weeks after surgery, the thickness of retinal macular central fixation is statistically different from that of pre-operation in group A. 2 to 6 weeks after surgery, 11 eyes showed postoperatively macular edema, including 9 eyes showed fovea thickened and 2 eyes showed cystoid macular edema. The results were similar with previous studies. 2 to 8 weeks after surgery, the fovea thickness in group B was lower than group A, and the difference was statistically significant. The incidence of macular edema in group B was significantly lower than group A after the surgery, and the difference was statistically significant. It indicated that administration of huoxuehuayu decoction could protect the macular area significantly. Possibly by inhibiting lipid per-oxidation and oxidation, eliminating free radicals and free radical reaction, enhancing the ability of hypoxia tolerance, it could reduce the incidence of macular edema. By improving the microcirculation, reducing the postoperative inflammation, inhibiting collagen synthesis to prevent the tissue proliferation, it could promote the restoration of macular edema. However, 2 cases of macular edema occurred in group B. It suggested that taking huoxuehuayu decoction solely could not completely prevent macular edema and taking huoxuehuayu decoction could alleviate or prevent the edema indeed to some extent. The proportion of patients whose visual acuity is more than 1.0 in group B was significantly higher than group A, and the difference was statistically significant. It indicated that oral administration of huoxuehuayu decoction can obviously improve the visual acuity of the patients after cataract surgery.

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活血化淤汤对超声乳化白内障吸除术后黄斑区的保护作用

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摘要

目的:探讨活血化淤汤对超声乳化白内障吸除术后黄斑区的保护作用。

方法:单纯年龄相关性白内障患者130例140眼分为A、B两组,A组80眼常规超声乳化吸除术;B组60眼行超声乳化吸除术后给予活血化淤汤口服两个疗程,A、B两组分别于术前、术后1d;1,2,4,6,8wk及3mo观察最佳矫正视力、角膜及房水情况、黄斑中心凹视网膜厚度及黄斑区组织变化情况。

结果:术后3mo,B组视力 ≥ 1.0 的比例明显高于A组,差别有统计学意义。术后1wk,B组房水轻度闪辉比例明显低于A组,差别有统计学意义。术后1,2,4,6,8wk;3mo白内障超声乳化术后出现中心注视点厚度增加,A、B两组术后2~8wk与术前比较差异均有统计学意义;其中A组11眼(13.7%)出现术后黄斑水肿,均发生于术后2~6wk,包括9眼中心凹增厚及2眼黄斑囊样水肿,其中7眼3mo内水肿消失;B组2眼(3.3%)出现术后黄斑水肿,包括1眼中心凹增厚及1眼黄斑囊样水肿,发生于术后4~6wk,到术后3mo水肿消失。术后2~8wk,B组中心凹厚度低于A组,差别有统计学意义。

结论:白内障超声乳化术后黄斑部呈现厚度增加的趋势,造成一定程度的视力下降,少数人会出现黄斑囊样水肿,术后口服中药活血化淤汤后视力 ≥ 1.0 的比例明显提高,黄斑中心凹的厚度及黄斑水肿的发生率大大降低,提示了活血化淤汤对超声乳化白内障吸除术后黄斑区的保护作用。

关键词:活血化淤汤;超声乳化白内障吸除术;黄斑水肿;光学相干断层扫描