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Intravitreal triamcinolone acetonide in the treatment of macular edema due to retinal vein occlusion

Meng-Xiang Guo[1], *Chang-Xian Yi*[2], *Dao-Man Xiang*[1]

[1]Department of Ophthalmology, Guangzhou Women and Children's Medical Center, Guangzhou 510120, Guangdong Province, China
[2]Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou 510610, Guangdong Province, China
Correspondence to: Meng-Xiang Guo. Department of Ophthalmology, Guangzhou Women and Children's Medical Center, Guangzhou 510120, Guangdong Province, China. gmengxiang@ yahoo. com. cn
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Abstract

• AIM: To evaluate the efficacy and safety of intravitreal triamcinolone acetonide (TA) as treatment for macular edema associated with retinal vein occlusion(RVO).

• METHODS: The study group consisting 30 patients (30 eyes) with RVO combined with macular edema received intravitreal 4mg TA. Changes in best-corrected visual acuity (BCVA), intraocular pressure(IOP), examination with slit-lamp microscope, fluorescein angiography and optical coherence tomography (OCT) were observed during the follow-up. Statistical analysis was conducted with SPSS 12.0 software.

• RESULTS: The visual acuity(VA) of all patients was significantly improved and the central macular thickness (CMT) was significantly relieved. There was no correlation between course, age, CMT before injection and the type of RVO. There was positive correlation between visual acuity before injection and after injection.

• CONCLUSION: Intravitreal injection of TA is an easy-operated and safe therapy. After injection, macular edema can be rapidly relieved. VA at baseline is the predictor for the prognosis of VA. Some patients experience recurrence of macular edema between 3 to 6 months after injection.

• KEYWORDS: macular edema; retinal vein occlusion; triamcinolone acetonide
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INTRODUCTION

Macular edema is the leading cause of central vision impairment from retinal vein occlusion (RVO). Long-term macular edema will result in the apoptosis of retinal photoreceptors, which leads to blindness at last. The traditional treatments of macular edema including topical and oral corticosteroids, oral acetozolamide and grid pattern laser photocoagulation have been proved with uncertain effect. Recently vitrectomy and intravitreal triamcinolone acetonide (TA) have been used in clinic trial. We reported our results on intravitreal TA as a treatment of macular edema associated with RVO from March 2003 to December 2006.

MATERIALS AND METHODS

Patients Thirty patients 30 eyes were treated with intravitreal TA from March 2003 to December 2006. Among the cases, there were 14 males and 16 females, who were aged from 18 to 77 and the average age was 54. Among them, there were 20 cases with central retinal vein occlusion (CRVO), who were categorized in two forms: ischemic and non-ischemic, according to Hayreh's standard [1]. Until now, there are no unify categorization standards of branch retinal vein occlusion (BRVO), so we had not classified those cases with BRVO. All the patients were followed after injection from one week to three months, 24 cases were followed for six months. The visual acuity(VA) of all patients was below 0.4 before treatment. Patients who had photocoagulation within one month of enrollment were excluded. Those patients who had intraocular pressure(IOP) greater than 25mmHg or history suggesting glaucoma, or had choroidal neovascularization were excluded. All the patients signed an informed content.

Methods The entire patients received antibiotic eye drops three days before injection. The procedure was performed in our outpatient clinic operation room under sterile condition. The eye was prepared with alcaine eye drops as a topical anesthetic, then applied povidone iodine to eyelid margins, eyelashes, and conjunctival surface; After that, 0. 1mL TA (40g/L, Kunming Jida Pharmaceutical Co., LTD, China) was intravitreal injected at inferior temporal quadrant 3. 5 or 4mm posteroid to limbus with 27 gauge- needle. Because TA is a kind of white suspension, so it must be shaken before injection. After injection the IOP was reduced by digital massage. A small amount of Chlortetracycline ointment was instilled at the end of the procedure, and after that, it was instilled once a day for one week.

The measurement of best-corrected visual acuity (BCVA) was performed with Snellen Chart. IOP was measured using Goldmann applanation tonometry. A masked clinical observer graded cataracts using slit-lamp microscope. The average thickness of the central macula (CMT) (1mm in diameter) was measured with optical coherence tomography (OCT), because this represents the most significant area for central visual acuity. Fundus fluorescein angiography (FFA) was observed. The grading of steroid-related adverse events was

Table 1 VA changes before and after TA injection ($\bar{x} \pm s$, LogMAR)

t/mo	All eyes($n=30$)	CRVO/I($n=8$)	CRVO/N($n=12$)	BRVO($n=10$)
Preinjection	1.16 ± 0.56	1.59 ± 0.49	0.94 ± 0.35	1.10 ± 0.66
Postinjection				
0.25	0.70 ± 0.50[b]	0.92 ± 0.62[a]	0.60 ± 0.34[b]	0.69 ± 0.54[b]
1	0.61 ± 0.52[b]	0.93 ± 0.55[b]	0.46 ± 0.33[b]	0.53 ± 0.61[b]
3	0.62 ± 0.46[b]	0.97 ± 0.54[a]	0.49 ± 0.33[b]	0.54 ± 0.43[a]
6	0.67 ± 0.43[b]	0.99 ± 0.47	0.57 ± 0.26[a]	0.50 ± 0.42[a]
Final	0.73 ± 0.45[b]	1.08 ± 0.47	0.57 ± 0.32[a]	0.69 ± 0.40

[a]$P<0.05$, [b]$P<0.01$ *vs*preinjection, CRVO/I: Ischemic CRVO; CRVO/N: Non- ischemic CRVO.

Table 2 CMT changes before and after TA injection ($\bar{x} \pm s$, μm)

t/mo	All eyes($n=30$)	CRVO/I($n=8$)	CRVO/N($n=12$)	BRVO($n=10$)
Preinjection	749 ± 318	947 ± 489	673 ± 250	683 ± 129
Postinjection				
0.25	314 ± 170[b]	390 ± 264[b]	270 ± 135[b]	307 ± 94[b]
1	224 ± 116[b]	301 ± 191[a]	185 ± 41[b]	205 ± 63[b]
3	255 ± 155[b]	230 ± 138[b]	263 ± 183[a]	268 ± 155[b]
6	338 ± 179[b]	373 ± 171	288 ± 165[b]	355 ± 208[b]
Final	317 ± 186[b]	310 ± 174[a]	290 ± 181[b]	354 ± 212[b]

[a]$P<0.05$, [b]$P<0.01$ *vs*preinjection, CRVO/I: Ischemic CRVO; CRVO/N: Non- ischemic CRVO.

defined prospectively. Significant elevation of the IOP was defined as an increase of more than 5mmHg or >21mmHg. Postoperative lens status was determined using the Lens Opacities Classification System Ⅲ (LOCS Ⅲ). Significant progression of cataract was defined as an increase of 2 or more grades. All the patients were examined at 0.25, 1, 3 and 6 months after the treatment.

Statistical Analysis Preinjection and postinjection changes of VA, IOP and CMT were analyzed by paired-sample *t* test, and $\alpha = 0.05$ with SPSS 12.0 software. The correlation between age, duration of disease, CMT at baseline and final VA was analyzed by Pearson correlation analysis. All the Snellen VA were changed to LogMAR VA according to formula[2]. VA changes were graded according to 0.2 LogMAR as increased VA (VA increased more than 2 lines), unchanged VA (VA unchanged or changed less than 1 line) and reduced VA (VA reduced more than 2 lines).

RESULTS

Visual Acuity The average preinjection VA of all the 30 patients was 0.13. The average VA of postinjection was all significantly increased, $P \leqslant 0.001$. Among them, 22 patients gained VA increase (22/30, 73%), 7 had VA unchanged (7/30,23%), 1 had VA reduced (1/30,3%). The final VA of 10 patients was less than 20/200. Among them, 6 were ischemic central retinal vein occlusion (CRVO), 1 was non-ischemic CRVO and 3 were branch retinal vein occlusion (BRVO). Among the 12 non-ischemic CRVO patients, 5 cases had baseline VA between 20/200 and 20/50, after injection, 2 patients had VA more than 20/40, 3 patients had VA unchanged, no one experienced VA reduced (Table 1). CRVO/I: Ischemic CRVO; CRVO/N: Non-ischemic CRVO.

Thickness of Central Macular Edema OCT showed diffused edema of macular neuroepithelial retina and cavitations before injection. After injection macular edema was reduced. All the patients had significantly reduced CMT during follow-up period, $P<0.01$. The statistical difference of postinjection CMT changes was showed both in non-ischemic CRVO patients and BRVO patients. However, no statistical difference of postinjection CMT changes was showed in patients of ischemic CRVO six months later, $P=0.066$ (Table 2).

FFA Proinjection FFA showed that leakage of fluorescein and macular edema were reduced, however, one patient revealed enlargement of non-perfusion area, who needed photocoagulation at last.

Correlation Analysis Age, course, the type of RVO and preinjection CMT had no correlation with VA prognosis, R^2 respectively were 0.86 ($P=0.126$), 0.217($P=0.25$), -0.338 ($P=0.67$), 0.068($P=0.72$). However, baseline VA was positively correlated with postinjection final VA, $R^2=0.405$ ($P=0.026$).

Recurrence According to our statistics, of the 30 patients, 14 patients (47%) had macular edema recurred, among them, 1 (7%) was recurred at 1 month postinjection, 5 (36%) were recurred at 3 month postinjection, 8 (57%) were recurred at 6 month postinjection. 4 cases of ischemic CRVO recurred (4/8, 50%), 4 cases of non-ischemic CRVO recurred (4/12, 33%), 6 patients of BRVO recurred (6/10, 60%). After recurrence, one patient received reinjection of TA 4mg. 1 week after injection, the VA was increased and CMT reduced from 508μm to 172 μm, but 3 months later it recurred again.

Complication The mean preinjection IOP was 13.2mmHg, 1 week, 1 month and 3 months after injection, the IOP was statistically increased, $P<0.05$, the IOP of 6 month and final follow-up had no statistical increase compared with baseline IOP. 6 cases had IOP increased (6/30, 20%),

among them, 2 cases occurred at 1 week after injection, 4 cases occurred at 1 month after injection. The IOP of 1 case temporarily increased at 1 month and after given some eye drops the IOP reduced, it increased again at 3 month. Using eye drops could control all the increased IOP. 3 cases of mild posterior capsule opacification occurred after 8 months to 11 months. No case of endophthalmitis and vitreous hemorrhage occurred during follow-up period.

DISCUSSION

Macular edema is the leading cause of lower central visual acuity of retinal vein occlusion, until now, it has no ideal therapeutic measurement[1-4]. Triamcinolone acetonide (TA) is a glucocorticosteroid with water-fast prolonged action. Intravitreal injecting TA could prevent blood-retinal barrier breakdown by reducing inflammatory reaction and suppressing the effect of vascular endothelial growth factor (VEGF)[5] to inhibit retinal vessel leakage and neovascularization[6]. Our results showed that intravitreal injecting TA could reduce macular edema and increase VA in a short time, however some cases experienced edema recurrence. According to our observation, the majority recurrence occurred form 3 months to 6 months after injection. We suppose that the absorption of TA in vitreous maybe one of the causes of recurrence. The other cause was that it was still a symptomatic treatment but not an etiological treatment. Although it was reported that TA could inhibit VEGF, thereby inhibit neovascularization, it is interesting that of our cases, one patient with BRVO had retinal ischemic developed and macular edema recurred and had to receive photocoagulation at last. These results suggest that the mechanism of macular edema is complex and it was insufficient to simply intravitreal injection of TA. Our statistical analysis showed that course, age, baseline CMT and the type of retinal vein occlusion had no relationship to VA prognosis, but baseline VA had positive correlation with final VA. The report of CRVO study group also showed that the VA prognosis was deeply depend on baseline VA[7]. The period of disease course had no relationship to VA prognosis because course was a subjective index, some patients couldn't remember their right course. Alternatively, it may also be because our group was too small and our follow-up period was too short. In theory, the type of retinal vein occlusion may be the important factor to affect VA prognosis, however, in our study it showed opposite result. Maybe our sample was too small and the follow-up period was too short to get right conclusion. It is shown in some research[8] that the VA prognosis of retinal vein occlusion has correlation with ages, the older of patients, the poorer of VA prognosis will get. As we know, vessel inflammation may be the cause of retinal vein occlusion of young, therefore, the relationship of VA prognosis and ages may be influenced by pathogenic. According to this, it needs to carry further study.

In conclusion, intravitreal injection of TA could relieve macular edema and improve VA in a short period, without serious complications. It must be a cost-effective treatment. However, it can't block the recurrence of macular edema. Great sample and further clinic study are needed.

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玻璃体腔注射曲安奈德治疗视网膜静脉阻塞黄斑水肿

郭梦翔[1], 易长贤[2], 项道满[1]
(作者单位:[1]510120 中国广东省广州市妇女儿童医疗中心眼科;[2]510610 中国广东省广州市,中山大学中山眼科中心)
作者简介:郭梦翔,女,博士,研究方向:玻璃体、视网膜疾病。
通讯作者:郭梦翔. gmengxiang@yahoo.com.cn

摘要

目的:评价玻璃体腔注射曲安奈德治疗视网膜静脉阻塞合并黄斑水肿的疗效及并发症。

方法:患者 30 例 30 眼玻璃体腔注射曲安奈德 4mg 治疗视网膜静脉阻塞合并黄斑水肿,观察治疗前、后的最佳矫正视力、眼压、裂隙灯显微镜检查、眼底荧光血管造影和光学相干断层扫描的变化,采用 SPSS 12.0 软件进行统计学分析。

结果:所有患者手术后视力均显著提高,平均黄斑中心凹厚度(CMT)显著减少。病程、年龄、注射前 CMT 及视网膜静脉阻塞的类型和视力预后无相关性,注射前视力与注射后末次视力呈正相关。

结论:玻璃体腔注射曲安奈德治疗视网膜静脉阻塞合并黄斑水肿简单、安全、易操作,短期内可以迅速减轻黄斑水肿,最终的视力预后取决于治疗前的视力,部分患者在注射后 3~6mo 可能复发。

关键词:黄斑水肿;视网膜静脉阻塞;曲安奈德