Intravitreal triamcinolone acetonide for patients with macular oedema due to central retinal vein occlusion in Taiwan

K-C Cheng¹, W-C Wu² and C-J Lin³

Abstract

Purpose To evaluate the safety and outcome of intravitreal triamcinolone acetonide as treatment for macular oedema secondary to central retinal vein occlusion (CRVO) in Taiwanese.

Methods The prospective clinical interventional study included 43 patients (43 eyes) with macular oedema due to CRVO. The study group consisted of 22 patients who had accepted an intravitreal injection of 4 mg of triamcinolone acetonide. The control group included 21 patients without intravitreal triamcinolone acetonide. Examination included assessment of best-corrected visual acuity, slit-lamp biomicroscopy, measurement of intraocular pressure, ophthalmoscopy, and optical coherence tomography (OCT).

Results The mean follow-up was 283.00 ± 70.62 days in the study group and 354.05 ± 173.18 days in the control group, respectively. In the study group, visual acuity measurements improved significantly ($P = 0.007$) from 1.00 ± 0.45 logMAR preoperatively to a best postoperative visual acuity of 0.67 ± 0.65 logMAR. Seventeen eyes (77.3%) gained improvement in visual acuity with 12 eyes (54.5%) showing an increase in visual acuity of at least two Snellen lines. All 22 patients showed significant macular oedema resolution in OCT examination ($P < 0.001$) from $594.36 \pm 177.78 \mu\text{m}$ preoperatively to a mean retinal thickness of $317.23 \pm 196.83 \mu\text{m}$ postoperatively postintravitreal injection. In the control group, baseline best-corrected visual acuity and best-

corrected visual acuity during the follow-up did not vary significantly ($P = 0.457$).

Conclusion Intravitreal triamcinolone acetonide can lead to a significant improvement in visual acuity and a resolution of macular oedema in patients with CRVO.

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Keywords: central retinal vein occlusion; macular oedema; intravitreal triamcinolone acetonide

Introduction

Central retinal vein occlusion (CRVO) is the second most common retinal vascular disorder in the eye after diabetic retinopathy and can be associated with significant visual morbidity. Patients have intraretinal haemorrhage in all four retinal quadrants, tortuous and dilated retinal veins, and in some cases, optic disc oedema. The pathologic finding suggests that the site of obstruction is located in the lamina cribrosa.¹ The two major vision-limiting complications of CRVO are macular oedema and neovascularization. The degree of macular involvement determines the level of visual impairment. Usually, the patients of CRVO often suffer severe irreversible visual loss and have improvement of vision in only 20% of cases.² However, an effective strategy to treat CRVO has not been forthcoming.^{3–5} The standard of therapy currently remains limited to the management of the neovascular sequelae with panretinal photocoagulation. The Central

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Table 1 Baseline clinical characteristics

	<i>Study group</i>	<i>Control group</i>
Number	22 patients (22 eyes; 10 right eyes)	21 patients (21 eyes; 12 right eyes)
Male:female	9:13	10:11
Mean age (years)	56.45 ± 14.67	64.57 ± 8.77
Mean follow-up time (days)	283.00 ± 70.62	354.05 ± 173.18

Vein Occlusion Study showed that grid pattern photocoagulation definitely reduced macular oedema on fluorescein angiography but did not translate to a visual acuity improvement.⁶ Recent reports have suggested various treatment options including intravitreal tissue plasminogen activator, radial optic neurotomy, surgical recanalization of the retinal vein, and laser-induced chorioretinal venous anastomosis^{3,7–9} to improve the circulatory status of the retina after CRVO.

However, these reports, although encouraging, are pilot studies, which lack larger well-controlled studies to demonstrate the efficacy of these procedures. Recently, the effect of intravitreal anti-VEGF drugs has been widely discussed. However, the number of patients in this pilot study was limited and the follow-up is too short to make any specific treatment recommendations. A recent addition to the options for the treatment of macular oedema due to CRVO has been intraocular injection of corticosteroids. Previous studies about intravitreal injection of triamcinolone acetonide for macular oedema due to CRVO were almost prospective or retrospective methods, which lacked control group data and papers mentioning this issue are rare in Taiwan. Therefore, we designed a prospective comparative nonrandomized clinical interventional study for Taiwanese to evaluate the efficacy of intravitreal triamcinolone acetonide in the management of macular oedema secondary to CRVO.

Materials and methods

Patient selection

The prospective comparative nonrandomized clinical interventional study included 43 consecutive patients (43 eyes) with central retinal vein occlusion. All patients had clinical evidence of CRVO with intraretinal haemorrhage and dilated, tortuous veins in all four quadrants in addition to macular oedema. There were 22 patients (9 men and 13 women; 22 eyes; 10 right eyes) in the study group and 21 patients (10 men and 11 women; 21 eyes; 12 right eyes) in the control group. No cataract surgery was performed either before, in combination

with, or after the intravitreal injection. Those patients enrolled in the study group agreed to accept an intravitreal injection of 4 mg of triamcinolone acetonide. Patients who refused an intravitreal injection of triamcinolone acetonide were assigned to the control group. Six eyes (28.57%) in the control group (cases 10, 13, 15, 16, 17, and 18) were classified as ischaemic CRVO; a panretinal argon laser photocoagulation was performed as treatment of CRVO to prevent neovascular complications during the follow-up, others accepted only regular follow-up visit. The mean age of the study group was 56.45 ± 14.67 years and the mean age of the control group was 64.57 ± 8.77 years. The mean follow-up times were 283.00 ± 70.62 days (ranging from 185 to 423 days) in the study group and 354.05 ± 173.18 days (ranging from 183 to 598 days) in the control group, respectively (Table 1). We performed a series of ophthalmic examinations at baseline of the study and in repeated intervals afterwards as visual acuity (the best-corrected visual acuity was determined from Snellen chart and converted to the logarithm of minimal angle of resolution (logMAR) equivalents to perform the appropriate statistical manipulation; Counting fingers and hand movements at 1 m were converted to 1.6 and 1.9, respectively), slit-lamp inspection of the anterior segment, pneumotonometry (Full auto Tonometer TX-F; Canon, NY, USA), dilated fundus examination with indirect ophthalmoscopy and Goldmann 3-mirror contact lens, and optical coherence tomography (Stratus OCT™ III Model 3000; Zeiss Humphrey, NY, USA). In each patient, the same instrument (optical coherence tomography) was used throughout with 6-mm radial lines employed. Retinal thickness mapping was performed and the 1-mm mean central retinal thickness was recorded.

Eye was categorized as nonischaemic CRVO, if there was no rubeosis iridis and capillary nonperfusion on fluorescein angiography less than 10 disc areas. Otherwise, eyes with 10 or more optic disc areas of nonperfusion on fluorescein angiography or rubeosis iridis were classified as ischaemic CRVO.

For the study group, we performed the above examinations during the first week postinjection, and twice at two-weekly intervals, then at routine monthly intervals. For the control group, the same examinations were performed once a month. Main outcome measures were best-corrected visual acuity, macular thickness assessed with optical coherence tomography, and postoperative complications.

Surgical procedure

The intravitreal injection of triamcinolone acetonide was performed under sterile conditions in the

ophthalmologic operation theatre with an operation microscope. After informed consent was obtained, the affected eye was anesthetized with a drop of proparacaine hydrochloride (0.5%) ophthalmic solution. Povidone-iodine (Saint-iodine[®]; Patron, Gangshan, Taiwan) was applied before the intravitreal injection. Then the patient was completely draped. We used lid speculum to stabilize the eyelids. A paracentesis into the anterior chamber was performed and 0.1 ml of aqueous fluid was aspirated by 26-gauge needle with a 1.0-ml tuberculin syringe to decrease the volume of the eye, thereby avoiding a rise in intraocular pressure (IOP). The injection of 4 mg (0.1 ml) crystalline triamcinolone acetonide (Kenacort[™]-A; Bristol-Myers Squibb, Taipei, Taiwan) into the vitreous cavity was performed using a sharp 27-gauge needle through the pars plana, at 4 mm from the limbus. The inferior pars plana was preferred to minimize postoperative floaters, because the injected triamcinolone acetonide rapidly deposited to dependent areas of the vitreous cavity following treatment. After that, an antibiotic eyedrop (Tobramycin-Tobrex[®]; Alcon, Belgium, China) was applied.

Statistic analysis

Visual acuity and retinal thickening at the baseline and follow-up visits were summarized using mean $\pm$ SD. Statistical calculations were carried out using standard software (MS Excel 2003, Microsoft Co., Redmond, WA, USA). Data were compared using paired *t*-test. Statistical significance was taken at *P*-value ≤ 0.05 .

Results

In the study group, visual acuity measurements improved significantly (*P* = 0.007) from 1.00 ± 0.45 logMAR preoperatively to a best postoperative visual acuity of 0.67 ± 0.65 logMAR. Seventeen eyes (77.3%) showed visual acuity improvement, two eyes (9.1%) remained the same, and three eyes (13.6%) became worse during the follow-up period compared with the baseline measurement of the study. Measured in Snellen lines, 12 eyes (54.5%) showed an improvement by at least two Snellen lines or more (Table 2). In the control group, after argon laser panretinal photocoagulation or just continuous observation, only seven eyes (33.33%)

Table 2 Clinical data of the patients before and after intravitreal injection of triamcinolone acetonide

Case no.	Age	Gender	Type	Preoperative data		Postoperative data				Visual acuity improvement	Visual acuity improvement ≥ 2 Snellen lines
				BCVA (logMAR)	Foveal thickness (μ m)	Final BCVA (log MAR)	Final foveal thickness (μ m)	Foveal thickness change (%)	Follow-up (days)		
1	49	F	Non-ischaemic	1.0	590	0.7	210	-64.41	185	Yes	No
2	70	F	Non-ischaemic	1.0	597	0.3	203	-66.00	251	Yes	Yes
3	66	M	Non-ischaemic	1.0	663	0.4	190	-71.34	190	Yes	Yes
4	46	M	Non-ischaemic	0.5	632	0.0	180	-71.52	331	Yes	Yes
5	77	M	Non-ischaemic	1.0	623	1.1	603	-3.21	223	No	No
6	53	F	Non-ischaemic	1.0	579	0.7	221	-61.83	235	Yes	No
7	70	F	Ischaemic	1.6	889	1.6	742	-16.54	238	No	No
8	75	M	Non-ischaemic	1.4	775	1.1	703	-9.29	363	Yes	No
9	75	F	Non-ischaemic	0.4	483	-0.1	188	-61.08	217	Yes	Yes
10	51	F	Non-ischaemic	1.3	848	0.5	260	-69.34	303	Yes	Yes
11	68	F	Non-ischaemic	1.3	369	0.3	333	-9.76	272	Yes	Yes
12	45	F	Non-ischaemic	0.7	854	0.3	280	-67.21	274	Yes	Yes
13	57	M	Non-ischaemic	1.0	587	0.2	169	-71.21	191	Yes	Yes
14	24	F	Non-ischaemic	0.5	526	0.0	193	-63.31	275	Yes	Yes
15	24	F	Non-ischaemic	0.5	345	0.1	219	-36.52	393	Yes	Yes
16	69	F	Non-ischaemic	1.5	613	1.3	413	-32.63	382	Yes	No
17	55	M	Non-ischaemic	0.3	350	0.0	209	-40.29	423	Yes	Yes
18	64	F	Ischaemic	1.2	459	1.4	165	-64.05	319	No	No
19	51	M	Non-ischaemic	0.7	435	0.1	185	-57.47	375	Yes	Yes
20	56	M	Non-ischaemic	1.5	649	1.3	354	-45.45	287	Yes	No
21	49	F	Non-ischaemic	0.5	315	1.9	206	-34.60	185	No	No
22	48	M	Ischaemic	1.9	895	1.9	753	-15.87	251	No	No

BCVA = best-corrected visual acuity; F = female; logMAR = logarithm of minimal angle of resolution; M = male.

Table 3 Clinical data of the control group during the follow-up

Case no.	Age	Gender	Type	Baseline data		Final OPD visit data				Visual acuity improvement	Visual acuity improvement ≥ 2 Snellen lines
				BCVA (log MAR)	Foveal thickness (μm)	Final BCVA (log MAR)	Final foveal thickness (μm)	Foveal thickness change (%)	Follow-up (days)		
1	72	F	Non-ischaemia	0.4	501	1.6	587	17.17	574	No	No
2	62	M	Non-ischaemia	0.7	721	1.0	914	26.77	221	No	No
3	66	M	Non-ischaemia	1.6	343	1.6	495	44.31	210	No	No
4	85	F	Non-ischaemia	1.4	708	0.7	335	52.68	245	Yes	No
5	55	M	Non-ischaemia	0.4	624	0.7	540	-13.46	207	No	No
6	72	F	Non-ischaemia	1.9	807	1.6	593	-26.52	302	Yes	No
7	73	F	Non-ischaemia	1.5	232	1.6	452	94.83	215	No	No
8	58	F	Non-ischaemia	0.7	452	0.7	341	-24.56	196	No	No
9	64	F	Non-ischaemia	0.7	398	0.3	263	-33.92	185	Yes	Yes
10	58	M	ischaemia	1.0	542	1.4	183	-66.24	540	No	No
11	58	F	Non-ischaemia	1.4	780	1.3	478	-38.72	539	Yes	No
12	70	F	Non-ischaemia	0.1	629	1.0	576	-8.43	236	No	No
13	57	M	ischaemia	0.7	401	0.7	443	10.47	571	No	No
14	70	M	Non-ischaemia	1.4	745	1.5	707	-5.10	181	No	No
15	73	M	ischaemia	1.5	803	1.6	817	1.74	575	No	No
16	52	M	ischaemia	1.9	799	1.9	785	-1.75	545	No	No
17	60	M	ischaemia	1.0	567	0.5	312	-44.97	572	Yes	Yes
18	63	F	ischaemia	1.5	779	1.4	698	-10.40	598	Yes	No
19	68	F	Non-ischaemia	1.6	555	1.6	503	-9.37	205	No	No
20	72	M	ischaemia	0.3	327	0.7	303	-7.34	183	No	No
21	48	F	Non-ischaemia	0.2	360	0.0	264	-26.67	335	Yes	Yes

BCVA = best-corrected visual acuity; F = female; logMAR = logarithm of minimal angle of resolution; M = male; OPD = outpatient department.

showed visual acuity improvement. Five eyes (23.81%) had the same visual acuity during the follow-up compared with the baseline measurement of the study. For nine eyes (42.86%), visual acuity measurements after baseline measurement were worse than those at the start of the study (Table 3). In the study group, the visual acuity was significantly increased postoperatively ($P=0.007$). On the other hand, the visual acuity of the control group did not vary significantly ($P=0.457$) between baseline best-corrected visual acuity (1.04 ± 0.57 logMAR) and best-corrected visual acuity during the follow-up period (1.11 ± 0.53 logMAR).

The decline of cotton wool spots, retinal haemorrhage, and macular oedema were noted in all of the study group during fundus examination after intravitreal injection of triamcinolone acetonide (Figure 1) and the fluorescein angiography showed vascular leakage decrease postoperatively (Figure 2).

The optical coherence tomography examination of the study group demonstrated clinical improvement in macular oedema ($P<0.001$) postoperatively (Figure 3). The preinjection foveal thickness ranged from 315 to $895 \mu\text{m}$ (mean, $594.36 \pm 177.78 \mu\text{m}$). The final foveal thickness ranged from 180 to $753 \mu\text{m}$ (mean,

$317.23 \pm 196.83 \mu\text{m}$) with an average decrease of 46.95% in foveal thickness (Table 2). In the control group, the foveal thickness measured by optical coherence tomography between baseline data and final data did not show significant resolution ($P=0.062$). The baseline foveal thickness ranged from 232 to $803 \mu\text{m}$ (mean, $574.90 \pm 183.82 \mu\text{m}$). The final foveal thickness ranged from 183 to $817 \mu\text{m}$ (mean, $504.24 \pm 200.43 \mu\text{m}$) with an average decrease of 8.33% in foveal thickness (Table 3).

Recurrence of macular oedema and a concomitant decrease in visual acuity occurred in six cases of the study group (cases 10, 17, 18, 19, 20, and 21) with an average of 269.33 ± 100.46 days (ranged from 133 to 403 days) postoperatively. Subsequently, all these six patients accepted a second injection of triamcinolone acetonide. After that, the macular oedema in all six patients subsided and visual acuity improvement in four patients (cases 10, 17, 19, and 20) again.

Seven patients (31.82%) in the study group had ocular hypertension (IOP ≥ 22 mmHg). Six patients (cases 2, 12, 14, 20, 21, and 22) could be controlled to a normal range by topical antiglaucomatous medication. One patient (case 19) required trabeculectomy. No cases of neovascular glaucoma occurred.

Figure 1 (a) Preinjection colour fundus photograph of left eye (51-year-old male; case 19 in the study group) with central retinal vein occlusion intraretinal haemorrhage in all four quadrants and macular oedema. The veins dilated and tortuous. (b) After 2 months of intravitreal triamcinolone injection, intraretinal haemorrhage with macular oedema subsided.

In the study group, 19 cases were assigned as nonischaemic CRVO and three patients (cases 7, 18, and 22) were assigned as ischaemic CRVO. Panretinal photocoagulation was performed on these three cases (cases 7, 18, and 22) during the follow-up periods to prevent neovascular sequelae. Those who were ischaemic CRVO got no improvement in visual acuity and those who were nonischaemic CRVO had visual acuity improvement (78.95%) at the end of the follow-up.

Adverse events

Excluding elevated IOP, no obvious complication was noted in the study group postoperatively except for one patient who developed a mature cataract during follow-up. No serious side effects, such as postoperative endophthalmitis or retinal detachment, occurred.

Discussion

Intravitreal triamcinolone acetonide was first used by Antcliff to treat uveitic cystoid macular oedema;¹⁰

Figure 2 (a) Preinjection late-phase fluorescein angiography of the left eye (case 19 in the study group) shows a central retinal vein occlusion with severe leakage around the macula. It also demonstrated severe fluorescein leakage and blockage secondary to retinal haemorrhage. (b) Resolution of macular oedema with restoration of normal foveal contour was noted 2 months after intravitreal triamcinolone injection. Fluorescein angiogram shows no macular leakage.

consequently many scholars tried intravitreal triamcinolone acetonide to treat macular oedema associated with diabetic macular oedema,^{11–13} proliferative diabetic retinopathy,¹⁴ Vogt-Koyanagi-Harada syndrome,¹⁵ sympathetic ophthalmia,¹⁶ branch retinal vein occlusion,¹⁷ and diabetic papillopathy.¹⁸ In addition, several case series demonstrated anatomical and vision improvement after intravitreal triamcinolone acetonide for patients with central retinal vein occlusion.^{19–22}

Park *et al*²⁰ demonstrated that after 4 mg intravitreal triamcinolone acetonide for macular oedema due to nonischaemic CRVO, all 10 eyes revealed biomicroscopic improvement in cystoid macular oedema with visual gain and 6 of 10 eyes had ≥ 2 lines of visual

Figure 3 (a) Preinjection cross-sectional optical coherence tomography (case 19 in the study group) shows cystoid macular oedema in the left eye. The retinal thickness map demonstrates marked retinal thickening. The mean central (1 mm diameter) thickness is $435\ \mu\text{m}$ (normal mean central thickness is $<210\ \mu\text{m}$). (b) Two months postinjection, optical coherence tomography demonstrates decline of the cystoid macular oedema. The mean central thickness is $221\ \mu\text{m}$.

improvement. Ip *et al*²³ reported that at the 6 months follow-up after 4 mg intravitreal injection of triamcinolone acetonide, five eyes with nonischaemic CRVO demonstrated improved anatomically and four of five patients had significant improvement functionally ($P=0.003$). Eight eyes with ischaemic CRVO also had good anatomical response. However, these patients do not appear to respond as well functionally. Cekic *et al*²⁴ studied visual acuity and macular thickness changes in 24 eyes with macular oedema due to CRVO ($n=21$) and hemiretinal vein occlusion (HRVO, $n=3$). Of the 24 eyes, 14 were treated with a single intravitreal injection of 4 mg triamcinolone acetonide, six were injected twice, three were injected three times, and one received four injections. After an average of 10 months follow-up, the mean central foveal thickness reduced by 55% of preinjection value and 41.67% of eyes gained ≥ 2 Snellen lines. In a retrospective study of 40 CRVO patients treated with intravitreal injection of triamcinolone acetonide, Gregori *et al*²⁵ found median Snellen visual acuity was 20/400 at baseline, increasing to 20/300 at 1 month, 20/300 at 3 months, 20/400 at 6 months, and 8/200 at 1 year. Ramezani *et al*²⁶ performed a randomized sham-controlled clinical trial for CRVO patients. The study group (13 eyes) received 4 mg intravitreal injection of triamcinolone acetonide and the control group (14 eyes) received a sham subconjunctival injection. The results revealed that the improvement in visual acuity and the reduction in central macular thickness of the

study group were more significant than control group only at 1 month ($P=0.013$) and at 2 months ($P=0.003$) after injection, respectively. Gelston *et al*²⁷ designed a retrospective comparative case series of nine patients with macular oedema associated with CRVO (six non-ischaemic and three ischaemic) treated with an intravitreal injection of 4 mg triamcinolone acetonide, compared with 10 control (observation) patients (six non-ischaemic and four ischaemic). No statistically significant improvement in visual acuity was observed between the study group and the control group at 1, 2, or 6 months. Similarly, a subgroup analysis of the non-ischaemic CRVO treatment patients compared with the non-ischaemic controls also showed no statistically significant increase in visual acuity at 1, 2, or 6 months. From the results of this study, we found that intravitreal triamcinolone acetonide may be effective in treatment of macular oedema and increase visual acuity in patients with central retinal vein occlusion. These patients of the study group experienced a significant increase in visual acuity ($P=0.007$) from 1.00 ± 0.45 logMAR preoperatively to a best postoperative visual acuity of 0.67 ± 0.65 logMAR, while the visual acuity of the control group did not vary significantly ($P=0.457$) during the follow-up period. Twelve eyes (54.5%) of the study group gained ≥ 2 Snellen lines. It also appears effective in decreasing vascular leakage. All 22 patients showed a decrease in central foveal thickness in optical coherence tomography examination. There was a significant

improvement in central foveal thickness ($P < 0.001$) from presentation of $594.36 \pm 177.78 \mu\text{m}$ to $317.23 \pm 196.83 \mu\text{m}$ at the end of the follow-up with an average decrease of 46.95%. On the other hand, the central foveal thickness of the control group did not show significant resolution ($P = 0.062$) at final visit.

The mechanism of action of corticosteroids for macular oedema in CRVO is still unclear, but it is believed that anti-inflammation, vascular endothelial growth factor downregulation and antipermeability functions of corticosteroid were the major roles for its effect.^{28–30} The effect of intravitreal triamcinolone acetonide may be transient and the duration of the effect is related to its clearance from the eye. The pharmacokinetics of intravitreal triamcinolone acetonide has been studied in rabbit eyes. Schindler *et al*³¹ found triamcinolone acetonide (0.5 mg) disappeared rapidly in eyes that underwent a combined vitrectomy and lensectomy (average, 6.5 days) and more slowly in eyes that underwent vitrectomy only (average, 16.8 days) compared with unoperated normal rabbit eyes (average, 41 days). How these findings may influence the optimal number of injections and the suitable timing of injections is still unknown. Ip *et al*²³ observed that there were four of 13 CRVO patients who received intravitreal triamcinolone acetonide developed a recurrence of macular oedema between the 3- and 6-month follow-up examination. Cekic *et al*²⁴ reported that eyes required second injection were performed at an average of 7 months after the first injection, and the third injection was at 12 months, thus indicating that the therapeutic effect of triamcinolone acetonide probably maintained 6 months to 7 months with CRVO and HRVO. Gregori *et al*²⁵ found that 50% of eyes of CVRO received more than one intravitreal injection of triamcinolone acetonide after 1 year follow-up period. In our series, six patients (cases 10, 17, 18, 19, 20, and 21) of the study group suffered from a recurrence of macular oedema and a concomitant reduction in visual acuity with an average of 269.33 ± 100.46 days postoperatively. Reinjection of triamcinolone acetonide led to a reduction in macular thickness in all six cases and a visual acuity improvement in four patients (cases 10, 17, 19, and 20). Two patients got worse visual acuity and one of them (case 21) developed mature cataracts finally. From the result of our study, we found retreatment may be effective in reducing retinal thickening and/or improving visual acuity in some patients.

Intravitreal triamcinolone acetonide has been shown to be nontoxic in animal studies,³² as was the vehicle used in the commercial preparation.³³ In our case series, no toxic effects of triamcinolone acetonide on the retina and optic nerve were noted. Previous clinical and

experimental studies also demonstrated the safety of using intraocular steroid.^{32–35}

The most common side effect reported after intravitreal injection of triamcinolone acetonide is an IOP rise. The prospective study of Williamson *et al*²² to use intravitreal triamcinolone acetonide for the treatment of macular oedema associated with nonischaemic CRVO revealed that 11 of 18 eyes suffered from IOP rises requiring topical medications and one of them needed trabeculectomy. Cekic *et al*²⁴ reported that 9 of 18 CRVO or HRVO patients without preexisting glaucoma developed steroid-induced elevated IOP after intravitreal triamcinolone acetonide injection and controlled with topical antiglaucomatous medication. Trabeculectomy was required for two eyes with preexisting glaucoma during the postinjection follow-up period. Gregori *et al*²⁵ observed that after intravitreal triamcinolone acetonide for 40 CRVO patients, IOP increased more than 10 mmHg in 24% of eyes at 1 year. Two of twelve eyes with a history of glaucoma needed trabeculectomy. In our study, ocular hypertension (IOP ≥ 22 mmHg) occurred in seven eyes (31.82%). This problem could be controlled by topical antiglaucomatous treatment or trabeculectomy surgically.

An increase in cataract formation has been described in patients after intravitreal injection of triamcinolone acetonide. Park *et al*²⁰ found a progression of cataract after intravitreal triamcinolone acetonide in 1 of 10 CRVO eyes. Cekic *et al*²⁴ reported that 8 (50%) of 16 phakic eyes with CRVO showed cataract progression after intravitreal injection of triamcinolone acetonide, and two eyes underwent cataract extraction during the study period. In our study, one case (case 21) developed mature cataracts and visual acuity deterioration during the follow-up.

No other complications were noted in this case study. Our low incidence of adverse events suggests that intravitreal triamcinolone acetonide is relatively safe, but the possibility of elevated IOP cannot be understated.

Ip *et al*²³ declared that both nonischaemic and ischaemic eyes with CRVO had a meaningful reduction in retinal thickness following intravitreal triamcinolone acetonide. However, only nonischaemic eyes revealed statistically significant visual acuity improvement at each time point. In the study of Ramezani *et al*,²⁶ the decrease in retinal thickness and visual acuity improvement showed significant changes after intravitreal injection of triamcinolone acetonide in both of nonischaemic and ischaemic types of CRVO. In the study group of our series, 19 cases were classified as nonischaemic CRVO and three patients (cases 7, 18, and 22) were classified as ischaemic CRVO. Those who were ischaemic CRVO got no improvement in visual acuity and those who were nonischaemic CRVO had visual acuity improvement

(78.95%) at the end of the follow-up, favouring improvement for the nonischaemic group. The results from our present study suggest that patients with nonischaemic CRVO have both favourable anatomical and functional responses to intravitreal triamcinolone injection. Patients with ischaemic CRVO also have a favourable anatomical response but do not appear to respond as well functionally. We cannot demonstrate a statistically significant difference between these two groups due to inadequate sample size of ischaemic group. However, it does suggest that patients without ischaemia may have a better response to intravitreal triamcinolone acetonide.

The advantages of intravitreal triamcinolone acetonide include avoiding the systemic adverse effects, having simultaneously high concentrations of drug at the site of action, and no toxic effect on intraocular tissue.

The major limitations of our study are non-randomized selection between study group and control group, small number of patients in both the study and the control group, and inadequate follow-up periods. A large prospective, randomized clinical trial is warranted to assess the long-term efficacy and safety of intravitreal triamcinolone acetonide for patients with macular oedema due to CRVO.

Recently, the effect of intravitreal anti-VEGF drugs such as bevacizumab (Avastin), ranibizumab (Lucentis) and pegaptanib sodium (Macugen) had been widely discussed. Iturralde *et al*³⁶ demonstrated that neither intraocular nor systemic side effects were observed in this study after intravitreal injections bevacizumab. Current results suggest that intravitreal anti-VEGF therapy is a promising option in macular oedema secondary to central retinal vein occlusion. However, the number of patients in this pilot study was limited and the follow-up is too short to make any specific treatment recommendations, but the favourable short-term results suggest that further study is needed. We look forward to a large series study comparing the benefit of intravitreal injection of triamcinolone acetonide and bevacizumab.

Conclusion

The application through intravitreal injection of triamcinolone acetonide showed a significant increase in visual acuity and decrease in macular oedema and vascular leakage in patients with central retinal vein occlusion. Our data indicate that a single intravitreal injection of triamcinolone acetonide may not provide a sustained visual acuity benefit for patients with macular oedema associated with CRVO and some patients needed reinjection. A frequent side effect in our study was an elevation in IOP, which can be readily solved by topical antiglaucomatous medication or surgical

intervention. The results of this study suggested that intravitreal triamcinolone acetonide might be a possibly effective treatment for patients with macular oedema due to central retinal vein occlusion.

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