

Visual and Anatomical Outcomes of Spironolactone Therapy in Patients with Chronic Central Serous Chorioretinopathy

Khalil Ghasemi Falavarjani, MD; Anahita Amirsardari, MD; Abbas Habibi, MD; Acieh Eshaghi, MD
Shohreh Bakhti, MD; Kaveh Abri Aghdam, MD, PhD

Eye Research Center, Rassoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran

Abstract

Purpose: To evaluate the effect of spironolactone on chronic central serous chorioretinopathy (CSC).

Methods: In this prospective interventional case series, patients with chronic CSC were treated with spironolactone (25 mg daily) for at least 6 weeks. If the subretinal fluid (SRF) had not completely resolved by this time, treatment was continued, and the dosage was increased to 25 mg twice daily. Primary outcome measure was the change in maximum SRF height at the final follow-up visit, as detected by optical coherence tomography. Secondary outcome measures were changes in best corrected visual acuity (BCVA) and central macular thickness (CMT).

Results: Sixteen eyes of 14 patients with chronic CSC were enrolled. Mean follow-up time was 6.4 ± 4.3 months. Baseline BCVA was 0.54 ± 0.44 logarithm of the minimum angle of resolution (log MAR), which improved to 0.42 ± 0.43 log MAR at the final visit ($P = 0.04$). Mean CMT decreased from 282.69 ± 103.23 μm at baseline to 236.75 ± 90.10 μm at final visit ($P = 0.11$), and the mean of maximum SRF height decreased from 155.63 ± 95.27 μm at baseline to 77.19 ± 95.68 μm at the final visit ($P = 0.04$). SRF resolved completely in seven eyes (43.75%).

Conclusion: In eyes with persistent SRF due to CSC, spironolactone therapy was associated with a statistically significant decrease in maximum SRF height, as well as an improvement in BCVA.

Keywords: Central Serous Chorioretinopathy; Optical Coherence Tomography; Spironolactone; Subretinal Fluid

J Ophthalmic Vis Res 2017; 12 (3): 281-289

INTRODUCTION

Central serous chorioretinopathy (CSC) is often associated with localized detachments of the neurosensory retina

Correspondence to:

Kaveh Abri Aghdam, MD, PhD. Department of Ophthalmology, Eye Research Center, Rassoul Akram Hospital, Sattarkhan-Niayesh St. Tehran 14456-13131, Iran. E-mail: kaveh.abri@gmail.com

Received: 14-07-2016

Accepted: 23-01-2017

and retinal pigment epithelium (RPE).^[1] The condition is six times more common in men than in women,^[2] and has an overall incidence of approximately 1 in 10,000.^[3] In chronic CSC, subretinal fluid (SRF) does not resolve spontaneously within a few months^[4], which causes anatomical damage to the RPE, and permanent damage to visual function.^[5]

Different treatment modalities, including systemic acetazolamide or rifampin,^[6] conventional and subthreshold laser photocoagulation,^[7] and intravitreal

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Ghasemi Falavarjani K, Amirsardari A, Habibi A, Eshaghi A, Bakhti S, Abri Aghdam K. Visual and anatomical outcomes of spironolactone therapy in patients with chronic central serous chorioretinopathy. *J Ophthalmic Vis Res* 2017;12:281-9.

Access this article online

Quick Response Code:



Website:
www.jovr.org

DOI:
10.4103/jovr.jovr_139_16

bevacizumab or ranibizumab,^[8,9] have been investigated as potential therapeutic options for chronic CSC. Photodynamic therapy (PDT) has been the most promising treatment in this regard, with a success rate approaching 90%.^[10,11] Lack of response, cost, and adverse effects are disadvantages associated with these treatment modalities.

Recently, inappropriate activation of mineralocorticoid receptors (MRs) located in the choroidal vasculature has been identified as a potential pathological pathway underlying the vascular choroidopathy in CSC.^[12] This finding suggests that therapeutic blockade of the MRs could reverse choroidal vasculopathy. Different steroidal competitive MR antagonists, such as eplerenone and spironolactone, are available and currently used in the treatment of congestive heart failure and primary hyperaldosteronism.^[13] Eplerenone is a more selective MR antagonist, but its affinity for the MR is 40-fold lower than that of spironolactone. For this reason, eplerenone is a less potent MR antagonist.^[1]

In the present study, we prospectively evaluated the clinical effects of oral spironolactone in 14 consecutive patients with chronic CSC.

METHODS

In this prospective, interventional case series conducted from September 2013 to January 2015, all patients with chronic CSC were admitted to the retina clinic at Rassoul Akram Hospital, Tehran, Iran. The study was approved by the Eye Research Center Ethics Committee of the Iran University of Medical Sciences, and adhered to the tenets of the Declaration of Helsinki. Photodynamic therapy (PDT) was offered to patients as the most effective treatment.^[14] The off-label use and possible adverse effects of spironolactone were explained to those patients who refused PDT, and informed consent was obtained before the start of spironolactone therapy.

Chronic CSC was diagnosed in eyes affected by symptomatic CSC with duration of at least 3 months, or presence of signs of disease chronicity, including intraretinal cysts or cystoid macular edema. Presence of subretinal fluid (SRF) anywhere in the macular area was detected by funduscopy and confirmed by optical coherence tomography (OCT). Exclusion criteria were as follows: (1) concomitant vitreoretinal or optic nerve disease, including diabetic retinopathy, uveitis, glaucoma, or optic disc pit; (2) previous PDT for CSC, previous laser photocoagulation, or intravitreal injections in the past 3 months; (3) signs of choroidal neovascularization, including subretinal or intraretinal hemorrhages or hard exudates; (4) history of kidney or liver diseases; (5) concomitant use of other potassium-sparing diuretics; and (6) pregnancy.

All included patients were treated with spironolactone (Iran Hormone Pharmaceutical Company, Tehran, Iran)

25 mg daily for 6 weeks. If SRF had decreased but not completely resolved by this time, or if its maximum height remained the same, treatment was continued with increasing the dosage to 25 mg twice daily. The drug was discontinued if there was complete resolution of subretinal fluid or if any systemic adverse events, including gastrointestinal upset, hypersensitivity reactions, or muscle cramps occurred. Patients with an increase in subretinal fluid after 6 weeks were strongly recommended to receive PDT as rescue treatment; however, if they rejected PDT, the drug was continued with a dose of 25 mg two times daily.

All patients underwent comprehensive ophthalmologic examination, including measurement of best corrected visual acuity (BCVA) using Snellen charts, dilated fundus biomicroscopy, and OCT imaging at baseline. OCT was performed using Topcon spectral domain OCT instrument (OCT 1000 mark II; Topcon Inc., Japan) with a 6 × 6, 3D protocol. To detect the maximum height of the SRF, we used the built-in caliper scale of the spectral domain OCT software to measure SRF height in B-scans around the maximum height of subretinal fluid according to the 3D cube and then chose the greatest value. The chosen section was used in the follow-up. Fluorescein angiograms were obtained in all patients who were suspected of having alternative diagnoses mimicking CSC.

Clinical and OCT examinations were repeated 6 weeks after the start of treatment, and every 6 weeks thereafter. Primary outcome measure was the change in maximum SRF height at both 6 weeks and final follow-up. Secondary outcome measures were the changes in BCVA and central macular thickness (CMT). SPSS software (version 15; IBM Inc., Chicago, IL, USA) was used for statistical analyses. Snellen visual acuity records were converted into logarithm of minimum angle of resolution (logMAR) scale. Paired *t*-test was used to analyze within-group changes from baseline. Results were reported as mean ± standard deviation. *P* values <0.05 were considered statistically significant.

RESULTS

Sixteen eyes of 14 patients, 11 men (78.6%) and three women (21.4%) were enrolled. Patients had a mean age of 39.57 ± 1.79 years (range: 26–53 years). Four eyes had history of intravitreal bevacizumab injections with no visual or anatomical response. Two patients had bilateral chronic CSC. Treatment was well tolerated and continued for at least 6 weeks in all patients. Table 1 shows baseline characteristics of cases included. Patients were treated for a mean of 3.1 ± 1.6 months (range: 1.5–7 months). Mean follow-up time was 6.4 ± 4.3 months (range: 1.5–12 months).

Table 1 also shows an overview of all the outcome measures. Mean changes in BCVA were -0.10 logMAR

Table 1. Patients' characteristics and study outcome measures at baseline, 6 weeks, and final visit

Eye number	Patient's age (years)	Gender	Symptom duration before spironolactone treatment (months)	Previous treatment before spironolactone	Drug dosage (mg)	Duration of treatment (months)	Follow-up (months)		BCVA (decimal)		Central macular thickness (µm)		Maximum SRF height (µm)			
							Baseline	6 weeks	Final visit	6 weeks	Final visit	Baseline	6 weeks	Final visit	Baseline	6 weeks
1	31	F	36	None	25	1.5	1.5	0.70	0.70	0.70	312	327	327	70	108	108
2	42	M	9	MPC	25 then 50	3	3	0.10	0.10	0.10	202	164	164	95	49	50
3	31	F	18	None	25	1.5	1.5	0.20	0.20	0.20	410	495	495	172	261	261
4	26	M	Several months*	None	25	3	3	0.90	0.90	0.90	224	173	179	83	60	0
5	37	M	48	IVB	25 then 50	7	10	0.10	0.20	0.40	169	149	149	73	25	0
6	35	M	9	None	25 then 50	6.5	6.5	1.00	1.00	1.00	502	502	177	328	284	43
7	40	M	12	None	25	1.5	1.5	FC at 3 m	FC at 3 m	FC at 3 m	352	206	206	350	0	0
8	51	F	6	IVB	25 then 50	3.5	6	0.40	0.90	0.90	248	192	193	121	64	76
9	53	M	24	None	25 then 50	3	12	0.20	0.20	0.20	150	169	164	73	67	86
10	32	M	4	None	25	1.5	3	0.90	1.00	1.00	291	215	215	130	0	0
11	45	M	Several months*	None	25 then 50	3	3	0.20	0.40	0.40	466	354	267	302	226	137
12	48	M	9	None	25 then 50	3.5	4.5	FC at 4 m	FC at 4 m	FC at 4 m	193	168	357	137	153	283
13 [†]	35	M	36	IVB	25 then 50	3	12	0.20	0.70	0.70	290	216	233	79	80	191
14 [†]	35	M	36	IVB	25 then 50	1.5	10.5	1.00	1.00	1.00	255	254	253	236	0	0
15 [‡]	48	M	12	None	25 then 50	3	12	0.30	0.30	0.30	228	359	186	124	156	0
16 [‡]	48	M	12	None	25 then 50	3	12	0.70	0.70	0.70	231	226	223	117	134	0

BCVA, best corrected visual acuity; F, female; FC, finger counting; IVB, intravitreal bevacizumab; M, male; MPC, macular photocoagulation; SRF, subretinal fluid; *Unknown duration, but with signs of chronicity; [†]Two eyes of the same patient; [‡]Two eyes of the same patient

and -0.12 ± 0.01 logMAR at the 6-weeks and final visits, respectively ($P = 0.04$ for both time points; Table 2). No statistically significant changes were found in CMT measurements at either the 6-weeks or final follow-ups (mean changes: $-22.13 \pm 10.92 \mu\text{m}$, $P = 0.2$ and $-45.94 \pm 13.13 \mu\text{m}$, $P = 0.1$, respectively). There was no significant change in the maximum height of SRF at 6 weeks (mean change: $-51.44 \pm 3.93 \mu\text{m}$, $P = 0.08$; Table 2). However, the maximum height of SRF decreased significantly at the final visit (mean change: $-78.44 \pm 0.41 \mu\text{m}$, $P = 0.04$; Table 2). SRF decreased in ten eyes (62.5%) and completely resolved in three eyes (18.75%) six weeks after initiation of treatment. Three eyes had 6 weeks of follow-up; in two cases, the drug was discontinued due to an increase in SRF. In the other case, SRF completely resolved and the patient decided to discontinue both the medication and follow-up. No adverse events occurred in this patient during the course of treatment. The treatment period was extended past 6 weeks in 11 eyes with persistent SRF which was completely resorbed in four of these eyes at the final visit. Thus, seven out of 16 eyes (43.75%) showed complete resolution of SRF at the final visit.

DISCUSSION

The pathogenesis of CSC is still not definitively known. Exogenous glucocorticoids may induce or exacerbate the disease.^[1] They facilitate fluid accumulation beneath the retina in patients with CSC; this effect contrasts with their role in macular edema, where they lead to fluid absorption.^[15] Glucocorticoid/mineralocorticoid balance is necessary to control hydro-electrolytic regulation. In most tissues, glucocorticoids activate MRs at physiologic levels, while excessive activation of the MR pathway is pathogenic.^[16] Increased choroidal thickness in patients with CSC has been identified using enhanced depth imaging spectral domain OCT.^[17] Moreover, a thickened choroid was observed not only in the affected eyes of patients with unilateral CSC, but also in the unaffected eyes.^[18] This finding suggests that CSC is essentially a bilateral disorder involving choroidal dysfunction, which may be an appropriate target for treatment strategies.

The rationale behind suggesting MR antagonists in the treatment of CSC is that the MR pathway

upregulates the expression of KCa2.3/SK3—the vasodilatory, small conductance, Ca²⁺-activated potassium channel 3—in choroidal endothelial cells. This channel induces dilation of choroidal vessels,^[2] and inactivates endothelial potassium channels, which are upregulated by aldosterone. So this group of drugs can prevent aldosterone-induced choroidal thickening, which might be involved in the pathophysiology of CSC.^[12]

The natural course of chronic CSC has not been well studied, and the control groups of studies that have reported a treatment for chronic CSC have been limited in size. In addition, such studies generally report changes in BCVA and retinal thickness, rather than complete absorption of the fluid. For instance, Gramajo et al^[19] reported that patients with chronic CSC who had been treated with placebo showed no absorption of SRF after 1 month. In a prospective, randomized, double-blind, sham-controlled pilot trial, Roisman et al^[7] showed that patients with chronic CSC in the sham group all needed treatment after 3 months.

Results of the current study indicate that, spiroglactone treatment results in a significant reduction in maximum SRF height and improvement in final BCVA in eyes with persistent SRF due to CSC. However, complete SRF resolution was achieved in less than half of the eyes, and while there was a significant change in BCVA, CMT changes were not significant. Indeed, several studies have shown that no correlation exists between VA and retinal thickness,^[20-22] perhaps because statistical significance is not equivalent to clinical significance. Findings of the current study are in line with the results of several previously published studies, which reported a reduction in SRF and improvement in BCVA, after treatment with MR antagonists.

A summary of the studies that explored the effects of treatment with eplerenone and spiroglactone on CSC is given in Table 3. As shown therein, MR antagonists had a positive influence on the course of chronic CSC in those studies. In a randomized crossover study involving 16 eyes with chronic CSC, Bousquet et al^[23] reported a significant decrease in subfoveal choroidal thickness in spiroglactone-treated patients ($P = 0.02$), but not in placebo-treated cases. However, in the same study, changes in BCVA were not significant ($P = 0.48$).

Table 2. Statistical overview of subretinal fluid, central macular thickness, and best corrected visual acuity

	Baseline	6 weeks	Final visit
Best corrected visual acuity (LogMAR)	0.54±0.44	0.44±0.44 $P=0.043^\dagger$	0.42±0.43 $P=0.045^\dagger$
Central macular thickness (µm)	282.69±103.23	260.56±114.15 $P=0.21^\dagger$	236.75±90.10 $P=0.11^\dagger$
Maximum subretinal fluid height (µm)	155.63±95.27	104.19±91.34 $P=0.08^\dagger$	77.19±95.68 $P=0.04^\dagger$

LogMAR, logarithm of the minimum angle of resolution; [†]Paired *t*-test: the values were compared to the baseline measurements

Table 3. Characteristics of the included studies

Authors, location, and year	Study type	Inclusion criteria	Number of Eyes	Intervention	Mean age (years)	Follow-up period	Results of BCVA (log-MAR)	Results of CMT	Results of SRF	Adverse effects	Conclusion
Bousquet et al. ^[23] France, 2015	Prospective, randomized, double-blinded, placebo-controlled crossover study	CSC and persistent SRF for at least 3 months	16; the analysis of data from 15 eyes was reported	Either spirono-lactone (50 mg) or placebo once a day for 30 days, followed by a washout period of 1 week and then a crossover to either placebo or spirono-lactone for another 30 days	46.5±8	67 days	No significant changes in BCVA (P=0.48)	A significant reduction in CMT in treated eyes, but not in placebo eyes (P=0.02).	Statistically significant reduction in SRF in spirono-lactone compared with the same eyes under placebo (P=0.04)	None	Spiro-lactone significantly reduced both the SRF and the CMT as compared with placebo
Bousquet et al. ^[23] France, 2013	Inter-ventional, prospective, uncontrolled open-label clinical trial	Patients with stable SRF (or intraretinal cysts in one patient) for >4 months	13	25 mg/day of oraplerenone for 1 week, followed by 50 mg/day for 1 or 3 months	54.2±8.9	3 months	0.52±0.24 to 0.27±0.19 (P<0.001)	352±139 µm to 189±99 µm (P<0.01)	175±123 µm to 36±55 µm (P<0.01)	Fatigue (two patients), sedative effect (one patient)	Eplerenone treatment was associated with a significant reduction in CMT, SRF levels, and an improvement in BCVA
Breukink et al. ^[24] The Netherlands, 2014	Retro-spective case series	Chronic CSC for at least 9 months and responded insufficiently to previous treatments	Seven eyes of five patients	Eplerenone (25 mg/day then 50 mg/day)	55	2.5 months	Not reported	Not reported	Resolved in one eye, decreased in two eyes, remained unchanged in two eyes and increased in one eye	Not reported	Eplerenone only has a beneficial effect in a minority of patients with chronic CSC.
Chin et al. ^[20] USA, 2015	Retro-spective consecutive observ-ational case series	Patients treated with oral MA (epler-enone and/or spirono-lactone) were included, and a minimum of 1 month of MA treatment was required	30 (23 patients; seven cases of bilateral CSC). Sixteen patients (69.6%) had been recalcitrant to other inter-ventions prior to treatment with oral MAs	Treatment dose of both eplerenone and spirono-lactone ranged from 25 to 50 mg twice-daily	58.4±10.5	3.9±2.3 months	Median BCVA at the start of therapy was 20/30 (range: 20/20-20/250), and that at final follow-up was 20/40 (range: 20/20-20/125).	The mean decrease in CMT in all patients was 42.4 µm (range: -136 to 255 µm); 100.7 µm among treatment-naive patients, and 16.9 µm among recalcitrant patients.	Not reported	Nine patients (39.1%) experienced systemic side effects, of which three patients (13.0%) were unable to continue therapy.	MA treatment had a positive treatment effect in half of the study patients.

Contd...

Table 3. Contd...

Authors, location, and year	Study type	Inclusion criteria	Number of Eyes	Intervention	Mean age (years)	Follow-up period	Results of BCVA (log-MAR)	Results of CMT	Results of SRF	Adverse effects	Conclusion
Daruich et al. ^[31] Switzerland and United Kingdom, 2016	Retro-spective, inter-ventional case series	Persistent CSC with SRF lasting longer than 4 months; recurrent CSC with SRF lasting longer than 2 months; persistent CSC (SRF ≥ 4 months) with FAF gravitational tracks	54	Eplerenone (25-50 mg daily) or spiro-lactone (25-75 mg daily)	53.1	6 months	0.28 to 0.23 (P=0.041)	342 μ m to 285 μ m (P=0.0003)	93 μ m to 35 μ m (P<0.0001)	Spiro-lactone group: Gyneco-mastia (one patient), low systolic blood pressure (one patient) and hyper-kalemia (two patients). Eplerenone group: hyper-kalemia (two patients)	Response to treatment in the three subgroups: In persistent CSC with tracks, the response was delayed compared with that in the persistent and recurrent cases, suggesting that longer treatment durations would be beneficial in patients with gravitational tracks of RPE alteration.
Chadiali et al. ^[32] USA, 2016	Retro-spective, observ-ational case series	Chronic CSC for greater than 6 months; however, patients with an acute episode of SRF were also included.	23 (20 eyes with chronic CSC and three eyes with acute disease)	Spiro-lactone only (13 eyes), Eplerenone only (three eyes), Spiro-lactone and Eplerenone (seven eyes)	58.0 \pm 9.8	12 months	Mean difference in VA 12 months from base-line: 0.046 \pm 0.02 (P=0.043)	Mean difference in CMT 12 months from baseline: 31 \pm 12.88 μ m (P=0.125)	Mean difference in SRF 12 months from baseline: 62.25 \pm 17.65 μ m (P=0.035)	Hyper-tension (one patient), dizziness (one patient)	MAs may improve BCVA and decrease SRF in patients with CSC, but do not affect the choroidal or macular thickness.
Current study. Iran, 2016	Prospective, inter-ventional case series	CSC with a duration of at least 3 months, or signs of disease chronicity	Sixteen eyes of 14 patients	Spiro-lactone (25 mg daily) for at least 6 weeks. If SRF was not completely resolved, the treatment was continued, with the dosage increased to 25 mg twice daily	39.57 \pm 1.79	6.4 \pm 4.3 months	0.5 \pm 0.44 to 0.42 \pm 0.43 (P=0.04)	282.69 \pm 103.23 μ m to 236.75 \pm 90.10 μ m (P=0.11)	155.63 \pm 95.27 μ m to 77.19 \pm 95.68 μ m (P=0.04)	None	Spiro-lactone therapy was associated with a statistically significant reduction in maximum SRF height and BCVA improvement.
Herold et al. ^[24] Germany, 2014	Inter-ventional, un-controlled, prospective case series	Chronic CSC persistent for more than 6 weeks	18	Spiro-lactone (25 mg twice daily) for up to 12 weeks	45.7 \pm 8.00	3 months	0.32 to 0.20 (P=0.042)	405 μ m to 287 μ m (P=0.009)	219 μ m to 100 μ m (P=0.002)	Gastric pain (one patient) and dizziness (one patient)	There was a positive influence of spiro-lactone on the course of CSC.

Contd...

Authors, location, and year	Study type	Inclusion criteria	Number of Eyes	Intervention	Mean age (years)	Follow-up period	Results of BCVA (log-MAR)	Results of CMT	Results of SRF	Adverse effects	Conclusion
Leisser et al. ^[33] Austria, 2015	Retro-spective case series	Patients who had undergone photo-dynamic therapy (four patients), anti-vascular endothelial growth factor treatment (three patients), or had several episodes of CSC in the past (four patients)	Eleven eyes of 11 patients with long-term recurring CSC	Eplerenone (25 mg daily) as long as needed	60±9.7	10.6±9.9 weeks	Patients were able to read 2.3±2.2 more lines than they were before treatment	455±106 µm to 389±141 µm (P=0.083)	Not reported	Hyper-kalemia of short duration (two patients), increased liver parameters (two patients), and increased serum bilirubin levels (one patient). worsening of renal function parameters in a patient with a history of nephrectomy)	73% of patients had improvement in BCVA, although only 36.4% had full resolution of neurosensory detachment.
Salz et al. ^[34] USA, 2015	Retro-spective review	Chronic CSC for a minimum of 3 months prior to the start of treatment, without evidence of spon-taneous improvement in vision or SRF during this period	Fourteen eyes of 14 patients	Eplerenone (25 mg daily) for 1 week, followed by an increase to 50 mg daily	57	3 months	0.41 to 0.28 (P=0.02)	Not reported	130 µm to 21 µm (P=0.004)	None	Oral eplerenone may be effective in treating patients with chronic CSC.
Singh et al. ^[35] USA, 2015	Retro-spective consecutive case series	Chronic CSC with the presence of SRF for greater than 4 months without improve-ment	17 eyes of 13 patients	Oral eplerenone (25 mg or 50 mg daily)	57	90-240 days	0.42 to 0.29 at day 181+ (P=0.024)	339.5 µm to 270.3 µm at day 181+ (P=0.029).	131.5 µm to 15.3 µm at day 181+ (P=0.002).	Not reported	There was a significant reduction in SRF, a reduction in CST, and improved visual acuity in eyes with chronic CSC.

BCVA, best-corrected visual acuity; CMT, central macular thickness; CSC, central serous chorioretinopathy; FAF, Fundus autofluorescence; logMAR, logarithm of the minimum angle of resolution; MA, mineralocorticoid antagonist; RPE, retinal pigment epithelium; SRF, subretinal fluid

Herold et al^[24] in a prospective case series, evaluated 18 consecutive patients with CSC. Total central retinal thickness decreased from 405 to 287 μm after treatment with spironolactone ($P = 0.009$). At final visit, BCVA significantly increased compared to baseline value ($P = 0.042$). In a non-randomized pilot study involving 13 cases with chronic CSC, Bousquet et al^[25] treated patients with 25 mg/day of oral eplerenone for 1 week; they then increased the dosage to 50 mg/day for 1 or 3 months. CMT reduced significantly at both 1 and 3 months ($P < 0.05$ and $P < 0.01$, respectively). At 3 months, BCVA significantly improved over baseline ($P < 0.001$). In the current study, even though there had been no significant SRF absorption after 6 weeks, there was significant SRF resolution at the final visit [Table 2]. This result is comparable to those of other published studies. For example, Bousquet et al^[23] reported a statistically significant decrease in SRF in spironolactone-treated eyes, but not in placebo-treated eyes ($P = 0.04$). Herold et al^[24] observed a significant foveal SRF reduction 3 months after spironolactone therapy: from 219 μm to 100 μm ($P = 0.002$). Bousquet et al^[25] reported that, after 3 months of treatment with eplerenone, SRF was significantly reduced over baseline ($P < 0.01$). In the current study, 11 eyes showed resolution or reduction of the SRF. In four of these, the duration of follow-up was the same as the treatment period, so the possibility of recurrence after cessation of the drug cannot be excluded. In the other seven eyes, follow-up was 1.5–9 months longer than the duration of treatment. The final SRF height was slightly greater (1–12 μm) than that of the first visit; in 2 eyes and no increase over pre-treatment SRF occurred in the remaining five eyes.

Aldosterone receptor antagonism influences serum K^+ levels by weakening the effects of aldosterone on K^+ homeostasis in the principal cells of the kidney. Therefore, the probability of clinically significant hyperkalemia increases, which can result in unstable ventricular arrhythmias.^[26] Daily spironolactone therapy should be reduced in dosage by 50% when serum K^+ level is 5.5–5.9 mEq/L, and it should be stopped when serum K^+ level is ≥ 6.0 mEq/L until the level becomes less than 5.5 mEq/L.^[27] Interaction between progesterone receptors and spironolactone can cause dose-dependent hormonal side-effects, such as breast tenderness and gynecomastia, erectile dysfunction, low libido, and irregular menstrual cycles.^[1] Spironolactone should not be used concomitantly with other potassium-sparing diuretics and potassium supplements.^[28] The adverse effects are generally minor and avoidable with proper dosage and monitoring.

Major limitations of the present study are the small number of cases, short follow-up period to observe recurrences, lack of choroidal thickness measurements, and absence of a placebo-treated (control) group. Despite these limitations, our study showed that SRF resolved

completely in more than 40% of eyes after treatment with spironolactone.

In conclusion, because of insufficient evidence, large randomized controlled trials are needed to further elucidate the role of spironolactone as a treatment option for chronic central serous chorioretinopathy. If a positive effect is found, spironolactone should be considered as a low-cost alternative to the expensive treatments available.

Financial Support and Sponsorship

Nil.

Conflicts of Interest

There are no conflicts of interest

REFERENCES

1. Daruich A, Matet A, Dirani A, Bousquet E, Zhao M, Farman N, et al. Central serous chorioretinopathy: Recent findings and new physiopathology hypothesis. *Prog Retin Eye Res* 2015;48:82-118.
2. Wong KH, Lau KP, Chhablani J, Tao Y, Li Q1, Wong IY. Central serous chorioretinopathy: What we have learnt so far. *Acta Ophthalmol* 2016;94:321-325.
3. Kitzmann AS, Pulido JS, Diehl NN, Hodge DO, Burke JP. The incidence of central serous chorioretinopathy in Olmsted County, Minnesota, 1980-2002. *Ophthalmology* 2008;115:169-173.
4. Spaide RF, Campeas L, Haas A, Yannuzzi LA, Fisher YL, Guyer DR, et al. Central serous chorioretinopathy in younger and older adults. *Ophthalmology* 1996;103:2070-2079; discussion 2079-2080.
5. Taban M, Boyer DS, Thomas EL, Taban M. Chronic central serous chorioretinopathy: Photodynamic therapy. *Am J Ophthalmol* 2004;137:1073-1080.
6. Steinle NC, Gupta N, Yuan A, Singh RP. Oral rifampin utilisation for the treatment of chronic multifocal central serous retinopathy. *Br J Ophthalmol* 2012;96:10-13.
7. Roisman L, Magalhães FP, Lavinsky D, Moraes N, Hirai FE, Cardillo JA, et al. Micropulse diode laser treatment for chronic central serous chorioretinopathy: A randomized pilot trial. *Ophthalmic Surg Lasers Imaging Retina* 2013;44:465-470.
8. Kim GA, Rim TH, Lee SC, Byeon SH, Koh HJ, Kim SS, et al. Clinical characteristics of responders to intravitreal bevacizumab in central serous chorioretinopathy patients. *Eye (Lond)* 2015;29:732-741.
9. Ozdemir O, Erol MK. Morphologic changes and visual outcomes in resolved central serous chorioretinopathy treated with ranibizumab. *Cutan Ocul Toxicol* 2014;33:122-126.
10. Lim JJ, Glassman AR, Aiello LP, Chakravarthy U, Flaxel CJ, Spaide RF; Macula Society CSC Collaborative Study Group, Research and Education Committee and Website Committee. Collaborative retrospective macula society study of photodynamic therapy for chronic central serous chorioretinopathy. *Ophthalmology* 2014;121:1073-1078.
11. Bae SH, Heo J, Kim C, Kim TW, Shin JY, Lee JY, et al. Low-fluence photodynamic therapy versus ranibizumab for chronic central serous chorioretinopathy: One-year results of a randomized trial. *Ophthalmology* 2014;121:558-565.
12. Zhao M, Célérier I, Bousquet E, Jeanny JC, Jonet L, Savoldelli M, et al. Mineralocorticoid receptor is involved in rat and human ocular chorioretinopathy. *J Clin Invest* 2012;122:2672-2679.
13. Funder JW. Mineralocorticoid receptor antagonists: Emerging roles

- in cardiovascular medicine. *Integr Blood Press Control* 2013;6:129-138.
14. Naseripour M, Falavarjani KG, Sedaghat A, Moghaddam AK, Nasserisina S, Alemzadeh SA. Half-dose Photodynamic Therapy for Chronic Central Serous Chorioretinopathy. *J Ophthalmol Vis Res* 2016;11:66-69.
 15. Sarao V, Veritti D, Boscia F, Lanzetta P. Intravitreal steroids for the treatment of retinal diseases. *Scientific World Journal* 2014;2014:989501.
 16. Gomez-Sanchez E, Gomez-Sanchez CE. The multifaceted mineralocorticoid receptor. *Compr Physiol* 2014;4:965-994.
 17. Imamura Y, Fujiwara T, Margolis R, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in central serous chorioretinopathy. *Retina* 2009;29:1469-1473.
 18. Kim YT, Kang SW, Bai KH. Choroidal thickness in both eyes of patients with unilaterally active central serous chorioretinopathy. *Eye (Lond)* 2011;25:1635-1640.
 19. Gramajo AL, Marquez GE, Torres VE, Juárez CP, Rosenstein RE, Luna JD; Medscape. Therapeutic benefit of melatonin in refractory central serous chorioretinopathy. *Eye (Lond)* 2015;29:1036-1045.
 20. Aghdam KA, Pielen A, Framme C, Junker B. Visual and anatomic outcomes after conversion to aflibercept in neovascular age-related macular degeneration: 12-month results. *Eur J Ophthalmol* 2016;26:473-478.
 21. Dadgostar H, Ventura AA, Chung JY, Sharma S, Kaiser PK. Evaluation of injection frequency and visual acuity outcomes for ranibizumab monotherapy in exudative age-related macular degeneration. *Ophthalmology* 2009;116:1740-1747.
 22. Singh RP, Srivastava S, Ehlers JP, Bedi R, Schachat AP, Kaiser PK. A single-arm, investigator-initiated study of the efficacy, safety and tolerability of intravitreal aflibercept injection in subjects with exudative age-related macular degeneration, previously treated with ranibizumab or bevacizumab: 6-month interim analysis. *Br J Ophthalmol* 2014;98(Suppl 1):i22-i27.
 23. Bousquet E, Beydoun T, Rothschild PR, Bergin C, Zhao M, Batista R, et al. Spirolactone for nonresolving central serous chorioretinopathy: A Randomized Controlled Crossover Study. *Retina* 2015;35:2505-2515.
 24. Herold TR, Prause K, Wolf A, Mayer WJ, Ulbig MW. Spirolactone in the treatment of central serous chorioretinopathy—a case series. *Graefes Arch Clin Exp Ophthalmol* 2014;252:1985-1991.
 25. Bousquet E, Beydoun T, Zhao M, Hassan L, Offret O, Behar-Cohen F. Mineralocorticoid receptor antagonism in the treatment of chronic central serous chorioretinopathy: A pilot study. *Retina* 2013;33:2096-2102.
 26. Maron BA, Leopold JA. Aldosterone receptor antagonists: Effective but often forgotten. *Circulation* 2010;121:934-939.
 27. Pitt B, Bakris G, Ruilope LM, DiCarlo L, Mukherjee R. Serum potassium and clinical outcomes in the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS). *Circulation* 2008;118:1643-1650.
 28. Aldactone (spironolactone) Drug Interactions; Available at <http://www.drugs.com/pro/aldactone.html>. [Last accessed on 2016 Jul 10].
 29. Breukink MB, den Hollander AI, Keunen JE, Boon CJ, Hoyng CB. The use of eplerenone in therapy-resistant chronic central serous chorioretinopathy. *Acta Ophthalmol* 2014;92:e488-e490.
 30. Chin EK, Almeida DR, Roybal CN, Niles PI, Gehrs KM, Sohn EH, et al. Oral mineralocorticoid antagonists for recalcitrant central serous chorioretinopathy. *Clin Ophthalmol* 2015;9:1449-1456.
 31. Daruich A, Matet A, Dirani A, Gallice M, Nicholson L, Sivaprasad S, Behar-Cohen F. Oral Mineralocorticoid-Receptor Antagonists: Real-Life Experience in Clinical Subtypes of Nonresolving Central Serous Chorioretinopathy With Chronic Epitheliopathy. *Transl Vis Sci Technol* 2016;5:2.
 32. Ghadiali Q, Jung JJ, Yu S, Patel SN, Yannuzzi LA. Central serous chorioretinopathy treated with mineralocorticoid antagonists: A one-year pilot study. *Retina* 2016;36:611-618.
 33. Leisser C, Hirnschall N, Hackl C, Findl O. Eplerenone in patients with chronic recurring central serous chorioretinopathy. *Eur J Ophthalmol* 2016;26:479-484.
 34. Salz DA, Pitcher JD^{3rd}, Hsu J, Regillo CD, Fineman MS, Elliott KS, et al. Oral eplerenone for treatment of chronic central serous chorioretinopathy: A case series. *Ophthalmic Surg Lasers Imaging Retina* 2015;46:439-444.
 35. Singh RP, Sears JE, Bedi R, Schachat AP, Ehlers JP, Kaiser PK. Oral eplerenone for the management of chronic central serous chorioretinopathy. *Int J Ophthalmol* 2015;8:310-314.