

# Comparison of two common treatment methods in patients with Central Serous Chorioretinopathy (CSCR) referred to Imam Khomeini Hospital in Kermanshah in 2019 2020

Leila rezaee

Imam Khomeini hospital, Kermanshah University of medical sciences and health services

pezhvak azadi

Imam Khomeini hospital, Kermanshah University of medical sciences and health services

Ashkan Safarzadehkhoushabi (✉ [ashkans716@gmail.com](mailto:ashkans716@gmail.com))

Imam Khomeini hospital, Kermanshah University of medical sciences and health services

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## Research Article

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## Abstract

Central serous chorioretinopathy (CSCR) is an idiopathic disease most commonly seen in young men with a prevalence of 5.8 per 100,000. It is characterized by one or more cases of detachment serosa in the retinal neurosensory layer and may be associated with retinal pigment epithelial (RPE) detachment.

Eighty patients were divided into two groups of exposure (receiving eplerenone at a dose of 25 mg for one week and then at a dose of 50 mg for three weeks) and without exposure (without medication). Effectiveness-related variables including best visual acuity as primary outcome, central macular thickness, and choroid thickness as secondary outcomes before, 1 month, and 3 months later were assessed and recorded. Information such as central macular thickness, choroid thickness of 500 and 1000 microns on the nasal side and temporal superior and inferior were measured. Data were analyzed by SPSS version 23 software.

The mean reduction in choroid thickness in the macular group treated with eplerenone in the macula, as well as the 500 micron areas of the nasal, temporal, superior, and inferior, are:  $12.90 \pm 105.82$  microns,  $15.48 \pm 95.17$  microns, and  $16.07 \pm$ , respectively.  $94.45$  microns and  $14.48 \pm 94.96$  microns and  $15.10 \pm 95.94$  microns Also in the 1000 micron areas of the nasal, temporal, superior and inferior, respectively:  $.95$  microns and  $14.45 \pm 95.81$  microns and  $13.39 \pm 96.1.5$  microns. It was concluded that treatment with eplerenone was significantly associated with a decrease in choroid thickness in the macula and areas of 500 and 1000 microns of the nasal, temporal, superior and inferior. In our study, 70% of patients were men with a mean age of about 39 It was a year. In our study, more than 30% of patients had low visual acuity at 0.5 on the LogMar scale at the end of the first month without receiving eplerenone.

## Introduction

Central serous chorioretinopathy (CSCR) is an idiopathic disease most commonly seen in young men, with a prevalence of 5.8 per 100,000. It is characterized by one or more cases of detachment serosa in the retinal neurosensory layer and may be associated with retinal pigment epithelial (RPE) detachment. (1 and 2)

The disease has a wide range of clinical manifestations. The most common clinical manifestation is central scotoma, which may be associated with metamorphopsia. Other clinical manifestations include dyschromatosis, micropsy, hyperopia, and decreased sensitivity to contrast. (1 and 3)

Most cases of acute CSCR resolve spontaneously within 3 months and patients' visual acuity returns to normal. (3) But during CSCR recovery there are often areas of RPE atrophy and pigmented changes that can be seen in more than 90% of patients. (2 and 4)

In these patients, anatomically, Fovea depression returns to normal, but studies show that after the absorption of serous fluid, some of the density of Fovea cone cells is reduced, and this may indicate a slight decrease in patients' visual acuity compared to before. Be sick. (5)

In chronic cases (more than three months), the disease can be associated with complications such as geographic atrophy, chronic retinal cystic changes, subretinal fibrinosis accumulations, subretinal fibrosis, and secondary choroidal neovascularization, followed by permanent vision loss. (4 and 6) The pathogenesis of CSCR is not fully understood but is thought to be associated with impaired choroid circulation, which is confirmed by endocyanin

(ICGA) angiographic findings (7–9). Choroidal vasodilation and dilatation, choroid staining and hyperfluorescence in the intermediate and delayed phases of ICGA are seen in CSCR patients. (10)

Aldosterone causes vasodilation and leakage of the choroidal arteries, which may exert this effect through up-regulation of the potassium channels of the choroidal vascular endothelium cells. (10)

Another pathogenesis reported in this disease is dysfunction of the mineralocorticoid system. (11)

Risk factors for this disease include stressful personalities (type A personality), corticosteroid use, and hypertension. (11)

In animal models, activation of choroidal mineralocorticoid receptors caused vasodilation and leakage. This is inhibited by mineralocorticoid antagonists (12). It is estimated that 15–50% of patients with acute CSCR will experience a recurrence of the disease after spontaneous recovery, which seems to be a high statistic and reflects the approach of physicians in making the right decision to follow patients or perform appropriate interventions. Has been disrupted.

The most common way to treat this problem is to wait for spontaneous recovery after about three months, but other treatments such as laser, photodynamic therapies and mineralocorticoid antagonists have been proposed for it. (13)

Therefore, due to the high prevalence of this disease, it seems necessary to adopt a method of treatment that, while having good performance, has the least possible side effects. Since in many cases no treatment is prescribed for this problem, so the improvement of vision and complications of patients receiving the drug can be compared with patients for whom no treatment has been prescribed. Due to the lack of detailed studies comparing the effectiveness of corticosteroid mineral antagonist drugs such as eplerenone compared to untreated follow-up, researchers are interested in evaluating the effectiveness of this drug on CSCR.

## Material And Methods

This prospective cohort study protocol was reviewed and approved by the local university Institutional Ethics Committee and the tenets of the Declaration of Helsinki were followed throughout the study.

Effectiveness variables including best visual acuity as primary outcome, macular central thickness and choroid thickness as secondary outcomes before, 1 month and 3 months later were assessed and recorded. Patients in both groups were examined and paraclinical examinations were performed 1 month and 3 months after the start of treatment by Optovue's EDI OCT device, and information such as central macular thickness, nasal and temporal choroid thickness of 500 and 1000  $\mu\text{m}$ , superior and inferior were measured. There is no need to prove their validity and reliability, given that we have measured the required clinical variables directly and using routine, standard and accepted devices.

For eligible patients, after obtaining informed consent, their demographic characteristics including age, sex, duration of disease, medications, comorbidities, hypertension, and laboratory renal tests including BUN and creatinine were recorded.

Then, the patients underwent a complete evaluation of the ophthalmological examination, including the best visual acuity based on the ETDRS chart and determination of intraocular pressure, and a complete examination of

the retina and optic nerve. Patients should be treated in two groups of exposure (receiving appleronone at a dose of 25 mg for one week and then at a dose of 50 mg for three weeks) and without exposure, depending on whether they receive treatment with appleronone routinely and with the diagnosis of their physician. (Without medication).

Inclusion criteria:

1. Acute onset of the disease (less than 3 months)
2. Age over 18 years
3. Normal kidney tests for the treatment group.

Exclusion criteria: Receive previous treatment, including medication, PDT, laser photocoagulation, etc.

Presence of choroidal neovascularization, choroidal polypoid vasculopathy

Existence of any pathology and visual impairment in the patient's eye

Presence of ocular pathology such as glaucoma, retinal disease and uveitis

Taking corticosteroids

Existence of a history of non-disease-related visual impairment

Changing the diagnosis in the study stages

Previous CSCR attack history

Failure to refer the patient in the follow-up stages

Lack of complete and correct use of medicine

Use of other treatments during the follow-up period

Occurrence of a new complication affecting vision unrelated to the disease.

## Results

A total of 80 patients with acute serous chorioretinopathy were included in this study. Of these patients, 40 were treated with eplerenone at the discretion of their physician, and another 40 did not receive the drug. Of the total patients under study, 24 (30%) were female and 56 (70%) were male. Of these, 11 (27.5%) were female and 29 (72.5%) were female with eplerenone. Participants averaged  $6.15 \pm 35.92$  years. The mean age of the eplerenone-treated group was  $4.81 \pm 36.27$  years. Table 1

In specialized measurements performed by the researcher, it was found that the central thickness of the macula and the thickness of the choroid in the areas of 500 microns nasal and temporal and superior and inferior are 1000 microns nasal and temporal and superior and inferior respectively  $42.10 \pm 458.5$  microns And  $20.58 \pm 406.38$  microns and  $22.29 \pm 398.87$  microns and  $15.50 \pm 395.66$  microns and  $16.63 \pm 389.50$  microns and  $21.20 \pm 449.50$  microns and  $21.42 \pm 410.41$  microns And recorded  $20.10 \pm 394.50$  microns and  $25.15 \pm 391.55$  microns.

Table 1

Characteristics of study patients in two groups treated with eplerenone and without eplerenone treatment

P-Value	Total patients N = 80		Treated without Eplerenone N = 40		Treated with Eplerenone N = 40		male	sex
	Percentage	frequency	Percentage	frequency	Percentage	frequency		
0.152	70	56	67.5	27	72.5	29		
	30	24	32.5	13	27.5	11	□fema le	
0.404	5	4	10	4	0	0	0.8	Visual acuity
0.0745	12.5	10	25	10	0	0	0.7	
0.801	13.8	11	22.5	9	5	2	0.6	
0.066	17.5	14	20	8	15	6	0.5	
0.094	18.8	15	5	2	32.5	13	0.4	
0.489	15	12	7.5	3	22.5	9	0.3	
0.555	7.5	6	0	0	15	6	0.2	
0.891	5	4	0	0	□□	4	0.1	

## Results after the intervention:

After 1 month of treatment with eplerenone, both groups were tested again. The mean reduction in choroid thickness in the macular group treated with eplerenone in the macula as well as the 500 micron areas of the nasal, temporal, superior, and inferior are:  $1.89 \pm 98.77$  microns,  $25.48 \pm 85.27$  microns, and  $26.17 \pm 88$ , respectively. 41 microns and  $15.29 \pm 86.55$ . Microns and  $17.39 \pm 81.35$  microns Also in the areas of 1000 microns nasal and temporal and superior and inferior are  $27.39 \pm 86.45$  microns and  $24.48 \pm$  and  $85.75$  microns and  $77.10 \pm 83.25$  microns, respectively. And  $13.13 \pm 85.55$  microns. Table 3

After 3 months of treatment with eplerenone, both groups were tested again. The mean decrease in choroid thickness in the macular group treated with eplerenone in the macula as well as in the 500  $\mu\text{m}$  nasal, temporal, superior, and inferior areas are  $12.90 \pm 105.82$  microns and  $15.48 \pm 95.17$  microns and  $16.07$ , respectively..  $94.45$  microns and  $14.49 \pm 95.5$  microns and  $14.29 \pm 97.25$  microns. Also in the 1000 micron regions of the nasal and temporal and superior and inferior are  $17.19 \pm 96.55$  microns,  $15.89 \pm 96.95$  microns,  $31.29 \pm 94.44$  microns and  $26.18 \pm 9.7.61$  microns, respectively.

On the other hand, in the non-treatment group with apleronone in month 1, the average reduction of choroid thickness in macular as well as 500 micron areas of nasal and temporal and superior and inferior are 1000 microns of nasal and temporal and superior and inferior, respectively:  $10.82..$  12 microns and  $1.69 \pm 1.9$  microns and  $22.53 \pm 21.25$  microns and  $10.51 \pm 22.4$  microns and  $14.18.77$  microns and  $17.79 \pm 17.74$  microns and  $41.39 \pm 18.45$  microns and  $21.96 \pm 18.05$  Microns and  $33.39 \pm 1.25$  microns Table 2.

In the non-treatment group with applerone in month 3, the mean decrease in choroid thickness in the macula as well as the 500 micron nasal and temporal areas as well as the 1000 micron nasal and temporal and superior and inferior areas are: 11.92 ± 34.23 microns and 12, respectively. 79.29 microns and 12.73 ± 33.45 microns and 12.59 ± 32.4 microns and 12.28.97 microns and 14.49 ± 29.12 microns and 41.49 ± 29.24 microns and 14.49.30 microns And 15.79 ± 31.25 microns.

In statistical analysis with logistic regression test and analysis of variance of duplicate data with a significant limit of 0.05, it was found that the variance of data between the two groups in month 0, month 1 and month 3 are significantly different from each other and it was concluded that Treatment with eplerenone was significantly associated with a decrease in choroid thickness in the macula and areas of the nasal, temporal, superior, and inferior 500 and 1000 microns. It was also found that the changes in visual acuity scale in both groups were quite significant. (P-Value = 0.001) In the present study, patients' virulence improved from 0.61 to 0.28. (p-Value = 0.001). Based on the data of this study, no statistically significant relationship was observed between age and sex and reduction of macular and choroid thickness during treatment. (P-Value = 0.744).

Table 3 Comparison of visual outcomes one month after and 3 months after starting treatment in the two groups of treatment with eplerenone and not receiving eplerenone. In data analysis, the increase in visual acuity in the group without treatment was not significant in 1 and 3 months follow-up. (P-Value = 0.666). In data analysis, the increase in visual acuity in the group with treatment at 1 and 3 months of follow-up was significant. (0.001 ± (P-Value)).

Table 2

Visual acuity 3 months after treatment based on LogMar scale in two groups treated with eplerenone and without eplerenone treatment.

Percentage	frequency	Percentage	frequency	Percentage	frequency			
0.001 ± *	5	4	10	4	0	0	1.0	Visual acuity one month after treatment
0.001 ± *	5	4	10	4	0	0	0.9	
0.001 ± *	12.5	10	25	10	0	0	0.8	logMar
0.001 ± *	13.8	11	22.5	9	5	2	0.7	
0.001 ± *	17.5	14	20	8	15	6	0.8	
0.001 ± *	18.8	15	5	2	32.5	13	0.5	
0.001 ± *	15	12	7.5	3	22.5	9	0.4	
0.001 ± *	7.5	6	0	0	15	6	0.3	
0.001 ± *	5	4	0	0	10	3	0.2	

Table 3

Visual acuity 1 month after treatment based on LogMar scale in two groups treated with eplerenone and without eplerenone treatment.

P-Value	Total patient N = 80		Treated without Eplerenone N = 40		Treated with Eplerenone N = 40			
	Percentage	frecuency	Percentage	frecuency	Percentage	frecuency		
0.001*	5	4	10	4	0	0	1.0	Visual acuity one month after treatment  logMar
0.001*	20	8	20	8	0	0	0.9	
0.001*	12.5	19	25	10	0	0	0.8	
0.001*	37.5	15	22.5	9	15	6	0.7	
0.001*	17.5	14	17.5	7	17	7	0.6	
0.001*	17.5	14	2	1	32.5	13	0.5	
0.001*	22.5	9	2	1	17.5	7	0.4	
0.001*	12.5	5	0	0	12.5	5	0.3	
0.001*	5	2	0	0	5	2	0.2	

Reduction of central macular thickness and choroid thickness between 500 and 1000 µm of superior temporal and inferior nasal temporal was not observed in the group without treatment with apieronone at 1 and 3 months follow-up. (-P- Value = 0983). Decrease in central macular thickness and choroid thickness between 500 and 1000 µm of superior temporal and inferior nasal temporal was observed in the group with apieronone treatment at 1 and 3 months follow-up (P-Value 00 0.001).

## Discussion

Central serous chorioretinopathy (CSCR) is an idiopathic disease most commonly seen in young men, with a prevalence of 5.8 per 100,000. It is characterized by one or more cases of detachment serosa in the retinal neurosensory layer and may be associated with retinal pigment epithelial (RPE) detachment.

The disease has a wide range of clinical manifestations. The most common clinical manifestation is central scotoma, which may be associated with metamofopsia. Other clinical manifestations include dyschromatosis, micropsy, hyperopia, and decreased sensitivity to contrast.

Most cases of acute CSCR resolve spontaneously within 3 months and patients' visual acuity returns to normal. But during CSCR recovery there are often areas of RPE atrophy and pigmented changes that can be seen in more than 90% of patients.

In these patients, the anatomical depression of the fovea returns to normal, but studies show that after the absorption of serous fluid, some of the density of the foveal cone cells is reduced, and this may indicate a slight decrease in the visual acuity of patients compared to before. Be sick. In chronic cases (more than three months), the disease can be associated with complications such as geographic atrophy, chronic retinal cystic changes, subretinal fibrinosis accumulations, subretinal fibrosis, and secondary choroidal neovascularization, followed by

permanent vision loss.. The pathogenesis of CSCR is not fully understood but is thought to be associated with impaired choroid circulation, which is confirmed by endocyanin angiographic findings (ICGA).

Choroidal vas deferens and dilatation, choroid staining and hyperfluorescence are seen in the intermediate and delayed phases of ICGA in CSCR patients. Aldosterone causes vasodilation and leakage of the choroidal arteries, which may be exerted by up-regulation of the potassium channels of the choroidal vascular endothelial cells. Another pathogenesis reported in this disease is dysfunction of the mineralocorticoid system. Risk factors for this condition include stressful personality type (personality type A), corticosteroid use, and hypertension.

In animal models, activation of choroidal mineralocorticoid receptors caused vasodilation and leakage. This is inhibited by mineralocorticoid antagonists. It is estimated that 15–50% of patients with acute CSCR will experience a recurrence of the disease after spontaneous recovery, which seems to be a high statistic and reflects the approach of physicians in making the right decision to follow patients or perform appropriate interventions. Has been disrupted.

The most common way to treat this problem is to wait for spontaneous recovery after about three months, but other treatments such as laser, photodynamic therapies and mineralocorticoid antagonists have been proposed for it.

Therefore, due to the high prevalence of this disease, it seems necessary to adopt a method of treatment that, while having good performance, has the least possible side effects. Since in many cases no treatment is prescribed for this problem, so the improvement of vision and complications of patients receiving the drug can be compared with patients for whom no treatment has been prescribed.

Due to the lack of detailed studies comparing the effectiveness of corticosteroid mineral antagonist drugs such as eplerenone compared to untreated follow-up, researchers are interested in evaluating the effectiveness of this drug on CSCR.

In two separate studies in 2013 and 2002, Levy and Lowe reported that the disease was more common in young men (1), and in our study, 70% of patients were men with a mean age of about 39 years.

According to Berkinck's study, most acute CSCR cases resolve spontaneously over a period of 3 months, and patients' visual acuity returns to normal (3).

In our study, more than 30% of patients had a visual acuity above 0.5 on the LogMar scale at the end of the first month without receiving eplerenone. However, all patients referred to the hospital had less than 0.5 visual acuity upon arrival. In his study, Otto cited a decrease in the density of FuaH cone cells after serous fluid uptake as a possible reason for this inadequate repair (5).

Bojarborra also states in her study that during CSCR recovery, most areas of RPE atrophy and pigmentation changes are seen in more than 90% of patients (4).

In Zhao's study, 5-week treatment with eplerenone reduced retinal detachment and increased disease severity in 2 patients. This effect continued for up to 5 months after eplerenone was discontinued (12).

But in our study, the effects were measured only clinically and also the change in choroid thickness of its patients after one month. In a review article on the effect of eplerenone on CSCR in 2018, Chatzirali et al. Stated that oral

eplerenone at a dose of 25–50 mg per day is effective and tolerable for the treatment of chronic CSCR disease.

This study is in line with the recent study and Zhao's study to conclude that treatment with eplerenone has a significant effect on the treatment of the disease (13).

This finding was confirmed not only by improving patients' visual acuity, but also by accurate measurements of choroid thickness in the macula, as well as the 500- and 1000-micron temporal-nasal superior and inferior areas.

This study presented quite acceptable results by analyzing the mean changes in choroid thickness before and after treatment with eplerenone. On the other hand, the number of patients in the study (40 in the control group and 40 in the treatment group) in the field of data analysis is highly reliable.

The researcher also did not find a significant relationship between gender and age successfully in the study population. In 2015, Singh and colleagues treated a total of 17 eyes of 13 patients treated with 25 and 50 mg of oral eplerenone per day. LogMAR visual acuity improved from 0.42 (Snellen equivalent: 20/53) initially to 0.29 (Snellen equivalent: 20/39) on day 181 ( $P = 0.0024$ ) (14).

In the present study, the severity of patients improved from 0.28 to 0.61. In a 2019 study of short-term eplerenone therapy in the treatment of chronic CSCR in 13 affected eyes, Moin et al. Showed that oral eplerenone may be used as a safe and potentially effective treatment. But it has minimal short-term effects on subcutaneous fluid or visual acuity, so follow-ups longer than one month are necessary to demonstrate its benefits (15). However, the present study on more patients and more confidently stated that treatment with eplerenone can clearly improve visual acuity and choroid thickness. In a study of 114 patients (57 in each group), Professor Andrew Latry and colleagues found that Eplerenone was not superior to placebo for improving BCVA in patients with chronic CSCR after 12 months of treatment (16). But the present study did not confirm this view.

## Conclusion

It was concluded that treatment with eplerenone was significantly associated with a decrease in choroid thickness in the macula and areas of 500 and 1000 microns the nasal and temporal and superior and inferior. In our study, 70% of patients were men with a mean age of about 39 years. In our study, more than 30% of patients had low visual acuity of 0.5 on the LogMar scale at the end of the first month without receiving eplerenone.

## Abbreviations

Csr: Central Serous Chorioretinopathy

ACD: anterior chamber depth; AOD: Angle opening distance; ASOCT: Anterior segment optical coherence tomography; AT: Aspiration time; CCT: central corneal thickness; CDE: cumulative dissipated energy; IFU: Infusion fluid usage; IOP: Intraocular pressure; OHT: ocular hypertension; ONH: optic nerve head; PACG: Primary angle closure glaucoma; POAG: primary open angle glaucoma; PXF: Pseudoexfoliation; TISA: Trabecular-iris surface area; TM: trabecular meshwork

## Declarations

## Acknowledgments

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### **Authors' contributions**

FR designed the study and performed the surgeries. FR and MN conducted data collection, analysis and interpretation. FR and LR wrote the manuscript. All authors read and approved the final manuscript.

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### **Availability of data and materials**

The datasets generated and analyzed during the current study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author on reasonable request.

### **Ethics approval and consent to participate**

The Ethical Review Committee of Kermanshah University of Medical Sciences approved the study (no: IR.KUMS.REC.1398.1004). Informed written consent was taken from all participants. It was performed in accordance with the tenets of the Declaration of Helsinki.

### **Consent for publication**

Informed written consent was taken from all participants.

### **Competing interests**

The authors declare that they have no competing interests.

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