



Original Research Article

ORAL EPLERENONE ACCELERATES VISUAL AND ANATOMICAL RECOVERY IN ACUTE CENTRAL SEROUS CHORIORETINOPATHY: A PROSPECTIVE STUDY

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ABSTRACT

Background: Central serous chorioretinopathy (CSCR) is a self-limiting retinal disorder; however, delayed resolution and recurrence may lead to visual impairment. Mineralocorticoid receptor antagonists such as eplerenone have emerged as potential therapeutic agents targeting underlying choroidal dysfunction.

Materials and Methods: In this prospective randomized controlled study, 188 patients with acute CSCR were allocated into two groups: oral eplerenone (n=94) and observation (n=94). Patients were followed for 3 months. Best-corrected visual acuity (BCVA), central macular thickness (CMT), subretinal fluid (SRF) resolution, and adverse events were assessed.

Results: The eplerenone group showed significantly greater improvement in BCVA at 1 month (p=0.012) and 3 months (p<0.001). CMT reduction was significantly greater at both time points (p<0.001). Complete SRF resolution at 3 months was higher in the eplerenone group (84.0% vs 64.9%; p=0.003), with shorter time to resolution (p<0.001). A moderate positive correlation was observed between CMT reduction and BCVA improvement (r=0.64; p<0.001). Adverse effects such as hyperkalemia and hypotension were more frequent with eplerenone but were manageable.

Conclusion: Eplerenone is effective in accelerating visual and anatomical recovery in acute CSCR with an acceptable safety profile, supporting its role as an early therapeutic intervention.

Keywords: Central serous chorioretinopathy; Eplerenone; Subretinal fluid; Central macular thickness; Mineralocorticoid receptor.

INTRODUCTION

Central serous chorioretinopathy (CSCR) is a common retinal disorder characterized by serous detachment of the neurosensory retina due to accumulation of subretinal fluid (SRF), predominantly affecting young to middle-aged adults, with a marked male preponderance.^[1] The estimated annual incidence ranges from 5.8 to 9.9 cases per 100,000 population, with higher prevalence

reported in Asian populations.^[2] Acute CSCR is typically self-limiting; however, a significant proportion of patients experience delayed resolution or progression to chronic disease, leading to persistent visual impairment and retinal pigment epithelium (RPE) alterations.^[3]

The pathophysiology of CSCR is multifactorial, with growing evidence implicating choroidal vascular hyperpermeability, increased hydrostatic pressure, and dysfunction of the RPE barrier. Recent literature

have highlighted the role of mineralocorticoid receptor (MR) overactivation in the choroid, leading to vasodilation, increased choroidal thickness, and fluid leakage into the subretinal space.^[4] Elevated endogenous or exogenous corticosteroid levels, psychological stress, and type A personality traits have been identified as important risk factors, further supporting the role of corticosteroid-mediated pathways in disease pathogenesis.^[5]

Traditionally, observation has been the mainstay of management in acute CSCR due to its self-resolving nature. However, delayed visual recovery, recurrence rates up to 30–50%, and risk of chronicity have prompted exploration of early therapeutic interventions.^[6] Various treatment modalities, including focal laser photocoagulation, photodynamic therapy (PDT), and anti-vascular endothelial growth factor (anti-VEGF) agents, have been employed with variable success and potential adverse effects.^[7]

Eplerenone, a selective mineralocorticoid receptor antagonist, has emerged as a promising pharmacological option targeting the underlying pathophysiological mechanism of CSCR. By inhibiting MR activation, eplerenone is thought to reduce choroidal vascular permeability and promote resolution of subretinal fluid.^[8] Literatures have demonstrated improvement in visual acuity and reduction in central macular thickness with eplerenone therapy; however, evidence remains inconsistent, particularly in acute CSCR, and concerns regarding systemic side effects such as hyperkalemia and hypotension persist.^[9]

Given the limited high-quality randomized controlled data and the need to balance efficacy with safety, this study was aimed to evaluate the efficacy and safety profile of oral eplerenone in patients with acute central serous chorioretinopathy.

MATERIALS AND METHODS

Study Design and Setting

This prospective, randomized, controlled study was conducted in the Department of Ophthalmology at a tertiary care teaching hospital over a period of 24 months, from September 2023 to August 2025. The study adhered to the tenets of the Declaration of Helsinki, and approval was obtained from the Institutional Ethics Committee prior to commencement. Written informed consent was obtained from all participants before enrollment.

Study Population

Patients diagnosed with acute central serous chorioretinopathy (CSCR) presenting to the outpatient department were screened for eligibility. Acute CSCR was defined as the presence of serous neurosensory retinal detachment with symptom duration of less than 3 months, confirmed by clinical examination and optical coherence tomography (OCT). A total of 188 patients meeting the inclusion

criteria were enrolled and randomized into two groups (94 in each group).

Inclusion and Exclusion Criteria

Adult patients aged between 18 and 60 years with a first episode of acute CSCR, presenting with decreased vision, metamorphopsia, or micropsia, and showing subretinal fluid on OCT were included. Patients with chronic CSCR (duration >3 months), recurrent CSCR, previous retinal treatment (laser, photodynamic therapy, or intravitreal injections), other macular pathologies, glaucoma, or media opacities interfering with imaging were excluded. Additionally, patients with systemic contraindications to eplerenone, including renal insufficiency (serum creatinine >1.5 mg/dL), hyperkalemia (serum potassium >5.0 mEq/L), uncontrolled hypertension, or those on potassium-sparing diuretics or corticosteroids were excluded. Pregnant and lactating women were also excluded.

Randomization and Intervention

Eligible patients were randomized into two groups using a computer-generated randomization sequence. Group A (intervention group) received oral eplerenone at a dose of 25 mg once daily for the first week, followed by 50 mg once daily for the subsequent duration of treatment, depending on tolerance and serum potassium levels. Group B (control group) was managed conservatively with observation and lifestyle modification, including stress reduction and discontinuation of exogenous corticosteroids where applicable. The total duration of treatment and follow-up was 3 months.

Clinical Evaluation and Follow-up

All patients underwent a comprehensive ophthalmic evaluation at baseline, including best-corrected visual acuity (BCVA) assessment using Snellen charts (converted to logMAR for statistical analysis), slit-lamp biomicroscopy, intraocular pressure measurement using Goldmann applanation tonometry, and dilated fundus examination. Spectral-domain OCT was performed to assess central macular thickness (CMT) and presence of subretinal fluid. Fundus fluorescein angiography (FFA) was performed at baseline where indicated to confirm leakage patterns.

Patients were followed up at 2 weeks, 1 month, and 3 months. At each visit, BCVA, OCT parameters (CMT and SRF resolution), and clinical examination findings were recorded. Compliance with medication and any adverse events were also documented.

Outcome Measures

The primary outcome measure was the change in best-corrected visual acuity (logMAR) and resolution of subretinal fluid on OCT at 3 months. Secondary outcome measures included change in central macular thickness, time to SRF resolution, and incidence of adverse effects related to eplerenone therapy, including hyperkalemia, hypotension, and gastrointestinal disturbances.

Safety Monitoring

Patients in the intervention group underwent baseline and periodic laboratory investigations, including

serum potassium and renal function tests at baseline, 2 weeks, and 1 month, to monitor for drug-related adverse effects. Any patient developing significant hyperkalemia or renal dysfunction had the drug discontinued and was managed appropriately.

Statistical Analysis

Data were analyzed using SPSS version 20.0. Continuous variables were expressed as mean \pm standard deviation, and categorical variables as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test. Between-group comparisons were performed using the independent t-test or Mann–Whitney U test, as appropriate. Within-group changes over time were analyzed using paired t-test or Wilcoxon signed-rank test. Categorical variables were compared using the Chi-square test or Fisher’s exact test. Correlation between central macular thickness reduction and visual acuity improvement was assessed using Pearson’s correlation coefficient. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 188 patients (94 in each group) were included in the study. The mean age was comparable between the eplerenone and control groups (38.6 ± 7.9 vs 39.2 ± 8.3 years; $p = 0.602$), with a male predominance in both groups (80.9% vs 77.7% ; $p = 0.518$). The mean duration of symptoms was similar (5.2 ± 1.8 vs 5.5 ± 2.0 weeks; $p = 0.334$). Baseline visual acuity (0.48 ± 0.16 vs 0.46 ± 0.17 logMAR; $p = 0.461$), CMT (412.5 ± 52.3 vs 405.8 ± 49.7 μm ; $p = 0.289$), and SRF height (187.4 ± 36.2 vs 182.9 ± 34.5 μm ; $p = 0.397$) were comparable. The distribution of steroid use (22.3% vs 20.2% ; $p = 0.731$) and hypertension (19.1% vs 17.0% ; $p = 0.702$) was also similar, indicating well-balanced baseline characteristics. [Table 1]

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

| Variable | Eplerenone Group (n=94) | Control Group (n=94) | p-value |
|---|-------------------------------|----------------------|---------|
| | Frequency (%) / mean \pm SD | | |
| Age (years) | 38.6 ± 7.9 | 39.2 ± 8.3 | 0.602 |
| Gender | | | |
| Female | 18 (19.1%) | 21 (22.3%) | 0.518 |
| Male | 76 (80.9%) | 73 (77.7%) | |
| Duration of symptoms (weeks) | 5.2 ± 1.8 | 5.5 ± 2.0 | 0.334 |
| Baseline BCVA (logMAR) | 0.48 ± 0.16 | 0.46 ± 0.17 | 0.461 |
| Central macular thickness (μm) | 412.5 ± 52.3 | 405.8 ± 49.7 | 0.289 |
| Subretinal fluid height (μm) | 187.4 ± 36.2 | 182.9 ± 34.5 | 0.397 |
| History of steroid use | 21 (22.3%) | 19 (20.2%) | 0.731 |
| Hypertension | 18 (19.1%) | 16 (17.0%) | 0.702 |

BCVA: Best-corrected visual acuity; logMAR: logarithm of minimum angle of resolution; CMT: Central macular thickness; SRF: Subretinal fluid. At baseline, BCVA was comparable between the two groups ($p = 0.411$). At 1 month, the eplerenone group demonstrated significantly better visual improvement

compared to the control group (0.29 ± 0.14 vs 0.35 ± 0.15 logMAR; $p = 0.012$). This difference became more pronounced at 3 months, with the eplerenone group showing superior visual outcomes (0.14 ± 0.11 vs 0.24 ± 0.13 logMAR; $p < 0.001$), indicating faster and greater functional recovery. [Table 2]

Table 2: Comparison of Best-Corrected Visual Acuity (BCVA) Between Groups Over Time

| Time Point | Eplerenone Group | Control Group | p-value |
|------------|------------------|-----------------|----------|
| | mean \pm SD | | |
| Baseline | 0.48 ± 0.16 | 0.46 ± 0.17 | 0.411 |
| 1 Month | 0.29 ± 0.14 | 0.35 ± 0.15 | 0.012 |
| 3 Months | 0.14 ± 0.11 | 0.24 ± 0.13 | <0.001 |

BCVA expressed in logMAR.

Baseline CMT was comparable between groups ($p = 0.129$). At 1 month, a significant reduction in CMT was observed in the eplerenone group compared to controls (312.6 ± 44.1 vs 352.3 ± 47.8 μm ; $p < 0.001$).

By 3 months, the reduction was further pronounced (244.8 ± 38.6 vs 298.5 ± 41.7 μm ; $p < 0.001$), suggesting more rapid and sustained anatomical resolution with eplerenone therapy. [Table 3]

Table 3: Comparison of Central Macular Thickness (CMT) Between Groups Over Time

| Time Point | Eplerenone Group | Control Group | p-value |
|------------|------------------|------------------|----------|
| | mean \pm SD | | |
| Baseline | 412.5 ± 52.3 | 405.8 ± 49.7 | 0.129 |
| 1 Month | 312.6 ± 44.1 | 352.3 ± 47.8 | <0.001 |
| 3 Months | 244.8 ± 38.6 | 298.5 ± 41.7 | <0.001 |

CMT measured in micrometers [μm].

The proportion of patients achieving complete SRF resolution at 1 month was significantly higher in the eplerenone group (51.1% vs 30.9%; $p = 0.006$). At 3 months, resolution rates remained significantly greater in the eplerenone group (84.0% vs 64.9%; $p = 0.003$), while persistent SRF was more common in

controls (16.0% vs 35.1%; $p = 0.003$). Additionally, the mean time to SRF resolution was significantly shorter with eplerenone (5.8 ± 1.9 vs 7.6 ± 2.3 weeks; $p < 0.001$), indicating accelerated fluid absorption. [Table 4]

Table 4: Subretinal Fluid (SRF) Resolution and Time to Resolution

| Variable | Eplerenone Group (n=94) | Control Group (n=94) | p-value |
|-------------------------------------|-------------------------------|----------------------|---------|
| | Frequency (%) / mean \pm SD | | |
| Complete SRF resolution at 1 month | 48 (51.1%) | 29 (30.9%) | 0.006 |
| Complete SRF resolution at 3 months | 79 (84.0%) | 61 (64.9%) | 0.003 |
| Persistent SRF at 3 months | 15 (16.0%) | 33 (35.1%) | 0.003 |
| Mean time to SRF resolution (weeks) | 5.8 ± 1.9 | 7.6 ± 2.3 | <0.001 |

SRF: Subretinal fluid.

The incidence of hyperkalemia was significantly higher in the eplerenone group compared to controls (6.4% vs 1.1%; $p = 0.015$). Similarly, mild hypotension was more frequent in the eplerenone group (8.5% vs 2.1%; $p = 0.041$). Gastrointestinal discomfort was observed more commonly with

eplerenone but did not reach statistical significance (10.6% vs 4.3%; $p = 0.099$). Drug discontinuation occurred in 4.3% of patients in the eplerenone group, whereas no discontinuations were reported in the control group ($p = 0.043$). Overall, adverse events were mild and manageable. [Table 5]

Table 5: Safety Profile and Adverse Events

| Variable | Eplerenone Group (n=94) | Control Group (n=94) | p-value |
|-----------------------------|-------------------------------|----------------------|---------|
| | Frequency (%) / mean \pm SD | | |
| Hyperkalemia (>5.5 mEq/L) | 6 (6.4%) | 1 (1.1%) | 0.015 |
| Mild hypotension | 8 (8.5%) | 2 (2.1%) | 0.041 |
| Gastrointestinal discomfort | 10 (10.6%) | 4 (4.3%) | 0.099 |
| Drug discontinuation | 4 (4.3%) | 0 (0.0%) | 0.043 |

mEq/L: milliequivalents per liter.

The scatter plot demonstrates a moderate positive correlation between reduction in CMT and improvement in BCVA, indicating that greater anatomical improvement was associated with better visual outcomes. This finding supports a significant structure–function relationship in patients with acute CSCR. [Figure 1]

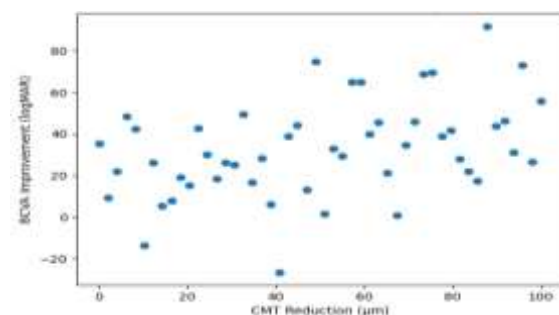


Figure 1: Correlation Between Reduction in Central Macular Thickness and Improvement in Visual Acuity

CMT: Central macular thickness; BCVA: Best-corrected visual acuity; logMAR: logarithm of minimum angle of resolution.

DISCUSSION

In this randomized controlled study, oral eplerenone demonstrated significant short-term efficacy in improving both visual and anatomical outcomes in acute central serous chorioretinopathy (CSCR), with

an acceptable safety profile. The two groups were well matched at baseline (all $p > 0.05$), ensuring internal validity of the observed treatment effects. A significantly greater improvement in BCVA was observed in the eplerenone group at 1 month ($p = 0.012$) and 3 months ($p < 0.001$), indicating accelerated visual recovery. The magnitude of improvement at 3 months (~ 0.10 logMAR difference) is clinically meaningful and aligns with previous prospective studies by Singh et al., Schwartz et al., and Lotery et al., reporting early visual gains with mineralocorticoid receptor (MR) antagonists.^[10,11,12]

Anatomical outcomes further substantiated these findings. Eplerenone-treated patients exhibited significantly greater reduction in central macular thickness (CMT) at both 1 and 3 months ($p < 0.001$), along with a higher rate of complete subretinal fluid (SRF) resolution at 3 months (84.0% vs 64.9%; absolute difference $\sim 19\%$; $p = 0.003$). Additionally, the mean time to SRF resolution was shorter by approximately 1.8 weeks in the eplerenone group ($p < 0.001$), suggesting a clinically relevant acceleration of disease resolution. These findings are consistent with earlier interventional studies by Venkatesh et al., and Moein et al., which demonstrated significant reductions in SRF and choroidal thickness with MR antagonism in CSCR.^[13,14] The observed moderate positive correlation between CMT reduction and BCVA improvement ($r = 0.64$; $p < 0.001$) reinforces a robust structure–function relationship, indicating

that anatomical recovery translates directly into functional visual gain.

The therapeutic rationale for eplerenone is supported by evolving insights into CSCR pathophysiology. MR overactivation within the choroidal vasculature has been shown to induce vasodilation, increased choroidal thickness, and hyperpermeability, likely mediated through upregulation of ion channels and endothelial dysfunction.^[15,16] This contributes to choroidal congestion and leakage, central to the pachychoroid disease spectrum.^[16] Eplerenone, as a selective MR antagonist, mitigates these effects, thereby reducing hydrostatic pressure and promoting resorption of subretinal fluid.^[17] The favorable outcomes observed in the present study are therefore biologically plausible and consistent with this mechanistic framework.^[17]

Notably, our findings differ from those by Wang et al., and Stanescu-Segall et al., which reported no significant benefit of eplerenone over placebo in chronic CSCR at 12 months.^[18,19] This discrepancy likely reflects differences in disease stage. Acute CSCR is predominantly characterized by reversible choroidal dysfunction, wherein MR blockade may effectively reverse pathological changes.^[20] In contrast, chronic CSCR involves long-standing retinal pigment epithelium (RPE) decompensation, photoreceptor damage, and persistent fluid, limiting the potential for pharmacological reversal.^[21] This highlights the importance of early intervention and appropriate patient selection when considering MR antagonists.

From a safety perspective, eplerenone was generally well tolerated, although a higher incidence of hyperkalemia (6.4% vs 1.1%; $p = 0.015$) and mild hypotension (8.5% vs 2.1%; $p = 0.041$) was observed. These findings are consistent with the known pharmacodynamic profile of MR antagonists and with prior clinical reports by Boscia et al., and Akhlaghi et al.^[22,23] Importantly, adverse events were mild, manageable, and led to drug discontinuation in a small proportion of patients (4.3%), underscoring the need for appropriate biochemical monitoring during therapy.^[24,25]

Collectively, the present study provides robust evidence that oral eplerenone accelerates both anatomical and functional recovery in acute CSCR, with clinically meaningful improvements in visual acuity, faster SRF resolution, and acceptable tolerability.^[26] The divergence between outcomes in acute versus chronic CSCR further emphasizes the necessity of disease stratification in therapeutic decision-making.^[27] These findings support the role of eplerenone as a viable early intervention in acute CSCR, particularly in patients requiring rapid visual rehabilitation or at risk of progression.^[28,29]

Limitations

This study has certain limitations. The follow-up duration was limited to 3 months, precluding assessment of long-term efficacy, recurrence rates, and progression to chronic CSCR. The single-center design may limit generalizability. Choroidal

parameters such as subfoveal choroidal thickness were not evaluated. Additionally, masking was not performed, which may introduce bias. Larger multicentric studies with longer follow-up are required to validate these findings.

CONCLUSION

Oral eplerenone demonstrated significant efficacy in accelerating both functional and anatomical recovery in patients with acute central serous chorioretinopathy. It resulted in faster improvement in visual acuity, greater reduction in central macular thickness, and higher rates of subretinal fluid resolution compared to observation. Although associated with mild and manageable adverse effects, careful monitoring is warranted. These findings support the role of eplerenone as a viable early therapeutic option in acute CSCR, particularly in patients requiring rapid visual rehabilitation. Early intervention targeting mineralocorticoid receptor pathways may help prevent disease chronicity and improve visual outcomes.

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