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Original Research Article

A Randomized Controlled Study on Eplerenone's Role in the Treatment of Chronic Central Serous Chorioretinopathy

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Abstract:

Background: (CSCR) is a retinal condition that can cause blindness and is characterized by damage to photoreceptors and chronic subretinal fluid. Acute CSCR may go away on its own, but persistent cases frequently need help. Eplerenone and other mineralocorticoid receptor antagonists have been studied as possible therapies, while the available data is still inconclusive.

Aim: To assess how well oral eplerenone therapy works and how safe it is for enhancing anatomical and visual results in patients with chronic CSCR.

Methods: Over the course of 11 months, this randomized controlled experiment was carried out at the Anugraha Narayan Magadh Medical College and Hospital's Department of Ophthalmology in Gaya. One hundred patients with chronic CSCR were recruited and randomly assigned to one of two groups: Group B received supportive care and monitoring, whereas Group A was given oral eplerenone 50 mg once daily for three months. At one, three, and six months, baseline and follow-up assessments included fundus examination, OCT, and BCVA. SPSS version 23.0 was used for the statistical analysis, and a p-value of less than 0.05 was deemed significant.

Results: Clinical and baseline demographic traits were similar among the groups. In comparison to Group B (0.62 ± 0.18 to 0.54 ± 0.16 logMAR, $p < 0.001$), Group A's mean BCVA improved significantly after 3 months (0.64 ± 0.15 to 0.32 ± 0.12 logMAR). Comparing Group A to Group B, OCT results revealed a larger decrease in central retinal thickness (395 ± 48 µm to 265 ± 34 µm, $p < 0.001$). 72% of Group A showed complete subretinal fluid clearance, compared to 34% of Group B. Mild side effects such as dizziness (6%) and hyperkalemia (4%) were reported in the eplerenone group but were manageable. No serious adverse events occurred.

Conclusion: In chronic CSCR, eplerenone therapy significantly improved anatomical and functional outcomes as compared to observation alone. The drug was well tolerated with minimal adverse effects, supporting its role as a safe and effective therapeutic option.

Recommendations: To validate these results, improve dosage regimens, and pinpoint patient subgroups most likely to benefit from eplerenone medication, more multicenter, long-term research is necessary.

Keywords: Chronic CSCR, Eplerenone, Visual Acuity, Optical Coherence Tomography, Randomized Controlled Trial

Introduction

Serous detachment of the neurosensory retina as a result of choroidal hyperpermeability and compromised retinal pigment epithelium function are hallmarks of central serous chorioretinopathy (CSCR), a chorioretinal condition [1]. It predominantly affects males aged 20–50 years and is often associated with stress and corticosteroid exposure [1]. CSCR may resolve spontaneously in its acute form; however, chronic cases—defined by persistent subretinal fluid beyond three to four months—pose a risk of permanent visual impairment and require effective therapeutic intervention [2].

Mineralocorticoid receptor (MR) antagonists have emerged as a pharmacological strategy in CSCR, proposed to counteract MR-mediated choroidal leakage and fluid accumulation [3]. Eplerenone, a selective MR antagonist, has demonstrated promising results in early small-scale and retrospective studies, including significant reductions in central macular thickness, subretinal

fluid, and improvements in visual acuity [4,5]. For instance, a retrospective real-world analysis reported BCVA improvement from 0.2 to 0.09 logMAR and SRF resolution in 67% of patients after three months of eplerenone treatment [4]. Similar findings were echoed in other case series and pilot studies, reinforcing the potential efficacy of eplerenone in chronic CSCR management [6].

Despite initial optimism, larger controlled trials have yielded conflicting results. There was virtually no difference between eplerenone and placebo in terms of best-corrected visual acuity at 12 months (mean difference 1.73 letters, $p = 0.24$), and the placebo group was favored by elevated subretinal fluid, according to the VICI trial, a multicenter, randomized, double-blind, placebo-controlled study that included 114 chronic CSCR patients [7]. The study concluded that eplerenone should not be recommended for chronic CSCR [7]. A recent systematic review and meta-analysis corroborated these mixed outcomes, indicating heterogeneity in therapeutic responses and underscoring the need for more nuanced investigations [8]. Real-world surveys further reveal that despite equivocal evidence, clinicians continue to prescribe eplerenone variably, often influenced by accessibility issues and multifactorial CSCR pathogenesis [9].

The discrepancy in the literature highlights a therapeutic dilemma—while smaller studies suggest benefit, large-scale trials question eplerenone's efficacy in chronic CSCR [7,8]. Contributing factors may include variations in treatment duration, timing of initiation, patient selection, and concomitant interventions [10]. Notably, discontinuation of therapy upon fluid resolution in the VICI trial may have attenuated its observed effectiveness, since recurrences are common when MR antagonists are abruptly withdrawn [10].

Given these inconclusive findings, there remains a compelling need to evaluate eplerenone under controlled yet contextually relevant settings—especially in resource-limited environments where advanced treatments like photodynamic therapy are less accessible. In order to provide significant evidence to support clinical decision-making in chronic CSCR, this study aims to evaluate the safety and effectiveness of eplerenone in a randomized controlled trial at Anugraha Narayan Magadh Medical College and Hospital, Gaya.

Methodology

Study Design: This study was designed as a prospective, randomized controlled trial.

Study Setting: The trial was conducted at the Department of Ophthalmology, Anugraha Narayan Magadh Medical College and Hospital, Gaya, Bihar, which caters to a large patient population with ocular disorders. The hospital provides tertiary care facilities, ensuring accessibility to advanced diagnostic tools and treatment modalities required for the study.

Participants

The study included 100 patients with a diagnosis of chronic CSCR. The acute and outpatient departments were used to recruit eligible individuals in turn. Patients were randomly assigned to one of two groups: the control group and the eplerenone therapy group. Before being included in the study, all individuals provided written informed permission.

Inclusion Criteria

- Patients aged 18–60 years diagnosed with chronic CSCR (symptoms persisting for more than 3 months).
- Presence of subretinal fluid on (OCT).
- No prior treatment with mineralocorticoid receptor antagonists.
- Willingness to provide informed consent and comply with follow-up visits.

Exclusion Criteria

- A history of further retinal conditions, such as diabetic retinopathy, age-related macular degeneration, or retinal vein occlusion.
- Patients with significant media opacities hindering fundus visualization.
- Individuals with systemic contraindications to eplerenone, such as chronic kidney disease (eGFR < 50 ml/min/1.73m²) or hyperkalemia.
- Patients on concomitant medications known to interact with eplerenone.
- Pregnant or lactating women.

Bias: A digitally generated randomization sequence was used to distribute participants in order to reduce selection bias. Sealing opaque envelopes guaranteed allocation concealment. Observer bias was reduced by masking the ophthalmologists assessing OCT images and visual acuity outcomes, who were blinded to the treatment allocation.

Data Collection: Age, gender, length of symptoms, and previous ocular history were among the baseline clinical and demographic information that was documented. OCT imaging, fundus examination, and best-corrected visual acuity (BCVA) were among the ophthalmological evaluations. At baseline, one month, three months, and six months, follow-up assessments were conducted. All information was entered into a secure electronic database after being captured on pre-made case report forms.

Procedure: For three months, participants who were randomly assigned to the treatment group took 50 mg of oral eplerenone once daily, while the

control group got supportive care and routine observation. Regular follow-up exams were performed on both groups to evaluate changes in visual acuity and subretinal fluid resolution. Regular counseling and pill count monitoring were used to ensure treatment compliance. Throughout the course of the investigation, adverse consequences were observed.

Statistical Analysis: SPSS version 23.0 (IBM Corp., Armonk, NY) was used for all statistical analyses. Whereas categorical data were displayed as frequencies and percentages, continuous variables were represented as mean ± standard deviation (SD). Continuous and categorical variables were compared using the independent t-test and chi-square test, respectively. To evaluate within-group changes from baseline to follow-up, a paired t-test was utilized. Statistical significance was defined as a p-value of less than 0.05.

Results

The study comprised one hundred patients with a diagnosis of CSCR. Group A (Eplerenone group, n = 50) and Group B (Control group, n = 50) were randomly assigned to them. The participants' average age was 41.6 ± 7.8 years, and 72% of them were men. The two groups' baseline clinical and demographic traits were similar ($p > 0.05$).

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Group A (Eplerenone, n=50)	Group B (Control, n=50)	p-value
Mean Age (years)	42.1 ± 7.5	41.2 ± 8.1	0.62
Male : Female ratio	37:13	35:15	0.68
Mean Duration of Symptoms (months)	4.8 ± 1.2	4.7 ± 1.4	0.79
Baseline BCVA (logMAR)	0.64 ± 0.15	0.62 ± 0.18	0.54
Mean Central Retinal Thickness (CRT, µm)	395 ± 48	388 ± 52	0.47

Comparability was ensured by the two groups' good matching in terms of age, sex distribution, symptom duration, baseline BCVA, and OCT characteristics.

Visual Acuity Outcomes: When compared to the control group, the eplerenone group's BCVA significantly improved at three months. Group B saw a slight improvement in mean BCVA from 0.62 ± 0.18 logMAR to 0.54 ± 0.16 logMAR, while Group A saw an improvement from 0.64 ± 0.15 logMAR to 0.32 ± 0.12 logMAR. A statistically significant difference between the groups was observed ($p < 0.001$).

Table 2: Change in Best-Corrected Visual Acuity (BCVA, logMAR)

Time Point	Group A (Eplerenone)	Group B (Control)	p-value
Baseline	0.64 ± 0.15	0.62 ± 0.18	0.54
1 Month	0.48 ± 0.14	0.58 ± 0.17	0.02
3 Months	0.32 ± 0.12	0.54 ± 0.16	<0.001
6 Months	0.28 ± 0.11	0.51 ± 0.15	<0.001

When compared to the control group, eplerenone medication resulted in a statistically significant and clinically meaningful improvement in visual acuity.

OCT Outcomes: The eplerenone group had a greater resolution of subretinal fluid and a decrease in CRT. By the end of three months, Group A's mean CRT decreased from 395 ± 48 µm to 265 ± 34 µm, while Group B's decreased from 388 ± 52 µm to 342 ± 39 µm ($p < 0.001$). 72% of patients in Group A and 34% of patients in Group B had complete clearance of subretinal fluid.

Table 3: Central Retinal Thickness (CRT) on OCT (µm)

Time Point	Group A (Eplerenone)	Group B (Control)	p-value
Baseline	395 ± 48	388 ± 52	0.47
1 Month	318 ± 41	367 ± 45	0.003
3 Months	265 ± 34	342 ± 39	<0.001
6 Months	258 ± 29	336 ± 37	<0.001

Significant anatomical improvement was seen in the treatment group, with faster and greater subretinal fluid resolution in relation to controls.

Safety and Adverse Effects: Eplerenone therapy was generally well tolerated. Mild side effects such as dizziness and fatigue were reported in 6 patients (12%), while hyperkalemia was observed in 2 patients (4%), which was managed with dose

adjustment. No serious adverse events were reported.

Table 4: Adverse Effects Observed

Adverse Effect	Group A (Eplerenone, n=50)	Group B (Control, n=50)
Dizziness	3 (6%)	1 (2%)
Fatigue	3 (6%)	1 (2%)
Hyperkalemia	2 (4%)	0 (0%)
Serious Adverse Events	0	0

Eplerenone was safe, with only mild and manageable side effects.

Summary of Findings

- **Visual outcomes**: Significant improvement in BCVA in the eplerenone group compared to controls ($p < 0.001$).
- **Anatomical outcomes**: Significant reduction in CRT and higher rate of subretinal fluid resolution with eplerenone ($p < 0.001$).
- **Safety**: Eplerenone had few adverse effects and was well tolerated.

Discussion

Plerenone therapy showed notable structural and optical improvements over the control group in this randomized controlled trial with 100 individuals with CSCR. We minimized confounding factors by comparing baseline characteristics between the two groups, such as age, sex distribution, duration of symptoms, and baseline OCT values.

The BCVA of patients receiving eplerenone treatment significantly improved. The therapy group's mean BCVA increased significantly by the end of three months (0.64 to 0.32 logMAR) whereas only a marginal improvement was seen in the control group (0.62 to 0.54 logMAR). This statistically significant difference ($p < 0.001$) suggests that eplerenone accelerates functional recovery in chronic CSCR. The sustained improvement at 6 months further highlights the long-term efficacy of therapy.

Anatomical outcomes on (OCT) strongly supported these findings. Eplerenone therapy resulted in substantial reduction in (CRT) and higher rates of subretinal fluid resolution compared to controls. By three months, the eplerenone group's mean CRT dropped from 395 µm to 265 µm, while the control group's CRT dropped somewhat from 388 µm to 342 µm. 72% of patients taking eplerenone experienced complete clearance of subretinal fluid, whereas only 34% of patients in the control group did so. This suggests that eplerenone improves fluid absorption and more successfully recovers retinal architecture.

Eplerenone was well tolerated in terms of safety. A small percentage of participants experienced mild adverse effects like weariness and dizziness while hyperkalemia occurred in only 4% of cases and was successfully managed with dose adjustments. No severe adverse events were observed, suggesting that eplerenone is a relatively safe therapeutic option in this population.

Overall, the results indicate that eplerenone provides superior visual and anatomical outcomes compared to observation alone in patients with chronic CSCR. The significant reduction in retinal thickness, higher rates of subretinal fluid resolution, and improvement in BCVA strongly support its clinical efficacy. Furthermore, the low incidence of mild and manageable side effects highlights its safety profile. These results support the use of mineralocorticoid receptor antagonists as therapeutic agents for the treatment of chronic CSCR and imply that eplerenone may be included in routine therapy regimens for certain patients.

The function of eplerenone and other mineralocorticoid receptor antagonists in the treatment of cCSC has been evaluated in a number of studies. Mineralocorticoid receptor antagonists (eplerenone and spironolactone) were shown to have variable efficacy in a systematic review and meta-analysis, with some small studies revealing anatomical improvements but no discernible or long-lasting visual effects [11].

Further comparative analyses indicated that photodynamic therapy (PDT) was more effective than eplerenone, both in terms of fluid resolution and functional visual gains, while systemic eplerenone carried risks of hyperkalemia and other adverse events [12]. Another review highlighted that spironolactone may provide slightly better or similar outcomes compared to eplerenone, though the overall evidence remains weak and inconclusive [11].

More recently, a randomized clinical trial reinforced these findings, demonstrating that eplerenone failed to provide meaningful benefit over placebo for cCSC, thereby discouraging its widespread clinical use [13]. Additionally, observational work investigating real-world data further supported that PDT should remain the first-line treatment for cCSC, with systemic mineralocorticoid receptor antagonists only considered experimental or adjunctive [14].

Conclusion

When compared to observation alone, eplerenone medication dramatically enhanced visual acuity and facilitated a quicker clearance of subretinal fluid in patients with chronic CSCR. With few side effects and good tolerance, the medication showed promise as a safe and efficient therapeutic approach for the treatment of chronic CSCR.

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