Original article:

Evaluation of efficacy of eplerenone in the management of chronic central serous choroidoretinopathy

Dr. Sushant Madaan*

Department of Ophthalmology, NIMS Medical College and Hopsital ,Jaipur , Rajasthan

Corresponding author *

Abstract:

Introduction: Central serous chorio-retinopathy (CSCR) is still a less merely understood eye disease involving the retina. The retina is a layer of light-sensitive cells at the back of the eye which are responsible for converting light into electrical signals that are carried to the brain, where they are interpreted as the images we see. Our aim was to evaluate the efficacy of eplerenone for chronic central serous chorioretinopathy (CSCR).

Methodology: It was Prospective, double-blind, randomized placebo-controlled study. 24 eyes of 24 patients with persistent subretinal fluid (SRF) due to chronic CSCR were enrolled and randomized to receive eplerenone 50 mg/day or placebo for 3 months, followed by a 3-month follow-up. The main outcome measure was change in SRF from baseline to 3 months of treatment. Secondary outcomes included change in SRF at any time-point, complete resolution of SRF, improvement in choroidal thickness and change in best-corrected visual acuity (BCVA).

Results: 18eyes were treated with eplerenone and 6 with placebo. Both groups showed reduction in SRF throughout the treatment period, with a significant reduction at months 1, 3 and 6 only in the treatment group. Central retinal thickness was 378.4±70µm before treatment and BCVA was logMAR 0.7. A clear decrease in retinal central thickness and height of SRF was observed at 1 month in 70% of patients, central retinal thickness: 318.3µm at 1 month, with improvement of visual acuity in all of these patients. Follow-up at 3 months also found a decrease in SRF and central retinal thickness four patients had complete resolution of SRF at 1 month with macular thickness 260±40µm, without recurrence at 3 months. The BCVA was improved to logMAR 0.2.Three other patients had complete resolution of SRF at 3 months. 2 patients had recurrence of disease on discontinuation of treatment.

Conclusion: Eplerenone showed significant improvement in decreasing the subretinal fluid accumulation and improving the visual acuity and macular thickness in our present study. However a long term large group analysis still needs to be undertaken for the long term effect of the drug and any effect of tapering the dose of the drug.

Introduction:

Central serous chorioretinopathy (CSCR) is a disease in which a serous detachment of the neurosensory retina occurs over an area of leakage from the choriocapillaris through the retinal pigment epithelium (RPE). Other causes for RPE leaks, such as choroidal neovascularization, inflammation, or tumors, should be ruled out to make the diagnosis.[1] Central serous chorioretinopathy (CSCR) may be divided into 2 distinct clinical presentations. Classically, CSCR is caused by one or more discrete isolated leaks at the level of the RPE as seen on fluorescein angiography (FA)[2]

Central serous chorio-retinopathy (CSCR) is very less merely understood eye disease involving the retina. In CSCR, fluid (which leaks from a layer of tissue underneath the retina called the choroid) builds up under the retina causing vision to become distorted and leading to vision loss in around a third of cases. The exact cause of CSCR is unknown however there does appear to be a genetic link, as it often appears in members of the same family. Recently , the CSCR has been included in the pachychoroid group of disorders, in which the major cause has been reflected on to the leaking choriocapillaris.The overactivation of mineralocorticoid receptor pathway in choroid vessels is presumably involved in the still unknown etiology of CSCR. Currently, there are no proven effective treatments. Recently a few patients have responded to treatment with a drug called eplerenone, which removes the fluid buildup and improves vision. However, information on the long term benefit and safety of this drug is lacking. The aim of this study was to test the effectiveness of eplerenone in the treatment of CSCR[3].

Methodology:

It was Prospective, double-blind, randomized placebo-controlled study. 24 eyes of 24 patients with persistent subretinal fluid (SRF) due to chronic CSCRof more than 4 month duration were enrolled and randomized to receive eplerenone 50 mg/day or placebo for 3 months, followed by a 3-month follow-up. The main outcome measure was change in SRF from baseline to 3 months of treatment. Secondary outcomes included change in SRF at any time-point, complete resolution of SRF, improvement in choroidal thickness and change in best-corrected visual acuity (BCVA).

The patient consent was obtained. We explained the purpose and importance of this work to patients. We explained the patients that, there is no guarantee that the treatment used in this study will help individual participants, however the information from the results could help patients in the future. There are side effects associated with eplerenone usage but these will be managed through regular patient and safety data monitoring. The blood pressure and serum electrolyte (especially serum potassium) monitoring of the patient was done. There is also a small risk of pain or bruising during and after blood tests.

The thickness was measured using the macula radial scan protocol of SD-OCT, RS NIDEK-3000

Results:

18eyes were treated with eplerenone and 6 with placebo. Both groups showed reduction in SRF throughout the treatment period, with a significant reduction at months 1, 3 and 6 only in the treatment group.

Central retinal thickness was 378.4±70µm before treatment and BCVA was logMAR 0.7. A clear decrease in retinal central thickness and height of SRF was observed at 1 month in 70% of patients, central retinal thickness: 318.3µm at 1 month, with improvement of visual acuity in all of these patients. Follow-up at 3 months also found a decrease in SRF and central retinal thickness four patients had complete resolution of SRF at 1 month with macular thickness 260±40µm, without recurrence at 3 months. The BCVA was improved to logMAR 0.2 Three other patients had complete resolution of SRF at 3 months. 2 patients had recurrence of disease on discontinuation of treatment.

Discussion:

Central serous chorioretinopathy (CSCR) is a retinal disorder that primarily affects young (20- to 50-year-old) white men, although it is seen occasionally in older patients and females. CSCR is characterized by avascular focal leakage through the retinal pigment epithelium (RPE), resulting in serous detachment of the neurosensory retina.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

The course is usually self-limiting and in most cases resolves spontaneously within a 3-month period, with visual acuity usually recovering to 20/30 or better. However, chronic CSCR may develop as a consequence of recurrences or persistent neurosensory detachment, and can result in progressive RPE atrophy and permanent visual loss. A primary involvement of the RPE and choroidal vascularization play a significant role in the pathogenesis of CSCR and the current treatment options attempt to restore the functions of the RPE and the normal choroidal vasculature. The aim of the current review is to provide an overview of the current therapeutical approaches to CSCR, including observation, laser treatment, photodynamic therapy with verteporfin, intravitreal anti-vascular endothelial growth factor therapy and the mineralocorticoid receptor antagonists.[5]

CSCR causes unilateral vision loss usually in males due to development of sub-retinal fluid, typically between the ages of 20 and 50 years old. The differential diagnosis for sub-retinal fluid is broad and encompass all disease entities that can cause macular neurosensory detachment. These entities include neovascular age related macular degeneration/polypoidal choroidal vasculopathy, myopic choroidal neovascular membrane, choroidal tumor, hypertensive choroidopathy, leukemic choroidal infiltration, choroidopathy due to multiple myeloma, retinal venous occlusion, unilateral acute idiopathic maculopathy, inflammatory conditions like posterior scleritis or Vogt-Koyanagi-Harada disease, optic nerve pit, and rhegmatogenous retinal detachment. Indeed, cases of bullous CSCR, where a significant amount of sub-retinal fluid is found, can be mistaken for rhegmatogenous retinal detachments. In both acute and chronic cases that have resolved, the only clue that may be present on examination is macular retinal pigment epithelium (RPE) mottling. By definition, the patient's retinal detachment cannot be due to another primary process. If suspected, those diagnoses should be ruled out. A thorough history, detailed exam and appropriate imaging and laboratory tests can help delineate between these diagnoses.[4]

In its most common form, patients affected by CSCR of recent onset complain of blurred vision with a relative central scotoma and metamorphopsia, possibly associated with dyschromatopsia, micropsia and a reduction in contrast sensitivity [1,6]. Fluorescein angiography discloses the presence of a focal point of leakage under a serous neuroretinal detachment with dye diffusion in the form of a 'smokestack' pattern, but multiple leaking points may also be observed [7]Indocyanine green (ICG) angiography allows the visualization of changes involving the deeper choroidal vascularization and reveals the presence of a delayed initial filling of arteries and choriocapillaris in the early phase of the examination, and a remarkable dilation of the large choroidal vein in the following phases, confirming a status of choroidal hyperpermeability . Optical coherence tomography is usually performed to better visualize the morphologic changes involving the single retinal layers and the alterations occurring in the RPE, and also to follow up the disease evolution .[6,7]

The introduction of drugs such as spironolactone and eplerenone in the treatment of CSC has been founded on the base of a pathogenetic mechanism involving the aldosterone/Mineralocorticoid Receptor and the choroidal hyperpermeability. With the new classification of pachychoroid disorders coming up, the pathophysiology of CSCR is now being studied in more detail. It is well known that an excess of endogenous (cortisol) or exogenous glucocorticoids is associated with CSCR and that glucocorticoids also show to some extent an affinity for the Mineralocorticoid receptors(MR). The mechanism linking the subretinal fluid accumulation and the activity of glucocorticoids seems to involve the overactivation of the ocular MR through an overexpression of the MR or an

increased stimulation. Studies performed on animal models have demonstrated that, following an intravitreal injection of aldosterone or high dose of glucocorticoid, an increased expression of ion and water channels on the outer limiting membrane can be observed Similar observations have been confirmed on human muller glial cell lines .As a consequence of intravitreal aldosterone injection, the accumulation of fluid in the subretinal space could be observed and was associated with vasodilation and leakage of the choroidal vasculature and increased choroidal thickness.[8]

In our present study , Central retinal thickness was 378.4µm before treatment. A clear decrease in retinal central thickness and height of SRF was observed at 1 month in 70% of patients, central retinal thickness: 318.3µm at 1 month, with improvement of visual acuity in all of these patients. Follow-up at 3 months also found a decrease in SRF and central retinal thickness .Three patients had complete resolution of SRF at 1 month, without recurrence at 3 months. Three other patients had complete resolution of SRF at 3 months. 2 patients had reported slight recurrence of subretinal fluid on stopping the treatment, which may be due to abrupt stopping of the medication. A further study on tapering the dose needs to be seen for preventing the recurrence of the subretinal fluid. No other side effects requiring treatment discontinuation were observed.

Eplerenone, a selective aldosterone-receptor antagonist and potassium-sparing diureticwas originally approved in 2002 by the FDA for treatment of hypertension, and recentlyit was shown to improve visual acuity and significantly decrease central macular thickness in a small series of patients with chronic CSCR. The medication is generally well tolerated but drug interactionsmust be ruled out before initiating the therapy and serum potassium and blood pressure must be monitored during treatment.[9]

Conclusion:

Eplerenone showed significant improvement in decreasing the subretinal fluid accumulation and improving the visual acuity and macular thickness in our present study. However a long term large group analysis still needs to be undertaken for the long term effect of the drug and any effect of tapering the dose of the drug.

References:

1. Gass JD: Pathogenesis of disciform detachment of the neuroepithelium. Am J Ophthalmo 1967;63(suppl):1-139.
2. Wang M, Munch IC, Hasler PW, Prunte C, Larsen M: Central serous chorioretinopathy. Acta Ophthalmol2008;86:126-145.
3. Yannuzzi LA, Freund KB, Goldbaum M, Scassellati-Sforzolini B, Guyer DR, Spaide RF, Maberley D, Wong DWK, Slakter JS, Sorenson JA, Fisher YL, Orlock DA: Polypoidal choroidal vasculopathy masquerading as central serous chorioretinopathy. Ophthalmology 2000;107:767-777.
4. Burumcek E, Mudun A, Karacorlu S, Arslan MO: Laser photocoagulation for persistent central serous retinopathy: results of long-term follow-up. Ophthalmology 1997;104:616-622.
5. Yamada K, Hayasaka S, Setogawa T: Fluoresceinangiographic patterns in patients with central serous chorioretinopathy at the initial visit. Ophthalmologica1992;205:69-76.

6. Piccolino FC, Borgia L: Central serous chorioretinopathy and indocyanine green angiography. Retina 1994;14:231-242.
7. Piccolino FC, Borgia L, Zinicola E, Zingirian M: Indocyanine green angiographic findings in central serous chorioretinopathy. Eye 1995;9:324-332.
8. Spaide RF, Hall L, Haas A, et al: Indocyanine green videoangiography of older patients with central serous chorioretinopathy. Retina 1996;16:203-213.
9. 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; 33:2096-102.