EFFECTIVENESS OF ORAL EPLERENONE IN THE TREATMENT OF CHRONIC CENTRAL SEROUS CHORIORETINOPATHY

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ABSTRACT

Objective: To determine the effectiveness of oral eplerenone in the treatment of chronic central serous chorioretinopathy (CSC).

Methodology: This non-randomized controlled trial conducted in Out Patient Department of Ophthalmology, Hayatabad Medical Complex, Peshawar from October 2015 to September 2016. 32 eyes of 32 patients who were diagnosed as cases of chronic CSC were included in the study. In all patients, visual acuity was recorded and the dilated fundoscopy was done followed by spectral domain optical coherence tomography (OCT) of macula to confirm the diagnosis. The macular thickness and subretinal fluid diameter was calculated using Spectralis OCT calipers. All patients were started on oral eplerenone 25mg once daily. All patients were reviewed after 1 month and 3 months with repeated OCT scans and visual acuity, OCT and fundus examination.

Results: Study was conducted on 32 eyes of thirty two patients. Mean age was 33.5 ±6.74 years. The mean baseline central macular thickness was 434.90 ±53.27µ. After 3 months, significant improvement in visual acuity was documented. There was marked reduction in central macular thickness after three months with mean of 325.41 ±52.55µ.

Conclusion: Oral eplerenone was an effective treatment for chronic serous dhorioretinopathy in terms of both anatomic and visual improvement.

Key Words: Eplerenone, Chronic central serous chorioretinopathy

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INTRODUCTION

Central serous chorioretinopathy (CSC) is characterized by disruption of outer blood retinal barrier with elevation of macular area due to accumulation of subretinal fluid[1]. The prevalence of CSC is 1:10000 with males more commonly affected than females[2,3]. Diffuse thickening of the choroid has been demonstrated by enhanced depth imaging by optical coherence tomography (OCT) in CSC patients suggesting the involvement of choroidal vessels in disease pathogenesis[4]. It has also been proposed that there is increased activation of glucocorticoids dependent choroidal vascular receptors which are responsible in the pathogenesis of CSC[5]. Because of this fact CSC is suggested to be associated with exogenous or endogenous glucocorticoids[6,7].

Central serous chorioretinopathy, is a diffuse retinal pigment epitheliopathy, in which there is widespread irregular, multifocal distribution of retinal pigment epithelium resulting in varying degrees of leakage[8]. Eexcessive glucocorticoid-dependent choroidal mineralcorticoid receptor activation in choroid vessels is another proposed theory for pathogenesis of CSC.

There are currently different treatment options available for CSC including focal laser photocoagulation, photodynamic therapy, anti-VEGF), corticosteroid inhibition and adrenergic receptor inhibition[9]. Eplerenone is a competitive antagonist of the glucocorticoid-dependent choroidal mineralcorticoid receptors[10]. Therefore, oral eplerenone which is a mineralocorticoids antagonist with good selectivity for mineralocorticoids receptors in choroidal vessels is considered as a treatment option for chronic CSC patients[11]. Recent studies have shown the potential benefits of eplerenone in chronic CSC patients , with promising results in terms of increase in visual acuity and decrease in central macular thickness on OCT[10].

As no data is available on the role of eplerenone in CSC in our population and it is not prescribed routinely to patients of CSC; so the purpose of the study was to establish the role of oral eplerenone in the treatment of chronic CSC in our community.

METHODOLOGY

It was a non-randomized controlled trial conducted in Out Patient Department of Ophthalmology, Hayatabad Medical Complex, Peshawar from October 2015 to September 2016. Patients between 10 to 60 years of age, with chronic CSC, diagnosed by the presence of subretinal fluid and reduced vision for more than 12 weeks were included in the study. Exclusion criteria were presence of choroidal neovascularization (CNV) identified by OCT angiography, Fluorescein angiography (FA), Indocyanine green angiography (ICG), photodynamic therapy, intravitreal injections, laser photocoagulation, vitrectomy, age-related macular degeneration, pathologic myopia, diabetic retinopathy, uveitis and contraindications for eplerenone such as severe renal, hepatic or cardiac disease and pregnancy.

A total of 32 eyes of 32 patients were included in our study. In all patients visual acuity (VA) was recorded and the dilated fundoscopy was done followed by spectral domain optical coherence tomography of macula to confirm the diagnosis. The macular thickness and subretinal fluid diameter was calculated using Spectralis OCT calipers.

All patients were started on oral eplerenone 25mg once daily. All patients were reviewed after 1 month and 3 months with repeated OCT scans, visual acuity and fundus examination. All the findings were recorded in the proforma. Effectiveness was determined in terms of increase in visual acuity of at least 2 lines on Snellen visual acuity chart from baseline visual acuity and decrease in macular thickness measured on SD-OCT of 200 microns from baseline macular thickness after 3 months.

Data were analysed using SPSS version 20.0. Quantitative variables included age, VA and central macular thickness; and qualitative variables included gender and effectiveness. Mean ± standard deviation was calculated for quantitative variables; while percentage and proportion was calculated for qualitative variables.

RESULTS

Total 32 patients were included in this study. Age ranges from 10 years to 60 years. Mean age was 33.5 ±6.74 years. Age distribution of patients is given in Table 1. Gender distribution was analyzed as 22 (68.75 %) patients were male while 10 (31.25 %) patients were female.

The baseline visual acuity and central macular thickness (CMT) is given in Table 2 and 3 respectively. After 3 months significant improvement in visual acuity was documented (Table 2). Similarly central macular thickness (CMT) was also reduced (Table 3).

Regarding effectiveness in visual acuity, eplerenone 25mg once daily was effective in 21 (65.62 %) patients (Table 4).

Regarding effectiveness in causing reduction in macular thickness, oral eplerenone 25mg once daily was effective in 24 (75%) of patients (Table 4).

The average duration of oral eplerenone 25mg once daily treatment was 3.9 ±2.3 months. Five patients (15.62%) experienced systemic side effects, e.g. fatigue, malaise, leg cramps, constipation and thirst. None of these was of such severity to discontinue the therapy.

DISCUSSION

One of the proposed treatment option for chronic CSC is oral mineralocorticoid antagonists. Currently two mineralocorticoid-specific receptor antagonists have got US Food and Drug Administration (FDA) approval for use in different systemic diseases[12]. The first, spironolactone is used for in the management of hypertension, hyperaldosteronism and congestive heart failure. However certain unwanted side effects including gynecomastia, impotence and abnormal menstrual cycles limit its use[13]. The second, eplerenone which has improved tolerability or specificity is similar to spironolactone except that the 17α-thoacetyl is replaced with a carbomethoxy group, resulting in decreased affinity for other steroid receptors such as those for androgen and progesterone[14].

Our results are comparable to the study conducted by Bousquet et al[15]. There was significant improvement in terms of increase in visual acuity, decrease in subretinal fluid and central macular thickness (CMT). They showed that with eplerenone 50 mg daily, the mean CMT decreased from 352µ at baseline to 246µ at one month and 189µ at three months. In our study, patients had an average decrease in CMT from 434.90µ to 325.41µ at 3 months with oral eplerenone 25 mg per day. One difference between our study and study conducted by Bousquet et al[15] was difference in drug dosing. They used 25 mg per day for a week followed by 50 mg daily for one or three months. While we used eplerenone 25 mg per day for 3 months. Despite the difference in dosing, we found significant improvement in visual acuity and significant decreases in central macular thickness.

Same dosing scheme as Bousquet et al[15] was used by Zhao et al[16] in their study with similar significant results. They also noted the recurrence rate and showed that there was no recurrent symptoms up to five months after discontinuation of therapy. In our study, because of small sample size we were not able to confirm that the benefits of eplerenone treatment were sustained in all patients over a longer period of time or re-accumula-

Table 1: Age-wise distribution of patients (n=32)

Age Ranges (Years)	Frequency	Percentage
10-20	2	6.26%
21-30	11	34.38 %
31-40	13	40.62%
41-50	5	15.62%
51-60	1	3.12%
Total	32	100%

Table 2: Baseline visual acuity (VA) compared to VA at 3 months (n=32 eyes)

Visual Acuity	Baseline		At 3 Months	
	Frequency	Percentage	Frequency	Percentage
<6/36	6	18.75%	2	6.26%
6/36–6/18	14	43.75%	4	12.50%
6/24–6/12	8	25.00%	5	15.62%
6/18–6/9	4	12.50%	21	65.62%
Total	32	100%	32	100%

Table 3: Baseline central macular thickness vs central macular thickness at 3 months (n=32 eyes)

Central Macular Thickness	Baseline		At 3 Months	
	Frequency	Percentage	Frequency	Percentage
>500 µ	5	15.62%	1	3.12%
400–500 µ	14	43.76%	6	18.76%
300–400 µ	12	37.50%	13	75.00%
200–300 µ	1	3.12%	12	3.12%
Total	32	100%	32	100%

Table 4: Effectiveness regarding visual acuity and central macular thickness (n=32 eyes)

Variable	Effectiveness	Frequency	Percentage	P Value
Visual Acuity	Yes	21	65.62%	0.02
	No	11	34.38%	
	Total	32	100%	
Central Macular Thickness	Yes	24	75.00%	0.001
	No	8	25.00%	
	Total	32	100%	

tion of sub-retinal fluid after discontinuation of treatment. Therefore we suggest that the optimal dosage and duration of eplerenone for chronic central serous chorioretinopathy need to be studied further[17].

Chin et al[18] found in their study that patients developed both tolerable and intolerable side effects with eplerenone. Tolerable side effects including malaise, fatigue and leg cramps were noted in 3 (13%) patients while 2 (8.7%) patients had intolerable side effects including constipation, thirst and dehydration. Five patients (15.62%) in our study experienced tolerable systemic side effects, e.g. fatigue, malaise and leg cramps of which none was of such severity to discontinue the therapy. Fatigue and leg cramps might have occured as a result of mild electrolyte imbalances. We make it possible to have frequent correspondence with the patient's physician or subspecialists, throughout treatment so that other associated systemic illnesses such as hypertension and renal function must be monitored and managed appropriately.

LIMITATIONS

Our study had certain limitations including small sample size and lack of control group. Similarly, our study did not work on acute versus chronic disease; however, prior treatment failures with oral, laser and intravitreal injections were in favor of chronic and recurrent nature.

CONCLUSION

Oral eplerenone 25mg once daily was an effective treatment for chronic CSC in terms of both anatomic and visual outcome. Further studies are required to determine the optimal dosage and duration of treatment.

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CONTRIBUTORS

OI conceived the idea, planned the study and drafted and critically revised the manuscript. IA and MR did data collection, statistical analysis and drafted the manuscript. IA did literature search, drafted and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.