Al-Kindy College Medical Journal (KCMJ)

Original Article

Possible role of Spironolactone in a sample of Iraqi patients with acute central serous chorioretinopathy

Marwa Majeed Hameed[1], Ahmed Majeed Rasheed[2], Furkaan Majeed Hameed[3]

[1] Opthalmology department, Ghazi Al- Hariri hospital, Baghdad, Iraq
[2] College of Medicine, Al-Nahrain University, Baghdad, Iraq
[3] College of Medicine, Al-Qadisiyah University, Diwanyah, Iraq

Corresponding author: majeedmarwa1@gmail.com

Article history:
Received 27 July 2021
Accepted 17 January 2022
Available online 30 April 2022

https://doi.org/10.47723/kcmj.v18i1.668

Keywords: Central serous chorioretinopathy, Spironolactone

ABSTRACT

Background: Central serous chorioretinopathy (CSCR) is an idiopathic condition aggravated by exogenous or endogenous glucocorticoids. Vascular deregulation in the choroid is a new hypothesis regarding central serous chorioretinopathy occurrence. The inhibition of choroidal mineralocorticoid receptors has a great role in shortening the duration of CSCR by inhibiting choroidal vasodilatation and leak.

Objective: To assess the effect of oral spironolactone on subretinal fluid, central macular thickness and visual acuity in patients with acute CSCR compared to observation.

Subjects and Methods: a hospital based, randomized clinical trial carried out at outpatient clinic in Ibn-Alhaitham Teaching Eye Hospital/ Baghdad, enrolling 60 patients with acute unilateral CSCR, allocated randomly (every other patient) to either receiving spironolactone 25 mg orally, twice daily for 2 months (30 patients) or observation only (30 patients). The follow-up included visual acuity measurement, central macular thickness and subretinal fluid height examinations by ocular coherence tomography (OCT) at one- and two-months post enrollment for all patients.

Results: Complete absorption of subretinal fluid was observed in 21(70%) of the eyes in the treatment group and in 6(20%) in the control group at two-months. Visual acuity and mean macular thickness improved significantly in both groups at the one- and two- months, mean changes was larger in treatment group compared to control group at the two-month-follow up endpoint.

Conclusion: Oral spironolactone imparted greater improvement in central macular thickness and faster resolution of sub retinal fluid in patients with acute central serous chorioretinopathy versus observation.

Introduction

Central serous chorioretinopathy (CSCR), is detachment of the sensory retina from retinal pigmented epithelia frequently seen in the macular area. It is the fourth most common nonsurgical maculopathy after diabetic retinopathy, choroidal neovascularization, and branch retinal vein occlusion. (1)

It typically affects middle‑aged men, it can be seen from 20 to 64 years with annual incidence of 9.9 per 100,000 men and

1.7/100,000 women in a population‐based study in United States. (2) Poorer visual acuity, diffuse retinal pigment epitheliopathy changes, and secondary choroidal neovascularization membrane occur frequently in elder patients. (3) Generally, CSCR is a self-limiting disorder, bulk of patients with acute state achieve natural resolution within three months, (4) 30% of patients sub retinal fluid (SRF) resolves in 8 weeks during the usual course of the disease, so observation is the first-line of management. (5)

To increase the chance of spontaneous resolution risk factors should be addressed, life style modification for patients with type A personality disorders and discontinuing intake of exogenous corticosteroids. (6) Various treatment modalities, including; systemic carbonic anhydrase inhibitors, conventional and subthreshold laser photocoagulation, anticorticosteroids (ketoconazole, mifepristone, rifampin), beta blockers, acetylsalicylic acid, intravitreal bevacizumab or ranibizumab, have been investigated as potential therapeutic options for chronic CSCR. (7)

Photodynamic therapy (PDT) with verteporfin has been the most promising treatment in this regard, with a success rate approaching 90%. (8) Lack of response, cost, and adverse effects are disadvantages associated with these treatment modalities. (9) Recently, unfortunate activation of mineralocorticoid receptors (MRs) situated in the choroidal vessels has been identified as a potential pathological pathway underlying the vascular choroidopathy in CSCR, this finding suggests that therapeutic blockade of the MRs could reverse choroidal vasculopathy. (10)

Activation MRs pathways by aldosterone or glucocorticoid increase vasodilator potassium channels KCa2.3 leading to the hyperpolarization of endothelial cells and underlying smooth muscles leading to vasodilatation of choroidal vessels. (11) Spironolactone, a synthetic 17-lactone steroid, acts as a non-selective mineralocorticoid receptor antagonist (MRa) with moderate affinity for both progesterone and androgen receptors. (12).

Subjects and methods

Study design: -

This study is a hospital based, randomized clinical trial conducted from April 2018 and last patient's response documented in February 2019.

Subjects:

In this study sixty patients with age range from 28-45 years, who attended the outpatient ophthalmic clinic at Ibn Al-Haitham Teaching Eye Hospital in Baghdad, were diagnosed with acute, first attack of unilateral CSCR with duration of symptoms ≤ 12 weeks enrolled in this study. Thirty patients were treated with (spironolactone 25 mg per oral, two times every day) for 8 weeks, and in the other group thirty patients subjected to observation only.

Randomization:

The patients were allocated into one of the two groups randomly during the study period as follows: the first patient was allocated into the treatment group and the next was allocated into the control group (every other patient) until reaching the targeted sample size of 60 patients.

Exclusion criteria:

1. Chronic CSCR (>12 weeks) or with history of recurrence.
2. Patient with other retinal diseases like diabetic retinopathy.
3. Previous treatment with laser photocoagulation, photodynamic therapy (PDT) or intra vitreal injection of (anti-VEGF).
4. Pregnancy.
5. Previous use of corticosteroid drugs or systemic diseases e.g endogenous hypercortisolism.
6. General illness for which spironolactone contraindicated like impaired renal, cardiac or hepatic function or standard serum potassium level >5.5 mmol/L.

Measurements:

At baseline, all patient included in the study underwent ophthalmic examination in form of distant best corrected visual acuity (BCVA) on Snellen charts (logMAR), intraocular pressure measurement, slit lamp biomicroscopy, spectral domain optical coherence tomography (OCT) (Heidelberg Engineering GmbH 69121 Heidelberg, Germany) for measurement of central macular thickness (CMT) and subretinal fluid height (SRFH) which manually measured from the retinal outer segment line to the pigment epithelia level at the center of macula and fundus fluorescein angiography (FFA). Patients then monitored at one- and two- months post-enrollment with visual acuity, slit lamp examination, OCT for CMT and SRFH measurement.

Statistical analysis:

Were carried out by using IBM® Statistical Package for Social Sciences (SPSS) ® version 20. Descriptive statistics included means ± standard deviations for quantitative data, and as frequency and percentages for categorical data. Chi-square test was utilized to investigate the statistical association between categorical data. Evaluations of age, duration of symptoms, BCVA, CMT, and SRFH in both groups were performed using the student independent samples T-test. Assessments of differences in BCVA, CMT and SRFH at baseline and at the two study-endpoints was done through analysis of variances (ANOVA) with least significant differences (LSD). A value of $P < 0.05$ was considered statistically significant.

Ethical issues:

The study design and data collection were done after getting approval of Iraqi committee for medical specialization. All patients were informed about methodology and purpose of study and written consents of patients were obtained.

Results

In treatment group the mean age was 34.56±1.68 years, males signified (80%) while the females (20%), duration of symptoms was 2.44 ±0.21 weeks, number of patients with leakage point in FFA was 16 (53.33%) in both groups. In the control group the mean age was 33.1±1.41 years, 83.33% were males, and the symptoms' duration was 2.49 ± 0.19 weeks. The male-to-female ratio between the two groups revealed no significant difference (p=0.739). Baseline BCVA (log MAR), CMT and SRFH were not significantly different between the two groups (p =0.052, p=0.771 and p=0.094 respectively). In addition, no statistically significant differences had

been found between both groups, in all demographic variables and in all comparisons (p. value > 0.05).

Table 1: Baseline demographic features in both groups

Demographic character		Groups: Treatment group N= 30	Groups: Control group N = 30	P Value
gender	male	24(80.0)	25(83.33)	0.739(NS)
	female	6(20.0)	5(16.66)	
Age (years) mean± SD		34.56±1.68	33.1±1.41	0.507(NS)
Duration of symptoms (weeks) mean± SD		2.44 ±0.21	2.49 ± 0.19	0.871(NS)
BCVA(logMAR) mean± SD		0.26±0.21	0.35±0.21	0.052(NS)
CMT (µm) mean± SD		442.4±93.06	450.1±110.26	0.771(NS)
SRFH (µm) mean± SD		216.96±102.37	262.86±106.36	0.094(NS)
Patients with leakage point	Yes	16(53.33)	16(53.33)	1(NS)
	No	14(46.66)	14(46.66)	

SD: standard deviation, S: significant difference (P<0.05), NS: Non-significant difference (P>0.05), BCVA: best corrected visual acuity, CMT: central macular thickness, MRa: mineralocorticoid receptor antagonist, SRFH: sub retinal fluid height.

Table-2 shows the mean BCVA at baseline, 1 month and 2 months in both groups, in spironolactone group, mean BCVA was 0.26±0.21 at baseline, 0.13±0.08 at 1 month and 0.09±0.12 at 2 months. The BCVA considerably improved related to base line in spironolactone group. In control group, the mean BCVA at baseline was 0.35±0.21, 0.25±0.14 at 1 month and 0.21±0.18 at 2 months. However, the mean difference in the BCVA was obvious in both groups relatively larger in spironolactone group.

Table 2:Distribution of participants according to PHQ questions

Check point	Treatment group: Mean BCVA (Log MAR)	Control group: Mean BCVA (Log MAR)	P.value between groups
Baseline	0.26±0.21	0.35±0.21	0.052
1 month	0.13±0.08	0.25±0.14	0.015
2 month	0.09 ± 0.12	0.21±0.18	0.017
P. value within group	0.032	0.042	-

Table-3 shows; mean changes in the CMT. In spironolactone group, the mean macular thickness declined considerably from 442.4±93.06 µm at baseline to 276.1±44.72 µm at 2 months. Regarding the control group the mean CMT was 450.1±110.26 µm at baseline, decreased to 371.26±70.34 µm at 1 month and to 339.6±81.80 µm at 2 months. There was a greater difference in the mean macular thickness between the two groups along the study period.

Table 3: Alterations in CMT (µm)

Check point	Treatment group: Mean CMT (µm)	Control group: Mean CMT (µm)	P.value between groups
Baseline	442.4 ± 93.06	450.1 ± 110.26	0.771(NS)
1 month	328.46 ± 74.39	371.26 ± 70.34	0.026(S)
2 month	276.1 ± 44.72	339.6 ± 81.80	0.001(S)
LSD	37.94 (S)	45.99 (S)	

LSD: Least significant differences.

Complete resolution of SRF was achieved in 70 % (21/30) of the eyes in the treatment group and 20 % (6/30) in the control group at 2 months. SRFH diminished significantly by mean of 216.96±102.37 µm at baseline to 104.06±60.65 µm after 4 weeks of treatment drop to 58.7±33.30 µm at 8 weeks. Regarding control group a significant decline from 262.86±106.36 µm at baseline to 179.36±62.50 µm at 1 month then to 134.86±82.05 µm at 2 months.

Table 4: alterations in SRFH (µm)

Check point	Treatment group: Mean SRFH (µm)	Control group: Mean SRFH (µm)	P.value between groups
Baseline	216.96±102.37	262.86±106.36	0.094(NS)
1 month	104.06±60.65	179.36±62.50	0.002(S)
2 month	58.7±33.30	134.86±82.05	0.003(S)
LSD	47.740(S)	51.962(S)	-

Discussion

Central serous chorioretinopathy is still an enigmatic condition in large part due to a natural progression of spontaneous improvement in a high proportion of patients and also to the fact that no single treatment has provided overwhelming evidence of efficacy in published randomized control trial .(13) Previous studies have shown a promising effectiveness of MRa in the treatment of chronic and recurrent CSCR, from this point other ophthalmic researchers studied the effect of oral spironolactone in patients with acute CSCR. (14)

The baseline characteristics of the patients revealed higher proportion of males among the studied groups and a mean age of 34.6 and 33.1 years in MRa and control groups respectively, indicated that the majority of the study participants were within their middle age, these findings came in line with the clinical picture of acute CSCR, where it more frequently affects middle aged males. (15-17)

The present study found that although the BCVA improved significantly in both study groups, the improvement was greater in treatment group as patients improved by five letters logMAR at one- and two-month endpoints compared to control group which indicated better and quicker improvement in treatment group. Improvement in the BCVA was similarly reported in previous studies, in term of BCVA, Pichi et al. reported in 2017 that treatment with spironolactone was effective in improvement of BCVA from the first month and concluded that spironolactone is better than eplerenone in refining visual acuity in patients with persistent CSCR. (18)

The present study found that CMT at 1 and 2 months decreased significantly in both groups. Despite the reduction in CMT was found in both groups, the change was larger in the MRa group and the difference between both groups was significant at one and two months, ($P<0.05$). These findings agreed with the previous study of Sun et al. from China where the researchers treat patients with acute serous retinopathy with MRa drug, approving a positive impact in most cases. (14)

Findings of the present study supported those reported in previous studies which documented similar changes and improvement, like in the study of Sun et al. who reported that complete resolution of SRF was reported in more than half, 55.6%, of the treatment group who received spironolactone for 2 months, compared to 8.3% in control group, and the mean BCVA improved with time compared to its baseline levels, in both groups. (14)

Zucchiatti et al. in 2018 showed the effect of eplerenone on patients with acute CSCR and compared the result with observation. The BCVA and CMT improved in eplerenone group at 3 months. Complete disappearance of subretinal fluid was observed in 80% of subjects in the treatment group, versus 25% in the control group. (4)

Kapoor and Wagner, in United States concluded in their case control study in 2017 that using MRa in patients with CSCR accelerated the resolution and improvement and there were improved visual acuity gain and reduction in the subretinal fluid at 1, 2 and 3 months compared to baseline, furthermore, they documented a significant improvement in the resolution of sub-retinal fluid and two-line visual acuity gain by month 2 in the treatment group compared to the observation group. (19)

Chin et al. used oral glucocorticoid antagonists for refractory cases of central serous retinopathy and concluded that MRa treatment had a positive treatment effect in half of the patients in the study. The decrease in CMT and macular volume was much less in the recalcitrant group compared to the group of no previous treatment for CSCR. (20)

Findings of the present study were comparable to the cure rates reported with other modalities which indicated that using spironolactone it is not inferior to other treatment modalities and could be a promising mode of treatment for CSCR.

Limitations

The main limiting factor in this study included a small sample size, that might be related to the limited duration of conducting research in the program of the Iraqi Board of Ophthalmology. Another limiting factor could be patients' compliance to treatment, which could affect the results as the disease could resolve spontaneously.

Conclusion

- Oral spironolactone achieved greater improvement in central macular thickness and faster resolution of sub retinal fluid in patients affected by acute CSCR compared to observation.
- This study endured the effectiveness of this treatment in Iraqi patients in which about 70% of the patients got complete absorption of the sub retinal fluid in a short period without any side effects.

Funding

This research did not receive any specific fund.

Conflict of Interest

No conflict of interest

References

[1] Wang M, Munch IC, Hasler PW, Prünte C, Larsen M. Central serous chorioretinopathy. Acta Ophthalmol. 2008 Mar;86(2):126-45. doi: 10.1111/j.1600-0420.2007.00889.x. Epub 2007 Jul 28. PMID: 17662099.

[2] Kitzmann AS, Pulido JS, Diehl NN, Hodge DO, Burke JP. The incidence of central serous chorioretinopathy in Olmsted County, Minnesota, 1980-2002. Ophthalmology. 2008 Jan;115(1):169-73. doi: 10.1016/j.ophtha.2007.02.032. PMID: 18166410.

[3] Manayath GJ, Ranjan R, Shah VS, Karandikar SS, Saravanan VR, Narendran V. Central serous chorioretinopathy: Current update on pathophysiology and multimodal imaging. Oman J Ophthalmol. 2018 May-Aug;11(2):103-112. doi: 10.4103/ojo.OJO_75_2017. PMID: 29930442; PMCID: PMC5991069.

[4] Zucchiatti I, Sacconi R, Parravano MC, Costanzo E, Querques L, Montorio D, Bandello F, Querques G. Eplerenone Versus Observation in the Treatment of Acute Central Serous Chorioretinopathy: A Retrospective Controlled Study. Ophthalmol Ther. 2018 Jun;7(1):109-118. doi: 10.1007/s40123-018-0121-2. Epub 2018 Feb 13. PMID: 29442283; PMCID: PMC5997595.

[5] Daruich A, Matet A, Marchionno L, De Azevedo JD, Ambresin A, Mantel I, Behar-Cohen F. ACUTE CENTRAL SEROUS CHORIORETINOPATHY: Factors Influencing Episode Duration. Retina. 2017 Oct;37(10):1905-1915. doi: 10.1097/IAE.0000000000001443. PMID: 28067724; PMCID: PMC5642321.

[6] Sahin A, Bez Y, Kaya MC, Türkcü FM, Sahin M, Yüksel H. Psychological distress and poor quality of life in patients with central serous chorioretinopathy. Semin Ophthalmol. 2014 Mar;29(2):73-6. doi: 10.3109/08820538.2013.793728. Epub 2013 Jun 12. PMID: 23758338.

[7] Abouammoh MA. Advances in the treatment of central serous chorioretinopathy. Saudi J Ophthalmol. 2015 Oct-Dec;29(4):278-86. doi: 10.1016/j.sjopt.2015.01.007. Epub 2015 Jan 24. PMID: 26586979; PMCID: PMC4625218.

[8] Lim JI, Glassman AR, Aiello LP, Chakravarthy U, Flaxel CJ, Spaide RF; Macula Society CSC Collaborative Study Group, Research and Education Committee and Website Committee. Collaborative retrospective macula society study of photodynamic therapy for chronic central serous chorioretinopathy. Ophthalmology. 2014 May;121(5):1073-8. doi: 10.1016/j.ophtha.2013.11.040. Epub 2014 Jan 16. PMID: 24439758.

[9] Falavarjani KG, Amirsardari A, Habibi A, Eshaghi A, Bakhti S, Aghdam KA. Visual and Anatomical Outcomes of Spironolactone Therapy in Patients with Chronic Central Serous Chorioretinopathy. J Ophthalmic Vis Res. 2017 Jul-Sep;12(3):281-289. doi: 10.4103/jovr.jovr_139_16. PMID: 28791061; PMCID: PMC5525497.

[10] Zhao M, Célérier I, Bousquet E, Jeanny JC, Jonet L, Savoldelli M, Offret O, Curan A, Farman N, Jaisser F, Behar-Cohen F. Mineralocorticoid receptor is involved in rat and human ocular chorioretinopathy. J Clin Invest. 2012 Jul;122(7):2672-9. doi: 10.1172/JCI61427. Epub 2012 Jun 11. PMID: 22684104; PMCID: PMC3386817.

[11] Daruich A, Matet A, Dirani A, Bousquet E, Zhao M, Farman N, Jaisser F, Behar-Cohen F. Central serous chorioretinopathy:

Recent findings and new physiopathology hypothesis. Prog Retin Eye Res. 2015 Sep;48:82-118. doi: 10.1016/j.preteyeres.2015.05.003. Epub 2015 May 27. PMID: 26026923.

[12] Layton AM, Eady EA, Whitehouse H, Del Rosso JQ, Fedorowicz Z, van Zuuren EJ. Oral Spironolactone for Acne Vulgaris in Adult Females: A Hybrid Systematic Review. Am J Clin Dermatol. 2017 Apr;18(2):169-191. doi: 10.1007/s40257-016-0245-x. PMID: 28155090; PMCID: PMC5360829.

[13] Salehi M, Wenick AS, Law HA, Evans JR, Gehlbach P. Interventions for central serous chorioretinopathy: a network meta-analysis. Cochrane Database Syst Rev. 2015 Dec 22;2015(12):CD011841. doi: 10.1002/14651858.CD011841.pub2. PMID: 26691378; PMCID: PMC5030073.

[14] Sun X, Shuai Y, Fang W, Li J, Ge W, Yuan S, Liu Q. Spironolactone versus observation in the treatment of acute central serous chorioretinopathy. Br J Ophthalmol. 2018 Aug;102(8):1060-1065. doi: 10.1136/bjophthalmol-2017-311096. Epub 2017 Oct 31. PMID: 29089356.

[15] Nicholson BP, Ali Idris AM, Bakri SJ. Central Serous Chorioretinopathy: Clinical Characteristics Associated with Visual Outcomes. Semin Ophthalmol. 2018;33(6):804-807. doi: 10.1080/08820538.2018.1503690. Epub 2018 Aug 1. PMID: 30067427.

[16] Mohabati D, Schellevis RL, van Dijk EHC, Altay L, Fauser S, Hoyng CB, De Jong EK, Boon CJF, Yzer S. GENETIC RISK FACTORS IN ACUTE CENTRAL SEROUS CHORIORETINOPATHY. Retina. 2019 Dec;39(12):2303-2310. doi: 10.1097/IAE.0000000000002333. PMID: 30300269.

[17] Ersoz MG, Arf S, Hocaoglu M, Sayman Muslubas I, Karacorlu M. Patient characteristics and risk factors for central serous chorioretinopathy: an analysis of 811 patients. Br J Ophthalmol. 2019 Jun;103(6):725-729. doi: 10.1136/bjophthalmol-2018-312431. Epub 2018 Jul 12. PMID: 30002072.

[18] Pichi F, Carrai P, Ciardella A, Behar-Cohen F, Nucci P; Central Serous Chorioretinopathy Study Group. Comparison of two mineralcorticosteroids receptor antagonists for the treatment of central serous chorioretinopathy. Int Ophthalmol. 2017 Oct;37(5):1115-1125. doi: 10.1007/s10792-016-0377-2. Epub 2016 Oct 18. PMID: 27757733.

[19] Kapoor KG, Wagner AL. Mineralocorticoid Antagonists in the Treatment of Central Serous Chorioretinopathy: A Comparative Analysis. Ophthalmic Res. 2016;56(1):17-22. doi: 10.1159/000444058. Epub 2016 Mar 17. PMID: 26982318.

[20] Chin EK, Almeida DR, Roybal CN, Niles PI, Gehrs KM, Sohn EH, Boldt HC, Russell SR, Folk JC. Oral mineralocorticoid antagonists for recalcitrant central serous chorioretinopathy. Clin Ophthalmol. 2015 Aug 11;9:1449-56. doi: 10.2147/OPTH.S86778. PMID: 26316684; PMCID: PMC4540165.

To cite this article: Hameed M, Rasheed A, Hameed F. Possible role of Spironolactone in a sample of Iraqi patients with acute central serous chorioretinopathy. Al-Kindy College Medical Journal. 2022;18(1):60-64.