Efficacy of oral rifampicin in chronic central serous chorioretinopathy

Ramesh Venkatesh, Manisha Agarwal and Meha Kantha

Ther Adv Ophthalmol
2018, vol. 10 1–6
DOI: 10.1177/2515841418807130

Correspondence to:
Ramesh Venkatesh
Dr. Shroff's Charity Eye Hospital, 5027, Kedarnath Road, Daryaganj, New Delhi 110002, India.
vramesh80@yahoo.com

Ramesh Venkatesh
Manisha Agarwal
Meha Kantha
Dr. Shroff's Charity Eye Hospital, New Delhi, India

Abstract

Objective: To evaluate the role of oral rifampicin in the management of chronic central serous chorioretinopathy.

Methods: Retrospective analysis of patients diagnosed with chronic central serous chorioretinopathy (duration >3 months) and treated with oral rifampicin 600 mg daily for a maximum period of 3 months was carried out. Baseline visual acuity, fundus fluorescein angiography, and optical coherence tomography were recorded and the patients were followed up. Resolution of subretinal fluid and improvement in visual acuity were the main outcome measures. Recurrence of subretinal fluid was noted. Any adverse reaction to the drug was monitored.

Results: Nine eyes of eight patients were included in the study. The average age of the patients was 41.90 years (range 32–52 years). Mean duration of symptoms was 16 months (range 3–60 months). Mean duration of follow-up was 10.11 months (range 3–33 months). Fluorescein angiography showed four eyes with subfoveal leaks and five eyes with diffuse retinal pigment epitheliopathy. Complete resolution of subretinal fluid was achieved in four of the nine eyes – two patients at the end of 1 month, one patient each at the end of 2 and 3 months, respectively. Visual acuity improvement was noted in four of the nine eyes. Three patients had one-line improvement and one patient had a two-line visual improvement. None of the patients had severe adverse events for which the drug had to be discontinued. None of the patients had recurrence of subretinal fluid after the discontinuation of the drug.

Conclusion: Oral rifampicin could provide a useful, effective, and cost-effective alternative for treatment of patients with chronic central serous choroidopathy and evidence of healthier retinal pigment epithelium, those with focal leakage. It was not effective in eyes with diffuse retinal pigment epitheliopathy.

Keywords: antitubercular, central serous chorioretinopathy, chronic, rifampicin, subretinal fluid

Received: 16 May 2018; revised manuscript accepted: 31 August 2018.

Introduction

Central serous chorioretinopathy (CSCR) is characterized by macular serous retinal and/or retinal pigment epithelium (RPE) detachment. It is most common in men aged 30 to 50 years. Most clinical studies have classified CSCR into acute and chronic forms based on the duration of subretinal fluid (SRF) accumulation.[1] Also, presence of retinal pigment epithelial changes on clinical examination also suggests chronicity. Multiple treatment modalities have been described for chronic CSCR, including focal laser, photodynamic therapy (PDT),[1,2] rifampicin,[3,4] and even anti-VEGF therapy.[5] In some patients, focal laser is contraindicated due to proximity of leaking spots to the fovea. Although PDT has been found to be effective, it is unavailable and not affordable to patients in many developing countries. Rifampicin has been described in anecdotal reports as an alternative treatment option due to its effect on serum cortisol and low cost.[3,4] This study retrospectively examined the efficacy of oral rifampicin in patients of idiopathic chronic CSCR.

Patients

After obtaining Institutional Review Board and Ethics committee approval (SCEH-2012-04-003), nine eyes of eight patients diagnosed with idiopathic chronic CSCR and treated with oral rifampicin were included in this study. The diagnosis of chronic CSCR was based on the presence of SRF >3 months duration with/without diffuse retinal pigment epithelial (DRPE) changes. All patients were men and the mean age was 41.90 years (range 32–52 years). The mean duration of symptoms was 16 months (range 3–60 months) and follow-up duration was 10.11 months (range 3–33 months). All eyes had SRF at the time of inclusion.

Results

Baseline ophthalmic evaluation included best-corrected visual acuity (BCVA) with Snellen chart, fundus examination, fluorescein angiography (FA; Topcon TRC-50 IA; Topcon, Tokyo, Japan) and optical coherence tomography (OCT; RTVue; Optovue, Germany). Indocyanine green angiography was done in select cases to identify the presence of a possible choroidal neovascular membrane (CNV). None of the eyes showed CNV. FA showed four eyes with focal subfoveal leaks and five eyes with DRPE. Investigations including complete hematological counts, chest X-ray, Mantoux test, and liver enzyme tests were performed to rule out active pulmonary tuberculosis (TB) in all patients. A written informed consent was obtained from all patients regarding understanding of the clinical condition, treatment modality offered, and its side effects. Patients were treated with oral rifampicin 600 mg daily for a maximum period of 3 months or till SRF resolved completely, whichever was earlier. BCVA and OCT were done in all follow-up visits. OCT was performed for measuring and monitoring the central retinal thickness and height of SRF. Complete resolution of SRF was achieved in four of the nine eyes. Details regarding the outcomes, follow-up, and adverse drug reaction of all the cases are mentioned in Table 1. A written informed consent for patient information and related images to be published was provided by all patients.

Discussion

Usually CSCR in its acute phase is a self-limiting condition associated with complete resolution of SRF and improvement of symptoms. However, long-term accumulation of SRF can lead to photoreceptor loss and extensive retinal pigment epithelial damage referred to as DRPE. This may result in permanent disturbances in visual acuity, color vision, and contrast sensitivity.[6] The standard of care for treating CSCR has evolved over the past three decades. Although focal thermal laser for extrafoveal leaks was found to decrease duration of SRF compared to observation, VA and recurrence outcomes were similar and thus observation was advocated for new-onset CSCR. As chronic CSCR could be associated with RPE damage and vision deficit, those with extrafoveal leakage spots had focal thermal laser as the recommended treatment. More recently, PDT with reduced fluence or reduced dose has been found to be more effective than observation in eliminating SRF and limiting vision loss.[7] In much of the developing world, PDT is not available as a treatment modality for those diagnosed with chronic CSCR. In such settings, thermal focal laser still has remained the standard of care. Focal laser to the leaking foci in CSCR could be associated with the complication of secondary choroidal neovascularization. Therefore, it may be advantageous to explore other treatments for management of chronic CSCR in this setting. Elevated levels of serum cortisol are associated with CSCR. An association between serum glucocorticoids and CSCR has already been established.[8] Anecdotal reports have shown that drugs targeting the cortisol pathways like ketoconazole, mifepristone (RU486), finasteride, rifampicin, and antiadrenergic agents like propranolol can be tried in CSCR.

Rifampicin is an inexpensive, antitubercular drug and readily available in the developing world. It is a cytochrome P4503A4 enzyme inducer which increases the metabolism of endogenous corticosteroids and thereby reduces their levels in the serum, helping in the faster SRF resolution. In a study by Shulman and colleagues,[9] 12 patients (with 14 involved eyes) were treated with oral rifampicin 300 mg twice daily. There was a significant reduction in SRF at the end of 3 months and complete resolution of SRF in six (42.8%) eyes. However, this study did not categorize fluorescein findings (type of leak) and had a short follow-up. The current series has the advantage of having long follow-up duration (mean of 10.1 months) and characterized fluorescein findings that prove to be clinically relevant. Three of the four eyes with complete resolution of SRF had focal leaks on FA. Four of the five eyes in the DRPE group did not achieve complete SRF resorption at month 3. Despite the small numbers, this suggests the need for a relatively healthy

Table 1. Patient characteristics, treatment outcomes, and adverse drug reactions of patients treated with oral rifampicin.

Patient no.	Eye	Age/ sex	Symptoms duration (months)	BCVA month 0	Type of leak	CRT presentation (µm)	Treatment duration	SRF month 3	SRF height (µm)	CRT month 3	BCVA month 3	Side effects	Final f/u duration (months)	SRF recurrence
1	RE	50/M	36	6/9	Focal	197	1	AB	0	184	6/6	Headache	15	No
2	RE	44/M	6	6/60	DRPE	221	1	AB	0	218	6/36	Diarrhea	33	No
3	RE	40/M	4	6/24	DRPE	226	3	P	73	229	6/12	None	6	No
4	LE	45/M	60	6/36	DRPE	271	3	P	41	262	6/36	None	7	No
5	LE	40/M	4	6/24	Focal	192	3	AB	0	181	6/24	None	9	No
6	RE	32/M	4	6/9	Focal	199	3	P	23	207	6/9	None	3	No
7	RE	52/M	9	FC 3 months	DRPE	265	3	P	44	241	6/60	None	6	No
	LE	52/M	9	6/18	DRPE	271	3	P	19	263	6/18	None	6	No
8	RE	32/M	5	6/60	Focal	201	2	AB	0	198	6/18	None	6	No

AB, absent; BCVA, best-corrected visual acuity; CME, cystoid macular edema; CRT, central retinal thickness; DRPE, diffuse retinal pigment epitheliopathy; F/u, follow-up; LE, left eye; P, present; RE, right eye; SRF, subretinal fluid.

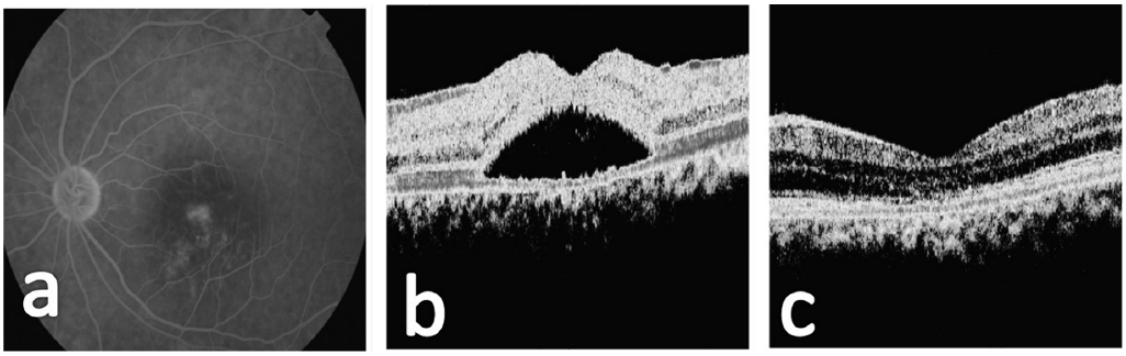

Figure 1. Patient 5. (a) Late-phase fluorescein angiogram showing focal leak at the subfoveal location with retinal pigment mottling noted inferior to the macula. (b) Pretreatment OCT showing the presence of subretinal fluid. (c) Posttreatment OCT showing complete resolution of subretinal fluid following treatment with oral rifampicin for 2 months.

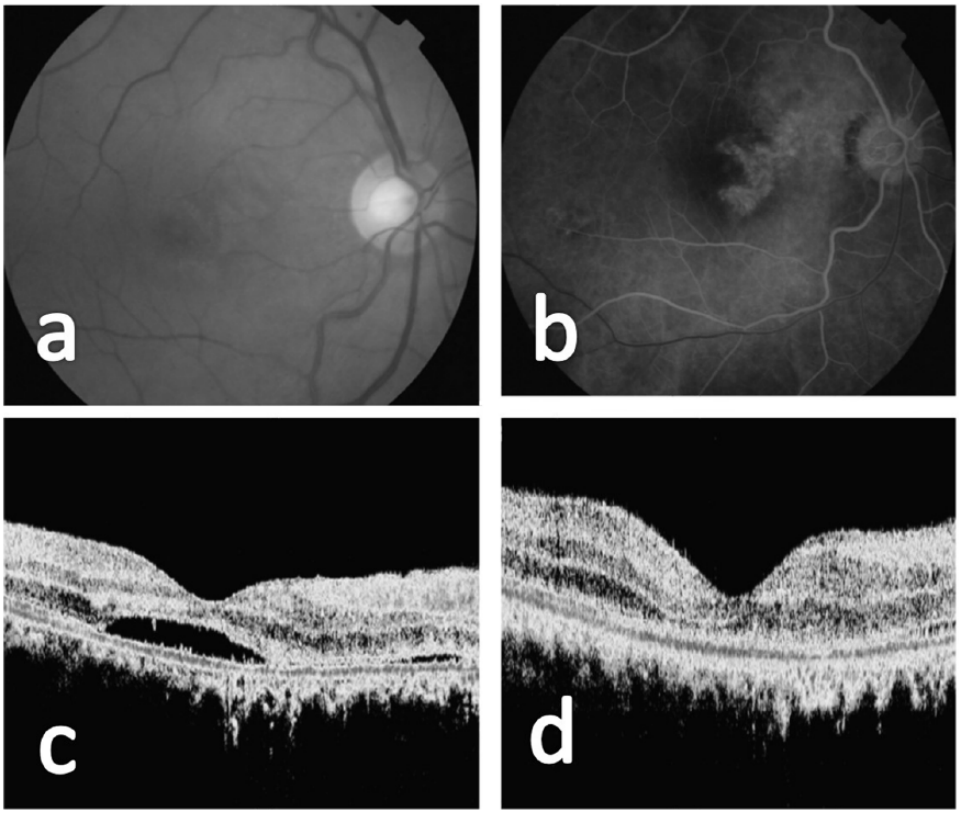

Figure 2. Patient 2. (a) Red-free fundus photo of a 44-year-old man showing diffuse retinal pigment epithelial changes (atrophy and pigment clumping) temporal to the disc. (b) Fluorescein angiogram showing diffuse retinal pigment epitheliopathy changes with no evidence of focal leaks. (c) Pretreatment OCT showing the presence of subretinal fluid. (d) Posttreatment OCT showing complete resolution of subretinal fluid following treatment with oral rifampicin for 1 month.

RPE to allow SRF absorption. Mean BCVA at presentation and at month 3 was 6/30 and 6/18, respectively. Vision improved in those eyes achieving resolution of SRF. Three (33.33%) eyes had one-line improvement and one (11.11%) eye had a two-line visual improvement. Eyes with persistent SRF at 3 months showed no improvement in three of the five eyes and the remaining two eyes had a two-line improvement in visual acuity. There have been reports that the efficacy of rifampicin in CSCR is limited to the duration of its use, with recurrences noted when treatment

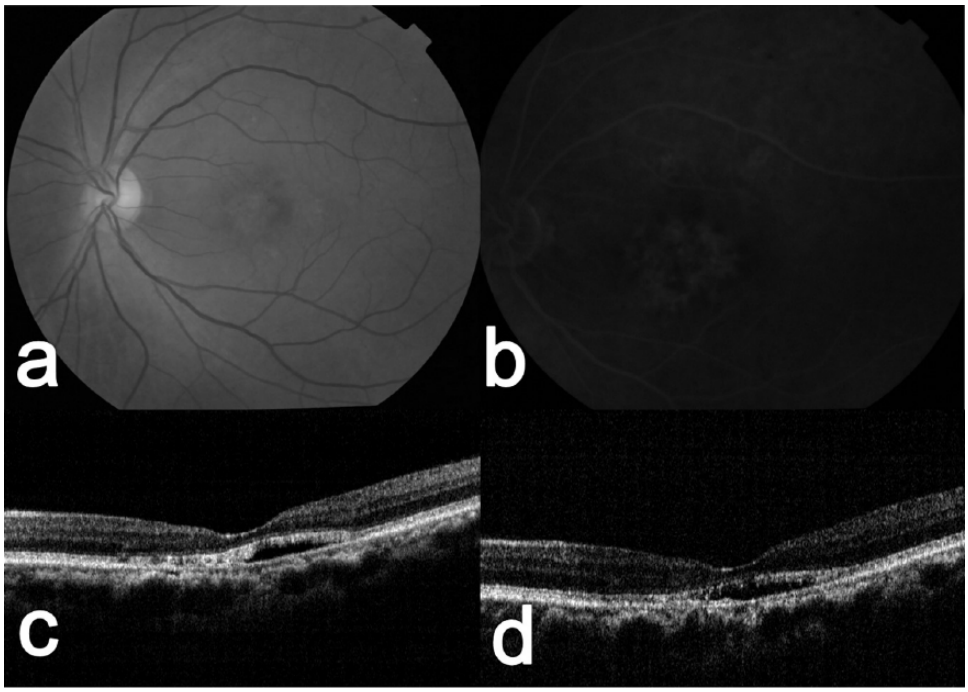

Figure 3. Patient 4. (a) Left eye red-free fundus picture of a 45-year-old man showing retinal pigment epithelial mottling and atrophic areas at the macula. (b) Late-phase fluorescein angiogram showing diffuse retinal pigment epitheliopathy changes at the macula with no focal leaks. (c) Pretreatment OCT showing the presence of subretinal fluid. (d) Posttreatment OCT following treatment with oral rifampicin for 3 months showing no resolution of SRF.

is discontinued.[4] In this series, the four eyes with resolution had no recurrences (after a mean of 16-month follow-up) despite a mean duration of treatment of only 1.75 months (rifampicin was discontinued when the CSCR resolved). Drug-induced hepatotoxicity has been reported following treatment with rifampicin in CSCR.[10] No serious adverse events were noted in our series that required discontinuation of treatment. One of the major concerns with the use of rifampicin in chronic CSCR is the development of drug resistance. TB is an endemic condition in India and rifampicin is commonly used in treatment regime for TB. Also, one of the secondary causes for CSCR is TB.[11] Thus, oral rifampicin has therapeutic benefits and lowers the risk of drug resistance. In our series, oral rifampicin was started only after excluding TB and was given for a maximum period of 3 months. We also noted resolution of SRF in four eyes where the mean duration of treatment was only 1.75 months. Thus, ensuring the use of the drug for a limited duration would not affect the chance of increasing drug resistance.

The limitations of our study are small patient numbers, lack of a control group, and use of Snellen rather than Early Treatment Diabetic Retinopathy Study (ETDRS) charts which may have provided a more uniform testing environment for visual acuity. Further randomized studies with a larger number of patients and controls will further elucidate the role of rifampicin for treatment in chronic CSCR in the developing world. However, the study has the strength of identifying the morphological changes with objective testing including FA and OCT. This allowed identification of two distinct groups based on fluorescein angiographic pattern of leakage (hotspots *versus* diffuse staining). Those with hotspots responded well to treatment with rifampicin, while those with diffuse staining indicative of DRPE (diffuse RPE epitheliopathy) did not benefit from this treatment (Figures 1–3).

Conclusion

This study found oral rifampicin to be an effective and affordable therapy for eyes with chronic CSCR. In eyes with extensive RPE damage, rifampicin is not very effective in causing resorption of SRF and improvement in vision. Alternative treatment options like PDT or observation should be considered in such scenarios.

Acknowledgements

R.V. was responsible in drafting and analyzing the scientific content of the manuscript. M.A. was responsible for reviewing the manuscript. M.K. was responsible for data acquisition. The manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work.

Conflict of interest statement

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Ramesh Venkatesh https://orcid.org/0000-0002-4479-9390

References

1. Shin JY, Woo SJ, Yu HG, *et al.* Comparison of efficacy and safety between half-fluence and full-fluence photodynamic therapy for chronic central serous chorioretinopathy. *Retina* 2011; 31: 119–126.
2. Ma J, Meng N, Xu X, *et al.* System review and meta-analysis on photodynamic therapy in central serous chorioretinopathy. *Acta Ophthalmol* 2014; 92: e594–e601.
3. Steinle NC, Gupta N, Yuan A, *et al.* Oral rifampin utilisation for the treatment of chronic multifocal central serous retinopathy. *Br J Ophthalmol* 2012; 96: 10–13.
4. Ravage ZB, Packo KH, Creticos CM, *et al.* Chronic central serous chorioretinopathy responsive to rifampin. *Retina Cases Brief Rep* 2012; 6: 129–132.
5. Lim SJ, Roh MI and Kwon OW. Intravitreal bevacizumab injection for central serous chorioretinopathy. *Retina* 2010; 30: 100–106.
6. Baran NV, Gurlu VP and Esgin H. Long-term macular function in eyes with central serous chorioretinopathy. *Clin Experiment Ophthalmol* 2005; 33: 369–372.
7. Chan WM, Lai TY, Lai RY, *et al.* Half-dose verteporfin photodynamic therapy for acute central serous chorioretinopathy: one-year results of a randomized controlled trial. *Ophthalmology* 2008; 115: 1756–1765.
8. Garg SP, Dada T, Talwar D, *et al.* Endogenous cortisol profile in patients with central serous chorioretinopathy. *Br J Ophthalmol* 1997; 81: 962–964.
9. Shulman S, Goldenberg D, Schwartz R, *et al.* Oral rifampin treatment for longstanding chronic central serous chorioretinopathy. *Graefes Arch Clin Exp Ophthalmol* 2016; 254: 115–122.
10. Nelson J, Saggau DD and Nielsen JS. Rifampin induced hepatotoxicity during treatment for chronic central serous chorioretinopathy. *Retina Cases Brief Rep* 2014; 8: 70–72.
11. Khan P, Khan L, Anjum N, *et al.* Central serous chorioretinopathy secondary to tuberculosis: cause or coincidence. *BMJ Case Rep*. Epub ahead of print 12 May 2017. DOI: 10.1136/bcr-2016-216471.