Published in final edited form as:

Retina. 2011 April ; 31(4): 766–771. doi:10.1097/IAE.0b013e3181f04a35.

Finasteride for Chronic Central Serous Chorioretinopathy

Farzin Forooghian, MD, Annal D. Meleth, MD, MS, Catherine Cukras, MD, PhD, Emily Y. Chew, MD, Wai T. Wong, MD, PhD, and Catherine B. Meyerle, MD

Division of Epidemiology and Clinical Research, National Eye Institute, National Institutes of Health, Bethesda, MD, USA

Abstract

Purpose—To evaluate the safety and efficacy of finasteride, an inhibitor of dihydroxytestosterone (DHT) synthesis, in the treatment of chronic central serous chorioretinopathy (CSC).

Methods—Five patients with chronic CSC were prospectively enrolled in this pilot study. Patients were administered finasteride (5mg) daily for 3 months, following which study medication was withheld and patients were observed for 3 months. Main outcome measures included best-corrected visual acuity (BCVA), center-subfield macular thickness and subretinal fluid volume as assessed by optical coherence tomography (OCT). Serum DHT, serum testosterone, and urinary cortisol were also measured.

Results—There was no change in mean BCVA. Mean center-subfield macular thickness and subretinal fluid volume reached a nadir at 3 months, and rose to levels that were below baseline by 6 months. The changes in both OCT parameters paralleled changes in serum DHT level. In four patients, center-subfield macular thickness and/or subretinal fluid volume increased following discontinuation of finasteride. In the remaining patient, both OCT parameters normalized with finasteride and remained stable when the study medication was discontinued.

Conclusion—Finasteride may represent a novel medical treatment for chronic CSC. Larger controlled clinical trials are needed to further assess the efficacy of finasteride for the treatment of CSC.

Summary—Pilot study to evaluate finasteride for treatment of chronic central serous chorioretinopathy suggests efficacy and tolerability.

Keywords

Finasteride; Chronic Central Serous Chorioretinopathy; Retina; Optical Coherence Tomography

INTRODUCTION

Central serous chorioretinopathy (CSC) is an acquired chorioretinal disease characterized by the presence of exudative detachment of the neurosensory retina and/or retinal pigment epithelium (RPE). The pathophysiology is poorly understood, but alterations in choroidal circulation and RPE function have been hypothesized to play a role. Indocyanine green (ICG) angiography and enhanced depth imaging spectral-domain optical coherence tomography (OCT) have provided evidence suggesting hyperpermeability and increased hydrostatic pressure within the choroidal circulation^{1–4}. Fundus autofluorescence (FAF) imaging has shown decreased autofluorescence in cases of chronic CSC, suggesting reduced metabolic activity of the RPE⁵. While acute CSC can sometimes be recurrent, it generally

resolves spontaneously with minimal sequelae. Chronic CSC, however, can result in significant visual loss⁶. Some patients may develop diffuse retinal pigment epitheliopathy, which is characterized by widespread RPE damage and destruction⁷. Chronic CSC can be challenging to treat; however, recent studies have demonstrated safety and efficacy using photodynamic therapy (PDT) at reduced-fluence or reduced-dosage^{8, 9}. Despite the improved safety of reduced-fluence PDT, complications such as tears of the RPE have been described¹⁰ and concerns over the potential for RPE atrophy with repeated treatments persist.

Based on the proposed role of glucocorticoids in the pathogenesis of CSC, inhibition of cortisol has been proposed as a medical treatment option¹¹. In one small study of chronic CSC, ketoconazole (a glucocorticoid antagonist) reduced urinary cortisol levels and resulted in a decrease in lesion height as measured by OCT¹². Another short-term study using a lower dose of ketoconazole for acute CSC did not show a statistically significant better outcome when compared to a control group¹³. Mifepristone, a glucocorticoid antagonist, showed some improvement in one case report^{14, 15}. In addition to glucocorticoids, androgens (testosterone) have been implicated in the pathophysiology of CSC^{16, 17}. Dihydrotestosterone (DHT) is an androgen similar to testosterone but with greater affinity for the androgen receptor¹⁸. Finasteride acts by inhibiting 5 α -reductase, the enzyme that converts testosterone to DHT. Finasteride is currently used in the treatment of benign prostatic hyperplasia, prostate cancer, androgenetic alopecia, and hirsutism^{19–21}. When compared to other medical treatments that have been used in the treatment of chronic CSC, finasteride is cost-effective and has a favorable side-effect profile. These findings, along with evidence suggesting that androgens may play a role in CSC, make finasteride a logical choice for a treatment trial.

METHODS

This was a single-center, prospective, uncontrolled, unmasked, phase I/II clinical trial of five patients designed to assess the potential safety and efficacy of finasteride as a novel medical treatment for chronic CSC. Eligibility criteria included patients with chronic CSC, which was defined in this study as: 1) the presence of subretinal fluid, as determined by spectral-domain OCT, **AND** 2) the subretinal fluid must have been present for at least 3 months, or there was a recurrence of subretinal fluid within the past 3 months, **AND** 3) the presence of characteristic fluorescein angiographic or autofluorescence features of CSC, such as one or more pinpoint leaks and/or diffuse RPE disease. Patients taking exogenous corticosteroids (oral, topical, or inhaled) were excluded, as were patients who had evidence of choroidal neovascularization or any other ocular disease that could confound the study. If both eyes qualified for the study, then both were allowed to be enrolled. Due to the teratogenic nature of finasteride on the male fetus, women who were pregnant or breastfeeding were excluded. Women who were of childbearing potential were allowed to enroll as long as two methods of birth control were used.

The duration of the study was 6 months, and study outcomes were assessed on a monthly basis. Main outcomes included best-corrected visual acuity (BCVA) using ETDRS charts, as well as center-subfield thickness and subretinal volume as assessed by spectral-domain OCT (CirrusTM HD-OCT, Carl Zeiss Meditec, CA, USA). Area of leakage seen on fluorescein angiography (FA), autofluorescence pattern documented on FAF imaging (TopconTM, Paramus, NJ, USA, and HeidelbergTM HRA2, Heidelberg Engineering, Heidelberg, Germany), serum testosterone, serum DHT, and 24 hour urinary cortisol were also assessed. Active questioning for adverse effects (impotence, loss of libido, gynecomastia) was performed at every visit. During the first three months, finasteride (5mg oral) was administered daily. A pill diary was used to document compliance with study medications.

Following the initial 3 month treatment period, study medication was withheld for the next 3 months and participants were observed. If BCVA, center-subfield thickness, or subretinal volume returned to baseline, then finasteride was allowed to be resumed. Subretinal fluid volume was determined by manually moving the segmentation lines of the OCT image using the “Edit Segmentation” function of the Cirrus™ HD-OCT software. The segmentation lines were edited to outline the inner and outer borders of the subretinal fluid pocket. This was manually done for all the individual B-scans of each OCT image, after which the software algorithm automatically calculated the subretinal fluid volume. In cases where a pigment epithelial detachment (PED) was present, the volume of the PED was included in the calculation of subretinal fluid volume. Center-subfield thickness was obtained from the standard output provided by the OCT software. The study was performed with informed patient consent and conducted under a protocol approved by the local institutional review board (IRB), and in accordance with the ethical standards stated in the 1964 Declaration of Helsinki. This clinical trial was registered on www.clinicaltrials.gov.

Although our results are primarily descriptive due to the small nature of the pilot study, the Kruskal-Wallis nonparametric test with Dunn’s post-test was employed in order to compare the baseline, 3-month, and 6-month study outcomes. Statistical testing was two-tailed, with statistical significance set at 5%, and was performed using GraphPad Prism software (version 4, GraphPad, La Jolla, CA, USA).

RESULTS

A total of five eyes of five patients were enrolled, with a mean age of 50 (range 37–62). All patients were male, and were followed up for the entire duration of the study. Only one patient had a PED. Study outcomes are summarized in Table 1. BCVA remained stable during the study, without any appreciable improvement or worsening. Center-subfield macular thickness and subretinal fluid volume declined to a nadir at 3 months and then rose slightly by 6 months. However, these parameters were all still lower at 6 months compared to baseline levels. The changes in center-subfield macular thickness and subretinal fluid volume paralleled serum DHT concentrations (Figure 1). Serum testosterone and urinary cortisol levels rose slightly at 3 months, but returned to approximately baseline levels by 6 months. With respect to visual acuity and OCT outcomes, the differences we saw were not statistically significant. However, the difference in subretinal fluid volume between baseline, 3 months, and 6 months approached statistical significance ($p = 0.08$). With respect to serum and urine parameters, serum DHT levels were significantly lower at 3 months compared to baseline ($p < 0.01$).

Following discontinuation of finasteride, re-accumulation of subretinal fluid was seen in four patients. Three patients had to be re-challenged with finasteride because subretinal fluid volume returned to baseline after discontinuation of the drug. Following reinstitution of finasteride, subretinal fluid volume decreased again in these patients. The fourth patient, whose fluid had almost completely resolved by month-3 while on finasteride, did not qualify for re-challenging because his fluid level, although worsened after stopping finasteride, had not returned to baseline by the time of the final study visit (Figure 2). One patient had complete resolution of subretinal fluid with decreased leakage on FA after two months of treatment, with no re-accumulation following discontinuation of finasteride (Figure 3).

Leakage on FA was decreased in three patients, and unchanged in the other two patients. With respect to changes in FAF pattern, three patients appeared to have a relative decrease in the amount of hyperautofluorescence, one patient had an increase in hyperautofluorescence, while another had an initial increase followed by a decrease. One patient experienced a worsening of previous libido loss while taking finasteride and another

reported some libido loss as well; but these symptoms returned to baseline in both patients when the drug was discontinued.

DISCUSSION

The goal of this pilot study was to observe trends and patterns that would warrant further study in a larger trial. Given the small sample size, achieving statistically significant results was not expected. We observed that the changes in center-subfield OCT thickness and OCT-derived subretinal fluid volume changed in parallel to serum DHT levels. All three parameters declined to a nadir at 3 months, and then rose slightly to a level that was still below baseline at 6 months. Furthermore, four patients worsened following discontinuation of finasteride. Finasteride was re-instituted in three of these patients, all of whom experienced a reduction in subretinal fluid volume with re-challenge. One patient experienced complete resolution of subretinal fluid volume by 2 months and remained fluid-free after discontinuation of finasteride throughout the study period of 6 months. These results suggest that finasteride may be efficacious in reducing subretinal fluid in chronic CSC.

Our study also supports the hypothesis that androgens, in particular DHT, may be involved in the pathophysiology of CSC. Although the pathogenesis of CSC is not known, choroidal hyperpermeability and/or defective RPE fluid transport may be involved. Choroidal hyperpermeability could lead to exudation of fluid into the subretinal space, while a defective RPE pump mechanism would result in an inability to remove the accumulating fluid. The putative role of DHT in the pathogenesis of CSC may be inferred from the known role of androgens in mediating blood flow and epithelial ion transport. Androgen receptors have been identified in mammalian choroid²². In animal models, DHT has been shown to increase blood flow in the prostate by upregulating expression of vascular endothelial growth factor (VEGF), an effect that was abolished with the administration of anti-VEGF antibodies²³. Interestingly, anti-VEGF antibodies have shown some benefit in treating patients with chronic CSC^{24, 25}. The precise role (if any) of DHT in regulating choroidal blood flow remains to be determined, but if its function in the choroid is similar to that in the prostate, then inhibition of its production using finasteride would conceivably help reduce choroidal blood flow and decrease exudation into the subretinal space. Human and *in vitro* work has shown that glucocorticoids have an inhibitory effect on the electric potential of RPE cells, which supports the hypothesis of a defective RPE pump mechanism in CSC²⁶. The enzyme inhibited by finasteride, 5 α -reductase, is expressed in human RPE cells²⁷. Analogous to the effect of glucocorticoids on RPE cells, DHT inhibits the electric potential in epididymal epithelium²⁸. The effects of DHT on the RPE pump (if any) are not known, but if DHT is indeed produced by 5 α -reductase in RPE cells and has a deleterious effect on the RPE pump, then its inhibition may help improve subretinal fluid resorption by RPE cells.

Ketoconazole and mifepristone have been proposed as novel treatments for chronic CSC based on their anti-cortisol effects^{12, 14, 15}. However, ketoconazole also lowers serum DHT levels²⁹. Hence, the potential beneficial effect of ketoconazole in chronic CSC could be attributed, at least in part, to its effect on serum DHT levels. Finasteride has an improved side effect profile and fewer drug interactions compared to ketoconazole³⁰. Thus, finasteride may be a safer alternative to ketoconazole for the medical treatment of CSC. The relatively cheaper cost of finasteride also makes it a more economically viable treatment option than mifepristone. The improved safety and cheaper cost of finasteride over other medical therapies warrant further investigation of this drug for treating patients with chronic CSC. Our study was a pilot study, and was thus limited by sample size in its ability to demonstrate statistically significant results. We are unable to exclude the possibility of our findings being

the result of chance alone. Larger controlled studies will be required to fully determine the efficacy of finasteride for chronic CSC.

Acknowledgments

National Eye Institute (NEI) intramural research program.

References

1. Imamura Y, Fujiwara T, Margolis R, et al. Enhanced depth imaging optical coherence tomography of the choroid in central serous chorioretinopathy. *Retina*. 2009; 29:1469–73. [PubMed: 19898183]
2. Iida T, Kishi S, Hagimura N, et al. Persistent and bilateral choroidal vascular abnormalities in central serous chorioretinopathy. *Retina*. 1999; 19:508–12. [PubMed: 10606450]
3. Prunte C, Flammer J. Choroidal capillary and venous congestion in central serous chorioretinopathy. *Am J Ophthalmol*. 1996; 121:26–34. [PubMed: 8554078]
4. Giovannini A, Scassellati-Sforzolini B, D'Altobrando E, et al. Choroidal findings in the course of idiopathic serous pigment epithelium detachment detected by indocyanine green videoangiography. *Retina*. 1997; 17:286–93. [PubMed: 9279943]
5. von Ruckmann A, Fitzke FW, Fan J, et al. Abnormalities of fundus autofluorescence in central serous retinopathy. *Am J Ophthalmol*. 2002; 133:780–6. [PubMed: 12036669]
6. Spaide RF, Campeas L, Haas A, et al. Central serous chorioretinopathy in younger and older adults. *Ophthalmology*. 1996; 103:2070–9. discussion 9–80. [PubMed: 9003341]
7. Castro-Correia J, Coutinho MF, Rosas V, et al. Long-term follow-up of central serous retinopathy in 150 patients. *Doc Ophthalmol*. 1992; 81:379–86. [PubMed: 1486812]
8. Reibaldi M, Cardascia N, Longo A, et al. Standard-fluence versus low-fluence photodynamic therapy in chronic central serous chorioretinopathy: a nonrandomized clinical trial. *Am J Ophthalmol*. 149:307–15. e2. [PubMed: 19896635]
9. Reibaldi M, Boscia F, Avitabile T, et al. Low-fluence photodynamic therapy in longstanding chronic central serous chorioretinopathy with foveal and gravitational atrophy. *Eur J Ophthalmol*. 2009; 19:154–8. [PubMed: 19123167]
10. Kim SW, Oh J, Oh IK, et al. Retinal pigment epithelial tear after half fluence PDT for serous pigment epithelial detachment in central serous chorioretinopathy. *Ophthalmic Surg Lasers Imaging*. 2009; 40:300–3. [PubMed: 19485297]
11. Jampol LM, Weinreb R, Yannuzzi L. Involvement of corticosteroids and catecholamines in the pathogenesis of central serous chorioretinopathy: a rationale for new treatment strategies. *Ophthalmology*. 2002; 109:1765–6. [PubMed: 12359592]
12. Meyerle CB, Freund KB, Bhatnagar P, et al. Ketoconazole in the treatment of chronic idiopathic central serous chorioretinopathy. *Retina*. 2007; 27:943–6. [PubMed: 17891021]
13. Golshahi A, Klingmuller D, Holz FG, et al. Ketoconazole in the treatment of central serous chorioretinopathy: a pilot study. *Acta Ophthalmol*. 2009
14. Nielsen JS, Weinreb RN, Yannuzzi L, et al. Mifepristone treatment of chronic central serous chorioretinopathy. *Retina*. 2007; 27:119–22. [PubMed: 17218929]
15. Nielsen JS, Bachhawat A, Jampol LM. A case of chronic severe central serous chorioretinopathy responding to oral mifepristone: update. *Retina*. 2008; 28:1363. [PubMed: 19430395]
16. Ahad MA, Chua CN, Evans NM. Central serous chorioretinopathy associated with testosterone therapy. *Eye*. 2006; 20:503–5. [PubMed: 15846380]
17. Grieshaber MC, Staub JJ, Flammer J. The potential role of testosterone in central serous chorioretinopathy. *Br J Ophthalmol*. 2007; 91:118–9. [PubMed: 17179128]
18. Grino PB, Griffin JE, Wilson JD. Testosterone at high concentrations interacts with the human androgen receptor similarly to dihydrotestosterone. *Endocrinology*. 1990; 126:1165–72. [PubMed: 2298157]
19. Townsend KA, Marlowe KF. Relative safety and efficacy of finasteride for treatment of hirsutism. *Ann Pharmacother*. 2004; 38:1070–3. [PubMed: 15100391]

20. Goetzl MA, Holzbeierlein JM. Finasteride as a chemopreventive agent in prostate cancer: impact of the PCPT on urologic practice. *Nat Clin Pract Urol.* 2006; 3:422–9. [PubMed: 16902518]
21. Kaufman KD, Rotonda J, Shah AK, et al. Long-term treatment with finasteride 1 mg decreases the likelihood of developing further visible hair loss in men with androgenetic alopecia (male pattern hair loss). *Eur J Dermatol.* 2008; 18:400–6. [PubMed: 18573712]
22. Wickham LA, Gao J, Toda I, et al. Identification of androgen, estrogen and progesterone receptor mRNAs in the eye. *Acta Ophthalmol Scand.* 2000; 78:146–53. [PubMed: 10794246]
23. Shibata Y, Kashiwagi B, Arai S, et al. Direct regulation of prostate blood flow by vascular endothelial growth factor and its participation in the androgenic regulation of prostate blood flow in vivo. *Endocrinology.* 2004; 145:4507–12. [PubMed: 15231711]
24. Schaal KB, Hoeh AE, Scheuerle A, et al. Intravitreal bevacizumab for treatment of chronic central serous chorioretinopathy. *Eur J Ophthalmol.* 2009; 19:613–7. [PubMed: 19551677]
25. Huang WC, Chen WL, Tsai YY, et al. Intravitreal bevacizumab for treatment of chronic central serous chorioretinopathy. *Eye (Lond).* 2009; 23:488–9. [PubMed: 18344956]
26. Arndt C, Sari A, Ferre M, et al. Electrophysiological effects of corticosteroids on the retinal pigment epithelium. *Invest Ophthalmol Vis Sci.* 2001; 42:472–5. [PubMed: 11157885]
27. Rocha EM, Wickham LA, da Silveira LA, et al. Identification of androgen receptor protein and 5 α -reductase mRNA in human ocular tissues. *Br J Ophthalmol.* 2000; 84:76–84. [PubMed: 10611104]
28. Leung GP, Cheng-Chew SB, Wong PY. Nongenomic effect of testosterone on chloride secretion in cultured rat efferent duct epithelia. *Am J Physiol Cell Physiol.* 2001; 280:C1160–7. [PubMed: 11287329]
29. Medda F, Puligheddu P, Parodo G, et al. Short term treatment with ketoconazole: effects on gonadal and adrenal steroidogenesis in women. *Clin Exp Obstet Gynecol.* 1987; 14:161–6. [PubMed: 2970350]
30. Venturoli S, Marescalchi O, Colombo FM, et al. A prospective randomized trial comparing low dose flutamide, finasteride, ketoconazole, and cyproterone acetate-estrogen regimens in the treatment of hirsutism. *J Clin Endocrinol Metab.* 1999; 84:1304–10. [PubMed: 10199771]

Figure 1.

Alterations in optical coherence tomography-derived center-subfield thickness and subretinal fluid volume in relationship to serum dihydroxytestosterone (DHT). Mean center-subfield macular thickness (first panel), mean subretinal fluid volume (second panel), and mean serum DHT (third panel) declined to a nadir at 3 months, and then rose slightly by 6 months. The changes in center-subfield macular thickness and subretinal fluid volume paralleled serum DHT concentrations.

Figure 2.

Treatment response to finasteride in a 54 year old patient with subretinal fluid persisting for 24 months prior to study enrollment. In this patient with subretinal fluid under the fovea at baseline with a subretinal fluid volume of 0.70 μl (top panel), near complete resolution of subretinal fluid to a subretinal fluid volume of 0.10 μl was seen after 3 months of treatment with finasteride (middle panel). The subretinal fluid re-accumulated once finasteride was discontinued; however, at 3 months following discontinuation of study drug the subretinal fluid volume was still below baseline at a subretinal fluid volume of 0.30 μl (bottom panel).

Figure 3.

Resolution of subretinal fluid and angiographic leakage following treatment with finasteride in a 37 year old patient with subretinal fluid persisting for 1 year prior to study enrollment. In this patient with subretinal fluid tracking inferior to the fovea (subretinal fluid volume of 2.00 μ l) and fluorescein angiographic leakage nasal to the fovea at baseline (first column), complete resolution of subretinal fluid and leakage was seen after 2 months of treatment with finasteride (second column). This effect was maintained during the study period after the drug was discontinued from month-3 through month-6 (third column).

Table 1

Main Study Outcome Measures at Baseline, 3 Months, and 6 Months

Outcome	Baseline (Mean $\pm$ SD)	Change from Baseline at 3 Months (Mean $\pm$ SD)	Change from Baseline at 6 Months (Mean $\pm$ SD)
Best-Corrected Visual Acuity (ETDRS letters)	70 ($\pm$ 12)	0 ($\pm$ 22)	-3 ($\pm$ 23)
Center-Subfield Thickness (μ m)	376 ($\pm$ 62)	-86 ($\pm$ 105)	-69 ($\pm$ 103)
Subretinal Fluid Volume (μ l)	0.79 ($\pm$ 0.69)	-0.58 ($\pm$ 0.71)	-0.53 ($\pm$ 0.72)
Serum DHT (pg/ml)	333 ($\pm$ 113)	-246 ($\pm$ 116)	-296 ($\pm$ 87) [*]
			-4 ($\pm$ 4) [†]
Serum Testosterone (ng/dl)	7.8 ($\pm$ 3.2)	+0.38 ($\pm$ 3.63)	-0.4 ($\pm$ 3.38)
Urine Cortisol (24 hour) (μ g/24h)	27 ($\pm$ 14)	+3 ($\pm$ 24)	-2 ($\pm$ 18)

SD = standard deviation

^{*} Mean change in serum DHT for the 3 participants who were re-challenged with finasteride after month-3.[†] Mean change in serum DHT for the 2 participants who did not resume finasteride after month-3.