

# Treatment of central serous chorioretinopathy (CSC) using diclofenac through different routes of administration, a comparative study

## Abstract

**Purpose:** To evaluate the effect of diclofenac nonsteroidal anti-inflammatory drug (NSAID) in the treatment of acute central serous chorioretinopathy (CSC) by different routes of administration and compare the results with control patients.

**Introduction:** Central serous chorioretinopathy (CSC) is an idiopathic disorder characterized by a serous detachment of the neurosensory retina at the macula, which is caused by active retinal pigment epithelial (RPE) leakage. Although the exact pathophysiology of CSC has not been clearly elucidated, the primary abnormality leading to RPE disruption and leakage is thought to be increased choroidal permeability. Studies using different imaging techniques have revealed the possible causes of abnormal permeability of the inner choroid. Ischemia and inflammation might lead to exudative changes within the choroid and the subsequent changes at the RPE. Topical diclofenac, ketorolac, nepafenac and bromfenac all belong to the NSAIDs class of medications. As an anti-inflammatory class, they function by inhibiting the enzyme cyclooxygenase, which blocks the synthesis of prostaglandins. A reduction in prostaglandin formation results a decrease in inflammation. It appears that the principle pathway involved in pain and inflammation is the COX-2 pathway where nonsteroidal anti-inflammatory drugs (NSAIDs) seems to play a significant role.

**Material and method:** All 57 patients in this study were diagnosed as having acute CSC relying upon visual acuity by standard Snellen chart, dilated fundus exam using slit lamp with 90D lens and OCT (ocular coherence tomography) findings. All patients were treated by diclofenac topical, oral or combination of topical and oral routes except those who were kept as control. Patients were followed on the 5<sup>th</sup> day, 10<sup>th</sup> day and 30<sup>th</sup> day after onset. Vision was recorded; dilated funduscopy and OCT were done on each visit. All 57 patients were male, divided into 3 age groups i.e group A (21-30yrs) includes 29(50.87%) patients, group B (31-40 yrs) includes 21(36.84%) patients and group C (41-50 yrs) included 7(12.28%) patients. 32(56.14%) were right eyes, 22(38.59%) were left and 3(5.26%) were bilateral. Vision recorded using standard Snellen chart, 32(56.14%) patients having vision 0.4, 17(29.82%) were 0.2, 6(10.52%) were having 0.1 while 2(3.50%) were recorded as CF at 1 meter. Macular thickness was recorded using OCT, patients were again divided into 3 groups on OCT findings, group 1, 30(52.63%) patients having macular thickness between 422-485 microns, group 2, 20(35.08%) patients between 535-565 microns while group 3, include 7(12.28%) patients having thickness between 612-640 microns. Out of these 57 patients 42 underwent intervention to treat acute CSC using diclofenac, nonsteroidal anti-inflammatory drug (NSAID) while 15 were kept as control without treatment. Out of these 42 patients, 13 (30.95%) were treated by oral diclofenac sodium 50mg tablets 12 hourly for 10 days, another 13(30.95%) were kept on topical diclofenac sodium 0.1% eye

## Introduction

Central serous chorioretinopathy (CSC) is an idiopathic disorder characterized by a serous detachment of the neurosensory retina at the macula,<sup>1</sup> which is caused by active retinal pigment epithelial (RPE) leakage.<sup>2,3</sup> The disease has a favorable natural course with the spontaneous resolution of the neurosensorial detachment in association with improvement of visual function. However, it is very difficult to

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Nisar Ahmed Khan,<sup>1</sup> Aftab Ahmed Khan,<sup>1</sup> Aisha Khan,<sup>2</sup> Atiqa Khan,<sup>2</sup> Jawaid Iqbal Memon,<sup>1</sup> Moin Shaikh<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Indus Medical College hospital, Mohammad Al-Dossary Hospital, Saudi Arabia

<sup>2</sup>Isra University Hospital Pakistan, Pakistan

**Correspondence:** Nisar Ahmed Khan, Assistant professor/ Consultant Ophthalmologist, Indus Medical College hospital Tando Mohammad Khan, Pakistan, Mohammad Al Dossary Hospital Khobar, Saudi Arabia, Tel +92-300-3014168/+966-548054283, Email nisargh2001@yahoo.com

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drops twice daily for 10 days, remaining 16(38.09%) were treated by combine oral as well as topical therapy for 10 days. All patients were observed for 30 days.

**Results:** Macular thickness in patients treated with oral diclofenac reduced from 622 microns to 465 microns on 5<sup>th</sup> day, down to 356 microns on 10<sup>th</sup> day and become 271 microns on 30<sup>th</sup> day. Visual acuity improved from 0.2 at onset to 0.4 on 5<sup>th</sup> day, 0.5 on 10<sup>th</sup> day while it becomes 0.8 on 30<sup>th</sup> day. In patients who were treated with topical diclofenac the macular thickness improved from 524 microns to 413 microns on 5<sup>th</sup> day, 362 microns on 10<sup>th</sup> day while 283 microns on 30<sup>th</sup> day. Visual acuity improved from 0.3 at onset to 0.4 on 5<sup>th</sup> day, 0.5 on 10<sup>th</sup> day and becomes 0.6 on 30<sup>th</sup> day. In patients who were treated with combination of oral and topical therapy with diclofenac, macular thickness improved from 636 microns to 574 microns on 5<sup>th</sup> day, 322 microns on 10<sup>th</sup> day and reduced to 214 microns on 30<sup>th</sup> day. Visual acuity improved from 0.2 at onset to 0.5 on 5<sup>th</sup> day, 0.6 on 10<sup>th</sup> day and remains 0.6 on 30<sup>th</sup> day. In patients who were kept as control (without treatment) the macular thickness improved from 636 microns to 467 microns on 5<sup>th</sup> day, 363 microns on 10<sup>th</sup> day and 252 on 30<sup>th</sup> day. Visual acuity improved from 0.2 on onset to 0.3 on 5<sup>th</sup> day, 0.4 on 10<sup>th</sup> day and was 0.5 on 30<sup>th</sup> day.

**Conclusion:** This treatment modality is non invasive, in affordable price and easily available all over the world. Patients with CSC, particularly leaving in remote rural areas where all new modalities are not available can be benefitted for this conclusion.

**Keywords:** khan NA, khan AA, khan A, khan A, memon ji, shaikh M, treatment, central serous chorioretinopathy(csc), diclofenac, indus medical college hospital/mohammad al-dossary hospital

predict the prognosis of CSC, and in some cases, progressive visual loss may be seen.<sup>4,5</sup> Although the exact pathophysiology of CSC has not been clearly elucidated, the primary abnormality leading to RPE disruption and leakage is thought to be increased choroidal permeability.<sup>6</sup> Studies using different imaging techniques have revealed the possible causes of abnormal permeability of the inner choroid. Ischemia and inflammation might lead to exudative changes within the choroid and the subsequent changes at the RPE.<sup>7,8</sup>

Topical diclofenac, ketorolac, nepafenac and bromfenac all belong to the non-steroidal anti-inflammatory drugs (NSAIDs) class of medications. As an anti-inflammatory class, they function by inhibiting the enzyme cyclooxygenase, which blocks the synthesis of prostaglandins. A reduction in prostaglandin formation results a decrease in inflammation. Inflammation functions to make the blood-retinal barrier more permeable. It appears that the principle pathway involved in pain and inflammation is the COX-2 pathway where non-steroidal anti-inflammatory drugs NSAIDs seems to play a significant role. The current uses for topical NSAIDs have been somewhat limited to the prevention of intraoperative miosis during phacoemulsification,<sup>9,10</sup> relief of postoperative pain, inflammation and photophobia.<sup>11</sup> therapy for ocular atopy,<sup>12</sup> and the reduction of post-cataract cystoid macular edema (CME).<sup>13</sup> Many cataract surgeons have used NSAIDs, such as diclofenac, preoperatively to block the formation of CME. For patients who develop a persistent postoperative CME, non-steroidal anti-inflammatory drugs NSAIDs have been dispensed to reduce postoperative edema and improve the patient's vision.

### Material and methods

It is a retrospective, interventional and comparative study conducted at Indus Medical College Hospital, Tando Mohammad Khan and Mohammad Al-Dossary Hospital from August 2014 to June 2016, includes 57 patients. Only patients with acute CSC included while those with chronic or recurrence were excluded. Careful history taken regarding peptic ulcer and sensitivity to diclofenac or any other non-steroidal anti-inflammatory drugs NSAIDs. All 57 patients were diagnosed as having acute CSC relying upon visual acuity by standard Snellen chart, dilated fundus exam using slit lamp with 90D lens and OCT (ocular coherence tomography) findings. All patients were treated by diclofenac topical, oral or combine topical and oral routes except those who were kept as control. Patients followed on 5<sup>th</sup> day, 10<sup>th</sup> day and 30<sup>th</sup> day after onset. Vision was recorded, dilated funduscopy and OCT performed on each visit.

All 57 patients were male (Table 1), divided into 3 age groups i.e group A(21-30yrs) includes 29(50.87%) patients, group B (31-40 yrs) includes 21(36.84%) patients and group C (41-50 yrs ) included 7(12.28%) patients (Table 2). 32(56.14%) were right eyes, 22(38.59%) were left and 3(5.26%) were bilateral (Table 3). Vision recorded using standard Snellen chart, 32(56.14%) patients having vision 0.4, 17(29.82%) were 0.2, 6 (10.52%) were having 0.1 while

2(3.50%) were recorded as CF at 1 meter (Table 4). Macular thickness recorded using OCT, patients again divided into 3 groups on OCT findings, group 1, 30(52.63%) patients having macular thickness between 422-485 microns, group 2, 20(35.08%) patients between 535-565 microns while group 3, include 7(12.28%) patients having thickness between 612-640 microns (Table 5). Out of these 57 patients 42 were underwent intervention to treat acute CSC using diclofenac non-steroidal anti-inflammatory drugs NSAID while 15 were kept as control without treatment. Out of these 42 patients, 13 (30.95%) were treated by oral diclofenac sodium 50mg tablets bid for 10 days, another 13(30.95%) were kept on topical diclofenac sodium 0.1% eye drops bid for 10 days, remaining 16(38.09%) were treated by combine oral as well as topical therapy for 10 days. (Table 6) all patients were observed for 30 days.

**Table 1** Male female ratio

Male	Female
57(100%)	Nil

**Table 2** Age at onset

Total patients	Group A 21-30 Yrs	Group B 31-40yrs	Group C 41-50 Yrs
57	29(50.87%)	21(36.84%)	7(12.28%)

**Table 3** Laterality

Total patients	Right eye	Left eye	Bilateral
57	32(56.14%)	22(38.59%)	3(5.26%)

**Table 4** Visual acuity at onset

Total patients	0.4	0.2	0.1	CF at 1meter
57	32(56.14%)	17(29.82%)	6(10.52%)	2(3.5%)

**Table 5** Macular thickness at onset.

Total patients	Group 1 30(52.63%)	Group 2 20(35.08%)	Group 3 7(12.28%)
57	422-485 Microns	535-565 Microns	612-640 Microns

**Table 6** Macular thickness in microns and visual acuity before and after intervention

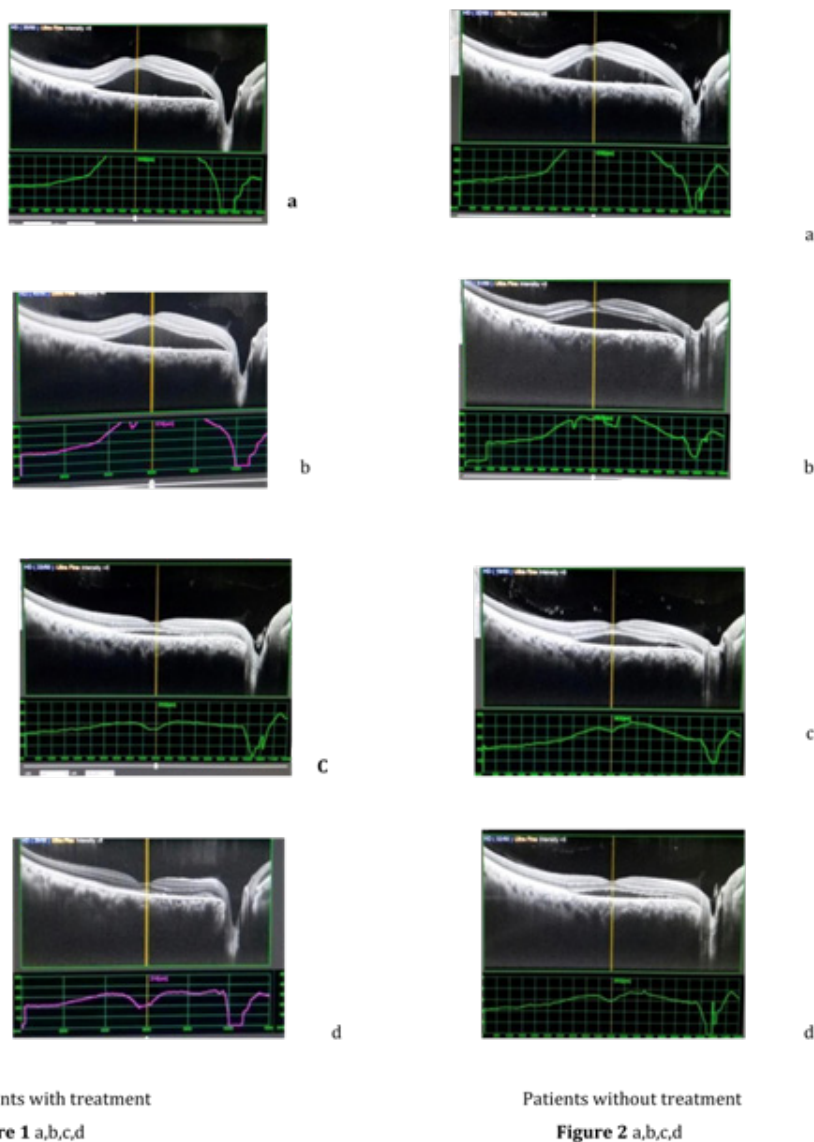
Days	With treatment (Intervention) 42(73.68%) patients			Without treatment (control) 15(26.31%) patients
	Oral diclofenac	Topical diclofenac	Combine oral and topical diclofenac	
	13(30.95%)	13(30.95%)	16(38.09%)	
	Patients	Patients	Patients	
Day 1	622	524	636	467
At Onset	With VA 0.2	With VA 0.3	With VA 0.2	With VA 0.2
Day 5	465	413	574	363
Day 10	With VA 0.4	With VA 0.4	With VA 0.5	With VA 0.3
	356	362	322	293
	With VA 0.5	With VA 0.5	With VA 0.6	With VA 0.4
Day 30	271	283	214	252
	With VA 0.6	With VA 0.6	With VA 0.6	With VA 0.5

## Results

This is an interventional, comparative study includes 57 patients who were diagnosed as acute CSC and followed from the day of onset to 30<sup>th</sup> day. Out of 57 patients 15(26.31%) were kept as control without any treatment while 42(73.68%) were underwent intervention. Out of these 42 patients 13(30.95%) patients were treated with oral diclofenac sodium 50 mg tablets bid for 10 days another 13(30.95%) patients who were treated with topical diclofenac sodium 0.1% eye drops bid for 10 days while remaining 16(38.09%) were treated with combine oral as well as topical therapy. All (except patients in control group) were followed with topical diclofenac drops bid for up to 30<sup>th</sup> days. Macular thickness and visual acuity recorded from the day of onset up to 30<sup>th</sup> day.

Table 6 shows all changes before and after treatment. Figures 1(a–d) shows early resolution of sub macular fluid as compared to control patients shown in Figure 2(a–d). Macular thickness in patients

treated with oral diclofenac was reduced from 622 microns to 465 microns on 5<sup>th</sup> day, up to 356 microns on 10<sup>th</sup> day and becomes 271 microns on 30<sup>th</sup> day. Visual acuity improved from 0.2 at onset to 0.4 on 5<sup>th</sup> day, 0.5 on 10<sup>th</sup> day while it becomes 0.6 on 30<sup>th</sup> day. In patients who were treated with topical diclofenac the macular thickness reduced from 524 microns to 413 microns on 5<sup>th</sup> day, 362 microns on 10<sup>th</sup> day while 283 microns on 30<sup>th</sup> day. Visual acuity improved from 0.3 at onset to 0.4 on 5<sup>th</sup> day, 0.5 on 10<sup>th</sup> day and was 0.6 on 30<sup>th</sup> day. In patients who were treated with a combination of oral and topical therapy with diclofenac, macular thickness reduced from 636 microns to 574 microns on 5<sup>th</sup> day, 322 microns on 10<sup>th</sup> day while 214 microns on 30<sup>th</sup> day. Visual acuity improved from 0.2 at onset to 0.5 on 5<sup>th</sup> day, 0.6 on 10<sup>th</sup> day and remains 0.6 on 30<sup>th</sup> day. In patients who were kept as control (without treatment) the macular thickness improved from 636 microns to 467 microns on 5<sup>th</sup> day, 363 microns on 10<sup>th</sup> day and 252 on 30<sup>th</sup> day. Visual acuity improved from 0.2 at onset to 0.3 on 5<sup>th</sup> day, 0.4 on 10<sup>th</sup> day and was 0.5 on 30<sup>th</sup> day.



**Figure 1** a (at onset),b (on 5th day), c(on 10th day), d(on 30th day) shows early resolution of sub- macular fluid in patients with treatment as compare to those patients who were without treatment as shown in Figure.

**Figure 2** a (at onset), b(on 5th day), c(on 10th day), d(on 30th day).

## Discussion

Central serous chorioretinopathy can lead to visual loss because of the accumulation of fluid in retinal layers for longer time that may lead to foveal attenuation, cystoid macular degeneration, and damage of the foveal photoreceptor layer.<sup>14-16</sup> Some therapeutic intervention may be helpful to resorb this fluid quickly and avoid dyschromatopsia and metamorphopsia along with other visual problems. Variety of treatment modalities like focal argon photocoagulation, PDT, anti-VEGF, topical non-steroidal anti-inflammatory drug (NSAID) are being used. In this study we only used diclofenac, one of the non-steroidal anti-inflammatory drug NSAIDs either oral or topical or combination of oral and topical therapy. We did not use any intravitreal injection, laser or PDT. We found that macular thickness reduced very early and vision returned to normal in those patients who received combine oral along with topical diclofenac.

Pradeep Venkatesh presented a contradictory opinion to what we found in this study.<sup>17</sup> It is his experience but lot of studies are there along with this study to prove the effect of non-steroidal anti-inflammatory drug (NSAIDs) in the treatment of CSC. Lucía Villarroel Salvatierra et al.<sup>18</sup> shows in their study that average macular thickness at center of the fovea prior to treatment was 431.55 microns, and post treatment macular average thickness was 198.77 microns though they treated CSR with intravitreal bevacizumab along with laser. We are having essentially the same outcomes but with diclofenac only as a combine oral along with topical therapy. Zeynep Alkin and coworkers used topical nepafenac 0.1%, and they have 82.3% results in resolution of macular sub retinal fluid at six months with the CFT decrease 349 microns to 257 at 1 month, 248 microns at 3 months and 221 at 6 months while in control group resolution was 42.8% with macular thickness reduced from 391 to 320 microns at 1 month 316 microns, at 3 months 301 microns and at six months 301 microns.<sup>19</sup> We got better results using diclofenac only and within 10 days though we followed these patients for 1 month.

Furthermore, no ocular or systemic side effects were observed in the treatment group during the follow-up period. Chan et al.<sup>20</sup> in their study, 63 patients treated with acute CSC using half-dose verteporfin PDT or placebo PDT in an attempt to demonstrate the safety of PDT. Subsequent to a follow-up time of 12 months, 94% of the eyes exhibited complete resolution of serous macular detachment in the half-dose PDT group versus only 57% of the eyes in the placebo group. Again, our results prove diclofenac combination therapy is more effective. While Ober et al Artunay O et al. and Lim JW et al.<sup>21-23</sup> showed in their studies that treatment of acute CSC with intravitreal injections of anti-VEGF agents has variable outcomes. But our results were excellent and consistent.

Pikkel et al.<sup>24</sup> demonstrated limited recovery in CSC patients with acetazolamide. In addition, its use is limited because of its potential side effects. It has been proposed that corticosteroid antagonists could be used for treatment of acute CSC such as mifepristone and ketoconazole. However, trials with these drugs have proven unsuccessful.<sup>25,26</sup> Metoprolol and propranolol, another treatment strategy with adrenergic receptor inhibitors, should be used very cautiously because of its significant side effects and potential morbidity.<sup>27</sup> So diclofenac is having better results without any side effects if care is taken for patients with peptic ulcer.

Former studies have suggested that choroidal ischemia and/or inflammation caused by nitric oxide, prostaglandins, and free radicals

might be involved in the pathogenesis of CSC.<sup>6-8</sup> Consequently, medications such as antioxidants or anti-inflammatories might be effective in decreasing the choroidal leakage especially in the early stages of CSC. Ratanasukon et al.<sup>28</sup> administered either high-dose antioxidant tablet or placebo tablets for 3 months or until complete resolution of sub retinal fluid. An additional treatment with laser or PDT was performed if any fluorescein leakage persisted following 3 months. They found no statistical difference in terms of VA and CFT between the groups at the end of the third month, but the patients treated with high-dose antioxidants revealed less fluorescein leakage. This somehow proves that diclofenac oral is having additive effect with topical therapy to get early rehabilitation of these patients suffering with CSC.

## Conclusion

Lots of studies carried out all over the world for the treatment of acute central serous chorioretinopathy using argon photocoagulation for leaking spot, PDT, anti-VEGF injections, topical anti-inflammatory (NSAIDs) etc, all are having their worth but our study is unique, we used only diclofenac oral along with topical drops and within 10 days, macular thickness as well as visual acuity came to almost at normal level. This treatment modality is non-invasive in affordable price and easily available all over the world. Patients with CSC, particularly leaving in remote rural areas where all new modalities are not available can be benefitted for this conclusion.

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## Conflicts of interest

Author declares that there is no conflict of interest.

## References

1. Jack J Kanski. *Clinical Ophthalmology: A Systemic approach*. 7th ed. 2011. p. 632.
2. Piccolino FC, Borgia L. Central serous chorioretinopathy and indocyanine green angiography. *Retina*. 1994;14(3):231-242.
3. Wang M, Munch IC, Hasler PW, et al. Central serous chorioretinopathy. *Acta Ophthalmol*. 2008;86(2):126-145.
4. Levine R, Brucker AJ, Robinson F. Long-term follow-up of idiopathic central serous chorioretinopathy by fluorescein angiography. *Ophthalmology*. 1989;96(6):854-859.
5. Loo RH, Scott IU, Flynn HW, et al. Factors associated with reduced visual acuity during long-term follow-up of patients with idiopathic central serous chorioretinopathy. *Retina*. 2002;22(1):19-24.
6. Guyer DR, Yannuzzi LA, Slakter JS, et al. Digital indocyanine green videoangiography of central serous chorioretinopathy. *Arch Ophthalmol*. 1994;112(8):1057-1062.
7. Prünte C, Flammer J. Choroidal capillary and venous congestion in central serous chorioretinopathy. *Am J Ophthalmol*. 1996;121(1):26-34.



8. Tittl MK, Spaide RF, Wong D, et al. Systemic findings associated with central serous chorioretinopathy. *Am J Ophthalmol.* 1999;128(1):63–68.
9. Ohara K, Ohbuto A, Miyamoto T, et al. Prevention of miosis during cataract surgery by topical bromfenac sodium. *Jpn J Clin Ophthalmol.* 2004;58:1325–1328.
10. Data on file. *ISTA Pharmaceuticals Xibrom US Phase III Trials.*
11. Seward MS, Cooke DL, Grillone LR, et al. *Topical Xibrom 0.09% Significantly Reduced Ocular Pain Following Cataract Surgery.* Presented at ARVO, Fort Lauderdale, Florida, USA, Poster B600. 2006.
12. Miyake K, Masuda K, Shirato S, et al. Comparison of diclofenac and fluorometholone in preventing cystoid macular edema after small incision cataract surgery: a multicentered prospective trial. *Jpn J Ophthalmol.* 2000;44:58–67.
13. Schainus R. Topical nonsteroidal anti-inflammatory therapy in Ophthalmology. *Ophthalmologica.* 2003;217(2):89–98.
14. Shukla D, Kolluru C, Vignesh TP, et al. Transpupillary thermotherapy for subfoveal leaks in central serous chorioretinopathy. *Eye (Lond).* 2006;22(1):100–106.
15. Iida T, Yannuzzi LA, Spaide RF, et al. Cystoid macular degeneration in chronic central serous chorioretinopathy. *Retina.* 2003;23(1):1–7.
16. Piccolino FC, de la Longrais RR, Ravera G, et al. The foveal photoreceptor layer and visual acuity loss in central serous chorioretinopathy. *Am J Ophthalmol.* 2005;139(1):87–99.
17. Pradeep Venkatesh. *Retinal Physician.* 2013;10:24–26.
18. Lucía Villarroel Salvatierra. Study of Best Corrected Visual Acuity and Macular Thickness After Bevacizumab or Bevacizumab with Laser in Acute Central Serous Chorioretinopathy. *EC Ophthalmology.* 2016;4(4):569–578.
19. Zeynep Alkin, Ozen Ayranci Osmanbasoglu, Abdullah Ozkaya, et al. Med Hypothesis Discov Innov Ophthalmol. *Winter.* 2013;2(4):96–101.
20. Chan WM, Lai TY, Lai RY, et al. Half-dose verteporfin photodynamic therapy for acute central serous chorioretinopathy. *Ophthalmology.* 2008;115(10):1756–1765.
21. Ober MD, Yannuzzi LA, Do DV, et al. Photodynamic therapy for focal retinal pigment epithelial leaks secondary to central serous chorioretinopathy. *Ophthalmology.* 2005;112(12):2088–2094.
22. Artunay O, Yuzbasioglu E, Rasier R, et al. Intravitreal bevacizumab in treatment of idiopathic persistent central serous chorioretinopathy: a prospective, controlled clinical study. *Curr Eye Res.* 2010;35(2):91–98.
23. Lim JW, Ryu SJ, Shin MC. The effect of intravitreal bevacizumab in patients with acute central serous chorioretinopathy. *Korean J Ophthalmol.* 2010;24(3):155–158.
24. Pikkell J, Beiran I, Ophir A, et al. Acetazolamide for central serous retinopathy. *Ophthalmology.* 2002;109(9):1723–1725.
25. Nielsen JS, Jampol LM. Oral mifepristone for chronic central serous chorioretinopathy. *Retina.* 2011;31(9):1928–1936.
26. Meyerle CB, Freund KB, Bhatnagar P, et al. Ketoconazole in the treatment of chronic idiopathic central serous chorioretinopathy. *Retina.* 2007;27(7):943–946.
27. Avci R, Deutman AF. Treatment of central serous choroidopathy with the beta receptor blocker metoprolol (preliminary results) *Klin Monbl Augenheilkd.* 1993;202(3):199–205.
28. Ratanasukon M, Bhurayanontachai P, Jirattanasopa P. High-dose antioxidants for central serous chorioretinopathy; the randomized placebo-controlled study. *BMC Ophthalmol.* 2012;20:20.