

Original Article**Effects of propranolol in patients with central serous chorioretinopathy***Farzan Kianersi\**, *Farnaz Fesharaki\*\****Abstract**

**BACKGROUND:** Central serous retinopathy (CSR) is a frequent disease often involves healthy men and causes visual disturbances. This study was undertaken to investigate the effects of propranolol tablet on improvement of CSR in referral cases to Farabi and Feiz hospitals in Isfahan in 2003-2004.

**METHODS:** This was a double-blind randomized controlled clinical trial. Patients with CSR referred to Farabi and Feiz hospitals were randomly divided into 2 groups: treatment group and control group, each one included 30 patients. Treatment group took propranolol tablets 20 mg twice a day, and control group took placebo tablets. Patients were examined weekly until complete improvement. Means of duration of disease and final visual acuity on the basis of log mar were compared by t-test. Relative frequency of final visual acuity of 10/10 in the two groups was compared using chi-square tests.

**RESULTS:** Two groups were comparable with respect to age, sex, involved eye, psychological tensions and clinical findings. The course of improvement in treatment group was  $62 \pm 29$  days and in control group was  $89 \pm 44$  days ( $P < 0.05$ ). Means of final visual acuities were not significantly different between the two groups ( $0.98 \pm 0.13$  log mar in treatment group compared to  $0.97 \pm 0.18$  log mar in control group). Relative frequency of vision  $< 10/10$  was 30% in control group and 3.3% in treatment group ( $P < 0.01$ ).

**CONCLUSION:** Duration of disease and need to laser therapy in patients with CSR were decreased by the use of propranolol but it had no effect on the amount of final vision. Because the patients are mostly in the years of active life, propranolol use is recommended for these patients.

**KEYWORDS:** Central serous chorioretinopathy, visual acuity, propranolol.

JRMS 2008; 13(3): 103-107

Central serous retinopathy (CSR) is a frequent disease often involves healthy men in the age of 30-50 years. Its signs are decreased visual acuity, vision obscuration, metamorphopsia, micropsia and color vision abnormality. <sup>1</sup> Persons suffering from this disease may have Marcus-Gunn pupil, disorders in electro-physiologic tests for the eyes, and visual evoked potentials disorders as well. This disease is one of the frequent disorders of retina and it is in fact an idiopathic detachment of sensory retina from pigmented epithelium in

macular region. <sup>2</sup> Today's suggestion for treating these patients with laser, which has side effects such as central visual scotomas and choroidal neovascularization, is only in special patients such as bilateral disease, persons with sustained signs and symptoms from previous episode of disease in contralateral or ipsilateral eye and in persons who have occupational need to subtle vision. <sup>1,3,4</sup> The etiology of CSR is not completely understood. This disease is episode of disease in contralateral or ipsilateral eye and in persons who have occupational

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need to subtle vision<sup>1,3,4</sup>. The etiology of CSR is not completely understood. This disease is more frequent in personality type A and in persons affected by psychological and physical tensions. Meanwhile, accompaniment with agents such as vasoconstrictors, presence of endogenous hypercortisolism<sup>5</sup> and use of systemic steroids<sup>6</sup> were seen in this disease. In animals, CSR can be induced by intravenous adrenaline injections. Tension causing conditions that followed by adrenergic hormones release were seen also with CSR.<sup>7</sup> These observations led to this theory that adrenergic receptor blocking agents may accelerate improving the disease. Yet, a few studies have been done on  $\beta$  blockers (metoprolol, nadolol and trimepranol) and their effects in improvement of CSR.<sup>8-12</sup> Propranolol also like nadolol is a  $\beta$ -adrenergic receptor blocker that blocks both  $\beta_1$  and  $\beta_2$  receptors, whereas metoprolol blocks only  $\beta_1$  receptors. Because metoprolol and nadolol and trimepranol may not be readily accessible in Iran, we decided to use propranolol, which is cheap and easily accessible. This study evaluated the effectiveness of propranolol in patients with CSR visited in two eye centers (Feiz and Farabi) in Isfahan in 2003-2004.

## Methods

This study was a double-blind randomized controlled clinical trial. Referral patients to Isfahan hospitals of Feiz and Farabi in 2003-2004 with diagnosis of CSR were referred to the first author (FK) and the diagnosis was confirmed by ophthalmoscopy and fluorescein angiography. In all patients, the time of the first visual complaint was considered as the start of the disease. CSR findings in ophthalmoscopy were circular shaped shallow eminent with marked limits in sensory retina and the presence of serous liquid beneath the retina, which was mostly clear but occasionally it was nonclear and obliterated choroidal pattern. Yellow delicate sediments in posterior surface of retina and/or light reflexes in marginal areas of serous detachment were sometimes seen. Very often, retinal pigment epithelium (RPE) de-

tachment in serous detachment was visible, which was a grey or yellow eminent usually small with marked limits. Sometimes RPE detachment occurred only in exterior of retinal detachment. Several cases of RPE detachment existed with or without retinal detachment<sup>8</sup>. In fluorescein angiography, a precocious small area of hyper-fluorescent and leak in proximity of RPE detachment site were seen. Sometimes, leakage ascended like cigarette smoke, which was dissipated and then, spread and filled serous detachment area in retina but mostly, local or diffuse leakage were seen. Usually, leakages were seen in one area that very often was 1 mm far from fovea center, in supranasal quadrant.<sup>1</sup> Inclusion criteria after confirmation of diagnosis were as follows: 1) no contraindication for propranolol use, 2) no other eye disease like cataract, retinal disorders and so on, which causes diminish visual activity, 3) no indication for laser therapy. Patients met the inclusion criteria were referred to the second author (FF), and according to the table of random numbers, they were assigned randomly in two groups; half of patients received propranolol (treatment group) and the other half received placebo with the shape and color similar to propranolol (Amin pharmaceutical company), which was supplied by Feiz Hospital Pharmacy. The amount of administered propranolol was 20 mg twice daily (anti-anxiety dosage), based on the advice of an expert in internal medicine. After drug administration, the patients were referred to the first author. Complete eye examination was performed once a week, and the drug adverse effects also were recorded. When the retina was flattened on examination, fluorescein angiography was requested. The time that the leakage disappeared was considered as recovery time. Those patients affected by drug adverse effects or another disease, which affected the visual acuity, were eliminated from the study. The duration of disease was considered as the time between the first report of symptoms by patients until recovery time. The mean duration of disease and the average final visual acuity of the two groups, after conversion to

lag mar, were compared by t-test. For comparison of relative frequency of visual acuity of 10/10 between the two groups, chi-square test was used.

## Results

Treatment group included 75% males and 25% females and control group included 69% males and 31% females. Mean age of all patients was  $35 \pm 8$  years (range, 26-60 years). The mean age in treatment group was  $34 \pm 7$  years and in control group was  $36 \pm 8$  years. Involved eye in 31 cases was the right eye and in 29 cases was the left eye. Psychological tension was seen in 68% of patients, including 76% in treatment group and 66% in control group. Differences between the two groups for this aspect had no statistical significant difference. Clinical finding of subretinal fleck was seen in 36% of control group and 30% of treatment group. In 12 months follow up, reappearance was seen in 8 cases (13.3%), which included 5 cases (16.7%) in control group and 3 cases (10%) in treatment group and this had no statistical significant difference. Because of elongation in duration of disease, one patient (3.3%) in treatment group and 9 patients (30%) in control group needed laser therapy ( $P < 0.01$ ). Five patients including 3 cases of kidney transplantation, one case of multiple sclerosis and one case of kidney disease used steroids. Duration of recovery in patients in treatment group was  $62 \pm 29$  days and in control group was  $89 \pm 44$  days; i.e., in treatment group was 27 days shorter ( $P < 0.05$ ). Visual acuity of patients in the two groups is presented in table 1, which shows in control and treatment groups 30% and 23.3% had visual acuity less than 10/10, respectively. It had no statistical significant difference ( $P < 0.8$ ).

**Table 1.** Frequency distribution of visual acuities in each group of patients.

Groups	Visual Acuity		Total
	10/10	< 10/10	
Control*	21 (70%)	9 (30%)	30 (100%)
Treatment*	23 (76.7%)	7 (23.3%)	30 (100%)
Total	44 (73%)	16 (27%)	60 (100%)

\*No significant difference was found between the two groups.

The mean of first visual acuity was  $0.71 \pm 0.12$  log mar in treatment group and  $0.72 \pm 0.15$  log mar in control group, which had no statistical significant difference. The mean of final visual acuity after the laser therapy in treatment group was  $0.98 \pm 0.13$  log mar and in control group was  $0.97 \pm 0.18$  log mar with no statistical significant difference. No one in the two groups of patients, had drug adverse effects or other disease that could be effective on visual acuity.

## Discussion

The investigation showed that propranolol use, 20 mg twice daily, could decrease CSR period. Have it in mind that if necessary, the control group, received laser therapy that diminished the disease period and if they were untreated, disease period (average 5 months) was more prolonged, in contrast with the treatment group disease period (about 2 months). Thus, it is clear that propranolol had significant effect on accelerated improvement in patients with CSR. Only 3.3% of patients in treatment group needed laser therapy while in control group 30% needed it and it seems that with the use of propranolol, the number of patients need laser therapy, will be diminished significantly. According to the recent investigations in pathophysiological basis of CSR with the use of indocyanine angiography, choroidal ischemia was found to be as the primary event. Release of chemical transmitters from hypoxic white blood cells causes choroidal venous and capillary congestion and liquid and protein leakage from choroidal capillaries and detachment of RPE. Detachment of RPE causes mechanical stress on RPE cells and destruction of external blood-ocular barrier, which in turn causes serous detachment of sensory retina and formation of CSR.<sup>13-16</sup> Disorder in sympathetic regulation and catecholamine levels causes choroidal ischemia. Propranolol, which is  $\beta$ -adrenergic receptor blocker, probably causes sympathetic system regulation and accelerates CSR improving. Due to higher prevalence of CSR in personalities type A and in tension conditions, and the effectivity of propranolol

as anti-anxiety in relieving the somatic symptoms of anxiety, the use of this drug in CSR has been considered logically. In Browning study in 1993, the effect of nadolol in decreasing the duration of CSR was seen.<sup>9</sup> Also, in the study of Fabianova in 1998 the effect of trimepranol (metipranolol) and metoprolol on decreasing the duration of the disease was seen and in all patients, remission of the disease occurred, on average of 4.5 to 4.8 weeks after the onset of treatment.<sup>10</sup> On the other hand, in the study of Chrapek in 2002, with the use trimepranol, remission occurred within four months of treatment, and he concluded that a therapeutic dose of trimepranol is not a reliable therapeutic solution for CSR.<sup>11</sup> In our study, by using propranolol, remission occurred, in an average of 9 weeks after the onset of treatment. In the study of Tatham in 2006, which was a comprise of a literature review and interventional case reports, the effect of propranolol on improvement of final visual acuity and remission of patients symptoms was seen.<sup>12</sup> However, in our study propranolol did not have any effect on final visual acuity, and just caused the decrease in the duration of the disease. In addition, because CSR mostly involves healthy persons in active years of life, shortening the disease duration and diminishing the disorders and disabilities caused by the disease are very

important. Then, propranolol, which is cheap and easily accessible and lacks visual adverse effects and has little systemic adverse effects, in patients with no contraindication is of great value. According to the results of this research and previous studies, administration of propranolol in patients with CSR is recommended. The effects of  $\beta$ -blocker agents on re-appearence rate and long-term complications of the disease should be studied. In a recent study, the effect of acetazolamide in improving CSR was studied and it decreased the time required for patients' feeling improvement in vision (treatment group,  $14.7 \pm 5.7$  days and control group  $34.3 \pm 4.5$  days) and also decreased the time required for clinical improvement (treatment group,  $3.3 \pm 1.1$  weeks and control group,  $7.7 \pm 1.5$  weeks). But, the reappearence rate and final visual acuity in treatment and control groups had no statistical significant differences.<sup>17</sup> According to this research, it seems that the effect of acetazolamide in improving CSR is comparable to the propranolol use. The use of acetazolamide in patients is difficult because of its adverse effects. If other studies confirm the results of this research, the use of acetazolamide in patients with any contraindications for propranolol is recommended.

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