**Therapeutic Use of Oral Propranolol to Treat Stubborn Central Serous Chorioretinopathy**

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**Abstract: Purpose:** To evaluate the prognosis of patients with stubborn central serous chorioretinopathy (CSCR) after oral propranolol. **Methods:** Two patients having CSCR with moderate to severe vision loss were treated at other hospitals but failed. They were introduced to our department. All the patients underwent the complete evaluation at the baseline and follow-up visits. This ocular examination included the bare and best-corrected visual acuity, fundus biomicroscopy and OCT in each visit (every 2 weeks). The medication of oral propranolol (20 mg qid per day) in our cases were used. **Results:** The follow-up time ranged between 3 and 6 months. Improvement of vision was observed, and they all had better spectacle-free vision within 2 months. The serous retinal detachment improved in all eyes and no ocular and systemic complications were noted. The detailed findings could be easily monitored by series of OCT. **Conclusion:** Many literatures had mentioned that the risk factors associated with CSCR including personality, psychological stress, or excessive steroid use. It is difficult to predict the exact reasons and will be bothered by the possibility of recurrence in this disease developed into chronic stage. How to select the correct drugs for patients became very important for clinicians. If failed, it may result in impaired permanent visual function. The oral propranolol (20 mg qid per day) was used to treat the patients with CSCR within 1.5 months in our study. No recurrent CSCR was noted after long time follow-up. Besides, the oral inderal showed safety concerns. The mechanisms of the beta-blockers were to reduce the adrenergic activity in the body and eyes. Propranolol had known, moreover, other advantage about the lowering the heart rate in patients with emotional stress which may be the impact factor of CSCR. Thus, we suggested that if the patients were vigorous and enthusiastic, the use of oral propranolol may be the first line medication to treat CSCR in clinics. [Chi-Ting Horng, I Yaun, Yuan-Ting Haung, Yi-Jun Chang, Chun-Sheng Wei, Ming-Ling Tsai. **Therapeutic Use of Oral Propranolol to Treat Stubborn Central Serous Chorioretinopathy.** Life Sci J 2014;11(5):499-505] (ISSN:1097-8135).

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1. **Introduction**

Central serous chorioretinopathy (CSCR) is the disorders characterized by serous retinal detachment, retinal pigment epithelial (RPE) detachment of dysfunction, and choroidal hyper-permeability (1,2). The pathology of CSCR is the sub-retinal fluid accumulation leaking from the impaired tight junction of choroid. Therefore, elevated and dome-shape macular region due to RPE detachment could be found in the posterior pole (3). The incidence of CSCR has been found to be approximately six times higher in men than women (4). Furthermore, the mean age of onset of this disease is about 41 years old (middle-age people) (5).

Although CSCR has been described as benign and self-limiting diseases, it has a tendency to re-occur with decreased vision. In cases of chronic CSCR, persisted sub-retinal pigment epithelia (RPE) atrophy, cystoid macular degeneration, choroidal neovascularization were found (6,7). Therefore, early treatment of CSCR was necessary which stressed the resolution of the neuroepithelial detachment. It also may reduce the incidence of retinal atrophy and the consequent vision loss (8). Hussain et al. had reported severe visual loss even happened in patients with chronic CSCR (9). There are many impacting factors associated with CSCR including stressful personality (Type A behavior), hypercoagulability, uncontrolled hypertension, preeclampsia, patients undergoing hemodialysis, bone marrow and solid organ transplantation, vasculitis, lupus, inflammatory bowel diseases, Cush’s syndrome, and excess exogenous glucocorticoids (10,11,12,13,14,15,16,17,18,19). Thus, different methods were used to treat the patients.

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with CSCR. For example, large doses of systemic steroids (20), ketoconazole (21), low-dose of aspirin (22), argon laser photocoagulation (20), Photodynamic therapy (PDT) (23), transpupillary thermotherapy (24), intravitreal injection (IVI) of Bevacizumab (Avastin) (25) or Ranibizumab (26) and even complicated retinal surgery such as perfluorocarbon liquid-assisted external drainage in case of bullous retinal detachment (27). Due to the complicated and uncertain pathogenetic model, we can not make sure to controlling the CSCR completely. Recurrence also developed in one third of patients and the cause may be from life style or personality. In this reports, we will demonstrate two cases of stubborn CSCR which were treated by oral propranolol finally in a short time (within one to two months).

2. Material and Methods

Material

From January 2013 to July 2013, two cases with diagnosis of CSCR were ever treated by any methods except propranolol. The patients had received various treatments including intravitreal injection (IVI) of avastin, argon laser photocoagulation and even PDT, but they all failed. Thus, they were tried to treat with oral propranolol in our hospital (Kaohsiung Armed Forced General Hospital). These patients did not have history of anticoagulant therapy or abnormal blood associated diseases. Before and after our treatment, the patients were followed at regular intervals (every two weeks) by various examinations including best-corrected visual acuity (BVCA) measurement (by Snellen chart), intraocular pressure (IOP), slit-lamp examination, OCT and ICG check-up at each follow-up visit. In the treatment regimen, we tried to treat the recurrent and stubborn CSCR only by oral propranolol.

Case Reports

Case 1:

A 45-year-old male patient (CEO of one company in Taiwan) presented with sudden visual loss in the left eye. Furthermore, the dim image and micropsia were also noted. He called at one teaching hospital of northern Kaohsiung and the BCVA had dropped to 6/30(OS) (by Snellen chart). Under the impression of CSCR, he received three times of IVI avastin and two times of laser photocoagulation within 6 months. Unfortunately the symptoms and signs did not improve. Apparently the laser did not seal the leakage and the bevacizumab also can not increase the occlusion between RPE cells and enhance the external retinal barrier (28). Thus, he was introduced to out clinics. After series of examination including FA, OCT (Figure 1A), and ICG were performed. The residual subretinal fluid for CSCR also persisted. His BVCA only revealed 6/30 in the left eye. He began to take oral propranolol (inderal) 20 mg qid (total 80 mg in one day) for one month and he came to our outpatient department for further evaluation every two week (Figure 1B and Figure 1C).

![Fig 1A (Day 1)](image1)

![Fig 1B (Day 14)](image2)

![Fig 1C (Day 28)](image3)

**Fig 1A, B, and C:** Series of OCT showed the disappearance of subretinal fluid of CSCR of right eye after oral propranolol within four weeks follow-up (Case 1). (OCT/ SLO, OPKO, E-Vision Instrument Company)
Two weeks later, the central retinal thickness of 320 microns had reduced to 250 microns by OCT. After one month, his bare visual acuity had returned to 6/6 and the resolution of CSCR was also noted. The patient remained asymptomatic over 2 months of follow-up.

**Case 2:**

A 42-year-old female (A management of foreign company in Taiwan) was bothered by metamorphopsia on her right eye. Her BCVA revealed only 6/60. During last year, series of evaluation including OCT, FAG and ICG were performed and CSCR was diagnosed at one medical center in Taipei. While tracing the past history, she did not have any other ocular disease and systemic disease. However, she was ever diagnosed as type A personality by several psychiatry doctor three years ago and received regular follow-up. At first, she had ever received IVI of avastin (total 6 times within one year) and her BCVA only mild returned to 6/30. Thus, she received the treatment of PDT again. However, the distortion image also remained. She was very depressed and introduced to our hospital. Fundoscopy revealed the dome-shape serous detachment in the macula. After detailed physical examination, she was suggested to take inderal 20 mg qid (equally to 80 mg every day) for 2 months. After the 5th weeks, her bare vision had returned to 6/7.5 dramatically. Three months later, decrease in central retinal thickness from 420 to 185 microns. The FAG findings also revealed the smaller leakage. After 6 months, we were surprised to find that her BCVA had come back to the initial situation (6/6). The fundus of her right eye revealed no elevated lesion in the posterior pole. In the same time, no subretinal fluid beneath macula region and the normal picture of cross-section of retina was found by OCT (the resolution of retina before and after treatment see the figure 2A, 2B and 2C).

### 3. Discussion

Many previous literatures about risk factors including male gender, personality, psychological stress (such as death, or divorce), pregnancy, or history of corticosteroid use were noted in clinics. The difficulty in predicting which patients will face a chronic and relapsing disease, resulting in impaired visual function, has led to a search for drugs and exact etiologies that can be effective in the treatment of CSCR. Due to the higher incidence of recurrence, the doctors may pay attention to the relationship between CSCR and the abnormal steroid regulation combined with anxious emotion induced stress. Most of CSCR may resolve within 4 to 6 months, and a good final acuity in 90% of cases (29,30). Furthermore, CSCR shows bilateral involvement in 30%, recurrence in 40% and severe visual loss in 5% of chronic course (31,32).

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![Fig 2A (Day 1)](image)

![Fig 2B (Day 15)](image)

![Fig 2C (Day 30)](image)

**Fig 2A, B, and C:** Series of OCT showed the resolution of CSCR of left eye after oral propranolol within regular follow-up (Case 2),(OCT, Stratus, Carl Zeiss).

Growing literature highlights how this type of treatment has a degree of effectiveness in sealing the leakage, reducing neuro-epithelial detachment and choroidal hypermeability for example the use of avastin and photocoagulation laser. However, the incidence of recurrence was frequently found. Hence, Yannuzzi et al. presented that the CSCR may be associated with life style, personality, and the altered pituitary-hypothalmic axis (HPA) response (10).
Nyklíček et al. also reported that patients with chronic psychological distress, with increased reactivity of HPA, frequency showed hypertension induced by a increase vascular resistance (33).

Furthermore, patients affected with CSCR were found to have various endocrine abnormalities. Some patients with CSCR often have higher levels of serum cortisol and catecholamines than healthy people (34,35). Wakakura et al. found that urinary epinephrine (Epi) and norepinephrine (NE) levels in patients with active CSCR were elevated compared with the control group (36). We know that adrenergic agents such as Epi and NE are components of the stress response and could maybe induce the transient hypertension, choroidal vasoconstriction, or direct effects on the RPE (37,38,39). The glucocorticosteroids and thyroid hormone have, moreover, been to sensitize the epinephrine receptors to the effects of circulating adrenergic hormones (40,41). In CSCR, patients are found to have the augmented vascular response, due to the glucocorticoid excess, to noradrenaline and angiotension II with consequent hypertensive response (42). In some cases, psychological stress had abnormal elevated 24 hour urine cortisol (a kind of glucocorticoid) and tetrahydrosterone (THA) which is usually found in CSCR. Though corticosteroids would strength the tight junction and many ophthalmologists used to treat CSCR (43), some articles also had mentioned that corticosteroid might reduce RPE fluid absorption, thus prolong the disease duration if not used carefully. Another explanation is that high levels of circulating glucocorticoids increase adrenergic sensitivity either through increased catecholamine excretion (36). In addition, type A personality attribute to increasing cortisol and catecholamine response to behavioral challenge. In our two cases with CSCR, they were all busy, aggressive and honorable in their occupation (type A personality) which was just the risk factors of CSCR (10).

Now the concept of treatment of CSCR had improved and many drugs helped the patients to recover as soon as possible. For example, Ketoconazole (a anti-fungus agents) exerts its effects by inhibiting the step of steroid synthesis and decreased in the level of cortisol (44,45). Besides, it owns the direct anti-glucocorticoid effect as an antagonist. The effects seem to be present at the minimum dosage of 400m/day, however, the effectiveness of drugs were limited by the serious complication including flushing of face, yellow skin, liver damage, shortness of breath, GI upset, giddiness, nausea, vomiting, tachycardia, confusion, and even CNS or respiratory depression. Mefepristone (known as RU-486) is also another agent to treat the CSCR. The mechanism is an antagonist of glucocorticoids and progesterone receptors. Besides, it may inhibit cortical-induced peripheral vasoconstriction (46). Unfortunately, the severe side effects such as the sepsis, carcinogenic, genotoxic potency and teratology may impact the human especially pregnancy mothers (47,48).

Recently some ophthalmologists identified low-aspirin as the drug better suited for the treatment of CSCR because of the reduction of stress response of the HPA axis, limitation of the elevated cortisol and catecholamines in serum (49,50). Its effectiveness in other vascular diseases and its low ocular and general toxicity deserved to use for a long time (36,51). In experience, the dose of 75-100mg appears to be safer. However, the side effects about bleeding tendency, hepatic toxicity, stress ulcer, allergy, skin rash and even brochospasm (4-19%) should be also kept in mind.

Another attempt was made with carbonic anhydrase inhibitors (CAI) (a diuretics) that act on RPE, taking part in resorption of the subretinal fluid (52). In general, any type of diuretics including CAI was used to excrete the extracellular cell fluid in physiology. Recent studies demonstrated that both systemic acetozolamide (Diamox) and dorzolamide (Trusopt or Azopt) for topical use all can increase the choroidal blood flow (52,53,54). In the specific case of CSCR, acetazolamide has been demonstrated to reduce subretinal fluid (55). In view of potential the side effects of diamox including electrolytes imbalance, metabolic acidosis, renal stone and even pulmonary edema, it make the hesitations from the doctors. Therefore, its use needs more intervention (56,57). Many years ago, the steroids had ever used to control CSCR by ophthalmologists. Recently many literatures had established that steroid may even exacerbate the serous detachment when treating CSCR. The mechanism of the complication is to increase the permeability of choriocapillaris, which could allow entry of large proteins (such as fibrinogen) into the sub-RPE and subretinal space (58). Despite multiple reports describing the onset of CSCR or aggravation of existing lesions with corticosteroids, they are still used by some clinicians for the treatment of CSCR. Thus, we had better to make the early detection and steroid dose adjustment for preventing from permanent visual loss.

Due to the relationship between stress and high levels of adrenergic activity, the receptors inhibitors could work as a treatment of CSCR. At first, Heinrich et al. used the α-adrenergic antagonists to reduce the
effect of vasoconstriction induced by glucorticoids (59). In physiology, alpha blockers may relax certain muscles and help small vessels remain open. This improves blood flow and lowers blood pressure, thus many doctors used the medications to treat different types of hypertension and urinary retention induced by benign prostate hypertension (BPH). However, the systemic side effects (such as hypotension and dizziness) were remarkable and now it was abandoned gradually. β adrenergic antagonist currently were popular for some ophthalmologists to treat CSCR (60,61). The propranolol, nadolol, trimetoprolol and metoprolol were the common used medication and proved to improve the symptoms and visual acuity of patients with CSCR (62,63). The mechanisms of beta blocker in treating CSCR was to reduce the adrenergic activity in the body and eye which were proposed by Avic et al (63). According to several studies, the patients did experience remission in 4.5-4.8 weeks (60) and the time is just the same as our report. Besides, the rate of resolution of serous retinal detachment is approximate to 90% (62). The dosage of Inderal is suggested 40 mg twice per day; however, the recurrence of CSCR were still found (64). In our cases, the two patients took oral propranolol 20 mg qid (total 80 mg in one day) and no repeated problems and systemic side effects were noted. Thus, the dosage and frequency of medication should be recommended.

4. Conclusion

Some clinicians had mentioned that the risk factors associated with CSCR including personality, psychological stress, or excessive steroid use. It is difficult to predict the exact reasons and will be bothered by the possibility of recurrence in CSCR. How to select the correct drugs for patients became very important. If failed, it may result in impaired permanent visual function. The oral propranolol (20 mg qid per day)(total 80 mg in one day) in our cases were used to treat the patients with CSCR within about 1.5 months. No recurrent CSCR was noted after long time follow-up. Besides, it showed safety concerns carefully. The mechanisms of the beta-blockers were to reduce the adrenergic activity in the body and eyes. Besides, Inderal had other advantage about the lowering the heart rate in patients with emotional stress which may be the impacting factor of CSCR. Thus, we suggested that if the patients were vigorous and enthusiastic personality combined with the occurrence of CSCR, the use of oral propranolol may be the excellent choice in clinics.

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**References**


