

**New Method to Treat the Patients with Central Serous Chorioretinopathy by Oral Propranolol**Chi-Ting Horng<sup>1,2,4</sup>, Chiai-Jung Shen<sup>1,4</sup>, Mei Fang<sup>3,\*</sup><sup>1</sup> Department of Ophthalmology, Fooying University Hospital, Pingtung, Taiwan.<sup>2</sup> Department of Pharmacy, Tajen University, Pingtung, Taiwan.<sup>3</sup> Department of Pharmacy, Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan.<sup>4</sup> contributed equally the work and therefore should be considered equivalent authors\* Corresponding Author : Fang Mei, Department of Pharmacy, Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan. E-mail: [h56041@gmail.com](mailto:h56041@gmail.com)

**Abstract: Purpose:** This is the first large population study in the world to evaluate the outcome of patients with central serous chorioretinopathy for 4-month-period follow-up. **Methods:** The patients with CSCR decreased vision and called at our hospital in the past 2 years. All 276 victims were enrolled in our protocol and underwent series of ocular examinations including best-corrected visual acuity, the fundus biomicroscopy and series of OCT scanning everyday. At the beginning, each patient took propranolol (10 mg tid to qid per day) and the whole experiment was scheduled for 4 months. If the sub-RPE fluid showed complete resolution and the elevated dome shape on the OCT imaging disappeared, the therapy of this subject had stopped oral propranolol and it was considered as “successful” treatment. Moreover, we recorded the age, sex, time of complete remission, and the change of vision before and after therapy in each subject. **Results:** The patients with CSCR were three times higher than in men than women. The mean complete remission time was mean 3.5 weeks and the percent of cases with vision recovery was up to almost 95% (262 patients). Furthermore, the mean initial visual acuity of all patients decreased to 0.54 LogMAR, and their mean vision returned to 0.15 Log MAR. Besides, no significant complication was found and no recurrence in the 262 successful patients after further 4 months follow-up. **Conclusion:** We suggested that oral propranolol may be the first line medication to treat CSCR in the future and this method also showed safe, cheap, efficacy, well tolerated and convenient for patients. Moreover, it shortened the remission time rapidly which is benefit for the patients who worried about the outcome and even became depression.

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**Introduction**

Central serous chorioretinopathy (CSCR) is one type of macular diseases characterized by serious retinal detachment, retinal pigment epithelial (RPE) detachment or dysfunction, and choroid hyper-permeability [1,2]. Therefore, the patients of CSCR may complain about various degrees of vision loss, color change, and a scotoma in the central visual field (like a doughnut) at times. Besides, other signs are increasing central macular thickness and macular edema. Moreover, the pathology of CSCR is sub-retinal fluid accumulation leaking from the impaired tight junction of the choroid. Therefore, we could find out an elevated and dome-shape at the posterior pole of retina [3,4]. It is surprising that the incidence of CSCR has been to approximately 6 times higher in men than women. We suggested that in Taiwan society, male labor is always the major source of family facility. Therefore, they should suffer from the psychological stress and endurance the associated physiologic fatigue [5]. Furthermore, many articles demonstrated that the mean age of onset

of CSCR is around 40 years old which is just the mainstay of their works [6,7]. Recently the subjects with sleepless and fatigue from long-term use and even overnight utilizing the modern 3C products also resulted in CSCR. When the people concentrated on the computers or smartphone for working or playing game, the high energy of blue light from the instruments may enter the eye and induce series of oxidative stress and impacted various cells damage [8]. For example, cataract, glaucoma and various retinopathies were reported in the world. Moreover, on the base of our current understanding of the disorder, multifactorial concept has evolved, involving several risk factors such as age, race, gender, blood pressure, certain systemic disorders and a behavioral pattern [9].

Although CSCR has been described as benign and self-limiting diseases, it has a tendency to reoccur. CSCR usually absorbed spontaneously, However, the incidence of this disease developed approximate to one third of patient and sometimes caused significant impairment of the visual acuity [10]. In clinics,

persistent RPE atrophy, cystoid macular degeneration, and even several choroidal neovascularization could possibly persist. Therefore, early prevention, diagnosis and treatment for CSCR is very necessary which exhibited complete resolution of sub-retinal fluid and caused impairment of visual acuity [ 12 ] . Some patients with severe CSCR cases even result the death of photoreceptors and retinal detachment in chronic stage [ 13 ] . Therefore, how to effectively block the formation of CSCR and further enhanced the absorption of sub-RPE fluid as soon as possible becomes the mainstay in the regiment of therapy.

The treatment of CSCR varied. For example, in the past it is firstly used by steroid from oral or intravenous routine. Recently intravitreal injection of steroid or bevacizumab (Avastin) becomes popular to ophthalmologists. Moreover, Gramko et al. concluded that 3g melantoin t.i.d could decreased central macular thickness and help to get better vision [ 15 ] . Moreover, Türkçü and his co-workers suggested that the relationship between free radical theory and CSCR is close. Therefore, to take stronger antioxidant is in benefit and better for the patients of CSCR [ 9 ] .

In this study, we adopted a new method to treat patients with CSCR by taking oral propranolol. Our purpose is to evaluate its safe, cheap, compliance and convenience for patients.

## Methods

Between January 2016 and December 2017, we conducted a prospective study of total 276 patients with CSCR, hence, the total subjects were recruit aged between 20 and 48 years. Informed consent was obtained from victims before participation before series of the experiments. In addition, the investigations were conducted in accordance with the Declaration of Helsinki. Ethical approval for this human study was obtained from the institutional review board (IRB) of Kaohsiung Armed Forced General Hospital (the approval number: KAFGH-105-18). Firstly, the exact diagnosis of CSCR was exact confirmed by the same doctor (Dr. Horng) and now the signs of CSCR could be easily detected by OCT (Optic Coherence Tomography; OPKO. E-Vision, Instrument. Company, Taiwan) techniques (Fig 1). At the same time, we recorded the initial vacuity acuity (by the LogMAR method), left or right eye, time of total resolution (by OCT), age, sex, occupation, and body weight of each people. In this tomography, we measured various changes of elevated height which means the amount of the sub-retinal fluid absorbed and the vision may become better slow by slow. Elevated dome shape was the predominant sign of CSCR of the accumulation of

sub-RPE space around macular region. In the past, we only found the mean radius of squared from CSCR by color photography. Besides, fluoresce angiography showed slow leaking on the macular region. However, we can not evaluate the disappearance correctly in times. In this study, we checked inverted U-shape of sub-RPE fluid by OCT images at every day morning (10:00AM). If the fluid complete remission and the OCT images became flat, we would record the final vision of this time (so called “recovery time”). In addition, the case was considered “successful”. Furthermore, the patient begins to stop taking propranolol. In our study, taking medication for 3 months is the end of time. Therefore, the “successful” and “un-successful” case would be requested to take medication anyway. However, the “successful” patients still receive 4-month follow-up which is to measure the incidence of recurrence.

At the beginning, the patients with severe cataract, glaucoma, uveitis, trauma, any abnormal lesion in the retina, s/p ocular surgery and any treatment for CSCR (for example, had received intravitreal injection of avastin or steroids) was all excluded. Because propranolol belongs to one type of non-selective  $\beta$  antagonist's agents, the patients with asthma or serious cardio-vascular disease were contra-indication. For safe concern, everyone had received the examination of 12- lead static EKG before our protocol starting and any abnormalities of EKG in each subject would be excluded out. Furthermore, the dosage of propranolol depended on the patients' weight. Our medication prescription is depending on the subjects' body weight. For example, the body weight > 60 Kg, propranolol is prescribed 30 mg in one day (10 mg propranolol t.i.d.). On the other hand, if the patient's body weight > 70 Kg, the subject would take 40 mg propranolol every day (10 mg propranolol q.i.d.).

Meanwhile, we recorded the visual acuity when the RPE layer attached and the sub-RPE fluid absorbed completely by OCT images (Fig 2). All the other subjects had continued to take propranolol until 3 months. At last, we recorded the final vision of each volunteer. Besides, if the volunteers felt about any degree of discomfortable (e.g.: short of breath, chest pain, cold sweating or bradycardia) during the 3 months, the patient should be quickly requested to dis-continue the therapy. Fortunately, there was no significant complication or personal discomfort in our study. Every one was all good compliance after taking drug. Moreover, the initial and final vision were also recorded by LogMAR which may enable a more accurate estimate of acuity, particularly in many research [ 14 ] . Finally, we compared and analyze the characters of the “successful” and un-successful” cases. Moreover all results are expressed as the mean



$\pm$  SD. A pair-t test was used to analyze the outcome of the change of best-corrected visual acuity. Analysis of

data was done by using SPSS version 13.0. *P* values of 0.05 were considered statistically significant.

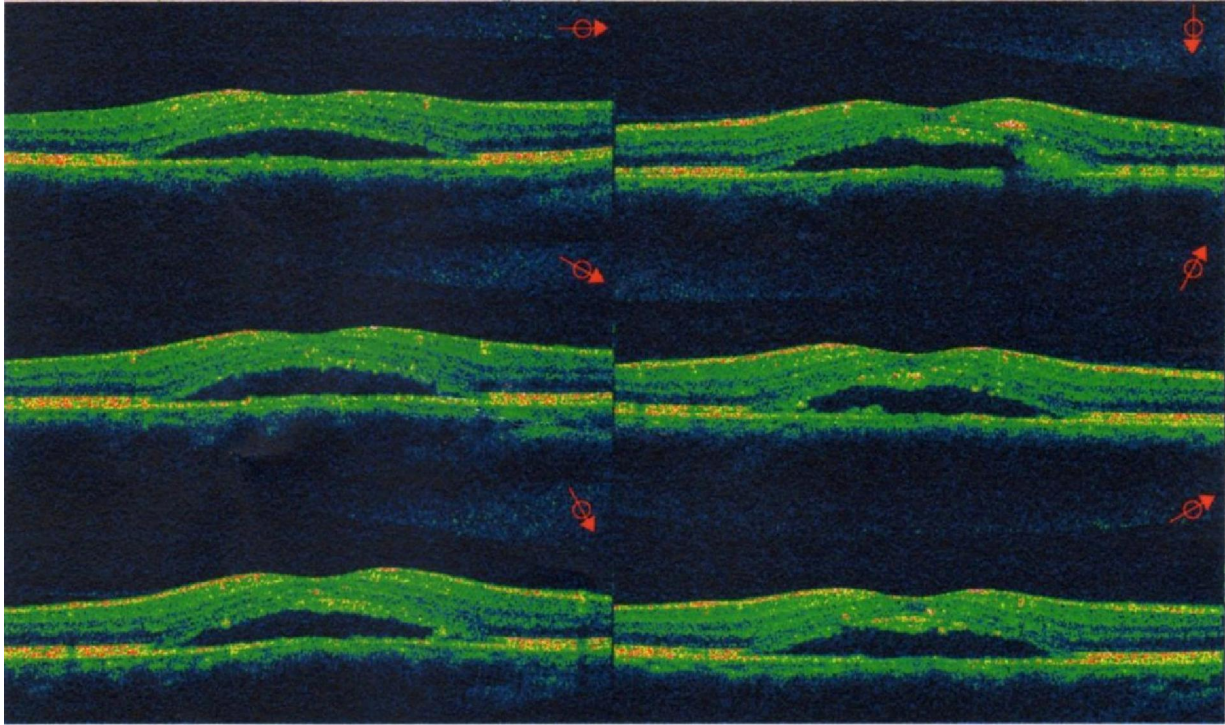


Fig 1: Serial ocular coherence tomography (OCT) in one CSCR patient showed retinal pigment epithelium detachment at day 1.

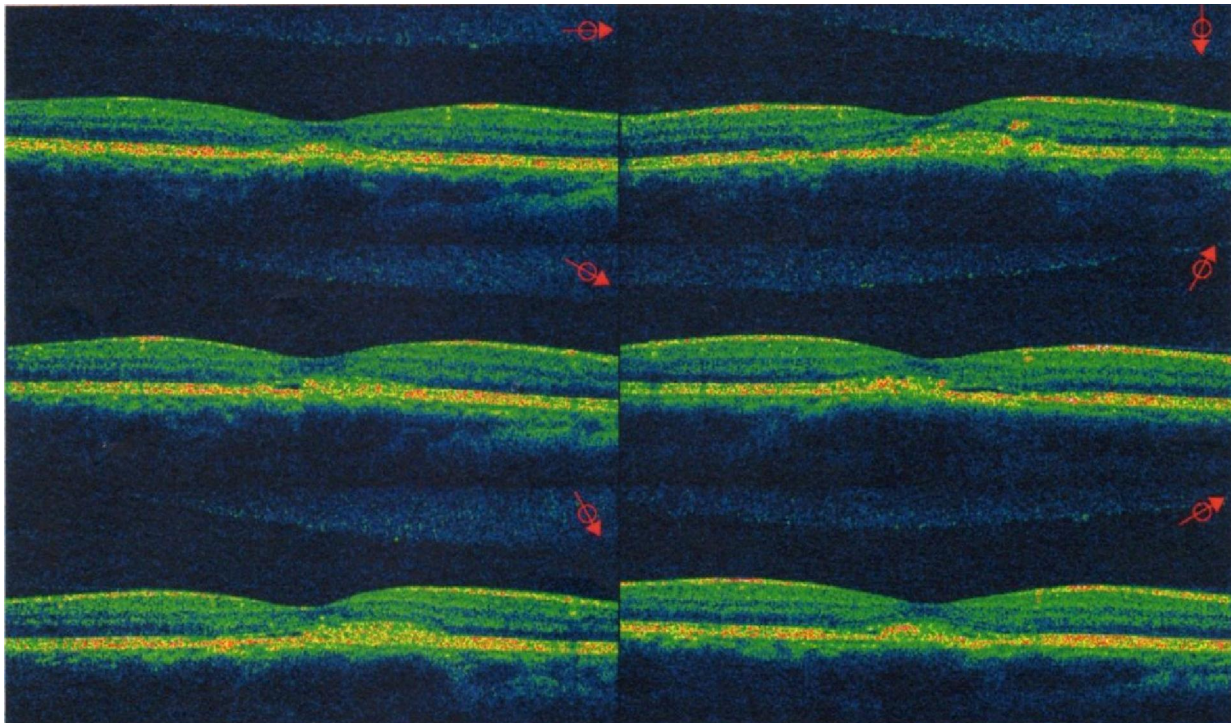


Fig 2: After oral propranolol for 27 days (Day 27), the retinal pigment epithelium detachment attached nearly by the view of OCT.

## Results

There were 276 volunteers took part in our treatment protocol with confidence and they knew that we had the ability treat the stubborn CSCR the stubborn and trouble problems in the past [ 28 ] . In that article, 2 case of stubborn CSCR had ever treated intravitreal avastin many time, however, still failed and went hospital shopping. They lose the money, the time and the uncalculated depressed mood. Fortunately, they were rescued from vision loss by our new treatment protocol. Therefore, we will perform the standard procedures and treatment protocols for the large population study of 276 patients of CSCR within 3 month.

According to analysis, the involved site is 54.4 % at right eyes, 45.5% cases of total CSCR at left eyes. Besides, 77 (28.5%) patients were with both eyes involved together. Therefore, we found that the percentage of involved eye is nearly equal.

All 276 volunteers took part in study and 262 (95%) patients of CSCR succeeded in our regimen. Hence, there are 212 (76.8%) male and 64 (23.2%) female patients were enrolled. The mean age was of all patients was  $37.5 \pm 2.5$  years which is similar to other reports. In other words, the male adults in family are the predominant group of victims of CSCR which the reasons are due to their social position, heavy work, anxiety and depression from their occupations. Besides, Only 14 (5%) patients did “not respond” to this treatment protocol (so called “unsuccessful”). However, we also found their vision mild improved and the dome shape in OCT scans disappeared in some degrees.

Moreover, we focused on the efficacy and it was exciting for us to demonstrate that the mean recovery time was only 3.5 weeks and the percent of “successful” patients was up to 95%. Moreover, the symptoms and signs in 262 patients with CSCR improved significantly. In a word, oral propranolol may enhance the sub-RPE fluid resolution completely and quickly, and modified the cell function after RPE layer re-attached. Furthermore, the mean initial visual acuity of all patients decreased significantly to 0.54 LogMAR, however, the final vision of total patients returned to mean 0.15 LogMAR ( $P < 0.05$ ). We concluded that the oral propranolol is a good strategy and the symptoms and signs of CSCR remission only after average 3.5 weeks. In addition, no remarkable physical complication or personal complainant was found. Moreover, after 4-months-follow-up, the 95% complete resolution of CSCR (successful cases) during treatment and revealed no more recurrence.

## Discussion

The central serous choroidoretinopathy (CSCR)

is one of the recurrent disorder characterized by the detachment of neurosensory retina and/or detachment of the RPE in the posterior pole, caused by fluid leakage from choroidal vessels, coming through retinal pigment epithelium (RPE) layer [ 17 ] . Furthermore, in some reach, alteration in the exudate state of the choroid may lead to serous detachment of the RPE and disruption of the tissue. Finally possible a small open or “blow out” of RPE. led to the characteristic fluorescein leak. To many ophthalmologists’ experience, sleepless, too tired and restless would result in CSCR formation. Mover, there are many associated diseases which may lead to CSCR including stressful personality (Type A behavior or personality), pre-eclampsia in pregnancy, hypercoagulability, the patients undergoing hemodialysis, bone marrow and solid organ transplantations, various vasculitis, tuberculosis, changed choroidal vascularity, lupus, smoking, steroid overuse (hypercortisolism), inflammatory bowel disease, Cushing’s syndrome, peptic ulcer and excessive exogenous glucocorticoids [ 17,18,19,20,21,22, 23, 24, 25, 26, 27,40 ] . Some habits, for example, playing the video computer games or using smartphone for a long time, especially overnight. Overexposure under high energy (near UV light) blue light and sequent oxidative stress happened. Hence, free radical formation begin to attack cells, organelle and human DNA, Finally the cells were damaged, induced CSCR and the users’ vision decreased significant because of cataract or various retinopathies. Moreover, Nakamura et al. indicated that oxidative stress was partially involved in blue LED light-induced retinal damage [ 29 ] . Li et al. even demonstrated that the blue light from the smartphone could induce severe photo-toxicity which plays an important role in retinal degeneration. Besides when exposure to LED blue light, RPE cells were subjected to blue light on activation of key apoptotic pathways which may cause fundus damage, decrease total retinal thickness, cause atrophy of photoreceptors, and even injure neuron transduction in retina. Hence, the blue light from 3 C population may be risk factor of formation of CSCR is possible [ 30 ] .

Indeed, more various risk factors of CSCR were taken into consideration from some researchers. For example, Islam et al and his colleagues suggested that the role of hypertension, uncertain steroid treatment and stress should be kept in mind when treated CSCR [ 7 ] . Goldhagen and his workers found that the shift work and sleep disturbance may be the etiologies of the CSCR [ 8 ] . Türkcü et al. suggested that free radicals and antioxidant mechanism would be one of



the pathogenesis [ 9 ] . It is interesting that Balkarli et al. found that the patients with CSCR have lower frequency of sexual dysfunction because of erectile dysfunction [ 31 ] . In summary, the relationship between CSCR and anxiety, or psycho-emotional state was suggested to be very closer. Therefore, when we scheduled to handle the cases of CSCR, the underlying causes should be not be neglected.

Many previous literatures about risk about various risk factors including male gender, emotional stress (e.g.: such as shift work, scolding by boss, family device and personal divorce), pregnancy, or over-corticosteroids used in clinics. According to many reports, 75 to 92% victims of CSCR were male subjects aged 35-40 years old who are always over duty working and in anxiety or depressed mood. Besides insomnia is also an independent risk factor. Furthermore, the difficulty in predicting which at least 1/3 patients will face a chronic and relapsing diseases, resulting in impaired visual function, has led to a search for various drugs and exact mechanisms that could be effective in CSCR. When we searched for the higher recurrence rate, many doctors paid attention to the abnormal steroid regulation and combined with anxiety-induced stress. Most CSCR patients may resolves within 4 to 6 months and returned to relative good acuity in 90% of the subjects finally [ 32,33 ] . Moreover, 30% of CSCR with bilateral involvement, 40% cases with recurrent rate and visual loss happened or remained poor vision in 5 -10 % of chronic CSCR [ 34,35 ] . However, even if one eye of CSCR with decreased visual loss, the patients may also loss of the static and dynamic stereopsis which could be inconvenient and induce anxiety or depressed mood. in life [ 36 ] . Furthermore, only one eye of the CSCR patient would only make patients walk slowly and vigorous movement must be forbidden.

Growing literature highlight how this type of treatment has a degree of effectiveness in sealing the leakage, reducing neuro-epithelial detachment and choroidal hyper-meability, for example, the use of intravitreal injection avastin or triamcinolone, conventional thermal photocoagulation, Transpupillary thermotherapy (TTT) and Photodynamic therapy (PDT) [ 37,38,39,53 ] . Moreover it is reported that Intravitreal bevacizumab injection (IVI), SM yellow laser (577nm) and standard-dose verteporfin PDT could result in reduction in the sub-retinal fluid height on OCT images, decreased the neurosensory detachment and improved the visual acuity after 2 to 8 months [ 37,38,39, 51,77 ] . These pharmacological interventions and various laser procedures may induce the anti-vascular endothelial growth factor

(anti-VEGF), seal the leakage and then has emerged to be a potentially effective treatment for CSCR. However, such invasive techniques would carry inherent risks or complication, and show poor outcome or offer questionable long- term benefit [ 69 ] .

Yannuzzi and his colleagues presented that CSCR may be associated with life style, personality, and the altered pituitary-hypothalamic axis (PHA) response [ 18 ] . Nykicek et al. al also reported that patients with chronic psychological distress and increased reactivity of PHA, frequency showed hypertension induced by an increase vascular resistance [ 41 ] . Furthermore, patients of CSCR were associated with various endocrine abnormalities. For instance, CSCR is associated with physiological changes including elevated blood pressure, serum cortisol and epinephrine. Rewai et al. ever found that patients with CSRC often have higher level of serum cortisol and catecholamine (epinephrine) than healthy control [ 42 ] . To our knowledge, the adrenergic agents such epinephrine and norepinephrine are components of the stress response and could maybe induce the transient hypertension, choroidal vasoconstriction, or direct effect on the RPE [ 43,44,45 ] . Yang established that alteration the alteration in RPE transport and a barrier might provide a way to modify human RPE transport for excessive endogenous adrenergic effects. Besides, the glucocorticosteroids has been to sensitize adrenergic receptors and to the effects of circulating adrenergic hormone [ 32,46,47 ] . In CSCR, patients are found to have the augmented vascular response, due to the glucocorticoid excessive, to noradrenaline and angiotension II with consequent hypertensive response [ 48 ] . Besides, in some CSCR cases, psychological stress has even elevated 24-hour-urine cortisol (a type of glucocorticoid) and tetrahydrosterone.

Excessive epinephrine may affect the retina through  $\beta$ -adrenergic receptors on the RPE. Activation of these receptors has been shown to produce a change in cyclic adenosine monophosphate concentration, (cAMP) which affects the RPE electrical activity. Besides, epinephrine has also been shown to induce apoptosis in RPE cells in vitro [ 32, 46,70 ] . Now it is known that the condition of hypercortisolism or hyperadrenalism and a catecholamine response are potential to risk factors in the well-recognized “speed and impatience nature” of patient with CSCR [ 32, 76 ] .

To our knowledge, CSCR may be present in various clinical forms with different prognosis now. Therefore, management of CSCR necessitates an individualized and selective treatment approach case

by case. There is overall poor evidence for the use of systemic and intravitreal corticosteroids. From various therapies, mineralocorticoid receptor antagonists appear to have the greatest potential. Because corticosteroids would strengthen the tight junction of choroid, some ophthalmologists favor using to treat patients with CSCR many years ago, however, the treatment regimen is instead of as a contraindication [ 49 ] . However, it is important to stress that in contrast to the current opinion, steroids can evoke or deteriorate CSCR and intensify its symptoms and signs. Therefore, it identified that any type of steroid is all a factor in the pathogenesis of the order are contraindicated in the treatment of this disease. Recently, in some articles, the steroids would reduce the RPE fluid absorption, and thus prolonged the disease duration if not used carefully. Many years ago, steroids had ever used to control. 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 choriocapillaries, which could allow entry of large proteins (such as fibrinogen) into the sub-RPE and sub-retinal space [ 50 ] . On the contrary, the steroid treatment for CSCR for ophthalmologists had become hesitated. For example, Siwiec-Prościńska J et al. found that the role of steroid treatment in course of CSCR was shown in many studies during past years and for that reason the correlation between those factors and the incidence and the course of CSCR was analyzed [ 17 ] . Kleinberger et al. presented that they found a bilateral CSCR resulting from intranasal corticosteroid use and they alarmed the side effects from steroid use [ 50 ] . Grixiti and his workers had reported that intravenous methylprednisolone induced central chorioretinopathy in giant cell arteritis. Therefore; the use of steroid for treating CSCR becomes controversial recently. Especially the use of systemic corticosteroids has significant CSCR [ 51 ] . Until now, Grixiti et al. concluded that corticosteroids own inflammatory abilities, however, it also disrupt RPE tight junctions which constitute the outer blood retinal barrier, leading to accumulation of the subretinal fluid. In addition increased choriocapillaries fragility, and hyper-permeability [ 51 ] .

Now, larger doses and systemic steroids for CSCR become contra-indication and should be avoided recently. Recently, the advanced mechanism of overload of mineralocorticoid receptor (MR) pathway in choroid vessels has been implicated in the pathophysiology of CSCR. Glucocorticoids also have affinity for MRs, further suggested of a targeted role for the MR pathways. Some animal studies showed that

They all have similar choroidal vascular dilation and leakage after activating the glucocorticoids and mineralocorticoid pathway, respectively [ 79 ] . In recent article, the prevalence of exogenous administration of glucocorticoid among patients developing CSCR was 3.3% and 9.1%. The mechanism of steroid-induced CSRC is that under the effects of endogenous or exogenous glucocorticoids, Karadium et al. postulated that glucocorticoids may affect the choroidal vasculature (causing increased capillary fragility, and hypermeabilities which could lead to choroidal circulation decompensation and leak of fluid in the subretinal space, or affecting the leakage of fluid in the sub-retina space, or affecting the production of nitric oxide, prostaglandins, and free radicals, and therefore affecting the autoregulation of blood) Hence, glucocorticoid use represents a risk factor for CSCR [ 80 ] . In previous publication, multiple routes of administration for steroid have been implicated in the advent of acute exudative changes of CSCR. Finally, Carvallo-Recchia CA, et al. reported that systemic steroid levels in otherwise normal patients with CSCR have been with CSCR have been found to be higher than match control [ 76 ] . It may be prudent for all CSCR patients to avoid the use of corticosteroid by any systemic routine of administration, unless there is a compelling medical indication.

In our experience (Not publication yet), we only could use the deeper peri-ocular or sub-tenon injection of a 3 ~ 4 ml of steroids once a week. There were no significant complications during therapy and the symptoms and signs of CSCR really disappeared 7~8 weeks later. Furthermore, no recurrence happened after sub-RPE layer well attached for 4 months in this study.

Ketoconazole (one type of anti-fungus agents) may inhibit the steps of steroid synthesis and decrease the level of cortisol. Besides, it owns direct anti-glucocorticoids effects as an antagonist [ 32,76 ] . The effects seem to present at the minimum dosage of 40g/day, however, the effectiveness of ketoconazole were limited by its severe complications including flushing of the face, yellow skin, liver damage, shortness of breathing, G-I upset, giddiness, nausea, vomiting, tachycardia and even CNS or respiratory depression [ 33 ] . Besides, Mifepristone (RU-486) is also another agent to treat CSCR. Its pharmacological mechanism is that mifepristone is an antagonist of glucocorticoids and progesterone. In addition, it may inhibit cortisol-induced peripheral vasoconstriction. Unfortunately, the serious side effects such as sepsis, carcinogenic, genotoxic, potency and teratology were found [ 58,59 ] .

Low-dose aspirin is another medication to treat

CSCR because it owns the ability to reduction of stress, and response of the HPA axis. Furthermore, low-dose aspirin may limited the elevation of cortisol and catecholamine in serum [ 60,61 ] . Moreover, its effectiveness in vascular diseases and combination of lower ocular and general toxicity deserved to be used. According to new medical text, the dose of 75-100 mg of aspirin appears to be safer for human. However, the side effects about bleeding tendency, hepatic toxicity, stress ulcer, allergy, skin rash, and even bronchospasm (4-19%) should be careful [ 62 ] . Besides carbonic anhydrase inhibitors (CAI) is a type of diuretic that act on RPE, taking part in resorption of the sub-retinal fluid. In general, the physiological function of diuretics were always used to excrete the excessive extracellular fluid [ 63 ] . Recent studies demonstrated that systemic acetazolamide (Diamox) and dorzolamide (Trusopt or Azopt) for topical use could also increase the choroidal blood flow [ 64,65 ] . Therefore, oral diamox could reduce sub-retinal fluid [ 66 ] and enhance the RPE layer attached in treating CSCR. However, the side effects, for example, electrolytes imbalance, metabolic acidosis, renal stone and even pulmonary edema [ 67,68 ] . We must pay attention to various serious when used.

Finally,  $\beta$ -blockers in our treatment protocol are competitive antagonist that blocks the receptor sites for the endogenous catecholamine epinephrine (adrenaline) and norepinephrine (noradrenaline) on adrenergic beta receptors of the sympathetic nervous system. In general,  $\beta$ -blockers interfere with the binding to the receptors of epinephrine and other stress hormones, and weaken the effects of stress hormones. In our study, the propranolol (30-40 mg) could dramatically made 95 % patients of CSCR complete absorption within 4 weeks and no other complication were found.

What is its mechanism? Possible explanation may relation to modification of the choroidal circulation of the choroid flow [ 76 ] . For example, choroidal blood flow is known to be regulated by both sympathetic and parasympathetic systems and steroids seems to act on synergistically with the sympathetic symptom and as an antagonist of the parasympathetic system, inhibiting the production of the vascular modulator nitric oxidase synthase [ 81 ] . Propranolol belongs to the non-selective  $\beta$ -adrenergic receptor antagonists.  $\beta$ - receptors are found on the cells of many tissues and organs and lead to stress response. In clinic, took propranolol may induce human vasodilation, decreased heart rate, blood pressure, cardiac output, and heart work, and preventing from hypoxia of heart and arrhythmia. Besides, propranolol also could decrease the incidence of angina pectoris,

stress, general anxiety, tension, headache, tremor and panic disorder, especially for people with prominent somatic or autonomic symptoms [ 75 ] . Therefore, the patients with asthma and severe cardiovascular disorders were excluded for safe. Moreover propranolol is a  $\beta$ -receptor has been proposed as potential means of treating CSCR because of choroidal circulation.

The  $\beta$ -blockers may prevent from changes in RPE activity and epinephrine- induced apoptosis that compromise integrity of the RPE and contribute to contribute to treat CSCR. This concept was supported by several studies just several years ago. Some  $\beta$ -blockers (propranolol, andolol, metoprolol) were used to decrease adrenergic activities. In clinic,  $\beta$ -adrenergic antagonist currently were popular for some ophthalmologists to treat CSCR in UK, USA, and Cesk Slov [ 71,72,73,74 ] . However, in our large population study (262 patients) succeed. In Tatham' study, only 2 CSCR were enrolled in propranolol treatment (40mg, twice). Unfortunately,

Patient 1 mild improved his vision, however, he did not return to his initial vision. Besides, in patient 2, no improvement occurred [ 74 ] . Besides, Browing et al. and his co-workers use the Nadolol (40 mg per day) for 8 patients with CSCR, however, they all failed. To our option, we prescribed the propranolol which is different from other researchers. Depending on the body weight, we order the lower body weight patients to take propranolol 10 mg three time in one day) and the heavy ones to oral propranolol (10 mg for time in one day). Another question is that propranolol and nadolol are all non-selective  $\beta$ -blockers. Why the patients took nadolol showed Unsuccessful? We suggested that other pharmacokinetic theories for propranolol and various pathway for different  $\beta$  blocker should further intervention.

## Conclusion

Central serous choroidretinopathy is a potential slight-threatening condition with a complex pathogenesis that up to this time has defined precise elucidation. Moreover, it is characterized by choroidal vascular thickness, and sub-retinal fluid accumulation. In general, subjects with CSCR usually could resolve spontaneously within 3 months; however, patients are naturally worried about that their recovery is as speedy and complete as possible. However, higher rate of recurrence developed in one third to one half of patients of CSCR and even very few subjects could not return to their initial vision unfortunately. In this large patient population study, we provide the better method for treating CSCR within rapid recovery time. The mechanism of failed to treat patients with CSCR

and the characters of recurrence of CSCR need further intervention in the future.

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