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Original Research Article

Evaluation of Risk Factors Associated with Central Serous Chorioretinopathy and Role of Systemic Propranolol as a Treatment Modality

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Conflict of interest: Nil

Abstract:

Background and Objectives: Central serous retinopathy (CSR) is an idiopathic condition characterized by accumulation of transparent fluid with acute serous detachment of neural retina at the macula. CSR mainly affects adults in the age group of 20 to 50 years with a male predominance. It usually present as acute onset of unilateral defective vision or metamorphopsia producing significant visual morbidity in young productive adults. Many forms of therapy had been employed for its treatment ranging from antihistamines, diuretics, NSAIDS, vasodilators, antitubercular drugs, osmotic dehydration and currently argon laser photocoagulation. But the results in all of these series had been equivocal and the clinical evaluation is difficult due to the tendency of the condition to recover spontaneously. Recently, few researches had shown a favorable role of beta blockers in the resolution of CSR.

This study was an attempt to study the various factors predisposed to CSR and effect of systemic Propranolol in the resolution of CSR.

Material and Methods: The study was done inside the setting of a hospital. Patients with clinical features of CSR were chosen from the Outpatient Department (OPD) at the Ophthalmology department of the Government Medical College and Hospital, Calicut, Kerala, India using a convenient sampling method. This was accomplished subsequent to receiving authorization from the Scientific Review Committee and Institutional Ethics Committee, as well as obtaining written consent from the patients. A detailed history was taken in each case to find the association of different risk factors.

In group P, 40 mg Propranolol tablet was started on daily basis at the time of first visit itself and the treatment continued till the resolution of CSR occurred or to a maximum of 2 months whichever is earlier. Similarly, in group C, control group tablet B complex were given. In group M, miscellaneous group, patients were allowed to continue the same treatment appropriately. All the patients were followed up at the end of 2 weeks, 1 month, 2 months, 3 months, 4 months and 6 months.

Results: The main victims of the disease were young people between 25 to 45 years. Among them also, the peak incidence was between 36 to 40 years of age. The male to female ratio was 2.9:1. The occurrence of CSR has a noticeable association with insufficient sleep pattern of the patient as a precipitating factor than other factors. It is evident that in Propranolol group only, the percentage of eyes showing resolution in the first two months remains unchanged in both occasions (41.7%). In the other two groups, when the whole course of disease is considered, the percentage of eyes showing resolution in the first two months are markedly decreased than the first visit.

Conclusion: Present study reflects a tendency of earlier occurrence of CSR in Indian people than Western people and does not affect the adolescents in the age group between 15-20 years. The occurrence of CSR has a noticeable association with insufficient sleep pattern of the patient as a precipitating factor than other factors. Propranolol 40mg daily for few weeks, considered to have a favorable role in the resolution time of CSR. Propranolol makes no difference in the final visual outcome of the disease as compared to placebo or other kinds of systemic therapy.

Keywords: Central serous retinopathy; Propranolol; Vision.

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Introduction

Central serous retinopathy (CSR) is an idiopathic condition characterized by accumulation of transparent fluid with acute serous detachment of neural retina at the macula. CSR mainly affects adults in the age group of 20 to 50 years with a male predominance. The male to female ratio is about 8:1 to 10:1. The diagnosis of CSR is clinical. It usually present as acute onset of unilateral defective vision or metamorphopsia producing significant visual morbidity in young productive adults. The etiology of CSR is still remains as an enigma and is mostly hypothetical. However several systemic conditions are described as predisposing conditions to CSR. This includes stress, Type A personality, pregnancy, migraine and steroid therapy.

Usually CSR is seen to be resolving spontaneously within 3-4 months. However it often recurred and complications compromising vision may sometimes occur.

Many forms of therapy had been employed for its treatment ranging from antihistamines, diuretics, NSAIDS, vasodilators, antitubercular drugs, osmotic dehydration and currently argon laser photocoagulation. But the results in all of these series had been equivocal and the clinical evaluation is difficult due to the tendency of the condition to recover spontaneously. The long natural history and the recurrent attacks resulting in gross visual impairment in many cases make a suitable treatment desirable. Recently, few researches had shown a favorable role of beta blockers in the resolution of CSR.

Aim and Objectives:

This study was an attempt to study the various factors predisposed to CSR and effect of systemic Propranolol in the resolution of CSR.

Material and Methods:

The study was done inside the setting of a hospital. Patients with clinical features of CSR were chosen from the Outpatient Department (OPD) at the Ophthalmology department of the Government Medical College and Hospital, Calicut, Kerala, India using a convenient sampling method. This was accomplished subsequent to receiving authorization from the Scientific Review Committee and Institutional Ethics Committee, as well as obtaining written consent from the patients.

Inclusion criteria: There were 35 patients and 37 eyes (2 bilateral cases) available as confirmed cases of CSR in 15-50 years age group in both sexes and without co morbidities.

Exclusion criteria:

- Age <15 years or >50 years
- Patients with history of ocular injury and other ocular pathology
- Patients having history of systemic conditions like hypertension, diabetes and others which can cause macular edema

Sample selection: To start with, there were 41 patients having features of CSR. Out of these 28 patients had typical features of CSR and were diagnosed clinically; 7 doubtful or atypical cases were confirmed by FFA. But 6 cases of doubtful or atypical

CSR were excluded either because of the evidence of other ocular disease or due to the noncompliance of the patients to confirm the diagnosis by FFA and to follow up. Except for 2 inpatients, all other cases were out patients. As there were 2 bilateral cases of CSR, total 37 eyes were included in the present study.

Methodology: A detailed history was taken in each case with special emphasis on points like the mode of onset of the symptom, the time of its first appearance and the duration. The incidences of similar illness in the same eye or in the fellow eye in the past were also elicited with its duration, course and the treatment taken for the same. Apart from the clinical symptoms, a detailed history of the personal habits, occupation, past history, and treatment history were also observed. An elaborated questionnaire regarding the occurrence of any concurrent history along with the appearance of the first symptom was put forward. This included details of sleep, food habit, physical stress, emotional stress, alcoholism, smoking, any kind of drug intake related to any other systems of medicine, work pattern, hours of work per day etc. Similarly, a detailed past history of migraine, epilepsy, hysteria, acid peptic disease, COPD and ischaemic heart disease were also enquired into.

The primary examination of the patient consisted of general examination and systemic examination. The ocular examination included a thorough anterior segment evaluation with slit lamp; Visual acuity testing, tests for Colour vision (Ishihara), near vision (Snellen) and tonometry (Schiots) were also done in each case.

Physician's opinion was sought in relevant cases regarding the systemic diseases. Apart from the tests described earlier to identify type – A behavior, psychiatrist's opinion was also sought whenever indicated. Routine investigations have been done in all patients.

Patients were randomly assigned into three groups.

- **In Group P (N=12, 12 eyes), Propranolol group**, 40 mg Propranolol tablet was started on daily basis at the time of first visit itself and the treatment continued till the resolution of CSR occurred or to a maximum of 2 months whichever is earlier.
- **In Group C (N=12, 13 eyes), control group**, tablet B complex as placebo were given.
- **In Group M (N=11, 12 eyes), miscellaneous group**, patients who had already been on other treatments from elsewhere before presenting to us. These patients are allowed to continue the same treatment appropriately.

The resolution was observed as the improvement of visual acuity and the symptoms like metamorphopsia along with the complete subsidence of ring reflex at the macula. The persistence of a few sub-retinal precipitates without a ring reflex was also considered as resolved. All the patients were followed up at the end of 2 weeks, 1 month, 2 months, 3 months, 4 months and 6 months.

In patients who are receiving other kinds of treatments before the first visit, the same regimen was allowed to continue. In all follow up visits, visual acuity testing, and test for colour vision and hyperopic correction were done. In addition, Amsler's grid testing was also repeated. All cases have undergone a detailed fundus evaluation as mentioned above in each visit. The findings observed in each occasions were recorded and statistically analyzed at the end of the follow up period.

Statistical Analysis:

Data was entered in Microsoft Excel and analyzed using STATA version 14. Categorical variables were summarized as proportions. Duration of follow up was summarized as median with inter-quartile range.

Association between categorical variables was done using chi square test of Fischer exact test. Statistical significance was defined as a P value of 0.05 or below.

Results:

As there were 2 bilateral cases of CSR, total 37 eyes were included in the present study. The demographic profile of study population was as shown in [Table 1].

The main victims of the disease were young people between 25 to 45 years. Among them also, the peak incidence was between 36 to 40 years of age. The male to female ratio was 2.9:1.

Table 1: Demographic variables (Total N=35)

Variables		N	%
Age groups Mean age: 35.31 years	20-25 years	01	2.86
	26-30 years	07	20.00
	31-35 years	09	25.71
	36-40 years	12	34.29
	41-45 years	05	14.28
	46-50 years	01	2.86
Gender	Male	26	74.30
	Female	09	25.70
Laterality	Right eye	14	40.00
	Left eye	19	54.30
	Both eyes	02	5.70
Presenting symptom	Defective vision	28	75.70
	Central scotoma	12	32.40
	Metamorphopsia	10	27.00
	Micropsia	02	5.40
	Photopsia	01	2.70
Recurrences	Recurrent cases	07	20.00
	Non-recurrent cases	28	80.00
Range of visual acuity at the time of presentation (Total 37 eyes)	6/6-6/12	19	51.40
	6/18-6/36	15	40.50
	6/60-5/60	03	8.10
	<5/60	00	00

Out of the 35 cases, 9 patients gave more than one specific concurrent history (one case had 3 and eight had 2) 18 patients gave single concurrent history; 8 patients had no concurrent history. [Table 2]

Table 2: Concurrent risk factors and systemic associations

Risk factors		N	%
1.	Insufficient sleep	20	54.0
2.	Insufficient food	01	2.7
3.	Physical stress	04	10.8
4.	Mental stress	04	10.8
5.	Alcohol	04	10.8
6.	Steroids	03	8.1
7.	Pregnancy	01	2.7
8.	NSAIDS	01	2.7
9.	Dapson	01	2.7
10.	B-Complex	01	2.7
11.	No specific history	08	21.6
12.	Acid peptic disease	13	37.0
13.	Migraine	04	11.4
14.	Type A behaviour	07	20.0
15.	Pregnancy	01	2.9
16.	Aphthous ulcer	03	8.6

In the Propranolol group and control group, the treatment started on the date of first visit itself. In the first instance, the resolution time in different groups were calculated from the first date of commencement of treatment until the resolution.In order to get the real course of the disease and the resolution time in this study, whether intervened with treatment or not, the date of commencement of the first symptom also included and considered in the course of the disease and its resolution time in all the 3 groups of patients. This is compared and analyzed with the data of resolution time taken from the date of commencement of the treatment. The days are rounded up to the nearest week. [Table 3]

Table 3: Comparison of resolution time in the three groups (Both from the first date of visit and first date of symptom)

Duration in weeks	Resolution time from					
	Group P (%)		Group C (%)		Group M (%)	
	Visit	Symptom	Visit	Symptom	Visit	Symptom
4-8	5 (41.7)	5 (41.7)	6 (46.1)	3 (23.1)	6 (50.0)	2 (16.6)
9-12	3 (25.0)	1 (8.3)	2 (15.4)	4 (30.8)	3 (25.0)	5 (41.7)
13-16	3 (25.0)	4 (33.3)	2 (15.4)	1 (7.7)	2 (16.7)	2 (16.7)
17-20	0 (0)	1 (8.3)	2 (15.4)	3 (23.1)	0 (0)	2 (16.7)
21-24	0 (0)	0 (0)	1 (7.7)	2 (15.3)	0 (0)	0 (0)
>24	1 (8.3)	1 (8.3)	0 (0)	0 (0)	1 (8.3)	1 (8.3)

Observing the above table, it is evident that in Propranolol group only, the percentage of eyes showing resolution in the first two months remains unchanged in both occasions (41.7%). In the other two groups, when the whole course of disease is considered, the percentage of eyes showing resolution in the first two months are markedly decreased than the first occasion (visit). [Table 3] The final visual acuity of the patients treated by various methods were analyzed below [Table 4]

Table 4: Comparison of final visual outcome in the three groups

Final Visual Acuity	Group P (%)		Group C (%)		Group M (%)	
	No. of eyes	%	No. of eyes	%	No. of eyes	%
6/6	6	50.0	8	61.5	9	75.0
6/9-6/12	5	41.7	5	38.5	1	8.3
6/18-6/24	1	8.3	0	0	1	8.3
<6/24	0	0	0	0	1	8.3
Total	12	100	13	100	12	100

Discussion:

CSR usually occurs in the age group 20-50 years and is most common in males and manifest unilaterally. The pathogenesis of this disease is considered to be due to an abnormal hyper permeable state of the choroid which leads to the

transudation of fluid producing a retinal and /RPE detachment.

In this study, the peak incidence of CSR was in the age group of 36-40 years; the mean age was 35.31 years. According to Yannuzzi et al, [1] Zweng et al, [2] Spaide RF et al [3], the mean age were 42, 41.6 and 51 respectively. Hence the present study shows the disease tends to occur earlier in Indians than in Japanese and Western people. Bennett [4] and others from B and S Mehkri [5], Gilbert CM et al [6] showed a very high male to female ratio which varied largely from 4:5 to 10:1. But in a study conducted by Spaide RF, [3] Haas A et al [7] in 1996 reported that in recent years, the female proportions affected are much higher than in the past. In the present study, even though males are more seen to be affected than females, the male to female ratio is very much decreased to 2.9:1. Even though many predisposing conditions and systemic associations of CSR like stress, Type A personality Migraine were described in the literature, what exactly trigger the occurrence of CSR; which is mostly acute in onset, is not enunciated. Among these precipitating conditions, the importance of physical and mental stress in the causation of CSR was emphasized by Bennett, [4] Gass [8] and Lipowski ZJ. [9] Its psychosomatic aspect was also supported by Fastenberg [10] and Yannuzzi LA. [1] There are reports of increased catecholamine level in the blood which have a role in the causation of CSR. This was shown by Yoshioka H et al [11] and Yasuzumi T [12] by creating animal models of CSR with intravenous epinephrine.

The present study shows clear cut evidence that patients with insufficient sleep have a propensity to develop CSR. The insufficiency of sleep was mostly because of the engagements of the patients to various tasks rather than sleeplessness due to emotional problems.

In this context, it is worth to correlate insufficiency of sleep with the multi-factorial theory of Yannuzzi LA [1] and the importance of steroids as predisposing factor of CSR shown by Wakakura M, [13] Harada T, [14] Pollak BCP [15] and Haimovici R. [16] When we consider all of these together, a different picture for the etio-pathogenesis of CSR is emerged. In stressful conditions, and in conditions of altered sleep, both ACTH and cortisol level increases in the blood, a condition which is favorable for precipitating an attack of CSR. When we compared the whole course of disease, with that taken from the first visit onwards also the Propranolol group was seen unchanged and mutually comparable, (that is 41.7% of eyes resolved in the first 8 weeks in both occasions). But the other

2 groups showed a marked difference in both occasions, indicating that these kinds of treatment (placebo and miscellaneous) have no role in the early resolution of CSR. Even though these placebo and miscellaneous groups showed most of the resolutions within 12 weeks, it is comparable with the natural spontaneous resolution of the disease (3 to 4 months). Hence in this study regarding the effectiveness of Propranolol gives a favorable role of Propranolol in the early resolution of CSR, as shown by several recent studies in this respect.

Observed findings regarding the final visual acuity, shows that beta-blockers (Propranolol) are no better than any other modalities of treatment for CSR, and has no role in the final visual outcome than placebo. All these observations in this study ultimately provides a picture that even though Propranolol is not effective in respect of final visual improvement, it has some beneficial role in the resolution time of acute CSR. This conforms to the recent reports shown by David R, [17] Spaide RF. [3]

Conclusion:

Present study reflects a tendency of earlier occurrence of CSR in Indian people than Western people and does not affect the adolescents in the age group between 15-20 years. The occurrence of CSR has a noticeable association with insufficient sleep pattern of the patient as a precipitating factor than other factors. Propranolol 40mg daily for few weeks, considered to have a favorable role in the resolution time of CSR. Propranolol makes no difference in the final visual outcome of the disease as compared to placebo or other kinds of systemic therapy.

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