

ORIGINAL ARTICLE

A Prospective Study of Dry Eyes Disease among Patients Using Oral Hydroxychloroquine at Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

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ABSTRACT

Background: Dry eye disease (DED) is a multifactorial disease of the interpalpebral ocular surface and tear film that leads to discomfort, fatigue, and disturbance in vision. In severe cases, DED can also lead to permanent visual impairment. **Materials and Methods:** It was a hospital-based prospective study, conducted at the Department of Ophthalmology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India, along with the coordination of the Department of Dermatology, Orthopedics, and Pathology from January 2019 to June 2020. **Results:** The mean age of the patients was 44.0 ± 8.63 years ranging from 24 years to 65 years. Majority (56%) were 41–60 years. Male-to-female ratio was 1:1. The difference between the mean ocular surface disease index (OSDI) on day 1 and day 90 was found statistically significant. The mean Schirmer's test value on day 1, 21.2 ± 5.1 , day 45 16.3 ± 6.3 , and day 90, 14.5 ± 6.6 . **Conclusions:** In the present study, patients OSDI scores increase as time of follow-up increases.

Key words: Dry eye disease, Hydroxychloroquine, Ocular surface disease index, Schirmer tear test

INTRODUCTION

Dry eye disease (DED) was defined as “a multifactorial disease of the tears and ocular surface” that is associated with hyperosmolarity of tear film which, in turn, leads to inflammation and damage of the ocular surface that accompanied with ocular symptoms of discomfort, fatigue, and disturbance in vision.^[1] Around the world, between 5% and 34% of people suffer from dry eye. Prevalence increases significantly with age. The large differences in prevalence figures are due to variations in study populations, geographical differences.^[2] DED is a common ocular surface disorder that considered a public health problem due to its impact on vision-related quality of life of the affected subjects.^[3]

Symptoms of dry eye vary among patients, and most commonly they include itching, grittiness, burning, sensitivity to bright light, foreign body sensation, irritation, pain, blurred vision, and contact lens intolerance. In severe cases, DED can also

lead to permanent visual impairment.^[4] Dry eye symptoms may be a manifestation of a systemic disease; therefore, timely detection may lead to recognition of a life-threatening condition. In addition, patients with dry eye are prone to potentially blinding infections, such as bacterial keratitis and also at an increased risk of complications following common procedures such as laser refractive surgery.^[5]

Hydroxychloroquine (HCQ), a commonly used conventional synthetic disease-modifying antirheumatic drug, is indicated for the treatment of rheumatoid arthritis and systemic lupus erythematosus.^[6] HCQ possesses a broad spectrum of antiviral effects against several viral infections, including coronaviruses such as severe acute respiratory syndrome coronavirus (SARS-CoV-1). *In vitro* experiments in China

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identified chloroquine as a promising therapeutic against SARS-CoV-2, while the immunomodulatory effects of its derivative HCQ may be more effective at targeting the cytokine storm.^[7]

Due to the increased prevalence of retinal toxicity in patients using HCQ American Association of Ophthalmology provided recommendation 2016 for screening of patients using HCQ which stated a baseline screening for every patients using HCQs and annual screening every 5 years or sooner if risk factors are present.^[8] The ocular side effects of long-term HCQ use include reversible corneal verticillata cornea deposits of salts within corneal epithelium to irreversible changes like bilateral bulls eye maculopathy which are rings of retinal pigment epithelium depigmentation in the macula sparing fovea leading to vision loss, central paracentral scotomas.^[9] This study has been designed to study the association of dry eyes in patients using oral HCQs, with this study, we aimed to evaluate the changes in ocular surface of a patient at the start of the therapy followed by day 45 and day 90 also to study various other ocular changes produced due to oral HCQs use.

Objective

The objective of the study was to determine the association of dry eyes in patients using oral HCQ at Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India.

MATERIALS AND METHODS

It was a hospital-based prospective study, conducted at the Department of Ophthalmology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India, along with coordination of the Department of Dermatology, Orthopedics, and Pathology from January 2019 to June 2020. Patients referred from various departments for evaluation of baseline ocular finding before start of oral HCQs were studied on day 1. The follow-up was done on day 45 and day 90. Non-probability purposive sampling technique was used to obtain data from all 30 patients.

Information was collected on a pre-structured, well-designed scheduled questionnaire. Patients referred from various departments, who were begun to start oral HCQ in between the age of 18 and 60 years were included in the study. Those who did not give their consent to participate in the study, patients who appear non-compliant and unreliable for follow-up and had ocular surface disease, pterygium, previous ocular surgery, diabetes, hypertension, history of renal diseases, history of previous retinal disease, history of tamoxifen use, patients using any other oral medication which may lead to dry eye, patients using contact lens, and females who are pregnant and lactating were excluded from the study.

The study subjects were explained with the purpose of the study and assured for confidentiality of the information which they provided us. After obtaining the written consent, the demographic data, visual acuity, and test for dry eyes were done and recorded. Symptoms of dry eye were recorded according to the ocular surface disease index (OSDI) questionnaire, Schirmer tear test. Data were entered into Microsoft Excel sheet and analyzed using Epi Info software. Descriptive statistics and inferential statistical tests were analyzed.

RESULTS

Table 1 shows that mean age of the patients was 44.0 ± 8.63 years ranging from 24 years to 65 years. Majority 56.70% of patients belonged to 41–60 years. Only 3.30% of the patients were elderly (>60 years) while 40% of the patients aged up to 40 years. Table 2 shows that in this

Table 1: Distribution of study subjects according to age

Age	Frequency	Percentage
≤40 years	12	40.00
41–60 years	17	56.70
>60 years	1	3.30

Table 2: Distribution of study subjects according to gender

Gender	Frequency	Percent
Male	15	50.0
Female	15	50.0

Table 3: For mean ocular surface disease index

Ocular surface disease index	Day-1	Day-45	Day-90
	12.9±3.2	13.7±3.8	15.7±5.3
P value	Day 1 versus day 90 <0.0001		

Table 4: Severity of dry eyes according to ocular surface disease index

Ocular surface disease index	Day-1		Day-45		Day-90	
	Number (%)	Number (%)	Number (%)	Number (%)		
Moderate	1 3.30	1 3.30	3 10.00			
Mild	12 40.00	15 50.00	12 40.00			
Normal	17 56.70	14 46.70	15 50.00			

Table 5: Table for mean Schirmer test

Schirmer's test	Day-1	Day-45	Day-90
	21.2±5.1	16.3±6.3	14.5±6.6
P value	Day 1 versus day 45 <0.0001		
	Day 1 versus day 90 <0.0001		
	Day 45 versus day 90 <0.0001		

Table 6: Severity of dry eye according to Schirmer test

Schirmer's test	Day-1		Day-45		Day-90	
	Number	(%)	Number	(%)	Number	(%)
Moderate	0	0	1	3.30	9	30.00
Mild	3	10.00	16	53.30	9	30.00
Normal	27	90.00	13	46.70	12	40.00

present study, 50% of the patients were male and 50% were female. Male-to-female ratio was 1:1.

Table 3 shows that the mean OSDI was on day 1, 12.9 ± 3.2 , day 45, 13.7 ± 3.8 , and day 90, 15.7 ± 5.3 . The difference between the mean OSDI on day 1 and day 90 was found statistically significant. Table 4 shows that day 1, 56.70% reported normal OSDI, 40.00% had mild score, and 3.30% had moderate score. On day 45, 46.70% reported no symptoms on OSDI, 50.00% had mild symptoms, and 3.30% had moderate symptoms, and on day 90, 50.00% had no symptoms on OSDI, 40.00% had mild symptoms, and 10.00% had moderate symptoms.

Table 5 shows that the mean Schirmer's test value on day 1 21.2 ± 5.1 , day 45 16.3 ± 6.3 , and day 90 14.5 ± 6.6 . The difference between the mean value on day 1, day 45, and day 90 was found statistically significant. Table 6 shows that, on day 1, 90.00% had normal Schirmer's test and 10.00% had mild Schirmer's test. On day 45, 46.70% had normal Schirmer's test, 53.30% had mild, and 3.00% had moderate, and on day 90, 40.00% had normal Schirmer's test score, 30.00% had mild, and 30.00% had moderate Schirmer's test score.

DISCUSSION

HCQ has been used for many years, initially for the treatment of malaria but now more commonly for the treatment of inflammatory diseases such as rheumatoid arthritis and lupus. It is now considered for new disease applications in adjunct cancer therapies. HCQ belongs to the quinolone family and has side effects, including retinal toxicity and dry eyes. However, there is lack of sufficient data in oral HCQ and dry eyes.

In this study, we aim to study the association of oral HCQ and dry eyes, also to study the short-term side effects of HCQ in eyes. In the present study, the mean age of the patients was 44.0 ± 8.63 years 56% ranging from 24 years to 60 years with only one patient above 60 years of age which was lower compared to a study done by Yavuz *et al.*^[10] in 2011 found that mean age of study participants was 57 years and study done by Gottenberg *et al.*^[11] in 2014 found that mean age of study participants was 56.3 years. In the present study, equal number of male and female participants was involved and there was no

statistical difference on basis of gender. Yavuz *et al.*^[10] in 2011 involved all female participants in his study.

Evaluation for dry eye was done based on subjective test OSDI, Schirmer's, and TBUT and cytology test impression cytology. In the present study, on day 1, 56.70% of patients had normal OSDI scores, 40.00% mild, and 3.30% moderate. On day 90, 50.00% reported normal scores, 40.00% mild, and 10.00% moderate range. The difference between average scores on day 1 and day 90 was found significant. However, a study done by Yavuz *et al.* in 2011^[10] reported no significant change in OSDI, but the mean OSDI 29.1 ± 18.5 was in range of severe-to-moderate score, also the symptom severity, "gritty sensation and burning sensation" changed compared to baseline evaluation.

The Schirmer's test measures the secretion of lacrimal gland. In dry eyes, the secretion of lacrimal gland is affected by various mechanisms. In the present study, Schirmer's test score was normal in 90.00% (>15 mm) and mild 10.00% of patients on day 1. On day 90, 40.00% normal, 30.00% mild (10–15 mm), and 30.00% moderate (5–9 mm). The difference between the mean Schirmer's value on day 1 (21.2 ± 5.1) and day 90 (14.5 ± 6.6) was statistically significant. A study done by Bunya *et al.*^[12] in 2013 reported that tear film osmolarity would increase in patients with decreased Schirmer's value.

CONCLUSIONS AND RECOMMENDATION

The present study evaluated the association of dry eyes in patients receiving oral HCQ. Oral HCQ results in mild-to-moderate dry eyes. Mean age of the patients was 44.0 ± 8.63 years ranging from 24 years to 65 years. Male-to-female ratio was 1:1. In the present study, patients OSDI scores increase as time of follow-up increases. We recommend that screening test such as OSDI, Schirmer's, and TBUT done at the start of therapy will be helpful to monitor the progression of dry eyes in patients using oral HCQ.

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REFERENCES

1. The definition and classification of dry eye disease: Report of the definition and classification subcommittee of the international dry eye workshop (2007). *Ocul Surf* 2007;5:75-92.
2. Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. *Continuing medical education. Dtsch Arztebl Int* 2015;112:71-82.
3. Shanti Y, Shehada R, Bakkar MM, Qaddumi J. Prevalence and associated risk factors of dry eye disease in 16 Northern West bank towns in Palestine: A cross-sectional study. *BMC Ophthalmol* 2020;20:1-8.
4. Kaercher T, Buchholz P, Kimmich F. Treatment of patients with keratoconjunctivitis sicca with Optive™: Results of a multicenter, open-label observational study in Germany. *Clin Ophthalmol* 2009;3:33-9.
5. Rao S, Revathi R, Durairajan R, Palanisamy S, Reddy SR, Nainappan M, *et al.* Spotlight on dry eye disease management. *TNOA J Ophthalmic Sci Res* 2017;55:321-4.
6. Rentsch CT, DeVito NJ, MacKenna B, Morton CF, Bhaskaran K, Brown JP, *et al.* Effect of Pre-exposure Use of Hydroxychloroquine on COVID-19 Mortality: A Population-Based Cohort Study in Patients with Rheumatoid Arthritis or Systemic Lupus Erythematosus. Available from: [https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(20\)30378-7/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30378-7/fulltext). [Last accessed on 2021 Mar 04].
7. Zabetakis I, Lorda R, Norton C, Tsoupras A. COVID-19: The inflammation link and the role of nutrition in potential mitigation. *Nutrients* 2020;12:1-28.
8. Marmor MF, Kellner U, Lai TY, Melles RB, Mieler WF. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision). *Am Acad Ophthalmol Statement* 2016;123:1386-94.
9. Tehrani R, Ostrowski RA, Hariman R, Jay WM. Ocular toxicity of hydroxychloroquine. *Semin Ophthalmol* 2008;23:201-9.
10. Yavuz S, Asfuroğlu E, Bicakcigil M, Toker E. Hydroxychloroquine improves dry eye symptoms of patients with primary Sjogren's syndrome. *Rheumatol Int* 2011;31:1045-9.
11. Gottenberg JE, Ravaud P, Puéchal X, Le Guern V, Sibilia J, Goeb V, *et al.* Effects of hydroxychloroquine on symptomatic improvement in primary Sjögren syndrome: The JOQUER randomized clinical trial. *JAMA* 2014;312:249-58.
12. Bunya VY, Langelier N, Chen S, Pistilli M, Vivino FB, Massaro-Giordano G. Tear osmolarity in Sjögren syndrome. *Cornea* 2013;32:922-7.