ORIGINAL RESEARCH

Ocular Toxicity Associated with The Short-Term Ingestion of Hydroxychloroquine

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ABSTRACT

Background: Early detection of ocular manifestations associated with hydroxychloroquine toxicity is imperative in the medical field. Due to the potential for irreversible ocular alterations that can ultimately result in vision loss, it is crucial to acknowledge that these changes may already be present by the time symptoms become apparent. **Methods:** During the two-year period, a prospective study was conducted within a hospital setting. The research encompassed a cohort of 50 individuals who were clinically diagnosed with either rheumatoid arthritis or systemic lupus erythematosus. These cases were selected from the departments of medicine and dermatology and were on the verge of initiating hydroxychloroquine (HCQ) treatment. Over a span of six months, each patient underwent a minimum of two subsequent visits, with a time gap of three months between each visit. A comprehensive ophthalmological evaluation was conducted, including optical coherence tomography (OCT) and perimetry, for each individual case. **Results:** The research findings indicated that the occurrence of ocular toxicities associated with hydroxychloroquine administration at low to regular doses (≤6.5mg/kg body weight) for a brief period (≤1 year) was observed to be 0%. **Conclusion:** Hydroxychloroquine is a pharmaceutical agent that exhibits a high degree of safety when administered within the recommended therapeutic range of low to regular doses (not exceeding 6.5 milligrammes per kilogramme of body weight). Furthermore, it is advisable to limit the duration of treatment to a period not exceeding one year.

INTRODUCTION

In the past, hydroxychloroquine, a member of the quinolone family of drugs and a derivative of the medication chloroquine, was used to treat malaria.[1] A number of rheumatic conditions, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), and Sjogren's syndrome, can be treated with hydroxychloroquine.[2] When the medicine is used to treat conditions other than malaria, the length of the treatment period and the daily doses are increased in comparison to when it is used to treat malaria. This is because the medication is less effective in treating conditions other than malaria.

The following ocular adverse effects can be caused by hydroxychloroquine: corneal deposits, posterior sub-capsular cataract, dysfunction of the ciliary body, and toxic retinopathy. [3] Hydroxychloroquine retinopathy is the most serious long-term complication associated with this medication. This condition affects the photoreceptors and also causes damage in the retinal pigment epithelium.[4] The classic form of HCQ toxic retinopathy is characterised by a bull's-eye maculopathy on both eyes. This maculopathy is brought on by a ring of parafoveal RPE depigmentation that spares the fovea.[5] Cornea verticillate, which is characterised by the diffuse punctuation deposits that accumulate over time into a vortex pattern in the corneal endothelium, has been observed to occur after 2-3 weeks of drug usage. This condition is characterised by the fact that the corneal endothelium develops a verticillate pattern as a result of the deposits. [6] It is generally believed to be a harmless ailment that goes away once the patient stops taking the medication in question and does not leave behind any lasting changes to the cornea. Verticillata, on the other hand, have been shown to generate visual disturbances such as halos and blurred vision due to the scattering of light.[7]

Therefore, both the patients and the physicians who are going to be administering the medications ought to be aware of the ocular side effects before the prescription is prescribed, and there ought to be a baseline ophthalmic evaluation performed in order to rule out retinopathy and other ocular alterations. Therefore, screening of patients who are currently being treated with HCQ continues to be one of the most significant aspects of its administration.[8]

METHODS

This prospective study was conducted on 100 eyes of 50 patients who were about to begin hydroxychloroquine medication and had been diagnosed with rheumatoid arthritis, systemic lupus erythematosus, and discoid lupus erythematosus at the medicine and dermatology department. The study was conducted on patients who were about to begin hydroxychloroquine medication. Every patient was required to attend a minimum of two follow-up appointments at three-month intervals during the course of a period of six months. The Department of Ophthalmology at VSSIMSAR in Burla, Odisha, was the location of this study. The research was conducted between the months of December 2020 and November 2022.

INCLUSION CRITERIA

- All patient who are about to begin hydroxychloroquine in the period December 2020 to May 2021.

EXCLUSION CRITERIA

- Patient who does not give consent for regular examination and follow up
- Ocular changes due to another drug
- Systemic disease [like diabetes, hypertension]

RESULTS

The present evaluation was carried out in the Department of Ophthalmology at the VSSIMSAR in Burla, Sambalpur, during the months of December 2020 and November 2022.

Table 1: Gender Distribution

Gender	No.ofPatients[n=50]	Percentage(%)
Male	8	16%
Female	42	82%
Total	50	100%

From Table-1 it is found in our study, we observed 16 % males and 82% females.

Table 2: Gender wise distribution of Ocular findings

Gender	Total no of patients	Positive ocular findings	Percentage
Male	8	0	0
Female	42	0	0
Total	50	0	0

From Table-2 it is found that ocular findings were absent in both male and female.

Table 3: Daily dosage of drug intake

Dose of the drug	No of Patients	Percentage
400mg	16	32%
200mg	34	68%
Total	50	100%

From table-3it is found that 68% patient, more no. of patients were advised 200mg/day and32% are advised 400mg/day.

Table 4: Maximum cumulative dose of HCQ in present study in a duration of one year

Daily doses	Maximum cumulative dose
200mg	73000mg
400mg	146000mg

In the current study, the length of HCQ treatment is greater than or equal to one year. Therefore, the maximum cumulative dose for patients who are advised to take 200 mg/kg per day is 73000 mg, which is equivalent to 73 grammes, and the maximum cumulative dose for patients who are advised to take 400 mg/kg per day is 146000 mg, which is equivalent to 146 grammes.

Due to the fact that autoimmune diseases are more prevalent in females than they are in males, the majority of patients who were evaluated came from the female population. Additionally, research suggests that females are more likely to consume hydroxychloroquine than males.

Table 5: Comparison of incidence of bull's eye maculopathy with other study

Studies	Percentage
Present study	0%
Levy et al (1997)	0%
Mavrikakis et al (2003)	<6yrs – 0%, >6yrs – 3.4%
Frederick and wolfe (2010)	>7yrs-1.8%
Melles-RB Marmor MF et al (2014)	5-10yrs – 2% ,>10yrs – 6%

Table 5 makes it abundantly evident that the incidence of HCQ toxicity might range anywhere from 0.8 to 6% after usage of HCQ for more than ten years, based on the findings of several investigations. In terms of the incidence percentage, our research is in line with those of Mavrikakis et al., Levy et al., and Mackenzie AH.

DISCUSSION

In the current study, there were no ocular results in either the male or female participants. The findings of this investigation are in line with the findings of the studies conducted by Mavrikakis et al [9], Levy et al [10], and Mackenzie AH [11].

According to the findings of our study, the younger age groups in our region have a higher incidence of autoimmune illnesses. According to wolfe and mamor's [12] research, however, 46% of participants are beyond the age of 60. Age greater than sixty years old is regarded as a major risk factor for an increased likelihood of developing retinopathy. All patients who were prescribed a dose of greater than or equal to 6.5 mg/kg per day are included in the present investigation. It's possible that this was the cause of 0% of the toxicity seen in our study caused by HCQ.

The accumulation of a cumulative dose more than one thousand grammes is an essential high-risk factor in the development of maculopathy. This dose is reached when patients take one tablet of 400 milligrammes each day for seven years. Since the period of HCQ medication in this study is less than one year, the cumulative dose is significantly less than one kilogramme. Patients who had failure in both their kidneys and their livers did not exhibit any signs of ocular damage. This indicates that a dose of hydroxychloroquine less than 6.5 milligrammes per kilogramme of body weight is safe even in these patients if the length of therapy is less than one year.

There are a number of conditions that have been linked to an increased likelihood of developing hydroxychloroquine or chloroquine retinopathy. It would appear that dose is one of the most critical factors, with researchers holding the belief that daily intake is more significant than cumulative dosage. [9,13,14] In point of fact, the vast majority of cases of retinal toxicity have been linked to a daily dosage of hydroxychloroquine that was greater than 6.5 mg/kg (calculated based on the patient's actual body weight). [9,13,14] We found that eight of the twelve patients in our series who were being treated with hydroxychloroquine and for whom the daily dosage could be computed had experienced retinal toxicity despite the fact that their daily dosages were below the threshold that is advised.

Age and duration of treatment are two other characteristics that increase the likelihood of retinal toxicity. Patients who are above the age of 60 and have been on medication for more than five years appear to be at a greater risk for retinal toxicity. [13,14] Only one of the patients in our series had been taking their medication for less than five years (although she had been taking a very high daily dosage), which suggests that, unless high-risk features are present, regular ophthalmologic assessment may not be warranted before 5 years, as is the case with the recommendations that are currently in place. Our series included four patients who were younger than 60 years old. When all of these data are taken into consideration together, they point to the possibility of additional risk factors for toxicity that are either not known at this time or are hypothetical. One example of this would be polymorphisms in the ABCA4 gene. [15] As is the case with many pharmacologic drugs, it is abundantly clear that idiosyncratic pathways might play a part in the progression of retinal toxicity in certain people.

CONCLUSION

With the growing use of the medicine, the various screening methods that are currently available for ocular toxicity, and the new screening guidelines, HCQ toxicity is becoming an increasingly serious issue in today's society. In our research, the ocular toxicity that can be caused by HCQ was not discovered. Hydroxychloroquine is a medicine that should only be used in low to regular doses (less than 6.5 milligrammes per kilogramme of body weight), and only for a short period of time (less than one year). If the daily dosage is less than 6.5 mg/kg, it is possible that routine ocular screening is not necessary during the first year of treatment.

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