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Ocular Affects of Hydroxychloroquine Treatment in Rheumatoid Arthritis Patients

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ABSTRACT

Hydroxychloroquine is an antimalarial drug which is used as a part of combination DMARD therapy in patients with Rheumatoid arthritis. Eye toxicity because of the accumulation of the drug in the Retina is the most serious adverse effect. The purpose of this study is to detect ocular affects of hydroxychloroquine treatment in low risk patients (without renal or liver disease) for longer duration. **Material and Methods:** Sixty two patients were studied who were taking hydroxychloroquine 200mg/day, after every six months. Best corrected visual acuity, color vision testing with ishihra chart, Amsler grid testing, slit lamp examination and fundus examination using 90D was done on each visit. Automated perimetry and ocular coherence tomography was done in suspected patients. The duration of treatment was four years. The patients selected were not having any renal or hepatic disease. Those suffering from diabetes mellitis were also excluded. The age limit was up to sixty year. **Results:** Out of sixty two patients studied over a period of seven years, only forty eight patients got their follow up examination completed for four years. All patients were females. Two patients suspected after amsler grid testing were further investigated with automated perimetry and ocular coherence tomography. These patients were found normal. Treatment in these patients was continued for four years. **Conclusion:** The recommended dose of Hydroxychloroquine 200mg/day given in RA patients is safe in low risk patients for a period of as long as four years.

Key Words: Hydroxychloroquine, rheumatoid arthritis, bull's eye maculopathy

INTRODUCTION

Hydroxychloroquine and chloroquine are antimalarial medications. These are also used in the treatment of rheumatoid arthritis and cutaneous lupus erythematosus and rashes associated with SLE. Hydroxychloroquine (HCQ) is used more frequently than chloroquine(CQ) as CQ is more likely to cause irreversible retinal damage.

HCQ mechanism of action is probably related to accumulation of the drug in the acid vesicular lysosomal system of the mononuclear cells, granulocytes, and fibroblasts. In macrophages, it may inhibit antigen presentation and IL-1 release. It is mainly used in combination with methotrexate in patients with RA. When administered in daily dosages of less than 6.5mg/kg body weight in patients with normal renal function adverse effects are uncommon. Mild side effects include headache, loss of appetite and skin rashes. These drugs are excreted slowly from the body. These are melanotropic drugs and are concentrated in melanocyte containing structures of the eye such as the retinal pigment epithelium and choroid. The ocular side effects of antimalarials are retinotoxicity and corneal deposits. These ocular side effects are the most serious ones and therefore it is recommended that eye examinations should be done at the start and then at six monthly intervals during the treatment with HCQ.

The clinical picture is charecterised by a paracentral visual scotoma with associated retinal pigment epithelial atrophy known as bull's eye maculopathy. The visual field, electroretinography, ocular coherence tomography (OCT) and amsler grid are the tests to detect toxic retinopathy.[1-4] Patients taking chloroquine are at more risk of developing classic bull's eye maculopathy than on HCQ. [5]

MATERIAL AND METHODS

Out of sixty two patients, forty eight patients who completed their followup examination were included in the study. HCQ in low dose of 200mg/day was given to each patient. Patients having renal or hepatic disease and diabetes mellitus were excluded. Their age range was 20-60years.Baseline examination was done in each patient before the start of treatment. The patients were examined after every six months. Examination include taking best corrected visual acquity, color vision by Ishihara plate, and slit lamp examination, Amsler grid testing and dilated fundus examination with 90D. Patients were asked about any distortion, blurring or blank areas on amsler grid testing. Two patients noticed slight blurring on amsler grid test. These two patients were further tested with automated perimetry and ocular coherence tomography. These tests were normal and the patients were advised to continue on HCQ.

RESULTS

We did not find any maculopathay or vortex keratopathy in fourty eight patients treated with HCQ at the end of four years. Age distribution of patients is shown in Table 1.

Most of the patients were in the age range 30-50. Twelve patients did not complete the follow up. These are excluded from the study.

Table 1: Age distribution in years.

Age (Years)	Number	Percentage
20-30	8	16.67
30-40	16	33.33
40-50	13	27.08
50-60	11	22.92

DISCUSSION

The critical dose of CQ or HCQ leading to maculopathy remains undetermined. The cumulative dose leading to signs of retinopathy was 170g to 1650g for CQ and from 57g to 1190g for HCQ. The highest cumulative doses without leading to signs of retinopathy were 790g for CQ and 1200g for HCQ. One tablet of HCQ is equivalent to 155mg base. So one tablet per day in one year corresponds to about 60g base. 6 A higher dosage per kg body mass, long duration of therapy, renal or hepatic disease are probably associated with an increased risk to develop a maculopathy.[7-8] Amsler grid testing of patients treated with CQ and HCQ is simple, rapid, reproducible and sensitive .Amsler grid is a suprathrshold target and may not detect relative central scotomas. By decreasing the perceived luminance of the amsler grid, threshold amsler grid testing provides a novel alternative to detect shallow scotomas and areas of depressed retinal sensitivity. Red amsler grid screening allows ophthalmologist to identify patients who are more likely to have HCQ maculopathy.

The main reason of having no ocular complication in our study is restriction of the prescription of HCQ only to low risk patients. Most of the patients were middle aged and all were below 60 years of age. Those having renal or hepatic disease or diabetes mellitus were excluded. Duration of treatment is very important. Most of literature review shows that ocular complications usually occur after five years. As we restricted our treatment for four years in these patients, this is the reason of having no ocular side effects in them.

CONCLUSION

HCQ is a safe drug when given in the dose required to treat RA (200mg/day) in risk free patients for reasonably long duration. Even then ophthalmological examination is necessary every six month and the drug should be stopped at the earliest sign of maculopathy.

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