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Research Article

Recording of Visual Evoked Potential in Rheumatoid Arthritis Patients with Hydroxychloroquine Treatment

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Abstract

Aim: Hydroxychloroquine HCQ is an antimalarial drug used to treat symptoms of Rheumatoid Arthritis (RA) diseases. This drug is having a certain side effect on the retina in visual system. The purpose of this study is to check the visual pathway of these patients using visual evoked potential (VEP).

Method: Thirty RA female patients with 25-35 of age range were selected. They were under 200 mg/day of HCQ treatment for at least three years. They had normal visual acuity. VEP test was examined in total subjects. Latency (msec) and amplitude (μv) were measured for each patient. Mean and standard deviation were calculated for a total case group. The result obtained was compared with the control group with the same demographical condition of the patients, but no HCQ intake.

Results: Two case and control groups had approximately same demographical conditions. The mean latency of VEP, P_{100} peak/S.D were 98/8.15 and 102/9.2 msec in control and case groups respectively. The mean amplitude of VEP, P_{100} Peak/S.D. were 8.2/2.25 and 7.4/2.18 μv in control and case group respectively. There were not statistical differences between mean latency and amplitude of VEP, P_{100} peak as far as case and control groups are concerned.

Conclusion: From the results of present study one can conclude that HCQ does not affect visual pathway which can be proved using visual evoked potential.

Keywords: Rheumatoid Arthritis; Hydroxychloroquine; Visual evoked potential

1. Introduction

Rheumatoid Arthritis (RA) is a chronic inflammatory disorder that can affect joints. RA also can damage a wide variety of body systems, including the skin, eyes, lungs, heart and blood vessels. Rheumatoid Arthritis occurs when the immune system attacks the body's tissue. It affects between 0.5 and 1% adults in developed countries. Hydroxychloroquine (HCQ) is a medication used for treatment of RA. Taking HCQ long term or at high doses may cause irreversible damage to different organs of body, including retina of the visual system. It occurs by seeing light streaks or flashes in the vision. It may be noticed by swelling or color changes in the eyes. It is important to diagnose the HCQ toxicity on retina before the patient have those symptoms. In this regard, recommend actions for screening chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy have recently been changed by American Academy of Ophthalmology taking in to account new published data on toxicity prevalence, risk factors, location of onset in retina and the efficacy of screening test. In fact, the risk of developing CQ or HCQ retinopathy depends on the daily dose and duration of treatment. With the recommended dose, the risk is <1% in the first 5 years, <2% in the first 10 years but increases to about 20% after 20 years of treatment. The maximum recommended daily dosage is 5.0 mg/kg for HCQ and 2.3 mg/kg for CQ. The two main risk factors are the daily dose and duration of treatment. The presence of kidney failure and treatment with Tamoxifen are also significant risk factors. A baseline examination should be performed at the initiation of treatment to rule out pre-existing maculopathy.

The screening test should be performed every year from the fifth year of treatment. The two tests recommended for screening are the automated Visual Field and spectral domain Optical Coherence Tomography (OCT). Multifocal Electroretinogram and auto Fluorescence Fundus imaging are only carried out secondarily to confirm the pathology [1]. In addition to the recommendations mentioned for screening HCQ retinopathy, using electro-ophthalmological techniques during the examination can be also useful. There are three electrophysiological techniques to examine the visual system as far as the pathological conditions are concerned. Visual evoked potential (VEP), electroretinogram (ERG) and electrooculogram (EOG) are among these techniques. Naser M and her colleagues on 2014 made a research on visual pathway disturbances of photophobia patients using VEP techniques. They used two types of techniques, i.e. pattern reversal checker board and flash one and they concluded that pattern reversal checker board is more efficient for this diagnosis rather than flash one [2]. Another research was made to look for retinal changes in multiple sclerosis (MS) patients with abnormal VEP using ERG techniques. The result of the survey shows retinal dysfunction of MS patients, which is proved by increase in latency of ERG, b wave [3]. Beside the pathological condition of visual system these techniques, i.e. VEP, ERG and EOG can be used to check the toxic effect of drugs on visual system.

A research work was done in 2014 to check the toxic effect of sodium valproate or Depakine on human retina using ERG. They made a cross-sectional study on 25 epileptic patients under Depakine treatment and compared the results with normal population as far as retina was concerned. They could not find any specific change in ERG of the patients, thereby Depakine does not affect the retina of epileptic patients [4]. Finally, a case was reported with visual disturbances due to Amiodarone treatment following refractive surgery. The patient was complaining from seeing

colored rings around the light after refractive surgery. VEP, ERG and EOG of the patient were not normal. The patient was instructed to stop taking the medication. The symptom improved after drug termination [5]. Base on above literature review, a research was set to look for possible visual pathway changes in patients taking HCQ.

2. Material and Method

Thirty Rheumatoid Arthritis patients that taking Hydroxychloroquine medication as treatment for at least three years, were selected for the purpose of present study. Patients uses 200 mg/day of HCQ. They were all female with an age range of 25-35 years. The visual acuity of the patients was 10/10 or otherwise corrected by suitable lenses. They did not have apparent changes in retina. An electrophysiological machine (Mangoni) capable of recording VEP, ERG and EOG was used for the purpose of recent work. Visual Evoked Potential (VEP) was tested in all patients. Three electrodes were used to connect the patient to Mangoni machine. Active, reference and earth electrodes were attached to occipital, vertex and forehead respectively. An electro-physiological paste was used between electrodes and respected places in head for better contact. VEP, P_{100} peak was taken into consideration for total patients (case) group. Latency (msec) and amplitude (μv) of VEP, P_{100} was measured for each patient. Finally, mean and standard deviation were calculated for two parameters. The same procedure was repeated for 30 subjects with normal visual system mainly retina. They were of same age range of case group, i.e. 23-35 years. The control group was females and their visual acuity was approximately similar to case group. The results obtained in two groups were compared together by SPSS version 24 to check for the significant differences between two groups.

3. Result

Case and control groups were selected for the present study. The case group included RA patients who were under HCQ treatment. Control group included normal population. There were statistical differences between the demographical conditions of the patients as for as age, sex and visual acuity was concerned. The mean latency of VEP, P_{100} peak/S.D were 98/8.15 and 102/9.20 (msec) in control and case group respectively. The mean amplitudes of VEP, P_{100} peak/S.D. were 8.2/2.25 and 7.4/2.18 μv in control and case group respectively. The differences between mean latency and amplitude of VEP, P_{100} peak were not statistically significant.

4. Discussion

The result of present work shows no demographical differences between case and control groups as far as age and sex was concerned. The result also shows no significant differences between mean latency and amplitude of VEP, P_{100} peak of case and control groups. This study was planned because other techniques beside VEP are rarely available and they are rather expensive, VEP is a technique which is used by neurologist and ophthalmologist and thereby more feasible. It is to mention that VEP is based on electrical information recorded from the visual cortex in response to stimulation of retina. Thus, the integrity of visual pathway can be tested using this method [6]. Considering above fact, it seems that retinal disturbances may affect visual pathway and this effect can be tested by VEP. So VEP was examined in Hydroxychloroquine consuming patients to look for possible changes in VEP parameters, but we could not find any alterations in VEP parameters. Recent work may be supported by following

research workers in related area. One of the early works was the report of Bishara SA and his colleague on 1989. They tested the patients receiving antimalarial therapy specifically hydroxychloroquine for different periods using contrast sensitivity test (CST), electro-retinography (ERG) and pattern reversal visual evoked potential (PVEP). The results of their work indicated CST to be most sensitive of other test in patients less than 40-year-old [7]. The above-mentioned work supports the result of present work. In 2002, Cavagna et al. worked on effectiveness of fundoscopy, electrooculography, electroretinogram and visual evoked potentials in early detection of hydroxychloroquine retinal toxicity in RA patients. They came to know that fundoscopy, electrooculography and visual evoked potentials are inefficient for early detection of hydroxychloroquine retinopathy whereas, electroretinogram allows early detection of retinal alterations during hydroxychloroquine treatment [8]. This study once more supports the result of our work. At the end it is to mention that there are some researches in contradiction with the result of present work which will be reviewed as follow, Heravian J and his team made a comparative study on the usefulness of color vision photo stress recovery time (PSRT), and visual evoked potential VEP test in early detection of ocular toxicity from hydroxychloroquine and they found that in the early stages of maculopathy, P_{100} latencies of VEP and PSRT are useful predictors of HCQ ocular toxicity and more over in patients without ocular symptoms and funduscopic changes the P_{100} latency of VEP predicts more precisely than the others [9]. Another work in this connection is reported by Fatemeh et al. [10]. They compared visual evoked potential and electrooculogram (EOG) tests in early detection of hydroxychloroquine retinal toxicity. They performed a prospective cross-sectional study on 100 patients with an age range of between 18 and 38 years. The patients were suffering from arthritis rheumatoid under hydroxychloroquine treatment. The result of their work was the efficiency of EOG and VEP for early detection of HCQ on retinal toxicity [10]. The present discussion on retinal toxicity and suitable techniques in this regard indicates the importance of this subject and still more work is necessary to reach a firm result.

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