



Probable Toxic Effect of Methotrexate on Retina Using Electroretinography

KEYWORDS

Methotrexate, Retina, Electroretinogram

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ABSTRACT Aim: Methotrexate is a drug generally prescribed to treat the patients with cancer and autoimmune diseases. The drug has different side effects on different organs of the human body. The aim of present work is to check the probable toxic effect of this drug on retina using Electroretinography.

Method: Twenty five patients taking methotrexate for one year, 2.5 mg three times per week were selected for the purpose of present study. Electroretinography was recorded in patients group. Flash ERG was the type of ERG used for this study. Latency (msec) and amplitude (μ V) of ERG b wave was measured in each patients. Mean and standard deviation was calculated for patient group.

The same procedure was repeated for 25 healthy population as far as visual system was concerned.

The results obtained in two groups compared together using SPSS version 13 to search for probable statistically significant difference among case and control groups.

Results: The mean latencies/ S.D. and amplitudes/ S.D. of ERG b wave were 47.12 ± 2.90 and 44.68 ± 1.80 and 108.92 ± 16.20 and 116.24 ± 12.30 in case and control groups respectively. The differences between two groups were not statistically significant as far as latency and amplitude of ERG b wave were concerned.

Conclusion: From the result of present work it is obvious that retina does not affected in methotrexate consuming patients which will be explained in full paper in detail.

Introduction

Methotrexate (MTX) is an antimetabolite and antifolate drug used in treatment of cancer, autoimmune diseases, ectopic pregnancy, and for induction of medical abortion. It acts by inhibiting the metabolism of folic acid. [1]

MTX can be taken orally or administered by injection. [2]

MTX has certain side effects include hepatotoxicity, ulcerative stomatitis, low white blood cell count and thus predisposition to infection, nausea, abdominal pain, fatigue, fever, dizziness, acute pneumonitis, rarely pulmonary fibrosis & kidney failure. MTX is also teratogenic and hence not used in pregnancy.

MTX has serious possible adverse effect on memory loss. It may produce neurologic damage. Neurotoxicity may result from the drug crossing the blood brain barrier and damaging neuron in the cerebral cortex. In this connection central nervous system reactions to MTX have been reported, especially when given via the intrathecal route, which include myelopathies and leucoencephalopathies. It has a variety of cutaneous side effects, particularly when administered in high doses. [3-4]

MTX may have side effect on visual system. Retina is a part of visual system which may be affected following MTX prescription in related patients. [5]

Related electrophysiological examination i.e. visual evoked potential (VEP). Electroretinography (ERG) and Electrooculography (EOG) are among the beneficial techniques to diagnose the toxic effect of drugs on retina & visual pathway. [6-8]

There exists few references available on the application of electrophysiological examination of retina in patients undergoing MTX treatment [9]. This discrepancy is more when retina of human subjects following methotrexate is concerned, and there by the present research try to overcome this discrepancy. ERG is the technique used for the purpose of this study.

ERG measures the electrical activity of various cell types in the retina, including the photoreceptors (rods and cones), inner retinal cells (bipolar and amacrine cells), and the ganglion cells. For recording ERG, the patient's eyes are exposed to standardized stimuli and the resulting signal is displayed showing the time course of the signals amplitude. Signals are very small and typically are measured in microvolts. The ERG is composed of electrical potentials contributed by different cell types within the retina, and the stimulus conditions (flash or pattern stimulus, whether a back ground light present and the colors of the stimulus and back ground) can elicit stronger responses from certain components.

ERG is used for the diagnosis of various retinal diseases [10]. Inherited retina degenerations in which the ERG can be useful may be listed as follow,

Retinitis pigmentosa, Lebers congenital amaurosis, choroideremia, Gyrate atrophy of the retina and choroid, congenital stationary night blindness cone dystrophy, usher syndrome and etc.

Base on above literature survey and lack of references on ERG and MTX toxicity the authors decided to work on probable toxicity of MTX on retina using ERG technique.

Method

In present study probable toxic effect of methotrexate on retina was worked out using Electroretinography. For this purpose 25 patients under methotrexate treatment were selected for the purpose of recent work. The patients might use any immunosuppressive drug but not the one which could produce abnormal ERG like Choloroquine. The patients were taking oral MTX 2.5 mg three times per week for 1 year. The patients were tested for ERG. Three electrodes were used to connect the patients to the machine i.e. Biomedica Mangoni which is capable of recording different electrophysiological tests including ERG. Active, reference and earth electrodes were attached to cornea, ear lobe & forehead respectively. It is to mention that active electrode was a hard contact lens. A thread shape cotton soaked with saline was placed in lens to extract the electrical response of retina and transfer it to electrode. For two other electrodes electrophysiological conductive paste was used between electrodes and skin. Before placing the contact lens the patient's eyes were dilated with standard dilating eye drops. Anesthetic drop were placed in the eyes to make them numb. After placing the electrodes, the patient eyes were stimulated by a standardized flash of light. The signal produced is an ERG wave form consisting of two waves a and b. In present work latency (msec) and amplitude (μV) of ERG, b wave were measured for each patients. Mean and standard deviation were calculated for patients group (case).

The same procedure was followed for 25 healthy population (control) as far as visual system was concerned. The patients and healthy population were matched as far as sex and age were concerned.

The results obtained in two groups were compared together using SPSS- version 13 to check the statistical relation between case and control groups.

Results:

Table 1 is the mean latency (msec)/ S.D. and amplitude (μV)/S.D. of ERG, b wave in case of patients (case) and healthy population (control) groups.

Group	ERG parameters	
	latency	Amplitude
Case	47.12/2.90	108.92/16.2
Control	44.68/1.80	116.24/12.3

Table 1: Mean latency/ S.D. and mean amplitude/ S.D. of ERG, b wave of case and control groups.

Analyzing the results obtained the differences between two groups are not statistically significant as far as latency and amplitude of ERG, b wave is concerned.

Discussion:

Result of present work is an indication of normal ERG, b wave in the patients using methotrexate for their illness or otherwise retina of these patients are intact.

Ponjavic V, and his colleagues worked on toxicity of MTX on retina using ERG. They worked on a 13 year old boy with psoriasis treated with methotrexate on a weekly basis for 8.5 year. The rod and cone responses in full-field ERG were markedly reduced in b-wave amplitude. Moreover his visual acuity(VA) was reduced to 0.3 in both eyes. After terminating the treatment, the situation was improved i.e. The ERG return nearly to normal values after 3 years and VA was also converge to approximately normal condition [5]. This study is in contradiction to the result of present study, but it should be noted that it is a case study and the treatment was continued for 8 years where as in present study the patients were administered for 1 year and their VA were not affected i.e. They had normal VA at the time of recording ERG or if at all they had any fall in VA it would have been corrected by suitable lenses.

Conclusion:

From the result of present work one can conclude that short term MTX prescription is a safe medication for retina as far as ERG b wave is concerned.

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