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Probable Toxic Effect of Methotrexate on Visual Pathway Using Visual Evoked Potential

KEYWORDS: Methotrexate, Visual pathway, Visual evoked potential.

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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 visual pathway using visual evoked potential.*

Method: Twenty five patients taking methotrexate for one year, 2.5 mg three times per week were selected for the purpose of present study. Visual evoked potential was recorded in patients group. Pattern reversal checker board was used to stimulate the eyes of the subjects. Latency (msec) and amplitude (μV) of VEP, P100 peak was measured in each patients. Mean & standard deviation were calculated for each group.

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

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

Results: The mean latencies /S.D. and amplitudes /S.D. of VEP, P100 peaks were 98.16±11.15 and 95.32±10.21 msec and 3.4±1.2 and 3.8±1.11 μV in case and control groups respectively. The difference between two groups were not statistically significant as far as latency and amplitude of VEP, P100 peak were concerned.

Conclusion: From the results of present work it is obvious that visual pathway is 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]

Methotrexate 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. Visual pathway 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 & visual pathway of the patient undergoing MTX treatment [9]. Among the tests the authors could not find the manuscript deals with toxic effect of MTX on visual pathway using VEP technique.

Visual Evoked Potential or VEP refer to electrical potentials initiated by brief visual stimuli which are recorded from the scalp overlying visual cortex. VEPs are used primarily to measure the functional integrity of the visual pathways from retina via the optic nerves to the visual pathways of the brain. VEPs better quantify functional integrity of the optic pathways than, scanning techniques such as magnetic resonance imaging (MRI). Any abnormality that affects the visual pathways or visual cortex in brain can affect the VEP. Examples are cortical blindness due to meningitis or anoxia, optic neuritis as a consequence of demyelination, optic atrophy, stroke, and compression of the optic pathways by tumors, amblyopia, and neurofibromatosis. In general, myelin plaques common in multiple sclerosis (MS) slow the speed of VEP wave peaks. Compression of the optic pathways such as from hydrocephalus or tumor also reduces amplitude of wave peaks [10].

Based on above literature review and lack of references on VEP and MTX toxicity the researches plan to work on probable toxicity of MTX on visual pathway using VEP technique

Method

In present study probable toxic effect of methotrexate on visual pathway was worked out using visual evoked potential. For this purpose 25 patients under methotrexate treatment were selected for the purpose of present work. The

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patients might use any immunosuppressive drugs but not the one which produce abnormal visual evoked potential. The patients were taking oral methotrexate 2.5 mg three times per week for 1 year. The patients were tested for visual evoked potential. Three electrodes were used to connect the patients to machine i.e. Biomedica Mangoni which is capable of recording different electrophysiological tests including VEP. Active, reference and earth electrodes were attached to occipital, earlobe and forehead respectively. Electrophysiological conductive paste was used between electrodes and skin.

To record VEP, pattern reversal checker board was selected to stimulate the eyes of the patients.

The machine parameters were selected according to standard ISCEV protocol.

Latency (msec) and amplitude (μV) of VEP, P100 peaks were measured for each patient. Mean and standard deviation were calculated for respected group.

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

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

Results:

Table 1 is the mean latency (msec)/ S.D and amplitude (μV)/S.D of VEP, P100 peak in case of patients (case) and healthy population (control) groups.

VEP parameters / Group	latency	Amplitude
Case	98.16/11.15	3.4/1.20
Control	95.32/10.21	3.8/1.11

Table 1: mean latency/ S.D and mean amplitude/ S.D. of VEP, P100 peak 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 VEP, P100 peak is concerned.

Discussion:

Result of present work is an indication of normal visual evoked potential, P100 peak in the patients using methotrexate for their illness, or in other word visual pathway of these patients are intact.

Cavaqna L, and his colleagues worked on concomitant therapy i.e. prednisone, methotrexate and hydroxycholoroquine in case of arthritis rheumatoid patients. They reported inefficacy of visual evoked potential in early detection of hydroxycholoroquine retinopathy. [9]

This research supports the results of present work because if methotrexate was harmful to visual pathway, they could have observe abnormal VEP.

Glare G et al reported progressive bilateral optic neuropathy with dense central scotomas and dyschromatopsia in a 66 year old woman following oral methotrexate treatment. This reference is in contradiction with the result of our work. [5] but it is to mention that the research is a case study and they have not record visual evoked potential in patient, where as it is a fact that optic neuropathy produce abnormal VEP.

Conclusion:

From the result of present work one can conclude that methotrexate is a safe drug as far as visual pathway is concerned and it can be proved by visual evoked potential.

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