ATYPICALITY IN PRESENTATION OF NEUROLEPTIC MALIGNANT SYNDROME CAUSED BY OLanzAPINE

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ABSTRACT

Neuroleptic malignant syndrome (NMS) is the most serious of acute neurological side effects produced by antipsychotic medication, characterized by hyperthermia, rigidity, altered consciousness and autonomic dysfunction, the prevalence of which varies from 0.4-1.4%. NMS is usually seen in treatment with high potency typical antipsychotics and very rarely with atypical antipsychotics. However, NMS cases have been reported with risperidone, clozapine, olanzapine and quetiapine. The presentations of NMS have often varied, and we report another atypicality in presentation of NMS due to olanzapine use.

Key words: Amantadine, electroconvulsive therapy, neuroleptic malignant syndrome, olanzapine

INTRODUCTION

Neuroleptic malignant syndrome (NMS) is the most serious of acute neurological side effects produced by antipsychotic medications, characterized by hyperthermia, rigidity, altered consciousness and autonomic dysfunction, the prevalence of which varies from 0.4-1.4%. NMS is usually seen in treatment with high potency typical antipsychotics and very rarely with atypical antipsychotics. However, NMS cases have been reported with risperidone, clozapine, olanzapine and quetiapine. The presentations of NMS have often varied, and we report another atypicality in presentation of NMS due to olanzapine use.

CASE REPORT

A 21-year-old male, was diagnosed as mania with psychotic symptoms, drug naïve on admission, was initially treated for 3 days with injectable haloperidol 10 mg intramuscular b.i.d. for the control of agitation and aggressive behavior. He had no past history of any psychiatric or medical illness. He was subsequently started on oral olanzapine 10 mg. However, on the seventh day of treatment with Olanzapine, he was found to have fever (temperature 98.4-99.6°F.), tachycardia (pulse rate: 100-120/min, regular), blood pressure fluctuations (150-110 SBP/ 80-100 mmHg).
DISCUSSION

The patient was suspected to be having NMS. Other differential diagnoses such as malignant hyperthermia, lethal catatonia, heat stroke, tetanus, CNS infections, septicemia, etc., however, were clinically ruled out. He had no physical or muscular injury. Laboratory investigations revealed the following: TLC-12600/cu. mm, Neutrophil-85%, CPKMB-37 µg/L (0-7 µg/L), SGOT-119 IU/L (0-45 IU/L), SGPT-66 IU/L (0-35 IU/L) and ECG suggesting sinus tachycardia.

Olanzapine was stopped and adequate hydration was maintained. In view of the unavailability of dantrolene, amantadine 100 mg b.i.d. was added. Within 3 days the patient showed improvement in terms of autonomic stability, absence of fever and reduction in rigidity. However, on the fifth day there was recurrence of the generalized rigidity. Hence bilateral electroconvulsivotherapy (ECT) was started, with patient showing adequate improvement in all the symptoms of NMS after 3 ECTs, following which he was put on quetiapine, gradually hiked to 200 mg/ day; and sodium valproate 1000 mg. All investigations, including CPK, were repeated after 1 week and were found to be within normal limits. Patient showed significant improvement in his clinical state and is maintaining well after 4 weeks of discharge from the hospital.

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Despite the patient's clinical picture, laboratory findings, and EEG results, the diagnosis of NMS was not straightforward. The patient was suspected to have NMS, but other possible diagnoses such as malignant hyperthermia, lethal catatonia, and heat stroke were ruled out. The patient's history, including a history of clozapine exposure, was also considered in the differential diagnosis.

Although extrapyramidal symptoms such as tremors, salivation, diaphoresis and orthostatic hypotension can be commonly seen with the use of olanzapine, our patient had marked rigidity and autonomic instability with absence of marked elevation of body temperature and Creatinine Kinase, an atypical form of NMS was seen in our patient.

REFERENCES

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LETTERS TO EDITOR

PHARMACOGENOMICS IN CLINICAL TRIALS: AN ANALYSIS

Sir,

Pharmacogenomics is a science that examines the inherited variations in genes that dictate drug response and explore the ways in which these variations can be used to predict whether a patient will have a good response to a drug, a bad response to a drug or no response at all. Pharmacogenetics refers to the study of inherited differences (variations) in drug metabolism and response. The distinction between the two terms is considered arbitrary, however, and now the two terms are used interchangeably.[1,2]

Clinical trials intended to evaluate the safety and efficacy of a new drug in development generally involve large number of patients and are critical to the evaluation and approval of a new drug. The role of pharmacogenetics in clinical trials is to focus on either the further exploration of genetically defined population or the confirmation of pharmacogenetic data from the population to support efficacy and safety of a drug.[3] A key component to successful pharmacogenetic research is the collection of samples during the conduct of clinical trials for a drug. Collection of whole blood samples even when no prior hypothesis has been identified may enable pharmacogenetic analysis to be conducted if at any time it appears that there is potential unexpected or unexplained variation in drug response. Since genotypes do not change in an individual, it should be possible to identify a group that will get clear benefit from the drug by reanalyzing the data from a previously completed trial through genetic stratification.[4]

The objective of the present study is to analyze the incorporation of pharmacogenetic study in ongoing clinical trials, the type of trials, indications and adequacy of informed consent form.

This was a prospective analysis of the clinical trial protocols with regard to pharmacogenetic component of the study, conducted at the Kasturba Medical College clinical research center, Mangalore. All the ongoing clinical trial protocols were reviewed to check whether any pharmacogenetic study is incorporated. Both blood sample study and tissue sample studies were considered. The informed consent forms were checked for adequacy of information. Of the 50 clinical trials that are ongoing clinical trials, 17 have incorporation of pharmacogenetics with the separately designed consent form. Common indications for pharmacogenomic studies include cancer studies with use of monoclonal antibodies (head and neck cancer, breast cancer, non-Hodgkin’s lymphoma), diabetes mellitus, hypertension, sepsis, rheumatoid arthritis, psychiatry disorders, ulcerative colitis, Crohn’s disease, atrial fibrillation. Regarding adequacy of information in the informed consent form, all the 17 trials had adequate information incorporated except that there was no information on the fate of sample collected after the specified duration of storage (15-20 years). All patients asked for consent had freely consented. Currently, there is an upward trend in the incorporation


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