Research Article

Haloperidol Induced Neuroleptic Malignant Syndrome

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ABSTRACT

Neuroleptic Malignant Syndrome (NMS) is a serious life threatening adverse drug reaction caused mainly by high potency neuroleptic agents. In this article we present a case on haloperidol induced neuromalignant syndrome. A 19 year old male patient was admitted to the hospital with complaints of high fever, muscle rigidity and extrapyramidal effects such as tremor, tardive dyskinesia. The patient was a known case of paranoid schizophrenia for 9 months and was on risperidone and olanzapine. On the previous visit to the physician the patient was prescribed with Haloperidol 5mg as risperidone and olanzapine showed no response. The patient developed mild-moderate EPS and NMS two months after the haloperidol therapy. On laboratory investigation the liver function test such as SGOT=82 IU/L and SGPT= 113IU/L were increased. The raised level of creatinine phosphokinase revealed the neuroleptic malignant syndrome. The patient was managed with supportive therapy, cessation of haloperidol and prescribed with dopamine agonist.

Keywords: Neuroleptic malignant syndrome,haloperidol, neuroleptics.

INTRODUCTION

Neuroleptic malignant syndrome is a rare but potentially life threatening idiosyncratic disorder caused by the use of antipsychotic or neuroleptic agents which results in dopaminergic blockage. The main characteristic features include hyperthermia (fever more than 38°C), muscular rigidity, altered mental status (confusion, stupor and delirium) and autonomic dysfunction.[1] The autonomic nervous system dysfunction may include tachypnea, tachycardia, diaphoresis, flushing and pallor.

In the laboratory investigation it seems an increase in creatinine phosphokinase(CPK), leukocytosis and mild elevation of lactate dehydrogenase, alkaline phosphatase and liver transaminase. In severe cases abnormalities in electrolyte level such as hypocalcemia, hyperkalemia, hypomagnesemia and metabolic acidosis can occur. The incidence of neuroleptic malignant syndrome ranges between 0.5%-3% of patient taking neuroleptic medications.[2] Most frequently associated drugs which develop neuroleptic malignant syndrome are potent typical antipsychotic agents such as haloperidol, fluphenazine, chlorpromazine and prochlorpromazine.[3]

NMS may develop within hours or day after the exposure to the causative agents, which increase the symptoms within 2 weeks or nearly within 30 days.[4] The pathogenesis in which NMS occurs is thought to be either from D_2 receptor blockade and decreased availability of dopamine.[5]

The treatment of neuroleptic malignant syndrome should always start with the withdrawal of the suspected offending agent and supportive care should be given. Commonly used pharmacological agents are dantrolene, bromocriptine and amantadine. We present a discrete case with neuroleptic malignant syndrome developed due to neuroleptic agent (haloperidol).

Case Report

A 19 year old male patient was admitted in the hospital with presenting complaints of suspicious fearfulness, auditory hallucination, insomnia, loss of appetite, suicidal behavior and fearful that family members want to kill him. He was a known case of paranoid schizophrenia for past 9 months and was under the treatment with risperidone and olanzapine. Before 2 months, the patient was switched to haloperidol 5 mg BD along with trihexyphenidyl 2mg and lorazepam 2 mg orally twice a day. After two days the frequency of haloperidol was changed to 1-0-2. On prior to hospital admission he has high grade fever and reduced oral intake. Upon hospitalization he experienced with mild rigidity over proximal upper limit (cog wheel type)tremor and tardive dyskinesia. On the first day of admission the patient has high grade fever at 104°F. He was diagnosed with severe extrapyramidal symptoms, moderate to severe suicidal risk and haloperidol induced neuroleptic malignant syndrome.

Laboratory investigation showed that the blood count were normal. In the liver function test there is an increase in SGOT 82 U/L (Normal <40 u/l) and SGPT 113 U/L(<38U/L) which reveals mild hepatic changes.

The creatinine phosphokinase level was 594U/L(normal 55-170U/L) and CK-MB was 26U/L (normal <28 U/L).All the physical examination and the laboratory interpretations where supporting the diagnosis of

haloperidol induced neuroleptic malignant syndrome with severe extrapyramidal symptoms.

On management he was first entailed with cessation of haloperidol. Then he was treated with amantadine 100mg orally once daily, trihexyphenidyl 2mg thrice a day and intravenous administration of promethazine 50 mg slow IV twice daily. The patient was also administered with paracetamol 1000mg intravenously three times a day for fever. Routine monitoring of laboratory parameter especially CPK was done. On the third day of hospital admission CPK was found to be 461 U/L, SGPT 95 U/L, and SGOT 69 U/L. The patient was given psychiatric follow up till the symptoms subside.

DISCUSSION

Haloperidol is a potent dopamine D_2 receptor blockade agent. Blockade of dopaminergic projection in the temporal and prefrontal areas which includes the limbic system and the mesocortical area was considered to be responsible for the antipsychotic activity of haloperidol.[6]

Neuroleptic malignant syndrome is considered as a neurologic emergency and the early detection and proper medical management improves the patient outcome. A wide range of antipsychotic drugs were associated with the occurrence of neuroleptic malignant syndrome including phenothiazines, butyrophenones, thioxanthenes, benzamide and miscellaneous agents such as clozapine and risperidone.[7] According to the previous reported cases young adult makes predominate with the incidence of neuroleptic malignant syndrome. The earlier physician recognition and better therapeutic modalities result in the decreased mortality rate in recent years.[8] The major complications associated with neuroleptic malignant syndrome are rhabdomylosis due to sustained muscle rigidity and muscle breakdown. The other common complications are renal failure pulmonary edema, pulmonary embolism, respiratory distress syndrome, sepsis and myocardial infraction.[9]

The management of neuroleptic malignant syndrome primarily requires prompt discontinuation of the offending neuroleptic agent. Intensive monitoring and supportive therapy should be provided to the patient. Dopamine agonists such as bromocriptine and amantadine were mainly used for the management of neuroleptic malignant syndrome. In this patient haloperidol was discontinued and the patient was first managed with IV fluids over 24 hrs. Amantadine, a dopamine agonist which act through presynaptic mechanism and counteract dopaminergic inhibition were prescribed. Amantadine was administered orally 100mg once daily and continued as discharge medication. Recurrences of NMS can occur when a patient is restarted on a typical antipsychotic with high potency or too quickly after their initial episode. In those patients who require continued antipsychotic treatment it should be prescribed after careful monitoring of 2 weeks for an oral antipsychotic or at least 6 weeks for a depot form.

CONCLUSION

NMS is a rare but potentially fatal complication which is caused by the dopamine receptor antagonist especially high potency neuroleptic agents such as haloperidol.

Physicians should be aware of this condition and the early detection, discontinuation of offending agents, supportive therapy, and reduction of risk factors improves the patient physically and economically.

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