Isoniazid Induced Psychosis

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Abstract

Tuberculosis is an important public health problem. First line therapy for tuberculosis includes isoniazid, rifampicin, ethambutol and pyrazinamide. A female patient aged 45 years, developed psychosis following first line antitubercular therapy (ATT). Patient was not taking pyridoxine along with ATT. Isoniazid was withdrawn and tablet pyridoxine was added in the therapy. Patient recovered from psychosis. Psychosis in a patient on ATT can be one of the complications of isoniazid.

Keywords: Tuberculosis, isoniazid, psychosis

INTRODUCTION

Tuberculosis is an important public health problem with more than one-third of the population in the world affected by the disease.¹ First line therapy for tuberculosis includes isoniazid (5 mg/kg once a day), rifampicin (10 mg/kg once a day), ethambutol (15-25 mg/kg once a day) and pyrazinamide (20–30 mg/kg once a day).² Isoniazid, also known as isonicotinic acid hydrazide (INH) was introduced in 1952 by Robitsek, Selikoff and Ornstein and has been the most widely and effectively used antitubercular drug.³ The common adverse effects of isoniazid are peripheral neuropathy, hepatitis, and rash. Rarely, psychosis, convulsions and even death have been reported.⁴ INH may cause psychosis by the inhibition of monoamine oxidase enzyme and decrease in N-Methyl D-Aspartate receptors caused by the INH induced oxidative stress. INH also interacts with the pyridoxine metabolism in the tissues to form a pyridoxal-INH complex which causes pyridoxine deficiency, that leads to the reduction in the concentration of inhibitory neurotransmitters.⁵ A case report of INH induced psychosis in tuberculosis patient is presented.

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CASE DESCRIPTION

A 45 year old female was admitted in the tertiary care hospital with chief complaints of several episodes of vomiting, fever, pain in abdomen and difficulty in breathing with cough. The patient was known case tuberculosis on irregular anti-tubercular therapy (ATT). The patient was admitted and was administered isoniazid (300mg), rifampicin (450mg), ethambutol (1000mg) and pyrizinamide (1200mg) once daily. For vomiting she was also given tablet pantoprazole and domperidone once daily, tablet ondansetron thrice daily and antacid four tea spoonfuls thrice daily. On day two, injection methylprednisolone sodium succinate 1000mg was also started.

On day three of the treatment, the patient developed abnormal behavior with altered sensation, for which psychiatric reference was sought. A computed tomographic examination of head (CT-head) was advised and treatment with tab lorazepam 2mg at night and tab etizolam 0.25mg once daily was started, keeping the ATT on hold for the time being. The CT-head ruled out any acute infarct or similar organic cause so after a thorough neurological examination the patient was diagnosed with psychosis. She was then started on injection dexamethasone 4mg thrice daily, injection mannitol 100ml intravenous thrice daily. On day four, isoniazid was excluded from the treatment and tablet pyridoxine 40mg once daily per orally was added. Injection methylprednisolone was also stopped. On day five onwards the condition of the patient started improving. After full recovery she was discharged with the advice to continue modified ATT with pyridoxine and was subsequently called for review in the OPD.

DISCUSSION

Mechanism of neuronal toxicity due to INH is not well defined. Destruction of vitamin B complex is well accepted mechanism in both acute psychosis and peripheral neuropathy due to INH. INH metabolites inhibit the activation of pyridoxine to pyridoxal 5-phosphate. Pyridoxal 5-phosphate is a cofactor of the enzyme glutamic acid decarboxylase which catalyzes the conversion of glutamic acid to gamma aminobutyric acid (GABA), the major inhibitory neurotransmitter in the central nervous system. The resulting GABA depletion leads to central nervous system dis-inhibition and seizures, following INH overdose. Further, INH also inhibits monoamine oxidase and decreases the NMDA receptors by the inducing oxidative stress. A number of psychiatric symptoms have been previously described to be associated with INH including paranoid delusions, auditory, visual as well as tactile hallucinations, suicidal ideation and mood disorders.

Cases of isoniazid-related psychiatric disorders reported in the literature include psychosis, obsessive–compulsive neurosis, and mania. The susceptibility to psychosis increases with age, personal and family history of psychiatric disorders, malnutrition, alcohol intake, diabetes, renal/hepatic insufficiency, hyperthyroidism, etc. Since this patient had not been taking the pyridoxine supplementation there was predisposition to central nervous system adverse effects. Conditions leading to vitamins and amino acids deficiency may
inhibit neurotransmitter (GABA) synthesis and may precipitate psychosis like condition. Supplementation of pyridoxine with INH is rational to prevent neurological adverse effects such as acute psychosis and peripheral neuropathy.

**CONCLUSION**

Pyridoxine tablet should be added to the ATT regimen as a prophylaxis to prevent neurological complications viz. peripheral neuropathy and acute psychosis.

**REFERENCES**