



## Case Report on Isoniazid Induced Generalised Tonic Clonic Seizure in Pediatric Department

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### ABSTRACT

Isoniazid, a vital drug in antitubercular regimen has reported many Adverse Drug Reactions (ADRs) in patients. The main adverse effect of Isoniazid includes neurotoxicity, psychosis, peripheral neuritis and hepatitis. Seizure, a minor complication of Isoniazid therapy has been reported. The mechanism behind the drug induced seizure has found to be inhibition of GABA synthesis. The keystone of the therapy is the administration of pyridoxine in a dose equivalent to ingested isoniazid. We are presenting a case that developed seizure after completing 2 months of ATT regimen containing Isoniazid.

**Keywords:** Isoniazid, Antitubercular regimen, Seizure

### INTRODUCTION

Isoniazid or isonicotinic acid hydrazine is a potent antimicrobial agent, acts by inhibiting the synthesis of mycolic acid, unique fatty acid component of mycobacterium cell wall. Isoniazid induced neurotoxicity includes neurological manifestation like seizures, memory loss, encephalopathy, ataxia, peripheral neuritis which usually occurs in slow Isoniazid acetylators<sup>1</sup>. It is among the common cause of drug induced seizure in USA<sup>2</sup>. The mechanism behind the Isoniazid induced seizure is thought to be inhibition of Gamma Amino Butyric Acid (GABA) synthesis. Isoniazid hydrazone, an Isoniazid metabolite inhibits pyridoxine phosphokinase. This enzyme is responsible for the conversion of pyridoxine (vitamin B<sub>6</sub>) to its active form, pyridoxal 5 phosphate. Pyridoxal 5 phosphate is a cofactor for glutamic acid decarboxylase enzyme, required for the production of GABA, one of the major inhibitory neurotransmitter. Decrease in GABA level increases susceptibility of seizure<sup>3</sup>. Our case report is a 14 year old child who developed seizure caused by Isoniazid.

### Case Report

A 14 year old female child was admitted in the hospital with the complaints of 2 episodes of generalized tonic clonic seizures 4 days before, 1 episode of vomiting containing food particles and occasional headache for past 2 months. She also complaints of loss of appetite, loss of weight, evening rise of temperature, cough with expectoration and breathlessness. She is a known case of pulmonary tuberculosis and completed her 2 months of ATT Category I regimen-Isoniazid 50 mg, rifampicin 100 mg, pyrazinamide 300 mg and ethambutol 800 mg in a thrice weekly schedule.

On examination she was conscious, oriented, afebrile with pulse rate of 78 bpm, BP 110/70 mmHg and

respiratory rate of 18 bpm. Her cerebral functions were normal with no meningeal irritation. Complete blood count showed Hb 11.4 g/dl, total WBC 7.8 X 10<sup>9</sup>/L with differential count of lymphocyte 28.6%, monocytes 8.5% and granulocytes 62.9%, ESR 20 mm/hr, RBC 3.83 X 10<sup>12</sup> L, PLT 150 X 10<sup>9</sup> /L and urine routine analysis was normal. Her peripheral smear implies few hypo chromic RBC, WBC adequate in number and distribution and PLT is adequate. LFT was normal (SGOT-15 IU/L & SGPT-12 IU/L). AFB sputum test was positive. Chest X-ray showed right sided effusion with lower lobe consolidation.

So, ATT withhold for first 2 days and started Injection Lorazepam 4mg. As a clinical pharmacist based on clinical examination and investigations, we suggest that Isoniazid can induce seizure as its minor complication and informed to the physician. On the third day, Lorazepam discontinued and ATT restarted along with T. Benadon (Pyridoxine) 40 mg twice a day. Patient improved after taking this regimen. Child was discharged with ATT and pyridoxine supplement. She felt better on her follow up.

### DISCUSSION

Isoniazid is an essential component of all antitubercular regimens. It is well tolerated by most patients. Peripheral neuropathy and neurological side effects including paresthesias, numbness and mental disturbance have been experienced in some patients.

Rarely seizure was also reported in some patients with no history of seizure<sup>4</sup>. In our case, all other possible causes of seizure were ruled out by clinical examination and relevant investigations. Child has no previous personal and family history of convulsion. Isoniazid induced seizure is thought to cause by absolute deficiency of pyridoxine (Vitamin B<sub>6</sub>). Pyridoxine is a vital cofactor for the production of the inhibitory neurotransmitter, GABA. This depletion in GABA levels increases the susceptibility of



seizures. So administration of pyridoxine helps to prevent the Isoniazid induced neurotoxicity<sup>5</sup>.

Lorazepam 4 mg administered intravenously as the initial approach to the seizure control with repeated required doses. Most of the authors recommend that pyridoxine should be given in the equivalent dose of the injected Isoniazid (gm/gm replacement)<sup>6</sup>.

If the amount of Isoniazid intake is unknown, IV administration of 5 gm Pyridoxine can be administered safely. If seizure persists, repeated dosing may require. But Gupta S.K noted that pyridoxine does not help in the seizure with single conventional dose of Isoniazid<sup>7</sup>.

In our case, though the patient was taking Isoniazid for the past 2 months, pyridoxine was not given to the patient who is very much essential.

She feels better after taking pyridoxine along with Isoniazid suggesting that pyridoxine deficiency due to Isoniazid was the reason for seizure and was corrected by the administration of pyridoxine.

### CONCLUSION

In our case we pointed out the complications of antitubercular regimen, Category-I mainly with the drug Isoniazid.

Physicians should be aware about the ADRs of Isoniazid. Prolonged use of Isoniazid might lead to pyridoxine

deficiency and thereby seizure. Sometimes it can even occur with single therapeutic dose.

So while prescribing Isoniazid, pyridoxine is must for preventing neurological complications due to the drug.

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