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ISONIAZID INDUCED SEIZURES IN TB/HIV PATIENT WITH SINGLE THERAPEUTIC DOSE

Medicine

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ABSTRACT

ISONIAZID is a potent antitubercular drug which has early bactericidal activity. INH acts on extracellular rapidly multiplying bacilli.The most common side effects reported with INH administration are Nausea, Vomiting, Abdominal discomfort, Gastritis, and rarely hepatotoxicity and peripheral neuropathy.

INH overdose can result in recurrent seizures, metabolic acidosis, coma and even death..Here we report a case of 30-year lady who developed generalised tonic clonic seizures after first dose of INH as a part of CAT-1 ATT Regimen.

KEYWORDS

INH, Seizures, ATT

INTRODUCTION

ISONIAZID is a potent antitubercular drug which has early bactericidal activity, prevents emergence of drug resistant mutants to any other added drugs and has a low rate of adverse drug reactions. It is cheap and widely used drug in TB treatment. INH acts on extracellular rapidly multiplying bacilli.

The most common side effects reported with INH administration are Nausea, Vomiting, Abdominal discomfort, Gastritis, and rarely hepatotoxicity and peripheral neuropathy.

INH overdose can result in recurrent seizures, metabolic acidosis, coma and even death. This can occur when INH dose exceeds 80-150mg/kg of body weight. But therapeutic dose of INH rarely cause seizures(600mg). Hence, we report a case of 30-year HIV POSITIVE lady who developed generalised tonic clonic seizures after first dose of INH as a part of CAT-1 thrice weekly intermittent antitubercular regimen with INH 600mg, rifampicin 450mg, ethambutol 1200mg and pyrazinamide 1500mg.

CASE REPORT

A 30-year-old female working in garments shop came to pulmonary medicine department in R.L. JALAPPA medical college with complaints of cough, fever, breathlessness, since 6 months. She gave history of weight loss and reduced appetite for the past 3months.Sputum examination was done from RNTCP lab, found to be negative but the chest x ray was showing upper and middle zone infiltrates characteristic of tuberculosis. We repeated the sputum but again it was negative for AFB.We went to lab and saw the slide. But the slide was full of saliva. She was diagnosed with smear negative PTB and was started on CAT-I ATT intermittent RNTCP regimen with INH 600mg, rifampicin 450mg, ethambutol 1200mg and pyrazinamide 1500mg thrice weekly. On the first dose of ATT, she developed 1 episode of GTCS after 2 hours of taking ATT.Patient was given stat dose of inj. lorazepam 4mg IV, the seizures subsided and there were no further episodes. Thorough nervous system examination revealed no abnormality, neurologist consultation was sought and advised CT brain which came to be normal. There was no family history or personal history of epilepsy and no other ill habits and was not on any long-term drugs.

The ATT was stopped temporarily for 2 days after the episode of seizures. Patient was again restarted with CAT-I ATT but patient developed one more episode of GTCS after 1 hour of treatment, which subsided with inj. lorazepam. Patient was restarted with altered regimen consisting of rifampicin 450mg, ethambutol 1200mg, pyrazinamide 1500mg, levofloxacin 500mg OD.INH was withhold. Patient tolerated this drugs without any further seizure episodes.

But the patient was permanently complaining of abdominal pain and difficulty in swallowing and we came to know that husband is not living with her for the past 10years.Initially patient denied ICTC testing but on further counselling she gave the blood sample which found to be retro positive. Patient was started on TAB.PYRIDOXAMINE and TAB.SEPTRAN-DS and continued with CAT-1 ATT with altered regimen and was referred for ICTC centre for further management. Her sputum was sent for culture and sensitive, report awaited.

DISCUSSION

INH is an important first line antitubercular agent, which has early bactericidal activity and prevents emergence of drug resistant mutants when combined with other antitubercular drugs. The side effects associated with INH are very minimal. The common side effects include nausea, vomiting, abdominal pain, gastritis, hepatotoxicity, and rarely peripheral neuropathy. Convulsions associated with INH therapy is rarely seen and has been reported in the past.

INH neurotoxicity characterised by recurrent seizures, metabolic acidosis, coma and even death. The neurotoxicity is usually associated with INH overdose of 80-150/kg of body weight. The first signs and symptoms of INH toxicity may appear with in 30minutes to 2 hours after ingestion and may include nausea, vomiting, fever, ataxia, slurring of speech, peripheral neuritis, dizziness and stupor. The symptoms are usually followed by grandma seizures and coma. The seizures are often refractory to anti convulsants. Respiratory failure and death can follow.

Convulsions are reported in patients treated with INH, with no prior history of seizure disorder or with family history of seizure disorder. However, convulsions with a single therapeutic dose of INH, few cases have been reported. In our case, there was no previous personal or family history of epilepsy. All other causes for seizures were ruled out by neurologist consultation and other relevant investigations.

The other thing what we noticed is patients with HIV/TB are more prone to produce INH induced seizures. There was similar case of TB/HIV in which patient developed seizures after first dose of INH. Whether TB/HIV patients are more prone to develop INH induced seizures, more data is needed.

INH is thought to cause seizures by interfering with synthesis of Gamma-amino butyric acid(GABA).INH metabolites hydrazones inhibit pyridoxine phosphor kinase which is an enzyme necessary for the conversion of pyridoxine (vitamin B6) to its active form pyridoxal 5 phosphate.Pyridoxal 5 phosphate is a cofactor in the synthesis of GABA which is a major inhibitory neurotransmitter in the brain. This

reduction in GABA levels increases the susceptibility to seizures. Thus, the neurotoxic effects of isoniazid are specifically encounteracted by the administration of pyridoxine.Pyridoxine 100mg/day oral/parenterally until symptoms subside can be given. If patient not responding will require treatment with amitriptyline.

To conclude, INH can induce seizures even with single therapeutic dose 600mg. There is an increased incidence of INH induced seizures in TB/HIV patients (more data required). Physicians should be aware that seizures can occur with the single therapeutic dose of INH in TB/HIV patients.

SUMMARY

INH is very effective first line anti tubercular drug having early bactericidal activity and prevents the emergence of drug resistant mutants when combined with other first line drugs. INH toxicity (characterized by seizures, metabolic acidosis, coma and death), is rarely seen with INH(80-130mg/kg). But seizures with single therapeutic dose of INH rarely reported and there is increased incidence of seizures in TB/HIV patients.

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