in the glutamate-GABA shunt.21-23 Until recently it was a common belief that high-dose pyridoxine therapy was without toxicity in humans. Patients who were treated with high doses of pyridoxine (eg, a total of 52 g [almost 1 g/kg] or single dose of 70 to 357 mg/kg) were described as having no toxicity.24 However, pyridoxine has neurotoxic properties, and recently, high doses of pyridoxine (132 and 183 g [a total amount >2 g/kg] given to two adults during a 3-day period for false mole mushroom poisoning) have been reported to cause acute, profound irreversible sensory loss.24 Because of such reports, only a gram-for-gram replacement with pyridoxine is recommended if the amount of INH ingested is known.9,21 The calculated amount of pyridoxine should be given in 15 to 30 minutes. If the INH dose is unknown, 5 g of pyridoxine should be given as a single dose and repeated at 6- to 20-minute intervals until the seizures are controlled.27 Multiple large doses of pyridoxine should be avoided.25

Commonly used anticonvulsants such as diazepam, phenytoin, and phenobarbital, when used alone, may not be effective in controlling INH-induced refractory seizures; however, when they are used with pyridoxine, seizures will be controlled.25 If the desired amount of parenteral pyridoxine (gram-for-gram of ingested INH) is unavailable, diazepam can be used simultaneously to potentiate the antidotal effect of suboptimal dose of pyridoxine26 (as seen in our case 3). If a parenteral form of pyridoxine is unavailable, pyridoxine tablets may be crushed and given orally as a slurry in a dose of 1 g of pyridoxine for each gram of INH ingested.27 Phenytoin should be used with caution, because slow acetylators of INH or those with high serum INH levels may develop phenytoin intoxication, because INH inhibits phenytoin metabolism.10,28

In a study of the pharmacokinetics of INH ingestions with and without accompanying oral-activated charcoal in volunteers, it was shown that when a single dose of oral-activated charcoal was taken simultaneously with INH, it totally prevented the measurable absorption of the test dose of INH.29 Because INH absorption is rapid, delayed administration of activated charcoal (eg, 1 hour after INH ingestion) may not be effective,30 thus, gastrointestinal evacuation and activated charcoal administration should be done as soon as possible after acute INH ingestion.

In conclusion, we have seen an increased incidence of acute INH neurotoxicity because of the resurgence of TB. Others as well may see a similar rise based on local trends in TB infection and disease. INH should be given only when clearly indicated, and all the patients receiving INH should be counselled about the harmful effects of overdose. Extra missed doses should not be taken all at one time. A clinician should evaluate all adolescent patients for medication-taking behavior as well as possible suicidal tendencies before INH is prescribed. With patients at high risk, INH therapy should be taken only in the presence of a parent or guardian to prevent accidental overdose. To prevent the availability of a large amount of INH, only a 1-month supply should be prescribed at a time. Acute INH neurotoxicity should be considered in children presenting with seizures with or without fever. Seizures should be considered to be caused by INH until proven otherwise in patients with a known access to the drug, which includes not only the patients but also household members taking INH. Parenteral pyridoxine, the specific antidote for INH-induced refractory seizures, should be placed in the emergency cart of every emergency department in areas where acute INH neurotoxicity is likely to be seen because of the resurgence of TB.

**ADDENDUM**

In the last 5 months, we have treated two more patients, girls ages 12 and 16, both receiving daily INH therapy for TB prophylaxis, who ingested INH in suicide attempts. One was admitted with status epilepticus and coma and the other with vomiting and abdominal pain.

**REFERENCES**

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