Asymptomatic rhabdomyolysis after pyridoxine treatment of an isoniazid intoxication

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Introduction
Isoniazid (INH) is an antibiotic and first-line medication in treatment of tuberculosis and is metabolized in the liver via acetylation. The metabolites are excreted in the urine without known renal toxicity. Intoxication with Isoniazid leading to elevated creatine kinase level is rarely described in literature.

Case report
A 22 year-old man of Asian origin deliberately ingested 75 x 100 mg tablets isoniazid. Half an hour later he developed a cerebral seizure. However, he was fully awake (GCS 15) 30 min after the ambulance arrived. The consulted emergency physician documented somnolence (GCS 8) and another seizure. The patient was sedated with midazolam and fentanyl, orally intubated and mechanically ventilated. At admission 90 min after ingestion he was cardiopulmonarily stable. However he had a marked metabolic acidosis (pH 6.98), an increased lactate (at admission 20 mmol/L, which declined to 0.7 mmol/L after 7 hours) and an increased serum-creatinine (1.2 mmol/L at admission). Creatine kinase (CK) rose within three hours from 581 U/L to 1135 U/L. ECG showed multiple ventricular extrasystoles.

The patient received 40 mg diazepam and 5 g pyridoxine intravenously within 30 min. The level of isoniazid fell from 16 µg/mL two hours after ingestion to 13.5 µg/mL 20 min later. The acidosis resolved and the patient regained sinus rhythm. After stopping sedation the patient could be extubated 18 hours after ingestion. The further course was uneventful and the patient was transferred to a psychiatric ward four days after ingestion.

Meanwhile, the patient had a remarkable course of rhabdomyolysis, which was clinically apparent. At admission (t=2h) his CK was 581 U/L and increased to 1135 U/L (t=5h). At day five it rose up to 29,000 U/L. The patient was therefore transferred back to the medical ward. Here, the CK returned to normal values under symptomatic observation. The patient never exhibited clinical symptoms of rhabdomyolysis nor renal failure.

Discussion
Rhabdomyolysis can be caused by intoxication, extreme physical exercise and seizures and has normally a linear relationship with the risk of acute renal failure. Isoniazid poisoning can show severe symptoms like seizures, coma, metabolic acidosis and rhabdomyolysis (2). Isoniazid at therapeutic doses can also cause rhabdomyolysis (1.3). The peak of creatine kinase was reached on day 5 and declined on day 6. In literature, 100% of intoxicated patients experienced seizures, but only 60% demonstrated rhabdomyolysis (2). This suggests that isoniazid and its metabolites may induce rhabdomyolysis on a direct toxic effect on the muscles. It is further known that treatment with pyridoxine can also cause rhabdomyolysis without clinical symptoms (4).

Conclusion
Rhabdomyolysis after isoniazid intoxication and pyridoxine treatment is an infrequent, but known complication. Specific treatment is not necessary. Repeated evaluation of renal function along with rehydration seems sufficient.

References