Case Report

Primidone and Liver Abnormalities: A Case Study

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Practitioners often encounter unavoidable polypharmacy for the elderly population. With significant evidence supporting a high prevalence of adverse reactions in this population (Beers Criteria), the need for appropriate medication selection becomes increasingly important. Inappropriate and/or unnecessary medication significantly increases hospital admission, morbidity, and mortality rates. Uncommon adverse effects are often discovered many years after medication introduction to market. In this case study, the connection between primidone and liver abnormalities is confirmed in an elderly patient.

PATIENT CASE

A 77 year old Caucasian female was admitted to the hospital due to right ankle dislocation caused by a fall following a syncopal episode. The patient's diagnoses prior to admission included: hypothyroidism, GERD, essential tremor, and borderline diabetes. Her home medications were as follows: esomeprazole 40 mg QD, levothyroxine 125 mcg QD, fluoxetine 20 mg QD, hydroxyzine 10 mg Q12h, milk of magnesia as needed, miralax as needed, and primidone 100 mg BID.

The causation of the syncopal episodes was addressed after completion of a ankle surgery. Internal medicine was consulted to help determine the reason for fainting. The patient reported a history of presyncopal episodes for the previous 10 years, but only 2 episodes of actual syncope. The first episode occurred about 2 months before hospital admission while outside gardening. She was worked up by a neurologist and cardiologist with no significant findings. The episode resulting in hospitalization occurred while the patient was taking a shower.

A full workup was ordered for completeness since this episode caused injury. This included: echocardiogram, MRI, MRA, CBC, BMP, TSH, and liver enzymes. Echocardiogram results showed an ejection fraction of 65-70% and grade 1 diastolic dysfunction. The MRI of the brain revealed mild atrophy and low grade sinusitis. Overall, the brain and heart were found to have no significant abnormalities which could explain her syncope. Therefore, the cause of the patient’s syncope was determined to be vasovagal in nature. The patient and family member were educated on the cause of the patient's syncope was determined to be vasovagal syncope, but her hospital stay was prolonged due to some worrisome incidental findings.

The patient was advised to stay away from this medication and all medications in this class. During the remainder of her hospital stay, liver enzymes were checked repetitively. A steady decrease in liver enzymes, especially bilirubin levels, was found which supported the diagnosis.

Possible diagnoses at this point were determined to be sclerosing cholangitis, primary biliary cirrhosis, and intrahepatic cholestasis. Multiple specialty tests were conducted such as antinuclear antibody, mitochondrial, and anti-smooth muscle antibody. All tests came back negative which ruled out sclerosing cholangitis and primary biliary cirrhosis as definitive diagnoses. The patient's jaundice was improving during this time, and she was also experiencing less itching. Therefore, primidone was decided to be the cause of intrahepatic cholestasis. This medication should have been stopped 2 weeks prior to admission due to itching. Despite physician recommendation to discontinue the medication, the patient continued to take it due to significant control of her essential tremor. Since an adverse reaction to this medication was documented previous to hospital admission, the patient was taken off the medication while inpatient. The patient was advised to stay away from this medication and all medications in this class. During the remainder of her hospital stay, liver enzymes were checked repetitively. A steady decrease in liver enzymes, especially bilirubin levels, was found which supported the diagnosis.

RESEARCH FINDINGS

PubMed, Galileo, and Qx Read were used to conduct research. Limited publications were found reporting a link between the anticonvulstant, primidone, and hepatic abnormalities. Many of our references are from the 1980s which can be considered outdated.

Primidone’s metabolism is through the liver, and the drug is a known CYP450 enzyme inducer. However, the drug’s adverse effects do not include liver abnormalities. Common side effects are ataxia and vertigo. The article “Factors that
affect the induction of gamma glutamyltransferase in epileptic patients receiving anti-convulsant drugs” had 3 of 5 patients in the Primidone study group with elevated GGT. In comparison to the other anticonvulsants studied, the primidone group was very small. Therefore, little can be concluded from this study. A study in 1986 by Deutsch and Fritsch showed highly significant differences were found between GGT activities of patients on primidone treatment vs. valproic acid and phenytoin treatments.

The best information came from a veterinarian case study of a 9 year old German Sheppard dog. The dog presented with jaundice and elevated liver enzymes. A biopsy revealed necrosis of hepatocytes, and the dog was diagnosed with cirrhosis. Primidone was the only medication the dog had been taking. Once removed from therapy, his liver enzymes decreased and hepatic function improved. The dog remained stable for many years with no long-term complications.

CONCLUSION/RECOMMENDATIONS

Much can be learned from this patient case. The importance of assessing patients for necessity and correct time to initiate therapy (especially for off-label use) is supported. The patient suffered from an unrecognized and uncommon adverse effect. Presentation of the liver abnormality was not noticeable, and the findings of elevated liver enzymes were incidental. If the medication’s side effect remained undiagnosed for a longer amount of time, then further liver damage would have occurred. Any sign such as pruritis should cause patient to call physician and discontinue medication. Given the possible severe consequence of liver failure, it may be prudent to begin monitoring the liver function of patients taking anticonvulsants, particularly primidone.

REFERENCES