An Unusual Case of Drug-Induced Liver Injury Secondary to Nitrofurantoin Use

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Introduction

Nitrofurantoin is an antibacterial drug of the nitrofuran family that is commonly prescribed for urinary tract infections (UTIs).

One of the most severe adverse effects of the use of nitrofurantoin is drug-induced liver injury (DILI).

If nitrofurantoin usage is discontinued early in DILI, there is a high chance of avoiding major long-term liver damage.

Parameters	Day 1	Day 2	Day 3	Normal Values
Platelets	245,000	250,000	225,000	150,000-400,000/mm3
Total Bilirubin	1.9	1.7	1.6	0.1-1.0 mg/dL
Direct Bilirubin	0.7	0.8	0.6	0.0-0.3 mg/dL
AST	> 717	406	135	8-20 U/L
ALT	476	520	331	8-20 U/L
Alkaline Phosphatase	120	129	104	20-70 U/L
Glucose	90	123	86	Fasting: 70-110 mg/dL 2-h postprandial: < 120 mg/dL
Albumin	4.5	4.1	3.7	3.5-5.5 g/dL
INR	1.0	1.2	1.2	0.8-1.2 secs
BUN	11	5	6	7-18 mg/dL
Creatinine	0.8	0.8	0.7	0.6-1.2 mg/dL
Sodium	135	138	137	136-145 mEq/L
Potassium	5.8	3.7	3.8	3.5-5.0 mEq/L
Chloride	103	106	106	95-105 mEq/L
ASA	<5.0			5.0-20.0 mg/dL
Acetaminophen	<1			5.0-20.0mg/dL
Alcohol	< 0.01			
Gammaglobulin	wnl			

Table 1: Labs after discontinuation of Nitrofurantoin on Day 1

Case Presentation

A 24-year-old obese female with a past medical history of GERD presented to the emergency department complaining of epigastric pain that started a few hours before admission.

The pain was associated with nausea and 2 episodes of non-bloody, non-bilious vomiting.

Medication history includes famotidine for GERD as needed and ibuprofen as needed for menstrual pain.

She had been recently diagnosed with a urinary tract infection and had been taking nitrofurantoin (50 mg every 6 hours) for the 3 days prior to admission.

On admission, the patient was afebrile with normal vital signs. Abdominal exam reviewed nontender non-distended abdomen with no signs of organomegaly.

Blood tests were significant for direct bilirubin of 0.7 mg/dL, total bilirubin of 1.9 mg/dL, aspartate aminotransferase (AST) of >717 U/L, and alanine aminotransferase (ALT) of 476 U/L. (Table 1).

The patient's liver function tests done at the primary care physician's (PCP) office a week before were normal.

Toxicology labs were negative for relevant drugs, viruses, and autoimmune markers.

Nitrofurantoin was immediately discontinued and after 3 days in the hospital, symptoms subsided.

Discussion

Acute liver injury from nitrofurantoin has a prevalence of ~ 0.3/100,000 prescriptions, while the prevalence of chronic nitrofurantoin liver injury is estimated to be 1 in 1500.

Risk factors include female sex, increased age, reduced renal function, and increased duration of treatment with the drug.

DILI can present with many symptoms however a patient presenting with jaundice should be of great concern as it is associated with a 10% mortality rate.

Both acute and chronic DILI generally present with elevated liver enzyme values, however, the chronic form is more associated with positive values for autoimmune markers.

Most cases of acute DILI due to nitrofurantoin will resolve on their own after discontinuation of the drug.

In chronic cases, liver biochemistry should return to normal after discontinued treatment, however, damage that has already occurred such as cirrhosis, fibrosis, or necrosis can require transplantation or lead to death.

After developing nitrofurantoin-induced DILI, patients have a high probability of relapse if the patient uses nitrofurantoin again.

Continued use of nitrofurantoin with elevated liver enzymes or subsequent rechallenge show the most severe symptoms, including a majority of the DILI-related fatalities.

Conclusions

Nitrofurantoin is an uncommon cause of DILI associated with various clinical phenotypes, natural histories, and treatments.

Patient demographic (age, sex, race) and laboratory features (serum ALT, bilirubin, INR) at DILI onset have been associated with the severity and outcomes of liver injury in patients with DILI.

Early withdrawal of the medication nearly always results in rapid normalization of the liver biochemistry. Many studies suggest that medical interventions such as the use of NAC and corticosteroids may provide benefits to some patients, but additional studies are needed.

Follow-up with hepatic function tests can be considered as a preventive measure after starting nitrofurantoin.

References

Livertox: clinical and research information on drug-induced liver injury. (2022). Accessed: June 2, 2022: https://www.ncbi.nlm.nih.gov/books/NBK548318/.

Hydes T, Wright M, Jaynes E, Nash K: Nitrofurantoin immune-mediated drug-induced liver injury: a serious complication of a commonly prescribed medication. BMJ Case Rep. 2014, 2014:bcr2013203136.

Björnsson E, Olsson R: Outcome and prognostic markers in severe drug-induced liver disease. Hepatology. 2005, 42:481-9.

Stricker BH, Blok AP, Claas FH, Van Parys GE, Desmet VJ: Hepatic injury associated with the use of nitrofurans: a clinicopathological study of 52 reported cases. Hepatology. 1988, 8:599-606.

Shen W, Hoener B: Mitigation of nitrofurantoin-induced toxicity in the perfused rat liver. Hum Exp Toxicol. 1996, 15:428-34.

Aksamija A, Horvat G, Habek D, Zalac D, Jendris E: Nitrofurantoin-induced acute liver damage in pregnancy. Arh Hig Rada Toksikol. 2009, 60:357-61.