Clinical Gastroenterology and Hepatology

To read this article in full, please review your options for gaining access at the bottom of the page.

Article in Press

Acetaminophen is Undetectable in Plasma From More Than Half of Patients Believed to Have Acute Liver Failure Due to Overdose

Thomas M. Leventhal
Division of Gastroenterology and Hepatology, University of Kansas Medical Center, Kansas City, KS, United States
Michelle Gottfried
Public Health Sciences, Medical University of South Carolina, Charleston, SC, United States
Jody C. Olson
Division of Gastroenterology and Hepatology, University of Kansas Medical Center, Kansas City, KS, United States
Ram M. Subramanian
Divisions of Hepatology and Critical Care, Emory University, Atlanta, GA, United States
Bilal Hameed
Division of Gastroenterology, University of California San Francisco, San Francisco, CA, United States

William M. Lee
Division of Digestive and Liver Diseases, The University of Texas Southwestern Medical Center, Dallas, TX, United States

Grant Support—This study was supported by a grant from the National Institute for Diabetes and Digestive and Kidney Diseases (U01-DK-58369) to the University of Texas Southwestern Medical Center at Dallas

Article Info

Abstract

Abstract

Background Aims

Evaluation of patients with acute liver injury (ALI) or acute liver failure (ALF) often includes measurement of plasma levels of acetaminophen, to determine exposure and/or toxicity. However, once liver injury has developed, acetaminophen might be undetectable in plasma. We investigated the association between level of acetaminophen measured and outcomes of patients designated as having ALF or ALI due to acetaminophen toxicity.

Methods

We performed a retrospective analysis of data from 434 subjects in the Acute Liver Failure Study Group who met criteria for ALF (coagulopathy and hepatic encephalopathy within 26 weeks of the first symptoms, without pre-existing liver disease) or ALI (severe liver injury with coagulopathy but no encephalopathy) due to acetaminophen toxicity from January 1, 2010 through December 31, 2014. We collected data on patient demographics, biochemical features, reported acetaminophen use, N-acetylcysteine therapy, liver transplant, and outcomes. Descriptive statistics were used to assess patient demographics, clinical characteristics, and outcomes whereas differences in continuous variables between patients with vs without acetaminophen detection on admission were analyzed using the Wilcoxon rank-sum test. The primary aim was to determine the proportion of patients with detectable plasma levels of acetaminophen.

Results

Acetaminophen was undetectable in serum samples from 227 patients (52%). There were no significant differences between groups of patients with detectable vs undetectable levels in demographic features, alcohol use, median levels of alanine aspartate, or use of N-acetylcysteine (given to 94.7% of patients with detectable acetaminophen vs 95.9% of those with undetectable acetaminophen; *P*=.63). We observed a significant difference in median dose taken between patients with detectable (29,500 mg; interquartile range, 15,000 mg–50,007 mg) vs no detectable parent compound (14,950 mg; interquartile range, 3960 mg–25,000) (*P*=.003). A lower proportion of patients with detectable plasma levels of acetaminophen (72.3%) survived without a liver transplant than of patients with undetectable levels (86.3%) in univariate analysis (*P*=.0006), although this was not significant in multivariable analysis (*P*=.12). Although most patients had unintentional overdoses, a higher proportion of patients with suicidal overdoses (43%) had detectable levels of acetaminophen than patients with accidental overdoses (29.3%; *P*=.01).

Conclusion

More than half of patients who present at the hospital with acetaminophen-induced ALI or ALF have undetectable levels of acetaminophen. Clinicians should not exclude acetaminophen toxicity because of undetectable levels or withhold N-acetylcysteine for patients with ALI or ALF when acetaminophen toxicity is suspected.

KEY WORDS:
ALFSG, overdose, NAC, hepatotoxicity

Abbreviations used in this paper:
ALF (acute liver failure), ALFSG (Acute Liver Failure Study Group), ALI (acute liver injury), APAP (acetaminophen), ICU (intensive care unit), INR (international normalized ratio), IQR (interquartile range), MELD (model for end-stage liver disease), NAC (N-acetylcysteine), US (United States of America)

Mechanisms of Acetaminophen Hepatotoxicity: Do We Need JNK for Cell Death?
Gastroenterology, Vol. 151, Issue 2

Mo1430 - Hepatocyte Release of HMGB1 During Acetaminophen-Induced Liver Injury and Deleterious Feed-Forward Process: Implication of Necroptosis Through TRIF/RIPK3 Axis
Gastroenterology, Vol. 154, Issue 6

Acetaminophen-induced Acute Liver Failure Is More Common and More Severe in Women
Clinical Gastroenterology and Hepatology, Vol. 16, Issue 6

352 Sex Differences in Acetaminophen-Induced Acute Liver Injury and Acute Liver Failure
Gastroenterology, Vol. 150, Issue 4

476 Determining Late Predictors of Outcome for Acetaminophen-Induced Acute Liver Failure Using Classification and Regression Tree (CART) Modeling Analysis
Gastroenterology, Vol. 146, Issue 5

View All

Disclosures--All authors must disclose any potential conflicts (financial, professional, or personal) that are relevant to the manuscript. If the author(s) has nothing to disclose, this must be stated.

1) Thomas M. Leventhal – nothing to disclose

2) Michelle Gottfried – nothing to disclose

3) Jody C. Olson – nothing to disclose

4) Ram M. Subramanian – nothing to disclose

5) Bilal Hameed – nothing to disclose

6) William M. Lee – nothing to disclose

1) Thomas M. Leventhal – study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content

2) Michelle Gottfried - study concept and design; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis

3) Jody C. Olson - analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content

4) Ram M. Subramanian - analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content

5) William M. Lee – study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; obtained funding; study supervision

6) Bilal Hameed - study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; study supervision