

CASE STUDY

Spurious hyperbilirubinemia secondary to Naproxen overdose**Muhammad Faizan Ahmed MD *, Abdullah Mahmood MD, Syed Rumman Ali Shah MD ,
Anaam Mubin***Brookdale University Hospital Medical Center***ABSTRACT**

Naproxen is one of the most commonly used NSAID in the world. It is metabolized primarily by the liver to 6-O-desmethyl naproxen which is then excreted through the kidneys. This can lead to spurious Hyperbilirubinemia due to interference in bilirubin assay by Naproxen metabolite. Herein we report a case of a 20 year-old-female with suicidal attempt by ingesting a high load of Naproxen leading to a Total bilirubin of 7.44 mg/dL without no signs of hemolysis or liver failure.

KEYWORDS:

Naproxen,
hyperbilirubinemia ,
drug interaction,
overdose

HISTORY

Received :08 February 2020

Accepted :09 April 2020

Published :14 June 2020

Volume : 6 Issue : 1

INTRODUCTION

Endogenous and exogenous substance interference with assays for clinical analytes is a common problem in laboratory medicine. Prescribed drugs constitute the major exogenous sources of interference; and there are a lot of examples of drug effects on clinical laboratory tests. Herein we report a case of hyperbilirubinemia attributed to interference of Naproxen or its metabolites with Total bilirubin assay.

Case presentation

A 20 year-old-female with no past medical history was brought in by EMS after a suicidal attempt. The patient stated she took 115 tablets of Naproxen (each of 250 mg) after she broke up with her ex-boyfriend 6 hours prior to admission. The patient had three episodes of vomiting in ED and her physical examination was unremarkable. Poison control center was contacted and recommended follow up blood gases and electrolytes. After her labs were drawn, the Hepatic panel showed normal liver enzymes with elevated Total bilirubin of 7.44 mg/dL (0.0-1.5) and after six hours it decreased to 6.3mg/dL with undetectable conjugated bilirubin. There were no signs of hemolysis as scleral icterus, elevated LDH, or decreased Haptoglobin; additionally, total CK was also normal. After careful assessment with the temporal relation of Naproxen intake the patient was labelled as spurious Hyperbilirubinemia due to interference in bilirubin assay by Naproxen metabolite. The same sample was also sent for confirmation to another lab and showed normal Bilirubin.

Discussion

aproxen is a nonsteroidal anti-inflammatory drug which is available as an oral tablet. It is an inhibitor of prostaglandins synthesis resulting in analgesia. Its time to peak concentration varies from 2 to 4 hours. It has a mean half-life of 13 hours, bioavailability of 95%, and strong protein 3 binding close to 99%. It is metabolized primarily by the liver to 6-O-desmethyl naproxen which is then excreted through the kidneys (1, 2). Hyperbilirubinemia can be divided into two major groups; indirect (unconjugated) and direct (conjugated) (3). Lab interference is a term used when the correct value of an analyte (concentration or activity) gets altered due to the effect of a substance present in the sample (4).

It can be positive or negative. Positive interference occurs when the measured concentration is greater than the true concentration of the analyte and vice versa for negative interference. Interference can result from both endogenous and exogenous substances. Hemoglobin, bilirubin, lipids, and paraproteins are the major endogenous compounds which can cause interference. Examples of exogenous interference include medications, additives, test materials, and matrix effects. Cefoxitin and cephalothin both can result in positive interference while measuring creatinine via the Jaffe method while ascorbic acid causes negative interference with glucose oxidase methods for glucose (5). Furosemide at a high dose can negatively interfere with the Jaffe method while measuring creatinine. These drugs undergo transformation and their resulting metabolites tend to be more reactive than the original form. Both endogenous and exogenous substances may interfere with accurate determination(6). However, there are a few tools available to detect possible interference. Delta check is one of the most commonly used detection methods and involves a comparison of a patient's current and past results (7) Physicians' feedback can also be helpful when they contact a laboratory after going over an

Address for Correspondence: Muhammad Faizan Ahmed ,
Brookdale University Hospital Medical Center

inconsistent result. Multiple options are available to resolve any interference, if it is present. Switching to a different method is a widely used modality in order to detect any possible interference. 4

Conclusion

Clinicians should be aware of interference in lab results as it may lead to expenses for more unnecessary tests or possible futile procedures, as well as time lost by performing them.

References

[1]. Segre EJ. Naproxen metabolism in man. *J Clin Pharmacol.* 1975 Apr;15(4 Pt. 2):316-23

[2]. Kroll MH, Chesler R. Rationale for using multiple regression analysis with complex interferences. *Eur J Clin Chem Clin Biochem* 1992;30:415-24

[3]. Martin H. Kroll' and Ronald J. Elimination of Interference with Clinical Laboratory Analyses *CLIN. CHEM.* 40/11, 1996-2005 (1994)

[4]. Watkins RE, Feldkamp CS, Thibert RJ, Zak B. Interesting interferences in a direct serum creatinine reaction. *Microchem J* 1976;21:370-84.

[5]. Siest G, Appel W, Blijenberg GB, et al. Drug interference in clinical chemistry: studies on ascorbic acid. *J Clin Chem Clin Biochem* 1978;16:103-10.

[6]. Murphy JL, Hurt TL, Griswold WR, Peterson BM, Rodarte A, Krouse HF. Interference with creatinine concentration measurement by high dose furosemide infusion. *Crit Care Med* 1989;17: 889-90.

[7]. <http://www.clinchem.org/content/25/12/2034.full.pdf> Lewis B. Shelner, Lawrence A. Wheeler,1 and John K. Moore The Performance of Delta Check Methods *CLIN. CHEM.* 25/12,