

Fatality Due to Acetaminophen-Ibuprofen Poisoning: A Rare Occurrence

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Abstract

Over-The-Counter (OTC) analgesics are very commonly used in our country and sometimes taken without the doctor's prescription. Though generally these medicines are considered safe, but they can produce complications when taken in excess doses. The authors report a case of an adolescent girl who consumed acetaminophen-ibuprofen combination pills present in her home for headache, which proved fatal. The authors aim to highlight and increase awareness about the hidden dangers in careless and unsupervised use of these medicines. The possibility of death with overdose of even commonly prescribed drugs should be understood, studied well and should be taught to patients to keep such medications away from their children. Accessibility and availability of OTC drugs should be restricted in accordance with the recommended daily usage.

Keywords: Ibuprofen Toxicity; Acetaminophen; Non-Steroidal Anti-Inflammatory Drugs (NSAIDs); Poisoning.

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Introduction

Over-The-Counter (OTC) analgesics are very commonly used in our country and sometimes taken without the doctor's prescription. Though generally these medicines are considered safe, but they can produce complications when taken in excess doses. The authors report a case of an adolescent girl who consumed acetaminophen-ibuprofen combination pills present in her home for headache, which proved fatal. The authors aim to highlight and increase awareness about the hidden dangers in careless and unsupervised use of these medicines.

Case Details

A 15-year old girl was allegedly doing a fast ritual and was on empty stomach since morning. In the

evening, she had headache for which she took six tablets of Ibuprofen 400 mg + Paracetamol 325 mg combination. Soon after, she started vomiting, which gradually worsened and then she developed frothing from mouth. She was taken to a private hospital where she was declared brought dead. The police seized a strip with fourteen white colored tablets of Ibuprofen 400 mg + Paracetamol 325 mg combination from the crime scene and it was sent for chemical analysis.

Autopsy Findings

Deceased was average built and rigor mortis was established all over the body. Clothes were intact. Lividity was present and fixed, in back and dependent parts, in supine position except pressure areas. Mouth was closed and white coloured

froth was seen oozing out of mouth. No external or internal injury was present over the Body. Genitalia was intact. The lungs were congested and edematous and weighed 420 gm and 380 gm respectively. Stomach contained around 150 ml of brown coloured fluid with black coloured particles. Mucosa was congested and a peculiar smell was present. Stomach and its contents, small intestine, liver, spleen, kidney and blood were preserved for toxicological analysis and opinion was reserved at that point of time.

Chemical analysis report could not detect any common poisons in blood or other viscera. On Chemical analysis of the tablets recovered from the crime scene, the composition of acetaminophen and ibuprofen were confirmed. The cause of death was concluded as "Poisoning due to combined effect of Ibuprofen and acetaminophen".

Discussion

Ibuprofen and Acetaminophen are Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).¹ Ibuprofen 400 mg and Paracetamol 325 mg combination is available in many trade names in India. The mechanism of action of both the drugs is cyclo oxygenase (COX) enzyme inhibition. Inhibition of COX enzymes affects the prostaglandin synthesis. Prostaglandins play an important role in pain pathway. They are also involved in fever mechanisms and they are inflammatory mediators. Therefore prostaglandin inhibition can significantly control pain, fever and inflammation thereby having a therapeutic effect.²

Ibuprofen, an Over-The Counter medication is commonly available in many countries. Although accessibility of ibuprofen is easy, ibuprofen overdose is seldom reported in literature. They usually present with nausea, vomiting, dizziness, drowsiness and blurred vision.³⁻⁴ Our case had history of vomiting immediately after ingestion of the tablets. Death due to acute ibuprofen overdose is rare. Reported deaths in literature are mostly associated with some other drug or some other cause as in our case. Deaths due to isolated ibuprofen poisoning is scarce as hen's teeth.⁵ Immediate life threatening complications following ingestion of ibuprofen are hepatotoxicity, coma, hypotension, respiratory arrest, thrombocytopenia, seizures, refractory multi system organ failure and death.⁶⁻⁷ In our case, we did not get any significant postmortem findings, which could explain the possibility of coma, respiratory arrest or hypotension contributing to the death of the deceased. Using NSAIDs for a longer period without prescriptions, especially in

patients suffering from chronic diseases can lead to other complications such as chronic renal failure and gastro intestinal ulcer followed by bleeding.⁴ Renal failure is one such complication, which can manifest in both acute and chronic overdose of ibuprofen. Glomerulus contains afferent arteriole, which receives the arterial blood from body for the process of ultrafiltration. PGE₂ (a type of prostaglandin) cause dilatation of afferent arterioles of glomerulus in normal individuals. This process will increase the renal plasma flow, which maintains homeostasis of Glomerular Filtration Rate (GFR). Use of NSAIDs can disrupt the above-mentioned homeostasis by inhibiting prostaglandin synthesis.⁸ We did not find any features of renal failure in our case. Another reported fatal complication is high anion gap metabolic acidosis which could be due to impaired kidney function and accumulation of toxic metabolites⁹ which again is difficult to pick up in postmortem examination. Ibuprofen induced apneic episodes can cause Aspiration Pneumonia³ which was not present in our case. These fatal complications have occurred only when the ingested amount of ibuprofen was greater than 400 mg/kg.¹⁰ In our case, according to the history, only about 5 to 6 tablets were consumed by the deceased, which amounts to only 2000 mg to 2400 mg. This shows ibuprofen could have had only contributory effects to death and not the sole factor that was responsible.

Acetaminophen (Paracetamol) is a commonly used OTC analgesic-antipyretic. It is metabolized in liver and is converted into non-toxic and toxic (NAPQI-N-acetyl-p-benzoquinone imine) products. Toxic products will be neutralized by glutathione. It is generally tolerated well and safe for healthy individuals, if prescribed in recommended doses. Overdose or chronic supra-therapeutic use can lead to hepatotoxicity and death.¹¹ Toxic dose when taken as a single dose is 140 mg/kg or 7.5 gm if taken over a 24-hour period.¹² The toxicity occurs in four stages. First stage is the immediate 24 period where patients will be asymptomatic or having non-specific symptoms. On second or third day initial stages of hepatotoxicity sets in. After this stage, some patients recover without any sequel and some develop characteristic findings like metabolic acidosis, renal failure, coagulopathy, encephalopathy, and recurrent gastrointestinal (GI) symptoms, which suggest Fulminant hepatic failure. Histopathology shows Centrilobular Hepatic necrosis. If the patient survives this stage, over the next week hepatic functions return to normal.¹² Acetaminophen poisoning cases presenting as brought dead is

seldom reported in literature and the contributory effect of ibuprofen could have had an impact in our case. Our case had symptoms of only vomiting and frothing after ingestion of tablets, collapsed rapidly and was declared brought dead in the casualty. Autopsy showed liver to be normal grossly. Other known complications are metabolic acidosis, lactemia and altered mental status. Usually metabolic acidosis develops late in the patients, after liver failure, but early occurrence of metabolic acidosis suggests excessive NAPQI accumulation.¹³

Drug absorption is increased generally in empty stomach. Presence of food always hampers absorption and has a control on any given drug. Faster gastric emptying increases absorption of drugs, since small intestine has large surface area due to presence of villi. Acetaminophen being a basic drug will be in unionized state in small intestine, which further increases absorption of the drug. In our case, the deceased was on empty stomach, which could have probably lead to erroneous absorption of both the drugs, especially acetaminophen.¹⁰ Consumption of combination tablet of ibuprofen and acetaminophen could cause synergistic adverse drug reactions. Metabolic acidosis is common in both the drugs, which could possibly explain cause of death in our case. Even though individual pathological feature of each drug is not visible structurally during autopsy, the combined functional pathology of both the drugs should be considered in opining the cause of death. The cause of death was concluded as "Poisoning due to combined effect of Ibuprofen and acetaminophen", despite the Viscera report being negative. A negative viscera report does not rule out death due to poisoning as the viscera tests has a lot of limitations and restricted to very few common poisons. As per judgments of the apex court, the doctor who has conducted the postmortem examination depending upon PM findings, the medical records, circumstantial evidences and after ruling out any other cause of death can very well give the manner of death as unnatural due to a poisonous substance, just as in this case.^{14,15}

Conclusion

The possibility of death with overdose of even commonly prescribed drugs should be understood, studied well and should be taught to patients to keep such medications away from their children. Accessibility and availability of OTC drugs should be restricted in accordance with the recommended daily usage. Even though gross findings are absent

and viscera turn out to be negative in chemical analysis, the pharmacopathology of the drugs should be understood well to opine cause of death under such circumstances. The autopsy surgeon should not be deterred by mere non detection of poison in the chemical analysis of viscera.

References

1. Wood D, Monaghan J, Streete P, Jones A, Dargan P. Crit Care. 2006;10(2):R44.
2. Nazu K: Ibuprofen: highly potent inhibitor of prostaglandin synthesis. *Biochim Biophys Acta* 1978, 529:493-494.
3. Hall AH, Smolinske SC, Conrad FL, Wruk KM, Kulig KW, Dwelle TL, Rumack BH: Ibuprofen overdose: 126 cases. *Ann Emerg Med* 1986, 15: 1308-1313.
4. Chyka PA, Seger D. Position paper: single-dose activated charcoal. *J Clin Toxicol.* 2005; 43 (2); 61-87.
5. Hall AH, Smolinske SC, Kulig KW, Rumack BH: Ibuprofen overdose - a prospective study. *West J Med* 1988, 148:653-656.
6. McElwee NE, Veltri JC, Bradford DC, Rollins DE: A prospective, population based study of acute ibuprofen overdose: complications are rare and routine serum levels not warranted. *Ann Emerg Med* 1990, 19:657-662.
7. Seifert SA, Bronstein AC, McGuire T. Massive ibuprofen ingestion with survival. *Clin Tox.* 2000;38:55-57.
8. Smetana M, Picard K, Boehm KM. An Acute Ibuprofen Overdose Masking a Severe Staphylococcus aureus Meningitis: A Case Report. *Case Reports in Emergency Medicine.* 2013:1-5.
9. Halpern SM, Fitzpatrick R, Volans GN: Ibuprofen toxicity. A review of adverse reactions and overdose. *Adverse Drug React Toxicol Rev* 1993, 12:107-128.
10. Smolinske SC, Hall AH, Vandenberg SA, Spoerke DG, McBride PV: Toxic effects of nonsteroidal anti-inflammatory drugs in overdose. An overview of recent evidence on clinical effects and dose-response relationships. *Drug Saf* 1990, 5:252-274.
11. Larson AM, Polson J, Fontana RJ, et al. Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. *Hepatology* 2005; 42: 1364-1372.
12. Hung O, Nelson LS. Acetaminophen. In Tintinalli JE, Kelen GD, Stapczynski JS. *Emergency Medicine: A Comprehensive Study Guide* 6th ed. New York, NY: McGraw Hill; 2004. 1088- 1094.
13. Ghannoum M, Kazim S, Grunbaum SA, Villeneuve E, Gosselinc S. Massive acetaminophen overdose: effect of hemodialysis on acetaminophen and acetylcysteine kinetics. *Clin Toxicol.* 2016; 54 (6), 519-22.

14. Jaiswal A K, Gupta S K, Millo T, Yadav A, Prasad K. Death is Due to Poisoning but Viscera Report is Negative. *Ind Journal of Forensic Med and Pathol.* 2015; 8(1): 29-36.
15. Yadav A, Gupta S K, Kulbhushan, Kumar A, Punia S, Jaiswal A K. Death Is Due To Poisoning: Negative Viscera Report-Intricacies Thereof. *Indian Police Journal.* 2015; 62 (1): 216-27.

