

Case Report

IRRATIONAL USE OF IBUPROFEN LEADS TO HEMATEMESIS; A CASE REPORT

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ABSTRACT

This case study has been designed to report an incident of irrational use of Ibuprofen (NSAID) in a 10 year old child brought to a local hospital in Rawalpindi and describe the seriousness of adverse effects that are to be associated with irrational use of NSAIDS. Complete chronological history of child was taken including his past medication history by direct interview of the mother. The study has revealed that the efficacy and wide availability of OTC preparations of NSAIDS and irrational prescribing of physician has lead to their irrational use resulting in serious adverse effects to the consumers. So it is the responsibility of the health care professionals to optimize and help rationalize the use of these OTC drugs by the consumer.

Key words: Irrational use, Ibuprofen, Hematemesis

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INTRODUCTION

Rational use of medicines requires the patients to take medications that are appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community¹. As stated by a famous humanitarian, A little simplification would be the first step toward rational living.

Thus simplifying ,Rational use of drugs require patients to take the Right medication, in the right dose, at right time through the appropriate route.² Failure to follow this scheme has lead to medically inappropriate, un productive and unprofitable use of pharmaceuticals world wide especially in the developed countries. This misuse of drugs has resulted in wastage of resources as well as worldwide health hazards. While; the non steroidal anti-inflammatory drugs (NSAIDs), now constitute perhaps the most frequently prescribed class of medications.³

Although these are the most widely prescribed medications in the United States for fever, arthritis and a number of other inflammatory conditions to reduce pain and inflammation, according to a research conducted on *Unnecessary prescribing of NSAIDs in 1997* it was proved that they are associated with a high incidence of side effects.⁴

In the last decades, epidemiologic studies have revealed the risk of upper gastrointestinal tract bleeding/perforation (UGIB) associated with individual nonsteroidal anti-inflammatory drugs (NSAIDs).⁵ A multicenter study revealed that long-term NSAID use is associated with the development of mucosal ulceration with an incidence of 20%.⁶

Many patients with Upper Gastrointestinal Bleeding who are taking NSAIDs present without dyspepsia but with hematemesis or melena as their first symptom, owing to the analgesic effect of the NSAID.⁷

The use of over-the-counter (OTC) formulations NSAIDs is very common. In this context, data of 4164 consecutively diagnosed patients with rheumatoid arthritis was collected on the GI risks of OTC doses of aspirin, ibuprofen, naproxen, paracetamol, and no drug, from eight Arthritis, Rheumatism, and Aging Medical Information System centers in North America. Serious GI events such as bleeding, requiring hospitalization were reported in these patients.⁸

Serious side effects have been reported due to NSAIDs especially in children. A large randomized controlled trial conducted by Lesko SM, Mitchell AA (1995) showed that ibuprofen and acetaminophen were equivalent in their risk of adverse events.⁹

CASE REPORT

A 10-year-old girl was brought to the emergency of a local hospital in Rawalpindi, Pakistan with chief complaints of epigastric pain (2 weeks), bloody vomiting (a week) and fever (last 2 days). There was a sudden onset of pain after having a meal. It was severe enough to hamper the child's activity. Her mother was called to school and the child was brought to the Emergency.

The pain had been accompanied by hematemesis i.e. vomiting of blood since a week.

It was sudden in onset and almost 2 tablespoons in volume. It was non-projectile, bright red in color associated with abdominal pain. No blood clots were seen. The child had intermittent, low-grade fever for the past 3 days. It was relieved by ibuprofen. There were no associated symptoms with fever such as rigors or chills, burning sensation on stooping, acidity retrosternally etc.

Her physical examination showed temperature 101°C, pulse 115/min, respiratory rate 22/min and B.P. She weighed 40 kg. Her examination had revealed pallor, weight loss and anorexia.

She had flank pain in the renal area and her CVS examination revealed palpitation and fatigue. CNS is normal and intact.

There was no history of constipation, diarrhea, malena, allergy and respiratory infection. While medical history showed sub-vaginal delivery (SVD), mild anemia and pancytopenia.

Patient's past medication history revealed frequent use of Ibuprofen (NSAID) for symptomatic relief of fever since thirteen months.

DISCUSSION

The patient presented with epigastric pain (2 weeks), bloody vomit (Hematemesis) (a week) and fever (last 2 days). The epigastric pain was sudden in onset after having meal and was severe enough to hamper her activities. The vomit was non projectile, contained blood and was almost 2 tablespoons in volume. Fever was mild intermittent and relieved by ibuprofen.

Past medication history of the patient showed frequent use of Ibuprofen for symptomatic relief of fever for the past 13 months (91 weeks).

Ibuprofen is an oral, Nonsteroidal Anti Inflammatory drug (NSAID) of the propionic acid chemical class. It competitively inhibits both cyclooxygenase (COX) isoenzymes, COX-1 and COX-2, by blocking arachidonate binding resulting in analgesic, antipyretic and anti inflammatory properties.

Cyclooxygenase 1 (COX-1) is responsible for the physiologic production of prostanoids, that regulates the normal cellular processes such as *gastric cytoprotection, vascular homeostasis, platelet aggregation and kidney function*. COX-2 cause's elevated production of prostanoids in case of a disease or at the site of inflammation. COX-2 is constitutively expressed in some tissues, such as brain, kidney and bone. Its expression at other sites is increased during inflammation.

Since ibuprofen is a nonselective COX inhibitor, it inhibits both of the COX enzymes resulting in wide range of side effects. Focusing on the above mentioned case, as already described, COX-1 is responsible for the physiologic production of prostanoids that regulate gastric cytoprotection i.e. Prostacyclin (PGI₂) which inhibits gastric acid secretion, whereas PGE₂ and PGF_{2a} stimulate synthesis of protective mucus in both the stomach and small intestine .In the presence of Ibuprofen, these prostanoids are not produced resulting in increased gastric acid secretion and diminished mucus protection respectively. This results in epigastric distress, ulceration and hemorrhage which increases with dose and duration and can occur at any time.¹⁰

This fact is supported by Geis GS, Stead H, Wallermark C-B (1991)¹¹ who reported the occurrence of mucosal lesions in patients, with rheumatoid arthritis, due to chronic use of NSAIDS. It was estimated that prevalence of NSAID induced gastric or duodenal ulcers, varies between 14.6% and 43.9%.

Gabriel and Bombardier (1990) estimated the absolute risk of gastric ulceration to be approximately 20%.¹²

The patient was prescribed ibuprofen 1 year back, when she had fever, by a local physician. She had immediate relief and from then onwards when ever she had fever in the past 13 months, she took ibuprofen for relief.

According to British National Formulary¹³, the dose for children under 12 years is 20 mg/kg of body weight in divided doses per day. As she weighed 40Kg, her total daily dose becomes 800mg in divided doses. Depicting irrational use, she took more then the required dose, according to her mother two 400 mg tablets at a time for fever .Thus by taking double dose each time ,the serum level for the drug increased then the required leading to exaggerated effect. Use of adult dosage form by the child also depicts irrational prescribing by the physician.

So as the child consumed ibuprofen for a long period, she developed ulceration leading to hemorrhage which presented as Hematemesis. The Blood CP of the child revealed mild anemia representing continuous blood loss and pancytopenia.

Lindblad R,Rödger S (1991) suggested that patients on prolonged therapy should undergo regular blood monitoring as ibuprofen causes iron deficiency anemia and pancytopenia.¹⁴

According to Autret-Leca E, Bensouda-Grimaldi L, Maurage C, Jonville-Bera AP (2007) ,Regional Centre of Pharmacovigilance, France; NSAIDS, when used in children for pain or fever relief, are associated with serious Gastro Intestinal complications which increase with the length of exposure and dose.¹⁵

So lowest effective dose should be given for the shortest period of time to limit these adverse effects.

CONCLUSION

Irrational use of OTC drugs is a major problem of present day medical practice. All NSAIDs can cause gastrointestinal discomfort and rarely serious but potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation, which may increase with dose or duration of use but can, occur at any time without warning. So it is the responsibility of the health care professionals to optimize and help rationalize the use of these OTC drugs by the consumer.

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