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CASE REPORT

# Thrombocytopenia after Ibuprofen: A Case Report

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## ABSTRACT

Ibuprofen, a propionic acid derivative, is an important non steroidal anti-inflammatory drug (NSAIDs) used freely for the treatment of various arthritic diseases, and as analgesic and antipyretic drug available over the counter (OTC) in Nepal.
Thrombocytopenia (TPA) is one of the rare haematopoitic adverse drug reactions (ADRs, <1%) of ibuprofen. This is a fatal case of ibuprofen induced TPA, reported from the Nepalese population. Ibuprofen is documented to be one of the safest anti-inflammatory, analgesic and antipyretic drugs used frequently.

**Key Words**: Adverse drug reactions (ADRs), thrombocytopenia (TPA), non steroidal anti-inflammatory drugs (NSAIDs), over the counter (OTC).

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## Introduction

Non steroidal anti-inflammatory (NSAIDs) are commonly used as analgesics, antipyretics and anti-inflammatory drug. Ibuprofen is one of the most common propionic acid derivatives used for the symptomatic treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gouty arthritis, and also it is used as an analgesic for acute tendonitis, bursitis, and primary dysmenorrhoea[1].

Ibuprofen is widely available as an over the counter (OTC) drug and it is a very frequently and widely used drug in Nepal and other developing countries. Some of the reported adverse drug reactions (ADRs) of ibuprofen are gastrointestinal intolerance, rashes, headache, dizziness, blurred vision and in few cases, toxic amblyopia, fluid retention and oedema[2]. Haematopoitic ADRs of ibuprofen include agranulocytosis, aplastic anaemia,[3] pure white cell aplasia[4] and thrombocytopenia[5]. Thrombocytopenia (TPA) may appear with or without purpura[6]. Some adverse events reported in the multimember study and of unknown association, include tachycardia, cardiac failure, abdominal distension, gastrooesophageal reflux, gastritis, ileus, inguinal hernia, injection site reactions, cholestasis, various infections, feeding problems, convulsions, jaundice, hypotension, and various laboratory abnormalities including neutropenia,

thrombocytopenia, and hyperglycaemia[6]. The post-marketing experience derived from spontaneous post-marketing reports or published literature: gastrointestinal perforation. As these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure[7].
We hereby report a case of fatal TPA (decreased platelet count), probably caused due to oral administration of ibuprofen tablets.

## Case Report

On 17th September 2004, a 14-year old school going boy (weighing 40 kg) was brought to the paediatrics out patient department of Nepal Medical College Teaching Hospital, Kathmandu, Nepal with c/o I. fever- six days, II. lesions in mouth, bruising in whole body and bleeding nose –four days duration.

## History of present illness

Till 11th September 2004, he was all right, when he developed gradual fever without rigor, during which he took ibuprofen tablet of 400mg, twice a day (5 tablets in two days) total dose 2.0.g, capsule amoxicillin 250 mg thrice daily, orally and some cough syrup for three days. There was no improvement in his condition which lasted for four days.

On examination,at the time of admission, his general condition was fair, Pulse 85/min, B.P. 100/70mmHg, normal respiration. Chest and abdomen were normal, except for oral examination, which showed small bruises and there were multiple bruises over the entire body, more in the central area of chest and abdomen and on the upper parts of the upper and lower limbs. Investigations showed that total leukocyte count (T.L.C) was 14,950 cub.mm, differential leukocyte count (D.L.C): was -N 55%, L 39%, and E 6%, haemoglobin was 11.5 g%, showing normocytic **and** normochromic anaemia. He was diagnosed as a case of thrombocytopenic purpura and was admitted to the hospital for treatment. First of all, the drugs being used by the patient were stopped and he was prescribed tablet prednisolone 20mg, 6hrly per day.

In spite of the treatment, there was no improvement in his condition and he had a mild episode of epistaxis. Same treatment was continued and his pulse was reduced to 60/min. On the fourth day (20th Sept 04), his platelet count dropped to 37000 cub.mm and he was given one bottle of blood transfusion.

On 21st Sept.04, his platelet count further dropped to 29,000. Cub.mm. and then, a second bottle of blood transfusion was given.. Following this treatment, he developed left sided hemiplegia and lower motor neuron paralysis of the left side of the face. Further, on the same day, he felt dizzy and fell down in the toilet, which was followed by headache, vomiting, his pupils became constricted and he was shifted to the intensive care unit (ICU) of NMCTH. But his condition remained unchanged, except that his bleeding stopped and there was no paplidema. Platelet transfusion was again repeated in the evening, followed by one bottle of blood and one more platelet transfusion. Even on the following day (22nd Sept.04), his platelet count did not improve and remained at 29,000.cub.mm. Further, at that time, the patient got an attack of tonic seizure. The treatment was revised and Phenobarbitone 60mg TDS I/V was added to control the seizures. On the same day, at 12.00 noon, he developed asystole ,but he was revived back by 2 ampoules of adrenaline and ventilation was started. His vitals at that time were: pulse 78/min, B.P. 120/60 mm. Temp-99 F and SPO2 97%.

On the same day,, at this stage he was given Pancuronium 1mg/2hrly IM, Diazepam 10mg I/V stat and then 5mg 4 hrly. Mannitol 100ml, 6hrly I/V was added and more platelet transfusion (100 ml) was given. However, there was no improvement in the patient's condition in the ICCU inspite of all these life saving measures. On 23rd Sept.04, the patient left the hospital against medical advice.

To conclude, it was strongly suspected that ibuprofen may be mainly responsible for this severe adverse drug reaction. The patient did not recover and probably died. Even after stopping Ibuprofen and other drugs there was no improvement in the patient's condition.

## Discussion

Thrombocytopenia can be a severe complication of non steroidal anti-inflammatory drug treatment. We were able to collect at least four pervious reports of NSAIDs induced TPA.

The first report is of 1991, from Department of Medicine, Ostra Hospital, Gothenburg University, Sweden. The patient developed severe neutropaenia, haemolytic anaemia and thrombocytopaenia associated with long-term use of ibuprofen. The blood parameters rapidly normalized when the drug was discontinued and only a short course of antibiotics was required for recovery[9]. Similar to this case, in1994, a case of life threatening TPA induced by Ibuprofen was reported from Al-Jahra Hospital, Kuwait[8].

In the second case, it is reported that an immune thrombocytopenic purpura temporally developed, related to the oral administration of ibuprofen in a patient of ankylosing spondylitis. Clinical manifestations were, a sudden onset of thrombocytopenic purpura occurring within 12 hrs of oral drug administration and a rapid increase of platelet counts following discontinuation of the drug. This adverse drug reaction was characteristic of an antibody-mediated immune reaction, as immunological studies in this case demonstrated. IgM and IgG antibodies in the patient's serum were capable of binding with allogenic platelets in the presence of a metabolite preparation[9],[10].

Similarly, the third report was of 2005 from Poland, of a patient of 58 years who developed severe thrombocytopenia during treatment with NSAID ketoprofen. Within several days of treatment, the platelet count decreased to undetectable values in the routine blood count of this patient. After discontinuation of ketoprofen and treatment with corticosteroids, the patient's platelet count returned to normal and was stable for 6 months of follow-up[11],[12].

In the fourth report in 1995, from the University of Western Ontario Canada, a 63 yrs old female patient of osteoarthritis was prescribed diclofenac sodium for her arthritis During her hospital admission for pneumonia, she was found to have developed severe thrombocytopaenia following diclofenac therapy. Thrombocytopaenia resolved after the dechallange of diclofenac[13],[14].

According to the literature, drugs can cause TPA by increasing platelet destruction or by bone marrow suppression. Patients developing TPA are thought to have drug related antibodies of both IgG/IgM classes that are involved in the destruction of the platelets. It can appear within a few hours following administration of a drug that causes TPA in patients who had taken the drug previously. In our case, we did not however perform any antibody tests. Most likely, it was a Type II adverse drug reaction.

Two mechanisms have been proposed as the cause for the development of TPA in this patient 1) Either the drug was bound to the platelet membrane and the antibodies were directed against the drug-membrane complex, with subsequent activation of the complex which induced injury to the platelet, or 2) There may have been circulating drug-antibodies which may have complexed with the platelets, playing a more or less passive role in the destruction of platelets, finally resulting in TPA. Immune complexes are phagocytosed by platelets and subsequently the platelets release some of their components, leading to intravascular platelet aggregation and TPA.11The precise incidence of TPA associated with ibuprofen is unknown, but less than 1% exists with a probable causal relationship.

## Conclusion

Painkillers like ibuprofen are often considered as the drug of choice for pain management in Nepal and are very widely used by professionals. Moreover, they are available as an OTC drug in Nepal. Innocent people who are unaware of the deadly ADR of this drug, use it without caution, and can endanger their lives. Even clinicians may not notice these things. Hence, it becomes important to observe patients for such life threatening ADR like TPA. Patients on ibuprofen and those who develop symptoms of TPA should have a complete blood count. As soon as this ADR develops, the culprit drug should be immediately withdrawn and treatment should be started at the earliest. Care must be taken not to put on the patient on the same drug again in the future.

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