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Case Report

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CASE REPORT: TRAMADOL INDUCED THROMBOCYTOPENIA

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ABSTRACT

Adverse Drug reaction is defined as the unintended response to a drug which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological functions'. Tramadol is a codeine analog which is commonly used as an analgesic. During Pharmacovigilance programme in a tertiary care hospital of Lucknow we came across a case of Thrombocytopenia and cutaneous rashes following the administration of tramadol. There were macular rashes evenly distributed all over the trunk, limbs and face along with Conjunctival congestion. The platelet count was decreased to 70,000/mm^3

KEYWORDS: Pharmacovigilance, prophylaxis, diagnosis, or therapy of disease.

INTRODUCTION

Adverse drug reaction as defined by the WHO is 'a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological functions'.[1]. Almost all drugs used for therapeutic purpose are associated with adverse reactions which may be serious, non-serious, life threatening or may even cause death

It has been seen that 0.7% of the total hospital admissions were due to Adverse drug reactions in India and 1.8% of these reactions were fatal in nature.[2]

The most common manifestation being cutaneous (38.8%) presenting as generalized rashes, itching and urticarial followed by Gastrointestinal manifestations (28.4%)

Tramadol is a synthetic codeine analog used as an analgesic that is a weak morphine opioid receptor agonist. Part of its analgesic effect is produced by inhibition of uptake of norepinephrine and serotonin. In the treatment of mild to moderate pain, tramadol is as effective as morphine or meperidine.[3]

Common side effects of tramadol include nausea, vomiting, dizziness, dry mouth, sedation, and headache. Tramadol can also cause seizures and possibly exacerbate seizures in patients with predisposing factors. During Pharmacovigilance programme in a tertiary care hospital of Lucknow we reported a case of Thrombocytopenia and cutaneous rashes following the administration of tramadol.

CASE REPORT

A 35 yr old male patient was admitted to the hospital with the complains of high grade fever and intense headache for the past 2 days. Preliminary examination did not reveal any abnormality. The patient was given Inj. Tramadol 50 mg/ml intravenously. The patient started developing intense itching within 30 minutes of giving injection and soon developed rashes which initially started over the limbs and spread to the trunk and back. Conjuctival congestion was also present.

On physical examination, the patient was well oriented with time, place and person, BP was 120/86 mm of Hg, Pulse- 90 beats/min, temperature 101 degrees F, Respiratory rate- 16/min, chest auscultation and abdominal palpation did not reveal any significant finding. The rashes were macular and evenly distributed all over the trunk, limbs and face. Conjunctival congestion was present.

The following investigations were done Hb 13.4 gm/dl, TLC 45OO/mm^3, ESR 30 mm/lst hour, platelet count was decreased to 70,000/mm^3. The kidney profile and the liver function tests were normal.

Patient was started with Intravenous fluids (1.5 liters/day), Inj. Pheniramine Maleate 25 mg and inj. Prednisolone 10 mg immediately.

Causality assessment using Naranjo's algorithm categorized the adverse drug reaction as probable (score=5) and by WHO scale was also classified to be probable. The Adverse event was reported to the WHO-UMC Vigiflow for the central assessment.

Patient started showing improvement after 12 hours of treatment, the itching was reduced and there was fading and shrinkage of the rashes in the next 24 hours. Systemic steroid was administered Inj. Prednisolone 10 mg was given twelve hourly for 3 days and 10 mg once daily for next 2 days and was then stopped. Patient showed complete remission of rashes in two days and the patient was finally discharged from the hospital on the third day. Patient was called for the follow up after one weak and the platelet count was done which were normal.

DISCUSSION

Thrombocytopenia or decrease in the platelet counts, results from one or more of three processes: (1) decreased bone marrow production; (2) sequestration, usually in an enlarged spleen; and/or (3) increased platelet destruction. Disorders of production may be either inherited or acquired. [4]

Drug-induced non-immune thrombocytopenia (DIT) can be distinguished from idiopathic thrombocytopenic purpura (ITP), a bleeding disorder caused by thrombocytopenia not associated with a systemic disease, based on the history of drug ingestion or injection and laboratory findings.

Various drugs have been attributed to cause DIT and common drugs amongst this include cytotoxic chemotheraptics, gold salts, thiazide diuretics, ethanol and Tolbutamide.[5] The frequency of DIT in acutely ill patients has been reported to be approximately 19–25%. Generally, platelet count falls rapidly within 2–3 days of taking a drug which has been taken previously, or 7 or more days after starting a new drug. When the drug is stopped, the platelet count rises rapidly within 1–10 days of withdrawal. Thus, the primary treatment for drug-induced thrombocytopenia is to discontinue the suspected causative agent.

The exact mechanism of platelet destruction is not clear however it may be attributed to the presence of drug-dependent antibodies (DDAbs) that bind the glycoproteins (GPs) on the platelets, most often GPIb/IX, GPV and GPIIb/IIIa and platelet-endothelial cell adhesion molecule-1 (PECAM-1) when the drug is present in soluble form. Remarkably, antibodies in an individual patient are often highly specific for a single GP.[6]

The target for these antibodies may be formed due to a conformational change in the GP molecule which is created in the presence of the offending drug or it may be also due to formation of the drug compound epitope which is formed due to the binding of the drug to the platelet GP molecule.[7] In some instances, not only the drug itself but also its metabolites are responsible for the immune response in the patient.[8]

CONCLUSION

This was a case of Tramadol induced Thrombocytopenia. The exact mechanism of platelet destruction is not clear but the reaction may be fatal hence re-administration should be avoided in patients with any history of such reaction.

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