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Pantoprazole induced Hypocalcemia: A case series

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ABSTRACT

Pharmacovigilance aims to guarantee the safe use of medicines. It is based on the reporting of adverse effects by health professionals, industry and the public. Pharmacovigilance is the monitoring of drugs and the prevention of the risk of adverse effects resulting from their use, whether this risk is potential or proven. It relies on the spontaneous reporting of adverse events by health professionals and patients, the collection of adverse effects for the detection of signals the establishment of preventive measures. One such adverse drug reaction is calcium deficiency due to reduced calcium absorption caused by an important group of medication namely, proton pump inhibitors. The data of the following three patients were evaluated and causality assessment further established a "probable" relationship between the drug intake and time of administration.

INTRODUCTION

Adverse drug reaction (ADR) has been implicated as a leading cause of considerable morbidity and mortality. It accounts for about 6-7% of the total hospital admissions [1]. One such adverse drug reaction of proton pump inhibitors is reduced calcium absorption leading to hypocalcemia and subsequently reduces the bone mineral density and it is also responsible for manifestations like muscular cramps and tingling sensation on the limbs.

Proton pump inhibitor therapy (PPI) is a gold standard treatment for the management of dyspeptic symptoms associated with gastritis, in the management of peptic ulcer disease, eradication of Helicobacter pylori infection and management of Zollinger-Ellison syndrome and to prevent complications related to NSAIDs [2]. Furthermore, these agents are often prescribed inappropriately, and patients are maintained on treatment for extended periods of time. As a result, PPIs have become one of the most commonly prescribed classes of medication since their introduction in the late 1980s, with a high prevalence of chronic use [3]. With the recent availability of both over-the-counter and generic formulations, PPI use continues to escalate. Herein, we present a series of 3 cases of Pantoprazole-induced hypocalcemia in patientsfollowing pantoprazole therapy for epigastric discomfort.

CASE 1

A 40 year old male suffering from GERD since past 2 months was prescribed capsule pantoprazole 40mg once daily. He presented to the medicine OPD of a tertiary care hospital with chief complaints of muscular cramps on lower limbs and flanks. On investigation, the serum calcium levels were found to be 6mg/dl (reference normal range is 8.6 to 10.3 mg/dL)

Calculated Naranjo's adverse drug reaction (ADR) scale of +6 was subsequently obtained which implies a probable adverse drug reaction. A definitive diagnosis of Pantoprazole-induced hypocalcemia was finally made following the subsequent review of his medical history, clinical examination findings, and the results of the laboratory investigations. Outpatient management commenced with the immediate withdrawal of the oral Pantoprazole medication was instituted and replaced with oral Famotidine 40mg twice daily and calcium supplements were added. The following measures led to the abatement of the muscle cramps.

CASE 2

A 25 year old female suffering from gastritis since past 1 month and was on capsule pantoprazole 40mg once a day. She presented to the medicine OPD of a tertiary care hospital with chief complaints of painful muscular spasm on lower limbs, flanks and abdomen. . On investigation, the serum calcium levels were found to be 5.5mg/dl (reference normal range is 8.6 to 10.3 mg/dL).

The causality assessment was done on Naranjo's adverse drug reaction (ADR) scale and a result of +6 was subsequently obtained which implies a probable adverse drug reaction. A definitive diagnosis of Pantoprazole-induced hypocalcemia was

finally made following the subsequent review of her medical history, clinical examination findings, and the results of the laboratory investigations. Outpatient management commenced with the immediate withdrawal of the oral pantoprazole medication was instituted and replaced with oral Famotidine 40 mg twice daily and calcium supplements were added. The following measures led to the relief of the spasmodic symptoms.

CASE 3

A 50 year old post-menopausal woman was diagnosed with hypertension 1 year back and was on anti-hypertensive medications such as tab Telmisartan 40mg, tab Aspirin 150mg once a day along with cap Pantoprazole 40mg. she was prescribed proton pump inhibitor for the indication of NSAIDs associated gastritis. 5months following the medications she developed muscular cramps which were painful and numbness and tingling sensation on the lower limbs and hands. On investigation, the serum calcium levels were found to be 4mg/dl (reference normal range is 8.6 to 10.3 mg/dL).

The causality assessment was done on Naranjo's adverse drug reaction (ADR) scale and a result of +6 was subsequently obtained which implies a probable adverse drug reaction. A definitive diagnosis of Pantoprazole-induced hypocalcemia was finally made following the subsequent review of her medical history, clinical examination findings, and the results of the laboratory investigations.

She was prescribed cholecalciferol granules sachet to be consumed per week and tab shelcal every day. Cap Pantoprazole was withdrawn and tab Famotidine 40 mg was instituted in its place to be taken once a day. The symptoms declined and the patient was relieved after 1 week of therapy.

DISCUSSION

PPIs are potent acid-suppressing medications that have proven efficacy against acid-related diseases. [4]

The main physiologic change induced by PPI therapy is profound suppression of gastric acid secretion. Gastric acid suppression results in hypergastrinemia, and may cause malabsorption of calcium. Both hypergastrinemia and calcium malabsorption may negatively influence bone and mineral metabolism. Several studies have directly examined the effect of PPI therapy upon calcium absorption [5][6] Few of the studies suggested that omeprazole therapy may impair dietary calcium absorption and they relied on demonstrating decreased plasma total calcium concentration with omeprazole therapy as evidence of calcium malabsorption [7][8].

CONCLUSION

Electrolyte disorders are becoming a common feature of the PPIs including Pantoprazole. Though common among the elderly, it could also occur among the younger age group. It becomes imperative that patients on PPIs (pantoprazole and omeprazole) irrespective of age be monitored regularly to avert potential complications of these electrolyte disorders.

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