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A Case Report of Pantoprazole Induced Hypomagnesemia and Hypomagnesemia Induced Cerebellar Edema

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ABSTRACT:Proton pump inhibitors are a group of medications for treatment of gastric acid–related disorders such as gastroesophageal reflux disease and peptic ulcer disease. Compared to H2 receptor antagonists like cimetidine, PPIs are more effective. Long-term use of PPIs has been linked with hypomagnesemia and more reports over current history of hypomagnesemia accompanied with cerebellar edema. Clinicians will use the treatment only in suitable therapeutic situations and be aware of any potential side effects.

A 53yrs old male patient was admitted to emergency ward with complaints of convulsion 2-3 episodes since 2 days and had a K/C/O reflux symptoms with Barrett's esophagitis on medication Tab. Pantoprazole 40mg once daily since 2 years. On examination, all the review of system were normal. An electrocardiogram showed sinus tachycardia, high peak QT waves. The routine baseline investigation were done. Elevated neutrophils and WBC count, decreased lymphocytes. In serum electrolytes, Magnesium level was decreased. Calcium, Sodium, Potassium, Chloride were normal. Based on this, provisional diagnosis was seizures. Advised Inj. Benzodiazepam 10mg IV as STAT and Inj. Magnesium Sulphate 1600 mmol. Left cerebellar edema was observed in CT Brain. Hence they diagnosed as Pantoprazole induced hypomagnesemia and hypomagnesemia induced cerebellar edema. Then Inj. Mannitol 100mg IV was given twice daily. Clinicians ruled out all possible causes for these symptoms (risk factors such as age, gender, poly pharmacy, concurrent disease effects etc.) and suspected as Pantoprazole induced seizures due to hypomagnesaemia. Hence they dechallagePPI. On 5th day, the level of serum magnesium normalised and his symptoms were resolved.

Our case report provides additional information about the existence of a relationship between the use of Pantoprazole and the occurrence of hypomagnesemia when used for a long term of Pantoprazole as an adverse effect though rarely seen. It is critical for the clinicians to explore and rule out other causes of electrolyte imbalance as well as to be aware of this uncommon adverse effect of proton pump inhibitors.

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KEYWORDS:PPIs, Pantoprazole, Adverse Drug Reaction, Hypomagnesemia

I. INTRODUCTION

Proton pump inhibitors (PPIs) are a group of medications for the treatment and prevention of non-steroidal anti-inflammatory drug (NSAID)–induced gastric damage, as well as the treatment of gastric acid–related disorders such as gastroesophageal reflux disease and peptic ulcer disease. PPIs are omeprazole, esmoprazole, pantoprazole, rabeprazole, lansoprazole, and dexlansoprazole. PPIs are frequently used in many nations due to its superior efficacy and regularity in suppressing gastric acid comparison to histamine H2 antagonists.[1] Compared to H2 receptor antagonists like cimetidine, PPIs are more effective. By forming a connection between the hydrogen–potassium ATPase pump on the secretory surface of gastric parietal cells, pantoprazole acts as an irreversible proton pump inhibitor (PPI), boosting stomach pH.[2] Long-term use of PPIs has been linked to unusual but serious side effects, including bone fractures, enteric infections, community-acquired pneumonia, diarrhoea caused by Clostridium difficile, hypergastrinemia, and nutritional deficiencies such vitamin B12 deficiency and hypomagnesemia.[1] Magnesium ion (Mg^{2+}), the most common divalent cation in live cells, is present in bloodstream and cerebrospinal fluid in addition to the intracellular compartment (CSF). Human serum Mg^{2+} content typically varies between 1.7 and 2.3 mEq/L and can drop under a number of clinical circumstances.[3] The Food and Drug Administration (FDA) identified PPIs as effective and safety drugs in 2011 strengthening the

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importance of long term use of PPIs prescription in this association.[5] The proton pump, which is a last stage in the production of acid by the parietal cells of the stomach mucosa, is inhibiting H+, K+-adenosine triphosphate (H+, K+ATPase) by pantoprazole to produce its pharmacodynamic activity.[6] In 2006, two individuals were the first to report a connection between PPI usage and symptomatic hypomagnesemia. Numerous studies have since confirmed the link between PPI usage and caused hypomagnesemia.[4] There have been more and more reports over current history of hypomagnesemia-induced cerebellar syndromes, which may represent a separate disease entity and are accompanied with cerebellar edema on MRI.[7] Clinicians will use the treatment only in suitable therapeutic situations and be aware of any potential side effects.[6]

MECHANISM OF INJUIRY

During the PPIs' clinical testing period, hypomagnesemia an uncommon but dangerous side effect went unnoticed. Despite the fact that the first PPI (omeprazole) was introduced in 1989, the first instance of PPI-associated hypomagnesemia was documented in 2006. Other case reports of hypomagnesemia brought on by PPIs have since emerged.[1] The brain may be harmed by a drop in Mg2+ levels inside cells in pathological situations, which can result in major biological and metabolic dysfunction. Reduced ATP production and utilisation in the Na+-K+ ATPase's role in maintaining the ion gradient are caused by falling intracellular free Mg2+ concentrations. Additionally, by encouraging the generation of free radicals, the decrease in Mg2+ concentration within the cell affects the stability of melanine. Focused haemorrhages and brain edema are brought on by a drop in Mg2+ levels in the cortical structures' microcirculation, which damages micro vessels quickly and gradually.[3]Tetany, seizures, delirium, and cardiac arrhythmias are just a few of the major side effects associated with hypomagnesaemia and hypocalcaemia that the TGA (Therapeutic Good Administration) has officially warned about.[6] The mechanism of PPI-associated hypomagnesemia is related to altered intestinal absorption of magnesium with long-term PPI use.[5]

CLINICAL FEATURES:

The adverse effects of hypomagnesemia, or low levels of magnesium, ranges from cramps, nausea, and vomiting to tetany, disorientation, seizures, QT prolongation, oscillopsia, and walking difficulties all the way up to being unable to walk.[1,7]

OUTCOME AND MANAGEMENT:

After using Pantoprazole for a prolonged duration, individuals had hypomagnesimia. When the medicine was withdrawn, the patients' serum magnesium levels returned to normal. Dechallenge the PPI and began using an H2 receptor blocker when test results confirmed this. According to studies, taking magnesium supplements can reduce the water content of localised brain tissue and lessen the development of brain edema by preventing Ca^{2+} antagonists from blocking the opening of paracellular channels. [3]

II. CASE PRESENTATION

A 53yrs old male patient was admitted to emergency ward with complaints of convulsion 2-3 episodes since 2 days. He was apparently normal 2 days back and developed convulsion 1 episodes lasting for 10-20 mins and had a K/C/O reflux symptoms with Barrett's esophagitis on medication Tab. Pantoprazole 40mg once daily since 2 years. His familial history was not remarkable. He had no history of smoking or alcohol abuse. On examination, his blood pressure was 140/70mm Hg, pulse rate was 86bpm and SpO2 was 97% under room air. An electrocardiogram showed sinus tachycardia, high peak QT waves. The routine baseline investigation including CBC, Serum electrolytes, RFT, LFT were done. Elevated neutrophils (88%) and WBC count (18900cells/cumm), decreased lymphocytes (6%). In serum electrolytes, Magnesium level was decreased (0.2 mg/dl). Calcium (5.8mg/dl), Sodium (141 mEq/L), Potassium (2.3 mEq/L), Chloride (99 mEq/L) were normal. Based on this, the provisional diagnosis was seizures. Advised Inj. Benzodiazepam 10mg IV as STAT and Inj. Magnesium Sulphate 1600 mmol. Left cerebellar edemawas observed in CT. Hence diagnosis was confirmed as Pantoprazole induced hypomagnesemia and hypomagnesemia induced cerebellar edema. Then Inj. Mannitol 100mg IV was given twice daily. Clinicians ruled out all possible causes for these symptoms (risk factors such as age, gender, poly pharmacy, concurrent disease effects etc.) and suspected as Pantoprazole induced seizures due to hypomagnesaemia. Hence they dechallengePPI. On 5 days, the level of serum magnesium normalised and his symptom were resolved.

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III. DISCUSSION

In patients with the proper reason, proton pump inhibitor treatment is still an useful, effective, and safe strategy.[6] Few controversial research on the long-term usage of proton pump inhibitors (PPI) with hypomagnesemia have examined the negative effects of hypomagnesemia caused by PPI.[4] If hypomagnesemia is not treated, PPI-associated hypomagnesemia can progress to additional electrolyte disorders such hypocalcemia and hypokalemia that are resistant to calcium and potassium supplementation. It is uncertain how often hypomagnesemia brought on by PPIs is. Due to polypharmacy, the prevalence of additional medical problems that may impact their serum magnesium level, and impaired renal function, the risks of PPI-associated hypomagnesemia might be exacerbated in the older population. Due to other risk factors including age, concurrent medications, or medical illnesses that might potentially cause hypomagnesemia, some particular groups may be particularly vulnerable to PPI-induced hypomagnesemia. Thiazide and loop diuretics are two frequently prescribed drugs that might cause hypomagnesemia. Diabetes mellitus, inflammatory bowel disease, chronic pancreatitis, diarrhoea, alcoholism, and congenital renal magnesium wasting are among the illnesses that can cause hypomagnesemia. Patients on long-term PPIs should have their serum levels of magnesium, calcium, and potassium checked on a regular basis since these tests can identify hypomagnesemiarelated to PPIs as well as any secondary hypocalcemia or hypokalemia before patient's exhibit over to symptoms. [1]

PPIs are among the most often prescribed drugs in the world, and treatment may extend for months or even years. The development of gastrointestinal Mg squandering, however, is a glaringly underappreciated adverse impact of long-term PPI therapy. This is likely due to a direct inhibitory influence on the active intestinal Mg absorption processes. In the complete absence of any gastrointestinal symptoms, this might result in the depletion of all body Mg reserves, which can cause severe hypomagnesemia.[7] Clinical signs of over to hypomagnesemia, as well as related hypocalcemia and hypokalemia, should be thoroughly monitored by healthcare professionals in patients. [1] Measuring renal Mg excretion in the 24-hour urine is the most helpful diagnostic procedure for differentiating between renal and gastrointestinal Mg losses. Renal Mg wasting is indicated by a daily excretion of more than 10 to 30 mg or a fractional excretion of Mg exceeding 2%. Treatment for hypomagnesemia entails removing the triggers (such as discontinuing or reducing drugs) and giving extra magnesium intravenously or orally. Depending on the severity of the clinical symptoms and indicators, the delivery route and corrective rigour are determined.

III. CONCLUSION

Looking In conclusion, our case report provides additional information about the existence of a relationship between the use of Pantoprazole and the occurrence of hypomagnesemia when used for a long term of Pantoprazole as an adverse effect though rarely seen. This adverse effect is fairly rare and typically dangerous if left untreated. It is critical for the clinicians to explore and rule out other causes of electrolyte imbalance as well as to be aware of this uncommon adverse effect of proton pump inhibitors.

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