

Electrolyte disorders in a young female following short-term omeprazole therapy

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Received: 02 March 2018

Accepted: 29 March 2018

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ABSTRACT

A 29 years old female presented to us in the metabolic clinic of the University of Port Harcourt Teaching Hospital (UPTH) on account of a week history of easy fatigability, weakness, and lower extremity muscle cramps associated with numbness and tingling sensation in the peri-oral area, fingers and toes. Two weeks prior to the onset of her presenting symptoms, she had visited a local pharmaceutical shop on account of a distressing epigastric discomfort and was subsequently placed on daily oral omeprazole 20mg daily for a month by a pharmacist. She had been on the omeprazole medication for two weeks before her present symptoms manifested. Her past medical history was not suggestive of hypoparathyroidism nor pancreatitis. She was married with three children and has an uneventful family, social and obstetric histories. On examination, she was a healthy well-oriented young female with positive Trousseau's, Chvostek's and epigastric tenderness signs. Further Laboratory evaluation revealed she had low plasma magnesium, low plasma albumin-corrected calcium, and low serum parathyroid hormone levels, while other laboratory parameters were essentially normal. A diagnosis of omeprazole-induced electrolyte disorders (hypomagnesaemia and hypocalcaemia) associated with hypoparathyroidism was made following the review of her clinical examination and laboratory findings. She was subsequently managed with oral magnesium supplements following the withdrawal of the omeprazole medication (replaced with oral ranitidine), monitored weekly, and full recovery was achieved after three weeks.

Keywords: Hypomagnesaemia, hypocalcaemia, Hypoparathyroidism, Omeprazole

INTRODUCTION

Omeprazole is a proton pump inhibitor employed in the management of dyspeptic symptoms.¹ It is one of the commonest medications prescribed in the management of peptic ulcer disease, eradication of *Helicobacter pylori* infection and management of Zollinger-Ellison syndrome in with very few side effects.^{1,2} Various case reports have been published in the literature implicating omeprazole as a culprit in a rare drug-induced electrolyte abnormalities notably hypomagnesaemia and hypocalcemia associated with hypoparathyroidism.³⁻⁸ These electrolyte abnormalities have been attributed to omeprazole-induced

hypomagnesaemia which leads to defective secretion of parathyroid hormone and the subsequent hypocalcemia.^{9,10} However, the majority of these cases which had been noted mostly in the western world had all been reported mainly after long-term medication with omeprazole especially among the elderly. Omeprazole-induced electrolyte disorders are rare following short-term omeprazole medication and among the younger age groups. Herein, we present a rare case of omeprazole-induced hypomagnesaemia and hypocalcemia associated with hypoparathyroidism in young female following short-term omeprazole therapy for epigastric discomfort.

CASE REPORT

A 29 years old female, who was referred from the General Outpatient Department of the University of Port Harcourt Teaching Hospital, Nigeria, presented to us in the Metabolic Clinic of the same hospital on account of a week history of easy fatigability, weakness, and lower extremity muscle cramps associated with numbness and tingling sensation in the peri-oral area, fingers, and toes. Two weeks prior to the onset of her presenting symptoms, she had visited a local pharmaceutical shop, where she was prescribed oral omeprazole 20mg (TEVA UK Limited) once daily for a month on account of a distressing epigastric discomfort that had affected her usual daily activities.

Her medical history was not suggestive of hypoparathyroidism nor pancreatitis. She was married with three children and her family, social, and obstetric histories had been uneventful. During her visit to the General Outpatient Department, she was subjected to the following investigations: liver function test, renal function test, thyroid function test, plasma electrolytes (sodium, potassium, and bicarbonate), fasting lipid profile, fasting plasma glucose, urinalysis, and an abdominopelvic ultrasound scan. The results of these investigations were all found to be essentially normal.

On clinical examination, she appeared healthy looking, well-oriented, in no distress, afebrile (36.3° C), not pale, not edematous, and not icteric. She weighed 81 kg, height of 1.72 meters and a calculated body mass index of 27.4kg/m², hence overweight. She had a blood pressure of 120/80mmHg, a peripheral pulse of 72 beats per minute and a respiratory rate of 14 cycles per minute. However, the Trousseau's and Chvostek's signs were positive. Auscultation of her breath and heart sounds were unremarkable. Palpation of her abdominopelvic region did not reveal any organ enlargements, however, tenderness was elicited in the epigastric region. No abnormality was observed on examination of her central nervous system, nose, throat, and eye. From the foregoing, an initial provisional diagnosis of hypocalcemia secondary to omeprazole therapy was made. To further evaluate the patient to define the diagnosis, the following investigations (Table 1) with their results were ordered prior to definitive diagnosis and subsequent management. Electrocardiogram (ECG) was not done due to financial constraints on the part of the patient. Calculated Naranjo's adverse drug reaction (ADR) scale of +6 was subsequently obtained which implies a probable adverse drug reaction. A definitive diagnosis of omeprazole-induced hypomagnesaemia and hypocalcemia associated with hypoparathyroidism was finally made following the subsequent review of her medical history, clinical examination findings, and the results of all the requested laboratory investigations as shown in Table 1.

Outpatient management commenced with the immediate withdrawal of the oral omeprazole medication was

instituted and replaced with oral ranitidine. With the understanding of the pathophysiology of omeprazole-induced electrolyte disorders which is based on initial hypomagnesaemia, the patient was placed on oral low-dose magnesium 500mg daily and monitored weekly with plasma total magnesium, plasma total albumin-corrected calcium concentrations and serum intact parathyroid hormone laboratory assays shown in Table 2. Full recovery from symptoms was achieved by the second week of treatment and a confirmatory investigation by the third and fourth week of treatment revealed complete resolution of hypomagnesaemia, hypocalcemia, and hypoparathyroidism.

Table 1: Investigations and their respective results.

Investigations	Values	Reference range/remark
Serum Intact PTH	6.4	10-65ng/l
Serum 25 (OH) Vitamin D	85.5	25-165nmol/l
Plasma Inorganic Phosphate	1.0	0.9-1.5mmol/l
Plasma Total Magnesium	0.5	0.7-1.0mmol/l
Plasma Albumin	35	34-50g/l
Plasma Total Calcium (Uncorrected)	1.8	2.1-2.6mmol/l
Plasma Albumin-corrected calcium	1.9	2.1-2.6mmol/l
Urinalysis	----	NAD
Abdominopelvic USS	----	NAD

ng/l = nanogram per liter; mmol/l = millimole per liter; g/l = gram per liter; HIV = Human Immunodeficiency Virus; NAD = No Abnormality Detected; PTH = Parathyroid Hormone; USS = Ultrasound Scan.

Table 2: Values of the weekly monitored laboratory parameter during treatment.

Parameter	Week one	Week two	Week three	Week four
Total plasma magnesium (mmol/l)	0.50	0.60	0.70	0.80
Total plasma albumin-corrected calcium (mmol/l)	1.90	2.10	2.20	2.20
Serum Intact PTH (ng/l)	6.40	9.60	18.90	33.20

ng/l = nanogram per liter; mmol/l = millimole per liter; PTH = Parathyroid Hormone

Oral magnesium was stopped following full recovery. She was counseled against self-medication and to subsequently seek medical advice from a trained physician before using any proton pump inhibitors in future.

DISCUSSION

The high efficiency and wide tolerability of the Proton Pump Inhibitors (PPIs) of which omeprazole is a prototype

has made them one of most prescribed drugs for acid-associated disorders of the gastrointestinal tract.¹ These PPIs functions mainly by inhibiting acid secretion from the parietal cells.^{1,2} These groups of drugs have a very high margin of safety and seem more superior to the histamine-2 receptor antagonist. However, various case reports have been published since 2006 regarding the association of various PPIs with mild, moderate and serious electrolyte disorders.³⁻⁶ This has even prompted the United State Food and Drug Administration (FDA) to issue an alert regarding these electrolyte disorders.²

Omeprazole-induced electrolyte disorders is one of the most reported in the literature of all the PPIs.³⁻⁶ These electrolyte disorders associated with omeprazole therapy is mostly reported among the elderly following a long-term therapy especially those taking other medications prone to the development of hypomagnesaemia.^{7,8} This norm is not in accord with the index patient who is relatively young and had been on only omeprazole medication for just two weeks prior to onset of symptoms. The mechanism of omeprazole-induced electrolyte disorders is hinged on the ability of omeprazole to inhibit active and passive absorption of magnesium from the gastrointestinal tract. The subsequent hypomagnesaemia leads to defective secretion of parathyroid hormone (PTH), the reduced PTH (hypoparathyroidism) culminates in the reduced plasma calcium (hypocalcemia).^{9,10}

The management of omeprazole-induced electrolyte disorders involves the initial withdrawal of omeprazole medication and supplementation with magnesium, calcium, and Vitamin D as noted in various case reports.^{3,6} However, we had managed the index case based on the general understanding that the core pathophysiology of omeprazole-induced electrolyte disorders is based on hypomagnesaemia. Although the reduced gastric acidity associated with omeprazole medication has been linked to reduced intestinal calcium absorption also and subsequent hypocalcemia, hypomagnesaemia is accepted as the likely trigger for the other associated electrolyte disorders and hypoparathyroidism.^{9,10} In the index case, we had only withdrawn omeprazole and supplemented the patient with only oral magnesium and the patient made a satisfactory recovery which supports the role of hypomagnesaemia in omeprazole-induced electrolyte derangements.⁹

CONCLUSION

Electrolyte disorders are becoming a common feature of the PPIs including omeprazole. Though common among the elderly, it could also occur among the younger age group. It becomes imperative that patients on PPIs

(omeprazole most importantly) irrespective of age be monitored regularly to avert potential complications of these electrolyte disorders.

ACKNOWLEDGEMENTS

The authors are grateful to Mr. Aleme BM for his expert laboratory assistance.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Amadi C, Owamagbe EM, Duru US. Electrolyte disorders in a young female following short-term omeprazole therapy. *Int J Basic Clin Pharmacol* 2018;7:1040-2.