Journal of Trace Elements in Medicine and Biology 26 (2012) 234–237

Contents lists available at SciVerse ScienceDirect

Journal of Trace Elements in Medicine and Biology

journal homepage: www.elsevier.de/jtemb

Clinical Studies

Effects of omeprazole consumption on serum levels of trace elements

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ARTICLE INFO

Article history:
Received 21 December 2010
Accepted 7 February 2012

Keywords:
Omeprazole
Trace elements
Gastroesophageal reflux disease

ABSTRACT

Project: Omeprazole is one of the most frequently prescribed drugs in patients with gastroesophageal reflux disease (GERD). It increases the gastric pH and this in turn may change the intestinal absorption of trace elements. This study was conducted to assess the effects of omeprazole consumption on the serum level of trace elements.
Procedures: The studied subjects were selected from the list of patients referred to the gastroenterology department of 5 Azar hospital in Golestan province of Iran for whom omeprazole was prescribed by a gastroenterologist. Blood samples were obtained before (phase I) and after an eight-week period (phase II) of omeprazole consumption. Serum levels of trace elements were assessed by the photometric method.
Results: Sixty seven patients were recruited of whom, 35.82% were males. There was no significant difference in serum levels of Fe, P, Ca and Cu between phases I and II. Serum concentration of Zn was significantly lower in phase II than I ($P=0.02$). The proportion of male patients with low Zn levels was significantly higher in phase II (50%) than I (16.7%) ($P=0.01$). We found no significant difference in the proportion of female patients with low Zn levels between phase I (37.2%) and phase II (27.9%).
Conclusions: We found no significant reduction in serum levels of Fe, P, Ca and Cu in phase II. However, our results showed that serum level of Zn was significantly lower after omeprazole consumption in males. So, nutritional supplement of Zn should be considered in male patients treated with omeprazole.

Introduction

Gastroesophageal reflux disease (GERD) is a kind of disease occurred when distal esophageal muscle does not close the sphincter completely. This change results in abnormal reflux of gastric acid into the esophagus. The typical symptom of GERD is heartburn [1]. It is estimated that GERD symptoms occur in up to 40% of population [2]. Omeprazole is one of the most frequently prescribed drugs in GERD patients. However, sometimes patients take it inappropriately and without physician's prescription [3]. Omeprazole is available in the form of 20 mg capsule [4]. It can relieve sign and symptoms of GERD. This drug is considered as an anti-gastric acid agent and its mechanism is to inhibit proton pump in the gastric mucosa and consequently, to reduce gastric acidity. Omeprazole inhibits proton pumps by blocking the production of gastric hydrochloric acid and changes the gastric pH to alkaline range. Gastric acidity plays an important role in absorption of food particles such as trace elements. Absorption of trace elements often takes place in acidic media of stomach and proximal part of small intestine. Some elements such as calcium (Ca), phosphorous (P) and iron (Fe) are soluble in acidic medium and insoluble in the alkaline environment [4]. Increasing gastric PH interferes with the absorption of the above mentioned elements [5]. In addition to indirect effect of omeprazole on the absorption of trace elements, some studies reported that omeprazole may directly block the absorption of Ca and other minerals [5].

Trace elements play important roles in a number of body functions. Ca is the most abundant mineral in the body and a large amount of it is deposited in bone and teeth. Reduction of Ca level in the body may cause some abnormalities such as osteoporosis and osteomalacia and rickets. The absorption of intestinal P follows the absorption of Ca. So, impairing the absorption of Ca due to omeprazole consumption may in turn lead to changes in the absorption of P [6]. Zinc (Zn) deficiency may results in growth delay, infertility in males, immune system dysfunction and cognitive impairment [7]. Copper (Cu) is a co-factor for at least 30 enzymes. It is directly absorbed through gastrointestinal (GI) tract [8]. Therefore Over-use of omeprazole may cause trace elements deficiency and this may lead to abnormalities in some of important body functions.

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doi:10.1016/j.jtemb.2012.02.002

Golestan province, located in northeast of Iran, is known as a high-risk area for upper GI (UGI) cancers. Symptoms of UGI problems, including GERD may wrongly be considered as manifestations of a malignant condition. These patients are frequently visited by various physicians. This in turn may result in inappropriate use and over-use of medicines such as omeprazole in this region. Therefore, we conducted this study to determine the effects of omeprazole consumption on the serum levels of Cu, Zn, Ca, P, Fe and erythrocyte indices of patients in Golestan province of Iran.

Materials and methods

The studied subjects were selected from the list of patients referred to the department of gastroenterology in 5 Azar hospital of Golestan province of Iran for whom omeprazole was prescribed by a gastroenterologist. Patients who did not take the drug regularly or consumed supplementary drugs containing Ca, P, Fe, Cu and Zn were excluded. Patients were referred to the biochemical laboratory of the Golestan University of Medical Sciences for blood sampling in two phases. The first sampling (phase I) was done before starting omeprazole therapy and the second sample (phase II) was collected after finishing an eight-week period of omeprazole consumption. Three ml of blood was taken from each of the participants. Complete Blood Count (CBC) was performed immediately after sampling by cell counter Sysmex KX-21, Japan. Then, serum was separated and stored at −80 °C until used. The trace elements were measured by Mindray BS-200 autoanalyzer, China. Ca, P and Fe were assayed by Parsazmoon kit (Iran). Cu and Zn were assessed by Greiner kit (Germany) and Elithec kit (France), respectively. To reduce the bias of the colorimetric and chemical methods, all tests were performed twice, and the mean values were considered for analysis. Paired *t*-test, Student's *t*-test, Mann–Whitney *U* test and Chi-square test were used for data analysis. *P*-values of less than 0.05 were considered as significant.

Results

Sixty seven 20–50 years-old patients were recruited in the study. Twenty four (35.82%) of the participants were male. Serum concentration of Zn was significantly lower in phase II than phase I ($P = 0.02$). There was no significant difference in serum levels of Fe, P, Ca and Cu between phases I and II. Table 1 shows the mean and standard deviation of trace elements before and after omeprazole consumption. The results of erythrocyte indices are shown in Table 2.

Serum levels of Ca and P in all male patients were within reference interval before omeprazole consumption. After omeprazole consumption, the levels of Ca and P in 16.7% of male patients were lower than reference interval. The proportion of male patients with low Cu levels was the same in phases I and II. The proportion of male patients with low Zn levels was significantly higher in phase II (50%) than phase I (16.7%) ($P = 0.01$). After omeprazole consumption, serum concentration of all variables except Fe and Cu were lower than reference interval in 16.7% of males.

Serum levels of Fe, Cu and Ca were within reference interval in all females both in phases I and II. All female patients had normal levels of P before omeprazole consumption, but serum level of P in 9.3% of females was lower than reference interval in phase II. We found no significant difference in the proportion of female patients with low Zn levels between phase I (37.2%) and phase II (27.9%) ($P = 0.36$).

Table 1
Mean (SD) of serum concentration of trace elements before (phase I) and after omeprazole consumption (phase II).

Trace elements	Fe (μg/dl)			P (mg/dl)			Ca (mg/dl)			Zn (μg/dl)			Cu (μg/dl)		
Phase	I	II		I	II		I	II		I	II		I	II	
Male ($n = 24$)	78.3 (23.4)	99.2 (65.3)		3.2 (0.5)	3.2 (0.8)		10.4 (0.8)	9.8 (1.1)		92.7 (22.6)	73.5 (26.2)		84.6 (26.6)	85.7 (28.3)	
Female ($n = 43$)	81.7 (22.6)	72.7 (39.9)	NS[a]	3.6 (0.5)	3.6 (0.5)	NS[a]	10.5 (0.8)	10.6 (1.0)	NS[a]	79.9 (23.7)	81.0 (29.9)	0.03[a]	121.0 (30.9)	126.1 (35.6)	<0.01[a]
Total ($n = 67$)	80.5 (22.8)	82.2 (51.6)	0.04[b]	3.4 (0.7)	3.5 (0.6)	0.01[a]	10.4 (0.8)	10.3 (1.1)	<0.01[a]	84.5 (23.9)	78.3 (28.7)	NS[a]	107.9 (34.1)	111.6 (38.3)	<0.01[a]

NS = not significant; μg/dl = microgram per deciliter; mg/dl = milligram per deciliter.
[a] Student's *t*-test.
[b] Mann–Whitney *U*.

Table 2
Mean (SD) of hemoglobin (Hb), hematocrite (HCT), erythrocyte count (RBC) and mean corpuscular volume (MCV) before (phase I) and after omeprazole consumption (phase II).

Erythrocyte indices	Hb (g/dl)			HCT (percent)			RBC ($\times 10^6$/μl)			MCV (femtoliters)		
Phase	I	II		I	II		I	II		I	II	
Male (n = 24)	13.2 (1.9)	13.4 (1.6)		40.6 (4.5)	40.3 (5.0)		5.6 (1.0)	5.5 (0.9)		73.5 (7.3)	73.6 (7.8)	
Female (n = 43)	12.9 (1.2)	NS[a]	13.1 (1.1)	0.04[a]	38.4 (4.2)	<0.01[a]	40.1 (4.2)	<0.01[a]	4.6 (0.6)	NS[a]	4.9 (0.5)	NS[a]	83.1 (6.5)	NS[a]	82.6 (5.4)	NS[a]
Total (n = 67)	13.0 (1.5)	13.1 (1.3)		39.2 (4.4)	40.2 (4.5)		5.0 (0.9)	5.1 (0.7)		79.7 (8.2)	79.4 (7.7)	

NS = not significant; $\times 10^6$/μl = million per microliter; g/dl = gram per deciliter.
[a] Student's t-test.

Discussion and conclusion

The aim of this study was to assess the effects of omeprazole consumption on serum levels of trace elements. There was a significant difference in serum levels of Zn and Cu between males and females before omeprazole consumption. This may be due to differences in nutritional status or physiological state of the disease between males and females. We found that Zn had more been affected by omeprazole consumption than other variables. Our findings showed a significant reduction in serum Zn levels after omeprazole consumption in males. In the other hand, the proportion of male patients with low Zn level was 16.7% and 50% before and after omeprazole consumption, respectively. Hiroshi et al. reported a significant lower serum Zn level in omeprazole treated rats than controls [9]. The result of a study by Ozutemiz et al. was in line with ours and suggested that omeprazole reduces intestinal Zn absorption by decreasing gastric pH [10]. The results of Alastair's study suggested that low gastric pH may not be necessary for intestinal absorption of Zn [11].

Our results showed no significant difference in serum levels of Ca, Fe, Cu and P between phases I and II. Mizunashi et al. reported that elimination of Ca through urine decreased after using omeprazole [12]. In the study of Graziani et al., serum level of Ca was decreased significantly after omeprazole consumption. They reported no significant difference in the placebo group. They also found no significant relationship between serum P level and omeprazole or placebo consumption [13]. Edemilson Cardoso da Conceic et al. reported a significant increase in serum transferrin and a decrease in hepatic Iron after four weeks as well as a reduction in Hb level after six weeks of omeprazole consumption in rats. Cases received Iron supplement (Fe or Fe^{3+}) in addition with omeprazole showed no difference in Hb and serum transferrin compare to controls [14].

Serfaty-Lacrosniere et al. suggested that omeprazole consumption led to a significant increase in gastric pH in omeprazole treated patients than controls. However, they did not find a significant difference in intestinal absorption of Ca, P, Mg and Zn between the two groups. So, they concluded that change in gastric pH may not be the only factor affecting the intestinal absorption of trace elements [15]. Parts of the results of our study considering Ca and P were in line with Serfaty-Lacrosniere's one. Although, chemical method is not the gold standard for assessing these trace elements, but it is routinely used in medical laboratories and physicians accept the results of this method for clinical judgment. Therefore, the results of the present research are near to the results reported in medical laboratories. Serum level of trace elements was assessed by the same method both in phases I and II. So, method variation was not an important concern for interpretation of the results in this study.

In conclusion, we found no significant reduction in serum levels of Fe, P, Ca and Cu in phase II compare to phase I. However, our results showed that serum level of Zn was significantly lower after omeprazole consumption in males. So, nutritional supplements of Zn should be considered in male patients treated by omeprazole.

Acknowledgement

This project was approved and supported by Golestan University of Medical Sciences.

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