Original Article

Prolong Omeprazole Therapy Impacts on Biochemical Parameters in Peptic Ulcer Disease Patients

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Abstract

Background: Prolonged use of proton pump inhibitors (PPIs) is associated with a range of potential adverse effects. Omeprazole, one of the most widely prescribed PPIs globally, is commonly used in clinical practice.

Objective: To assess the impact of prolonged omeprazole use on specific biochemical markers in individuals receiving treatment for a year or more.

Methods: This case-control study was conducted in the Department of Physiology of Armed Forces Medical College, Dhaka Cantonment using data obtained from at the Department of Medicine (Gastroenterology), Kurmitola General Hospital, Dhaka from October 2023 to March 2024, enrolling 122 participants; 62 patients diagnosed with uncomplicated peptic ulcer disease (PUD) (32 females, 30 males) and 60 age-matched healthy controls (30 females, 30 males)-selected from individuals aged 30 to 65 years presenting with epigastric symptoms and confirmed as diagnosed case of PUD through upper gastrointestinal endoscopy.

Results: While high-density lipoprotein levels were unaffected ($p>0.05$), prolonged use of omeprazole was related to significant increases in triglycerides, cholesterol and low-density lipoprotein levels ($p<0.05$). There was no discernible change in the levels of alanine aminotransferase ($p>0.05$), however there were elevated levels of alkaline phosphatase ($p=0.001$) and aspartate aminotransferase ($p=0.001$). Further, the group treated with omeprazole had significantly higher creatinine levels ($p=0.001$). Serum ferritin and calcium levels were also significantly lower ($p<0.05$) in peptic ulcer patients than in healthy controls.

Conclusion: The study's findings demonstrate that Omeprazole use for a prolonged period of time is related to substantial changes in lipid profiles, liver enzymes, kidney function indicators and essential minerals, implying potential impacts on patients' metabolic and biochemical state of health.

Keywords: PPIs, Prolong use, PUD, Lipid profile, Liver enzymes, Kidney function, Serum ferritin, Calcium levels.

Introduction

Peptic ulcer disease (PUD), which includes gastric and duodenal ulcers[1,2], is a common gastrointestinal condition characterized by painful sores in the stomach or duodenal lining.[2] It occurs when the protective mucus barrier is weakened, allowing acid to damage the tissue.[3] Histologically, it involves mucosal necrosis with lesions ≥0.5 cm deep. The most common cause is Helicobacter pylori infection, followed by the use of NSAIDs like aspirin and ibuprofen.[4] PUD affects about 4.1% of the population, with a lifetime prevalence of around 10%.[5]

Omeprazole, a substituted benzimidazole and the first approved PPI, is commonly used to treat acid-related gastrointestinal problems.[6] It inhibits the H^+/K^+-ATPase enzyme in gastric parietal cells, lowering acid output. It is extremely helpful in treating PUD, gastro-oesophageal reflux disease (GERD), erosive oesophagitis, and Zollinger-Ellison syndrome.[7] Clinical trials and real-world investigations demonstrate improved mucosal healing and symptom alleviation compared to H_2-receptor antagonists. Omeprazole is well tolerated in the short term; however, prolonged use may be associated with concerns such as vitamin deficits, kidney injury and cardiovascular consequences.[8]

Omeprazole rarely produces side effects in the short term, with the most prevalent being headaches, vomiting, diarrhoea, stomach distress and constipation. Serious side effects are exceptional; however they can include liver damage, joint discomfort from subacute cutaneous lupus erythematosus and allergic responses. Long-term usage (more than 3 months) might cause low blood magnesium levels and use for more than a year may raise the risk of bone fractures, gastrointestinal infections and vitamin B_{12} deficiency.[9] Long-term PPI medication may also have an effect on haematological markers, according to certain reports.[10] Reduced gastric acidity from proton pump inhibitors can impair the intestinal absorption of key trace elements like iron, zinc, selenium and copper potentially leading to deficiencies and weakened antioxidant activity. Given the widespread use of omeprazole and emerging adverse effects in long-term users, this study aims to evaluate its impact on specific biochemical markers in patients treated for 18 months or more.

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Materials and Methods

This case-control study was conducted in the Department of Physiology of Armed Forces Medical College, Dhaka Cantonment using data collected from the Department of Medicine (Gastro-enterology) at Kurmitola General Hospital (KGH) in Dhaka Cantonment, Bangladesh between October 2023 and March 2024. The study enrolled 122 individuals, 62 patients diagnosed with uncomplicated peptic ulcer disease (32 women, 30 men) and 60 healthy controls (30 women, 30 men); all aged between 30 to 65 years. Participants were selected from those presenting to the outpatient gastroenterology clinic with epigastric symptoms and underwent upper gastrointestinal endoscopy and were diagnosed as a case of PUD. Blood samples were obtained from every participant for biochemical analysis in the Kurmitola General Hospital's hematology laboratory.

Patients with Peptic Ulcer Disease who had comorbid conditions including inflammatory or autoimmune disorders, severe systemic illnesses, or those receiving medications that could influence white blood cell counts were excluded from the study. Specific exclusion criteria included hematopoietic system disorders, active infections, hypertension, diabetes mellitus, epilepsy, myocardial infarction, heart failure and other cardiac conditions, hepatic or renal failure, substance or alcohol addiction, severe head injury, intellectual disability, pregnancy and obesity (BMI >30kg/m^2).

All eligible participants were thoroughly informed about the purpose, objectives and procedures of the study and were encouraged to participate voluntarily. Written informed consent was obtained from each participant. Detailed histories covering personal, medical, family, socioeconomic, occupational and drug-related aspects were recorded. Comprehensive physical examinations were performed and documented. For biochemical analysis, blood samples were collected from the antecubital vein at approximately 8:00 AM and stored in hemogram tubes. Clinical biochemical tests were then conducted, including assessments of lipid profile, alkaline phosphatase (ALKP), alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IDBIL), serum ferritin, total calcium, urea, creatinine, uric acid, fasting plasma glucose, and HbA1c levels. The 2013 revised Declaration of Helsinki and its amendments or similar ethical norms, were followed in this study. The study was approved by the local Ethics Committee.

All data were presented as mean ± standard deviation (SD). Categorical variables, including frequencies and proportions, were analyzed using the Chi-square test (χ^2). Comparisons between two groups for normally distributed continuous variables were conducted using the independent samples t-test. Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS v26). A p-value of <0.05 was considered indicative of statistical significance.

Results

There were no statistically significant differences between the peptic ulcer disease patient group and the control group in terms of gender, age distribution, BMI, blood pressure (systolic and diastolic), educational status, socioeconomic status, or marital status (Table-I). This indicates that the two groups were well-matched demographically and clinically, minimizing confounding variables in the comparison of biochemical parameters.

Regarding biochemical parameters, it has been found that the long-term use could exert a variation in certain parameters. In serum cholesterol levels, we found a significant elevation (p=0.001) in the levels of total cholesterol in patients group (219.33±22.34 mg/dL) in comparison to healthy group (175.56±40.31 mg/dL), alongside significant elevation (p=0.001) of triglyceride levels in patients group (210.32±45.88 mg/dL) compared to healthy group (170.84±39.15 mg/dL). Analysis of lipoprotein parameters such as DLDL and vLDL showed significant increases (p=0.01) in patients group (147±40.11; 46.91±12.51 mg/dL), compared to healthy group (118.77±26.70; 30.21±7.73 mg/dL). However, there were no significant differences (p>0.05) between the two groups in HDL, as seen in Table-II and Figure-1.

Indicators of liver functions were also compared between the groups (Table-II). Significant increases in ALKP (p=0.001) and ASAT (p=0.01) levels were detected in patients group (90.33± 7.88; 25.55±5.70 U/L) when compared to healthy group (77.66±14.74, 15.34±5.71 U/L). Whereas, no significant change (p>0.05) in ALAT level (U/L) was found. Renal function parameters were compared between patient and healthy groups. As shown in Figure-2, creatinine level was significantly increased (p=0.001) in patients group (1.32±0.36 mg/dL) in comparison to healthy group (0.80±0.26 mg/dL). Also, significant differences (p=0.001) were observed in levels of blood urea between patients group (46.58±13.78mg/dL) and healthy group (28.24± 14.11mg/dL). Moreover, patients group had significantly lower (p=0.001) serum levels of ferritin (19.12±15.47mg/dL) than healthy group (65.77±49.51 mg/dL). Serum calcium concentration in long-term patients group (7.92±0.90mg/dL) was lower (p=0.001) than healthy group (9.40±1.40mg/dL). No significant changes were noticed between the groups in the levels of TBIL, DBIL and IDBIL (1.11±1.21 vs. 0.87±0.28 mg/dL, p>0.05; 0.33± 0.94 vs. 0.31±0.77mg/dL, p>0.05; 0.46±0.21 vs. 0.44±0.98 mg/dL, p>0.05, respectively) (Table-II).In addition as shown in Table-II, no significant changes were found between the groups as regards to the serum levels of fasting plasma glucose, HbA1c (%) and uric acid (97.8±18.6 vs. 97.4±18.6mg/dL, p>0.05; 5.8±0.4 vs. 5.7±0.3mg/dL, p>0.05; 5.09±1.58 vs. 4.90± 1.48mg/dL, p>0.05, respectively).

Table-I: Clinical characteristics of PUD patients and control groups (n=122)

Variables	Categories	PUD Patients Group (n=62)	Control Group (n=60)	*P* value
Gender	Female	32(51%)	30(50%)	0.781
	Male	30(49%)	30(50%)	0.812
Age (years)	30-35	15(25%)	15(25%)	0.910
	36-50	22(35%)	18(30%)	
	51-65	25(40%)	27(45%)	
BMI (kg/m^2)		22.12±3.10	23.8±4.10	0.612
Blood Pressure (mm Hg)	SBP	130±15	135±16	0.082
	DBP	85±12	80±10	0.074
Educational status	Illiterate	24(39%)	25(41%)	0.652
	Primary	16(26%)	14(24%)	
	Secondary	13(20%)	12(20%)	
	Higher level and above	9(15%)	9(15%)	
Socioeconomic status (score)		1.48±0.31 (1-4)	1.52±0.28 (1-4)	0.101
Married		48(78.12%)	45(75.18%)	0.124

BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure. Data were expressed as mean±SD. Statistical analysis was done with independent sample 't' test and Chi-square test

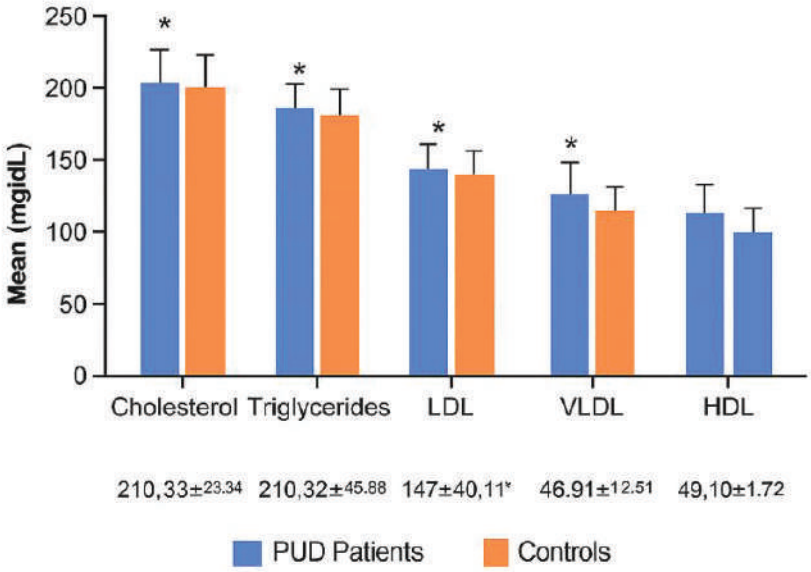

Figure-1: Comparison of lipid profiles between PUD patients and controls

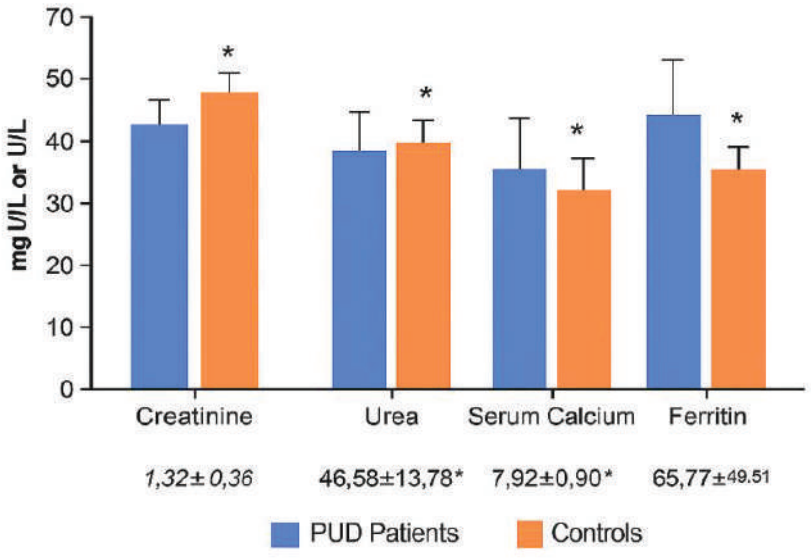

Figure-2: Comparison of kidney functions and mineral levels between PUD patients and controls

Table-II: Comparison of biochemical parameters between PUD patients and controls (n=122)

Variables	PUD Patients Group (n=62)	Control Group (n=60)	P value
DLDL (mg/dL)	147±40.11	118.77±26.70	0.001*
ALKP (U/L)	90.33±7.88	77.66±14.74	0.001*
ALAT (U/L)	28.54±12.73	24.23±228.65	0.214
ASAT (U/L)	25.55±5.70	15.34±5.71	0.001*
Total Bilirubin (mg/dL)	1.11±1.21	0.87±0.28	0.212
Direct Bilirubin (mg/dL)	0.33±0.94	0.31±0.77	0.125
Indirect Bilirubin (mg/dL)	0.46±0.21	0.44±0.98	0.124
Fasting Plasma glucose (mg/dL)	97.8±18.6	97.4±18.6	0.312
HbA_1c (%)	5.8±0.4	5.7±0.3	0.231
Uric acid (mg/dL)	5.09±1.58	4.90±1.48	0.215

*Significance at level <0.05. Data are presented as mean±SD. NS: Non-significant differences. Statistical analysis was done with independent sample 't' test.

Discussion

This study assessed the effects of prolonged omeprazole use on biochemical parameters, revealing notable alterations in patients' profiles. Suppression of gastric acid affects lipid digestion, with evidence suggesting that omeprazole enhances lipid absorption. This may be due to increased lipolytic activity in gastric juices and improved lipid uptake in the small intestine.[11] Additionally, PPIs may influence cholesterol metabolism. The observed rise in cholesterol, triglycerides and LDL in long-term users supports previous findings associating omeprazole to altered lipid metabolism.[12,13]

Optimal cellular metabolism depends on steady plasma mineral levels. Patients receiving long-term omeprazole therapy have lower plasma calcium levels, which is consistent with decreased intestinal calcium absorption.[14,15] Omeprazole causes achlorhydria and impairs calcium solubility and absorption by inhibiting the H^+/K^+ ATPase in the stomach parietal cells. In addition to impeding lipolysis, a crucial stage in calcium absorption, decreased stomach acidity raises the risk of hypocalcaemia.[15,16] Consuming protein may enhance the absorption of calcium, but long-term PPI use is still risky. Also, hypocalcaemia has been connected to possible cardiovascular side effects in long-term PPI users.[17]

This study observed considerably elevated serum ASAT and ALKP levels in long-term omeprazole users compared to healthy controls, with no notable changes in ALAT or bilirubin. These enzymes, primarily found in liver cells, serve as indicators of hepatic tissue damage when elevated.[18] Although levels remained within normal limits, the differences suggest potential hepatic stress. A case report also showed elevated ASAT, ALAT and GGT in an elderly patient on omeprazole, which normalized after discontinuation.[19] Conversely, recent studies in liver cirrhosis patients reported decreased ASAT and ALAT with PPI use. This study found substantial increases in serum creatinine and blood urea among omeprazole users, aligning with previous findings indicating possible renal effects.[20]

Elevated blood urea and serum creatinine, which have minimal sensitivity for early identification, were indicative of impaired kidney function among PPI users.[12,21] In line with other research that related persistent PPI usage to decreased iron storage, omeprazole patients also had noticeably lower serum ferritin levels than healthy controls. Iron deficiency anaemia may result from omeprazole's impairment of iron absorption, even though ferritin insufficiency seems to be uncommon. Serum iron was not tested, however its evaluation might have supported these results.[22,23] In line with earlier studies, no appreciable variations in fasting glucose, HbA1c or uric acid levels were discovered.[24,25]

Conclusion

Prolonged use of omeprazole in patients with peptic ulcers is associated with notable alterations in biochemical parameters, such as elevated blood urea, triglycerides, LDL, VLDL, ALKP, ASAT, creatinine and cholesterol, suggesting potential disruption of lipid metabolism, mild liver stress and renal impairment. Decreased serum ferritin and calcium levels may raise the possibility of hypocalcaemia and iron deficiency anaemia. HDL, ALAT, bilirubin, glucose, HbA1c and uric acid did not significantly change. Throughout long-term treatment, clinicians should keep an eye on these markers, use the lowest effective dose for the shortest amount of time and conduct routine biochemical assessments. Long-term users may require alternate therapies or supplements to avoid problems.

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