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Orginal Article

Do elevated blood calcium levels in patients with peptic ulcer facilitate perforation?

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Abstract

Aim: Calcium is primarily stored in bones in the body. The increase in blood calcium level due to primary or secondary causes leads to several impairments of the gastrointestinal system like nausea-vomiting, and peptic ulcer (PU). In this study, we want to compare and analyse the difference in blood calcium levels of patients who underwent surgery for peptic ulcer perforation (PUP) and were diagnosed with PU by endoscopy.

Material and Methods: Between May 2012-January 2017, patients' data for PU disease were recorded and our study was planned retrospectively. Patients were seperated into two groups: Group1, who was operated for PUP; and Group2, who were administered medical therapy for PU. Blood calcium levels during admission, age, gender and drug history of patients were recorded. Study exclusion criteria were patients whose data were missing (n=113), patients who had metabolic bone disease, patients who had been using calcium channel blockers and who were administered anti-ulcer drugs.

Results: Twenty-eight patients had PUP and 176 patients had PU disease. Group 1 had a lower mean age (p=0.017), and higher male gender rate (p<0.001). The mean calcium level of Group 1 was 9.7±0.6 mg/dl, while the mean calcium level of Group 2 was 8.8±0.7 mg/dl (p<0.001). Less than the cut-off value of 9.25, calcium showed a sensitivity of 78.6% and a specificity value of 73.1% between groups.

Conclusion: In our study, we found that in patients with PU diagnoses, elevated levels of calcium found in controls may increase both stomach acidity and the risk of PUP.

Keywords: Calcium; Peptic Ulcer; Perforation.

INTRODUCTION

The gastrointestinal system (GIS), which encounters acidic peptic activity, is defined as a chronic wound peptic ulcer (PU), that occurs in the mucosa and progresses to the submucosa, characterised by loss of specific tissue. The stomach also counteracts the harmful effects of acid and pepsin, the protective effects of prostaglandins, mucus secretions, saliva, food intake, HCO_3 and duodenal content. When this balance is degraded in favour of acid, the risk of developing PU increases. When PU develops, complications such as perforation, obstruction and bleeding may occur (1). Calcium found in the body mainly in the bones can lead to GIS diseases such as anorexia, nausea, vomiting, constipation, PU, and elevation of blood level due to primary or secondary causes. Few years ago, Pawlow's research began to explore the relationship between blood calcium level and PU (2). Increased serum calcium levels have been shown to increase gastrin, gastric acid and pepsinogen secretions by both direct and indirect effects (2-5). We aimed to reveal the difference in the blood values of calcium in the aetiology of PU in patients who were diagnosed with PU in the upper gastrointestinal tract by endoscopy performed electively with a diagnosis of peptic ulcer perforation (PUP) in our emergency department.

MATERIAL and METHODS

Our retrospective study examines file records of individuals who were patients at Kars State Hospital General Surgery Clinic and Kafkas University School of Medicine Department of General Surgery between May 2012 and January 2017. Following approval from the local ethics committee, file records of 317 consecutive patients undergoing either emergency surgery because of PUP or elective gastrointestinal endoscopy were recorded with complaints of pyrolysis, dyspepsia, retrosternal burning, pain in the epigastric region and both nausea and vomiting. Patients were assigned to Group 1, patients with PU activation, and Group 2, patients who underwent medical treatment for internalisation of PU activation. Blood calcium values, age, sex, and drug intake history were

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recorded at the time of admission. One hundred thirteen patients with bone metabolism disease and malignancy, calcium channel blockers and anti-ulcer treatment, and missing file records were excluded from the study. The upper GIS endoscopy was performed with an Olympus EVIS Exera II CLV-180, and the calcium measurement at the time the application was made with a Hitachi R P800 Automatic Analyser System® (Hitachi Co., Ltd., Tokyo, Japan. The reference interval for calcium was taken as 8.4–10.0 mg/dL.

Statistical Analysis

The data analysis was performed using SPSS for Windows, version 22 (Chicago, IL, USA). The normality of the distributions of continuous variables was determined via the Shapiro-Wilk test. The data were reported as mean ± standard deviation or median and range where applicable. The differences between the data from the groups were compared via Student's t-test or the Mann-Whitney U test where appropriate. The categorical data were analyzed using Pearson's chi-square test where appropriate. Logistic regression analysis was used to assess the differences between groups in age, gender and calcium values. The cutoff values of parameters for discrimination of the groups were determined using the receiver operating characteristic (ROC) analysis. At each value, the sensitivity and specificity for each outcome under study were plotted, thus generating an ROC curve. A p value less than 0.05 was considered statistically significant.

RESULTS

Of the 204 patients included in the study, 28 were found to have PUP, while 176 patients had PU. When sex and age distributions of the groups were examined, the median age of the perforation group was lower (p=0.017), and the male sex ratio was significantly higher (p<0.001) than those of the PU group. The calcium value in the perforation group was 9.7 ±0.6 mg/dl, while it was 8.8±0.7 mg/dl in the PU group (p<0.001). The demographic characteristics of the patients are shown in Table 1.

Table 1. Demographic features and regression analysis of age, gender and calcium values between groups

Parameters	PUP	PU	P values
Patients	28	176	
Age	45 (23-81)	54 (21-87)	P:0.017
Gender (Male/Female)	26/2	106170	P:0.001
Calcium value (mg/dl)	9.7±0.6	8.8±0.7	P<0.001

PUP : Peptic ulcer perforation group; PU : Peptic ulcer group

When the common effect of age, gender and calcium value was examined, the calcium level increased in the PUP group independently of the other two parameters (p<0.001). The cut-off value of 9.25 mg/dl between calcium groups was calculated as 78.6% sensitivity and 73.1% specificity. Distribution graphs between groups and roc curve analysis are provided in Figures 1 and 2, respectively.

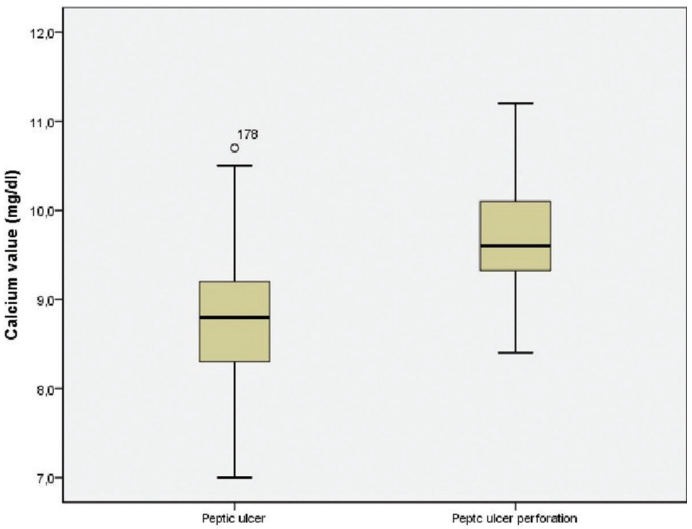

Figure 1. Distribution of calcium between groups

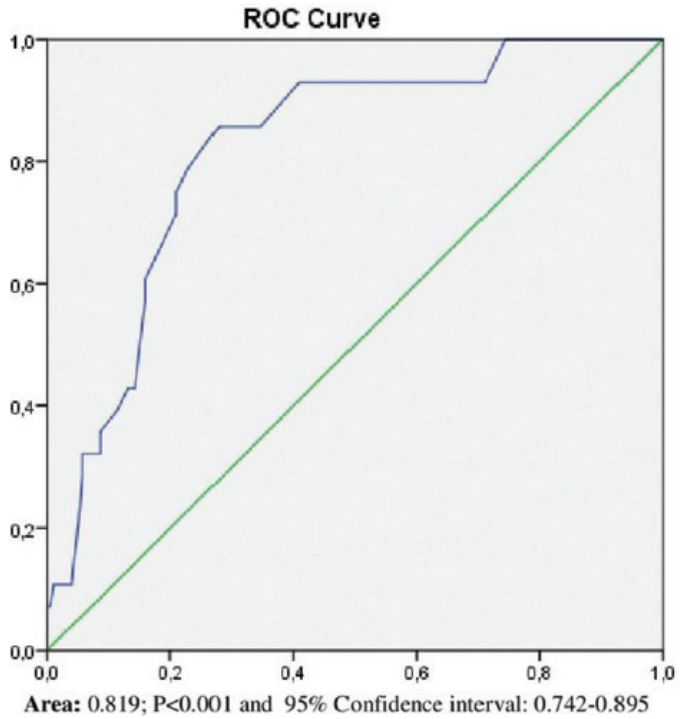

Figure 2. Roc curve anlysis between groups

DISCUSSION

Karl Schwarz's theory of "no ulcer is absent without acid" has been accepted as the theory that gastric acid is the most effective factor in ulcer pathogenesis (6). For this reason, researchers began to search for ways to stop the formation of ulcers by both discovering and blocking gastric acid-increasing mechanisms. In many published studies, calcium has been shown to increase the amount of acid that plays a primary role in the aetiology of PU. In our study of whether blood calcium levels in PUP patients differ from those in PU patients, we concluded that the increase in blood calcium levels might cause a perforation in PU patients. We realise that our study has several limitations.

The retrospective nature of our study lowers the level

of evidence. We could not prove homogeneity between patients because albumin, PTH and gastrin measurements affecting blood calcium levels could not be studied as standards. Detailed anamneses of factors that may be effective in the formation of PUP in patients' anamneses could not be achieved. Despite these limitations, the positive aspects of our work support the idea that the literature will both accept and make our study valuable.

Although many studies in the literature show the effect of calcium level on both PU pathophysiology and PU bleeding, we have been unable to find any information about the effect of calcium on perforation. Therefore, this is the first manuscript on that particular issue. Trained surgeons operated on patients in the same group in our study and endoscopies were performed by two general surgery specialists.

The most common clinical manifestation of elevated blood calcium levels is hyperparathyroidism. In fact, Chernin et al. who showed that there is an increase in blood calcium especially in patients with recurrent PU disease have also demonstrated a calcium-ulcer association in medical therapy-resistant PU patients. In addition, they argue that this connection is even stronger in favour of hypercalcaemia in calcium metabolism, especially in young male patients, as Fomina also points out (4,7). Our study supports the idea that when there is a likelihood of an increase in calcium, especially in young male patients, there is also an increased risk of perforation. Despite this evidence, there are many studies explaining the mechanism of action of calcium in PUs.

Although studies reporting the effect of calcium on the increase in gastric acidity are intense (2-4,7,8), other literature reports focus on either increased pepsinogen (3,7) or increased gastrin levels (2,9,10).

Donegan et al. demonstrated that the relation between calcium and ulcer was different from the general literature data as revealed by the deduction method. They showed that the level of stomach acid decreases when blood calcium level falls below 7 mg/dl (11).

Studies of calcium channel blockers conducted by Chernin et al. and McColl et al. have shown that gastric acid levels and recurrent ulcer attacks are reduced, and endoscopic findings are resolved (3,10).

When PU develops, complications such as perforation, obstruction and bleeding may occur. Güzel et al. declared that in the last decade, perforation became the most common complication (1). Menekşe et al. declared their mortality rates were 10.1% with their PUP patients (12). In contrast, we had no mortalities.

CONCLUSION

We think that two problems must be solved in light of our study results. The first is that if there are no contraindications in patients with PU disease and idiopathic hypercalcaemia, should treatment for hypercalcaemia be initiated even without clinical findings? The second problem is in patients with hypercalcaemic PU, should the dose of an anti-ulcer treatment be increased to reduce PUP risk? Answers to these problems require prospectively planned studies with high evidence power, detailed anamnesis and laboratory tests. However, in our study, we found that in patients with PU diagnoses, elevated levels of calcium present in controls may increase both stomach acidity and the risk of PUP.

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Conflict of Interest: None declared.

REFERENCES

1. Güzel H, Kahramanca Ş, Şeker D, Özgehan G, Tunç G, Küçükpınar T, et al. Peptic ulcer complications requiring surgery: What has changed in the last 50 years in Turkey. Turk J Gastroenterol 2014;25(2):152-5.
2. Pimparkar BD, Gandhi UM, Bodas PV. Serum calcium and gastric acid-pepsin secretion. J Postgrad Med 1981;27(2):90-8.
3. Chernin VV, Fomina LA. The calcium-regulating system and recurrent peptic ulcer. Ter Arkh 2016;88(2):10-5.
4. Fomina LA. Calcium-phosphorus ratio in relapse of peptic ulcer disease. Eksp Klin Gastroenterol 2011;(12):22-6.
5. Christiansen J, Kirkegaars P, Olsen PS, Petersen B. Interaction of calcium and gastrin on gastric acid secretion in duodenal ulcer patients. Gut 1984;25(2):174-7.
6. Kahramanca Ş, Güzel H, Şeker G, Azılı C, Bilgin BÇ, Gökce İE, et al. What should peptic ulcer patients do during Ramadan? Academic J Gastroenterol 2013;12 (3):118-22.
7. Chernin VV, Fomina LA. Calcium and phosphorus balance and its significance for the course of recurrent peptic ulcer disease. Ter Arkh 2013;85(2):13-6.
8. Kaur U, Agnihotri N, Kaur S, Khullar M, Bambery P, Sood G, et al. Duodenal ulcer. Calcium status in isolated parietal cells. Dig Dis Sci 1995;40(4):887-92.
9. Reeder DD, Jackson BM, Ban J, Clendinnen BG, Davidson WD, Thompson JC. Influence of hypercalcemia on gastric secretion and serum gastrin concentrations in man. Ann Surg 1970;172(4):540-6.
10. McColl K, Buchanan NM, Laferla G, Hearns J, Buchanan K, Crean GP. Effects of nifedipine on gastric acid secretion and gastrin release in man. Gut 1987;28(4):455-9.
11. Donegan WL, Spiro HM. Parathyroids and gastric secretion. Gastroenterology 1960;38:750-9.
12. Menekse E, Kocer B, Topcu R, Olmez A, Tez M, Kayaalp C. A practical scoring system to predict mortality in patients with perforated peptic ulcer. World J Emerg Surg 2015;10:7.