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Analysis of Possible Correlation with Associated Conditions of Patients with Gastric Fundic Gland Polyp

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Abstract

Gastric polyps are lesions that are often evaluated by the endoscopist. Among them incidence of Fundic gland polyp (FGP) showing an increasing pattern these days due to various associated conditions like long-term proton pump inhibitor (PPI) therapy. This study was designed to evaluate the conditions that were associated with the presentation of FGP including PPI therapy of ≥ 6 month. Our study concluded with a high incidence of 14% long-term PPI intake of ≥ 6 month among the patients presented with FGP. Beside that a high female predominance, potent association with gastritis and negative *Helicobacter Pylori* status, Personal habits like Smoking and alcohol intake also appeared as an important factor associated with FGP. Our current findings can serve as an assistance to evaluate associated conditions like FGP in patients with PPI intake of 6 month or more presenting with features of gastritis irrespective of HP status and give a high concentration on personal habit modification like alcohol and smoking in the treatment of FGP patients.

Keywords: Gastric polyp; Fundic gland polyp; Polyp; *Helicobacter pylori*; Proton pump inhibitor; PPI; Gastritis

Abbreviations

CUBT: C14 Urea Breath Test; FAP: Familial Adenomatous Polyposis; FGP: Fundic Gland Polyp; HP: *Helicobacter Pylori*; H/O: History of; OCP: Oral Contraceptive Pill; PPI: Proton Pump Inhibitor

Introduction

A gastric polyps are lesions that are often encountered during endoscopy. Among various types of polyps Fundic gland polyps (FGP) are being frequently evaluated by endoscopist due to increasing use of long-term PPI therapy and other conditions. Though FGP considered as benign lesion but its presence causes prolongation of patients suffering and might associate with other morbidities. Our aim of this study was concentrated to evaluate and develop the possible correlations between conditions that might be associated with FGP including long-term PPI intake of ≥ 6 month.

Method

A single centre prospective cross-sectional study was performed over a period of twelve months from July 2014 to July 2015 in the department of Digestive Disease-II, The first affiliated Hospital of Jiamusi University. After exclusion, 300 patients with primary diagnosis of gastric Fundic gland polyp/polyps of 18 to 78 years of age were included in the study. Endoscopic diagnosis of Fundic gland polyp was confirmed by further histopathology in all cases. Relative data of all patients were collected carefully, included and statistically analyzed for the study. Chi-square test was done to calculate the P value. A P value of ≤ 0.05 was considered significant. This included age, sex, number and size of FGP, History of (H/O) PPI (name and duration of intake), other drug history, patient habit (Smoking, alcohol, tea and others), C14 Urea breath test (CUBT) for *Helicobacter Pylori* (HP), other diseases and family history of stomach polyp. Among 300 patients, 35 had denied performing CUBT. In patients with multiple polyps, the size of polyps in an average was input in the data Table. For the study purpose, regular PPI intake of more than 6 months was considered as long time PPI use. Patients with previous H/O FGP, Adenomatous polyposis, carcinoma, advanced gastrointestinal disease, Inflammatory bowel disease, major metabolic diseases, gastric or duodenal ulcer, long term H/O antiplatelet therapy with aspirin or clopidogrel, long term H/O analgesic intake, very young and patient suffering of senile disorder were not included in the study.

Results

A total of 300 patients of primary FGP were included in this study, among them 102 (34%) men and 198 (66%) were female. In women, intake of PPI and number were dependent, there was a significant difference between them. 42 (14%) patients with FGP of the total had a long-term history of PPI intake (≥ 6 month), 144 (48%) had no history of PPI intake in last one year, 114 (38%) had a short time history of PPI (< 6 month). Out of 156 patient who had history of PPI intake irrespective of duration, 96 (30 male, 66 Female) had H/O Omeprazole, 18 (12 male and 6 Female) H/O Rabeprazole, 18 Female with H/O Pantoprazole and 6 Female with H/O Esmoprazole. Out of 42 patients with a history of PPI intake of ≥6 month 30 (71.42% - 12 Male and 18 Female), 6 Female (14.28%), 6 Male (14.28%) took Omeprazole, Pantoprazole and Rabeprazole respectively. The female patient took Omeprazole had a history of combine Lansoprazole

intake. 8% (24) of the total patients have a family history of gastric polyp-related to the first blood. No family history was detected in male patients. Out of 24 patients with family H/O of the gastric polyp, 12 had H/O PPI intake and 12 with no H/O PPI. Among those with H/O PPI, 6 (5.56%) had a family history of gastric polyp with sister and brother separately. Those without PPI intake, 6 (6.67%) patients had H/O Gastric polyp with sister and mother. 2% (6) patients were unable to provide family history. Male participants in this study with a history of intake of PPI were relatively older, compare to female. It was 54.25 ± 11.80 years against 50.44 ± 9.43 years. Significant differences were observed in the number of FGP among patients with a history of PPI intake and those who don't. Percentage of participants with gastritis as associated condition did not differ with the history PPI intake. 83% of patients without H/O PPI and 100% who were on PPI therapy showed evidence of gastritis in endoscopy and histopathology evaluation. Among them, 16.67% of those who had no H/O PPI and 33.33% with H/O PPI intake were found positive in C14 Urea Breath test for HP. Combine personal H/O smoking and drinking was found associated with 10% (30) of total (24 Male 8% and 6 Female 2%). Among which 25% and 22% of patients were with and without H/O PPI respectively. Smoking alone was found associated with 16% (48) of total (6 Male 2% and 42 Female 14%). This is 22.22% (24) and 20% (18) with and without H/O PPI among female patients and 11.11% (6) among male patients without H/O PPI intake. Smoking and regular tea drinking were notified in 12.5% and 22.22% patients with and without H/O PPI respectively. 14% (42) patients were Hypertensive (24 Male 8% and 18 Female 6%). This is 12.5%, 22.22%, 11.11% and 5.56% respectively in patients presented with Hypertension and Hepatitis B and in those with and without H/O PPI. Among the patients with and without H/O of PPI intake, 5.56% and 6.67% of had H/O prednisone and 5.56% and 6.67% had H/O OCP intake in regular interval respectively.

	Male (n=102)		**P value**	**Female (n=198)**		**p-value**
Age	H/O PPI (48)	No H/O PPI(54)		H/O PPI (108)	No H/O PPI (90)	
	54.25 ± 11.80	46.89 ± 0.26	0.228	50.44 ± 9.43	53.87 ± 8.70	0.291
Number of polyps						
<5	42	30	0	90	60	0.006
>5	6	24		18	30	
Size of polyp						
<0.5	24	24	0.575	60	60	0.111
>0.5	24	30		48	30	
Personal habit						
Smoking, alcohol	12 (25%)	12 (22.22%)			6 (6.67%)	
Alcohol, tea						
Smoking		6 (11.11%)		24 (22.22%)	18 (20%)	
Alcohol		6 (11.11%)		6(5.56%)	6	
Smoking, tea	6 (12.5%)	12 (22.22%)				
Smoking, alcohol, tea	6 (12.5%)	6 (11.11%)				
Tea				12(11.11%)	6	
H/O gastritis	36 (75%)	48 (88.88%)	0.066	90 (83.33%)	90 (100%)	
No H/O gastritis	12	6		18	0	
HP status						
Positive	6 (12.5%)	0		18(16.67%)	30 (33.33%)	
Negative	18 (37.5%)	18 (33.33%)		0	36 (40%)	
Menstrual history						
Regular				72 (66.67%)	60 (66.67%)	0.041
Irregular				18 (16.67%)	6 (6.67%)	
Menopause				18 (16.67%)	24 (26.67%)	

Duration of PPI intake	2			9		
	5			8		
Type of PPI use						
Omeprazole	30 (62.5%)			66 (61.11%)		
Rabiprazole	12 (25%)			6 (5.56%)		
Ome+lanso				6 (5.56%)		
Pantoprazole				18 (16.67%)		
esmoprazole				6 (5.56%)		
Drug history for prednisolone		6		6 (5.56%)	6 (6.67%)	
OCP				6 (5.56%)	6 (6.67%)	
Other disease						
HTN	6 (12.5%)	12 (22.22%)		12(11.11%)		
Hepatitis A		6 (11.11%)				
Hepatitis B				6 (5.56%)		
Familyhistoryofgastric FGP						
sister				6 (5.56%)	6 (6.67%)	
brother				6 (5.56%)		
mother					6 (6.67%)	

Table 1: Clinical features of participants with and without intake of H/O PPI.

Significant differences were observed in the number of polyp between the groups. Differences in age and size of polyps between the groups with and without the history of intake of PPI were not significant. 15.39% of patients with the history of PPI had a habit of smoking and 16.67% patients with no H/O PPI intake. This is 7.7% and 12.5% in case of Smoking and alcohol. CUBT was done in 265 patients. Among them, 145 patients had history of PPI/antacid preparation/ antibiotics intake within last 14 days or clinically inconclusive results were not considered. 120 patients obtained a conclusive HP status. HP was found positive in 15% (24) and 4.17% (6) with and without H/O PPI intake respectively. In patients with negative HP status, this was 23.07% (26) and 37.5% (54). The percentage of participants in gender wise, who were currently smoking and size of the polyp, did not differ with the H/O intake of PPI. PPI intake and HP status, PPI intake and Gastritis were found significant and related to each other.

	H/O PPI (156)	**No H/0 PPI (144)**	**p-value**
Age	51.61 ± 10.13	51.25 ± 10.50	0.901
Size of polyp			
<0.5	90	84	0.911
>0.5	66	60	
No of polyp			
<5	132	90	0.000**
>5	24	54	
Sex			
Male	48 (30.76)	54 (37.5)	0.219
Female	108 (69.23)	90 (62.5)	

Personal habit			
Smoking, alcohol	12 (7.7)	18 (12.5)	0.596
Alcohol, tea	6		
Smoking	24 (15.39)	24 (16.67)	
Alcohol		12 (8.33)	
Smoking, tea	6		
Smoking, alcohol, tea	6	12 (8.33)	
Tea	6	6	
HP status			
+ve	24 (15.39)	6 (4.17)	0
-ve	36 (23.07)	54 (37.5)	
Duration of intake of PPI			
1-3 months			
3-6 months	102 (68%)		
6-9 months	6 (4%)		
9-12 months	12 (8%)		
	30 (20%)		
Associated condition			
Gastritis	126	138	0
No gastritis	30	6	

Table 2: Differences in age and size of polyps between the groups with and without the history of intake of PPI.

Discussion

Gastric Fundic gland polyp (FGP) was first described by Elster [1] in 1976. They are mostly found in the fundus and upper part of the body of the stomach and usually considered as benign. Histologically FGPs are composed of cystically dilated glands lined by fundic epithelium. They are one of the common types of gastric non-neoplastic lesions encountered by endoscopist while performing gastroduodenoscopy, due to gastric or associated pathologies. They are most often found in people with familial adenomatous polyposis (FAP). FGPs are considered as one of the side effects that is related to long-term proton pump inhibitor (PPI) therapy. Several studies described hypertrophy and hyperplasia of parietal cells in patients with longstanding proton pump inhibitor therapy, which increase the risk of FGPs by 4-folds compared with control group [2]. Recently, FGPs are increasingly common findings in patients with long-term PPI intake [3-6]. Children's with multiple FGP were also described in several published literature following 6 months of PPI therapy. Though FGP is considered as benign but there is evidence of sporadic FGPs with low-grade or high-grade dysplasia in published literature [7-10] Adenocarcinoma of the fundic gland was recently proposed as a new variant of gastric adenocarcinoma [11,12]. Correlation between gastric polyps and metabolic syndrome like hyperlipidaemia was also described in recent literature [13]. Our primary aim was to correlate and investigate a possible relationship between the history of PPI intake and FGP. Several studies evaluated an increase in polyp risk and between the lengths of PPI use, especially after 12 months [14]. But for the study purpose and high frequency of intake of PPI among patients due to various reasons, we defined long-term PPI intake as the duration of 6 month or more regular intake. After primary exclusion, 300 case of primary FGP presented in the Department of digestive disease-II were included in this study. All relative information's were collected according to the methodology. In our study 42 (14%) patient of the total had a history of PPI intake of 6 months or more irrespective of type. This considerable percentage demands the special attention of the physicians toward patients having H/O PPI intake of ≥ 6 month. Fundic gland polyps are considered to be associated with familial adenomatous polyposis or Peutz-Jeghers syndrome [15,16]. Our finding revealed an association of 8% population related to the first blood with H/O FGP. We also found female dominance with no family history in male participants. This might be due to comparatively low sample size, undiagnosed cases or unawareness of family history. According to some authors, FGPs does not show any definite sex predilection and appear to have similar histology and genetic features to those developing without proton pump inhibitor use. But our study showed a female predominance of FGP 198 (66%) out of 300 against 102 (34%) male. This finding supports the study of Marcial MA which described a female predominance in non-familial FGPs suggesting that hormones might play a role in the development of FGPs [17]. Among 198 female participants 132 had a regular menstrual history, 24 were

with irregular menstruation and 42 were menopause. Out of this 12 had a history of OCP (Oral contraceptive pill). This finding does not support "hormonal imbalance" in the case of females as a probable role in the development of FGP. Most patients with fundic gland polyps on proton pump inhibitors were described *H. pylori*-negative in some publications, even with regression of FGP following the acquisition of *H. pylori* [18]. But among our described HP (+)ve patients only 16.67% were regular PPI users, 33.33% patient had no history of PPI in at least last one year. In this study, 83% of patients without H/O PPI and 100% who were on PPI therapy showed evidence of gastritis. This strongly develops "Gastritis" as a potent presenting feature and an associated condition regarding FGP. Some additional findings regarding this study were a personal habit, which included regular smoking, alcohol intake and tea. Smoking and tea together were found associated with 10% of total FGP patients. This is 25% and 22% of with and without H/O PPI respectively. On the other hand, smoking alone was associated with 16% (48) of the total. This is 22.22% (24) and 20% (18) with and without H/O PPI among female patients and 11.11% (6) among male patients without H/O PPI. Smoking and alcohol are proven a factor for gastritis and according to above findings, they might play a direct or indirect important role in the formation of FGP.

Conclusion

Our current study evaluated a high rate of 14% association of Fundic gland polyp and PPI intake of 6 months or more. We also found a high female predominance, potent association with gastritis and *Helicobacter Pylori* status with FGP. Personal habits like Smoking and alcohol intake also appeared to be an important factor which might be associated with FGP. The study has limitations which might include regional influences. But the patients presenting solely with primary Fundic gland polyp without associated disorders are remarkably rare. Despite this, we believe the above findings will help to evaluate associated conditions like FGP in patients with PPI intake of 6 months or more presenting with features of gastritis irrespective of HP status and give a high concentration on personal habit modification like alcohol and smoking in the treatment of diagnosed FGP.

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