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/polyplps 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.

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) | 0.228  | H/O PPI (108) | 53.87 ± 8.70 | 0.291  |
| 54.25 ± 11.80            | 46.89 ± 0.26 | 50.44 ± 9.43 | 0.006 |
| Number of polyps         |             |         |               |         |
| <5                       | 42          | 0       | 90            | 90      |
| >5                       | 6           | 24      | 18            | 30      |
| Size of polyp            |             |         |               |         |
| <0.5                     | 24          | 24      | 60            | 60      |
| >0.5                     | 24          | 30      | 48            | 30      |
| Personal habit            |             |         |               |         |
| Smoking, alcohol         | 12 (25%)    | 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 (8.67%) |             |         |
| Menopause                | 18 (16.67%) | 24 (26.67%) |            |         |
**Table 1:** Clinical features of participants with and without intake of H/O PPI.

| 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+lanoso            | 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%) |             |             |
| Family history of gastric FGP |             |             |             |
| sister                | 6 (5.56%) | 6 (6.67%)   |             |
| brother               | 6 (5.56%) |             |             |
| mother                |             | 6 (6.67%)   |             |

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

| Personal habit                | Group with PPI History | Group without PPI History | p-value |
|-------------------------------|------------------------|---------------------------|---------|
| Smoking, alcohol              | 12 (7.7)               | 18 (12.5)                 | 0.596   |
| Alcohol                       | 6                      |                           |         |
| Smoker                        | 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                     | Group with PPI History | Group without PPI History | p-value |
|-------------------------------|------------------------|---------------------------|---------|
| +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                         |         |

### 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 FGP 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). FGP 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 FGP by 4-folds compared with control group [2]. Recently, FGP 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 FGP 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 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, FGP 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 FGP suggesting that hormones might play a role in the development of FGP's [17]. Among 198 female participants 132 had a regular menstrual history, 24 were...
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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