

The Prevalence of Gastroduodenal Mucosal Injuries in Aspirin Users

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Background: Aspirin is a widely used medication for primary and secondary prevention of cardiovascular and cerebrovascular events. The gastrointestinal risks of aspirin are well known, but the frequency of gastroduodenal mucosal injuries in aspirin users in Thailand is currently unknown.

Objective: The present study was performed to investigate the prevalence of gastroduodenal mucosal injuries in asymptomatic aspirin users.

Material and Method: Asymptomatic patients taking low doses of aspirin without gastroprotective medication were enrolled and underwent esophagogastroduodenoscopy.

Results: One hundred four patients were endoscoped. The prevalence of gastroduodenal mucosal injuries (erosions or ulcer) was 63.5%.

Conclusion: The prevalence of gastroduodenal mucosal injuries was very high in asymptomatic aspirin users.

Keywords: Aspirin, Gastroduodenal mucosal injuries, Prevalence

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Low-dose aspirin (75-325 mg) has been widely used for primary and secondary prevention of cardiovascular and cerebrovascular disease⁽¹⁾. However, aspirin's efficacy is limited by the risk of gastrointestinal (GI) events. The GI events are ranging from dyspeptic symptom, occult GI bleeding to serious complication, such as GI bleeding and GI perforation. The serious complications are about two-to four fold higher than the control patients taking low doses of aspirin^(2,3). There are many factors increasing the risk of upper GI hemorrhage including old age, long-term use⁽⁴⁾, concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs)⁽⁵⁾, and a history of previous peptic ulcers⁽⁶⁾. There are a few studies about the prevalence of gastroduodenal mucosal injuries in patients taking low-dose aspirin, and the prevalence differ in different studies ranging from 10.7 to 63.1%⁽⁶⁾. The present study aimed to measure the prevalence of gastroduodenal mucosal injuries and other associated factors in asymptomatic aspirin users.

Material and Method

The present study was a cross-sectional descriptive analysis conducted between January 2012 and October 2012 at Bangkok Metropolitan Administration General Hospital. The study protocol was approved by the ethics committee and written informed consents were obtained from all patients before recruitment. The sample size was 104, calculated and plus 10% of drop out from $n = (1.96)^2(0.4)(0.6)/(0.1)^2$. The author enrolled 104 patients without dyspeptic symptom who were taking a low-dose aspirin (75-325 mg) daily for at least the preceding one month. All patients underwent esophagogastroduodenoscopy (EGD) without stopping aspirin. The exclusion criteria were concurrent medications (anticoagulant, NSAIDs, corticosteroids, bisphosphanate, gastroprotective drugs), aged less than 18 years, history of recent myocardial infarction, or heart failure.

The author investigated age, gender, underlying condition, concomitant medication, smoking, alcohol intake, dose and duration of aspirin, endoscopic findings, and *Helicobacter pylori* infection. Esophagogastroduodenoscopy (EGD) was performed after local anesthesia of the pharynx with lidocaine spray. Endoscopic findings were assessed by one experienced endoscopist. The reliability of the investigation tool was high, because of the standard of

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the gastroscopes which is used worldwide (Olympus brand). There was no intraobserver and interobserver variability, because the procedures were done by one experienced doctor and the pictures were recorded in all cases. The presence of *H. pylori* was tested by using rapid urease test from tissue biopsies at antrum. The definition of gastroduodenal mucosal injuries in the present study including erosion and ulcer in the stomach or the duodenum.

The “erosion” was defined as a mucosal defect if less than 3 mm, the term “ulcer” is used a mucosal defect of 3 mm or more in greatest diameter. The author measured the lesion size by using biopsy forceps (6 mm bite). Reflux esophagitis lesions were graded by Los Angeles (LA) classification. The author sent the tissue for pathological studies in cases of gastric ulcer or in suspected lesions.

Statistical analysis

The present study used the statistical analysis software SPSS version 17. Continuous data are expressed as mean \pm SD or median and categorical data are expressed as number (%). Multivariate logistic regression analysis was performed to determine factors for gastroduodenal erosions or ulcers. Frequency data were compared using Chi-square test or Fisher’s exact test where appropriate and continuous data were compared by using Student’s t-test. Statistical significance was set at $p < 0.05$.

Results

One hundred four patients were recruited (51.9% male). Patients characteristics are shown in Table 1. The mean age was 60.28 ± 9.96 years, and the male:female ratio was 54:50. The doses of aspirin were 81 mg per day in most of the patients (97.1%), 300 mg in one patient (0.96%), and two patients were taking enteric-coated aspirin. The authors recruited only asymptomatic patients who were taking aspirin as primary or secondary prevention without antiulcer drugs. The indication for primary prevention and secondary prevention was 91 (87.5%) and 13 (12.5%), respectively.

Prevalence of gastroduodenal mucosal injuries was 66 cases (63.5%). The most common endoscopic finding in this study was gastric erosion (32.7%) (Table 2). The common site of gastric ulcer was antrum. *H. pylori* infection rate was 43.3%. *H. pylori* infection was not a significant risk factor for gastroduodenal mucosal injuries in the present study ($p = 0.16$).

There were no correlation between age, gender, smoking, alcohol, underlying disease, or dose and duration of aspirin with gastroduodenal mucosal injuries (Table 3).

Discussion

The prevalence of gastroduodenal mucosal injuries in the present study was very high (63.5%). The author found gastric erosions in 32.7% and gastroduodenal ulcers in 30.8%. None of the patients had dyspeptic symptom during the use of aspirin. The importance of high prevalence of gastroduodenal mucosal injuries may identify hidden risk factors for

Table 1. Baseline characteristics (n = 104)

Age (years)	60.28 \pm 9.96
Gender (male:female)	1.1:1
Smoking (%)	9.6
Alcohol drinking (%)	7.7
Comorbidities (%)	
Diabetes	55 (52.9)
Hypertension	30 (28.8)
Dyslipidemia	6 (5.8)
Coronary artery disease (CAD)	9 (8.6)
Cerebrovascular disease (CVA)	4 (3.8)
Aspirin dose (mg)	
80 mg	101 (97.1%)
300 mg	1 (1.0%)
Enteric coated aspirin	2 (1.9%)
Duration of aspirin (%)	
Less than 6 months	16 (15.4)
More than 6 months	88 (84.6)
Objective of aspirin (%)	
Primary prevention	91 (87.5)
Secondary prevention	13 (12.5)

Table 2. Endoscopic findings and *Helicobacter pylori* infection (n = 104)

Endoscopic findings	Number (%)	<i>H. pylori</i> infection rate (%)
Normal	22 (21.1)	36.4
Esophagitis	6 (5.8)	16.7
Gastritis	10 (9.6)	40.0
Gastric erosions	34 (32.7)	44.1
Gastric ulcers	22 (21.1)	68.2
Gastric ulcer and duodenal ulcer	7 (6.7)	57.1
Duodenal ulcer	3 (2.9)	33.3

Table 3. Association between gastroduodenal mucosal injuries, patient characteristics and *H. pylori* infection

Variables	Gastroduodenal mucosal injuries	%	No gastroduodenal mucosal injuries	%	p-value
Age groups (years)					0.98
Less than 60	32	64.0	18	36.0	
60-70	23	63.9	13	36.1	
More than 70	11	61.1	7	38.9	
Sex (male)	38	70.4	16	29.6	0.13
Smoking	24	80.0	7	20.0	0.07
Alcohol	22	66.7	10	33.3	0.54
Comorbidities					
Diabetes	34	61.8	21	38.2	0.56
Hypertension	20	66.7	10	33.3	0.45
Dyslipidemia	4	66.7	2	33.3	0.90
Coronary artery disease (CAD)	7	77.8	2	22.2	0.38
Cerebrovascular disease (CVA)	1	25.0	3	75.0	0.09
<i>H. pylori</i> infection					0.16
Positive	32	71.1	13	28.9	
Negative	34	57.6	25	42.4	
Aspirin duration					0.86
Less than 6 months	10	62.5	6	37.5	
More than 6 months	56	63.6	32	36.4	
Aspirin dose					0.69
81 mg	64	63.4	37	36.6	
300 mg	1	100	0	0	
Enteric coated aspirin	1	50.0	1	50.0	

upper GI bleeding in the future. The real clinical problems that the authors confronted are the group of patients who were taking low-dose aspirin but seeking a doctor only when they have GI symptom (dyspepsia) or complications (most likely GI bleeding).

The high prevalence of gastroduodenal mucosal injuries in the present study will encourage doctors who prescribe aspirin about the awareness of GI complication. Low-dose aspirin use has been associated with a wide range of adverse events, which range from dyspeptic symptom with or without mucosal lesions to more serious GI events⁽⁷⁾.

The key points about low-dose aspirin usage are unclear. However, they include the lack of detection of the presence of gastroduodenal mucosal injuries. The reason being aspirin elevates the gastric sensory threshold of patients, thus more than half of patients with GI complications will not have warning symptoms⁽⁸⁾.

H. pylori infection rate was 48.5% of patients with gastroduodenal mucosal injuries and 34.2% of patients without gastroduodenal mucosal injuries. *H. pylori* infection rate was highest in patients

with a gastric ulcer (68.2%), 57.1% of patients with gastroduodenal ulcer and 33.3% of patients with a duodenal ulcer. There was a trend of high rate of *H. pylori* infection in a group of gastroduodenal ulcers (53.1%) more than a group of gastroduodenal erosions (44.1%), and a lowest *H. pylori* infection rate in a group of normal endoscopic findings or gastritis (34.2%).

The author could not demonstrate the significant risk factors of gastroduodenal mucosal injuries (age, gender, smoking, alcohol, underlying disease, *H. pylori* infection, dose, and duration of aspirin). In comparison with the previous studies, the author found the prevalence rate of gastroduodenal mucosal injuries in the present study to be similar to studies by Nema et al⁽⁹⁾ and Yeoma et al⁽⁶⁾. According to the high prevalence of gastroduodenal injuries in aspirin users in Thailand, the endoscopic surveillance of this group of patients may be important. From the previous reports, coadministration of proton pump inhibitor (PPI) with low-dose aspirin reduced the prevalence of gastroduodenal injuries⁽¹⁰⁻¹³⁾ and Tamura et al found no gastroduodenal ulcer in

asymptomatic patients taking a standard dose of PPI with low-dose aspirin⁽¹⁴⁾. In the practical point, PPI prophylaxis should be considered in aspirin users to reduce gastroduodenal mucosal injuries.

The prevalence of esophagitis was 5.8%, which is lower than the previous reports (7.9% and 9.4%)^(15,16). The author did not find cancer from endoscopic surveillance in the present study. The present study investigated only asymptomatic aspirin users because the symptomatic patients will seek doctors and will investigate and get treatment earlier than the asymptomatic group.

The author used the exclusion criteria to reduce other possible confounding factors. The present study excluded the patients who were taking concomitant medications that might affect the results such as anticoagulant, NSAIDs, corticosteroid, bisphosphonate, and gastroprotective drugs. The author could not control some factors including food (spicy) or drinks that might affect the result, but there was no evidence to support these effects. However, prospective RCTs are required in the future to clarify these factors that might affect the prevalence of gastroduodenal mucosal injuries.

The present study has some limitations. First, we did not have a control group to compare with an aspirin group, but the authors know from the previous study that the prevalence of gastroduodenal mucosal injuries are 10 to 13% in control group^(9,17). Second, the present study included only asymptomatic low-dose aspirin users, but from the previous study found the same prevalence of gastroduodenal mucosal injuries both in symptomatic and asymptomatic aspirin users⁽¹⁵⁾. Third, we did not have the baseline endoscopic findings before the administration of aspirin.

Conclusion

Endoscopic surveillance in aspirin users revealed high prevalence of gastroduodenal mucosal injuries. Consideration of the indication and GI risks of aspirin before prescription is very important.

What is already known on this topic?

Aspirin is a medication prescribed worldwide with a wide range of complication. The prevalence of gastroduodenal mucosal injuries varied in different studies ranging from 10.7 to 63.1%.

What this study adds?

This is the first study in Thailand about the prevalence of gastroduodenal mucosal injuries of

aspirin users. This study revealed high prevalence of gastroduodenal mucosal injuries (63.5%) in aspirin users.

Potential conflicts of interest

None.

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ความชุกของการเกิดรอยโรคในกระเพาะอาหารและลำไส้เล็กส่วนต้นในผู้ป่วยที่ได้รับยาแอสไพริน

จิวรีดา ทองใบ

ภูมิหลัง: ยาแอสไพรินเป็นยาที่ใช้กันอย่างแพร่หลายเพื่อป้องกันหลอดเลือดหัวใจและสมองตีบทั้งการป้องกันแบบปฐมภูมิและทุติยภูมิ เป็นที่ทราบกันดีถึงความเสี่ยงของยาแอสไพรินต่อการเกิดโรคทางกระเพาะอาหารและลำไส้เล็กส่วนต้น ในประเทศไทยยังไม่มีข้อมูลของความชุกของการเกิดรอยโรคในกระเพาะอาหารและลำไส้เล็กส่วนต้น

วัตถุประสงค์: เพื่อศึกษาความชุกของการเกิดรอยโรคในกระเพาะอาหารและลำไส้เล็กส่วนต้นในผู้ป่วยที่ได้รับยาแอสไพริน

วัสดุและวิธีการ: ศึกษาผู้ป่วยได้รับยาแอสไพรินที่ไม่ได้รับยาป้องกันกระเพาะอาหาร และไม่มีอาการปวดท้อง โดยการตรวจสอบกล้องทางเดินอาหารส่วนบน

ผลการศึกษา: ผู้ป่วยทั้งหมด 104 ราย ที่ได้รับการตรวจสอบกล้องทางเดินอาหารส่วนบน พบความชุกของการเกิดรอยโรคกระเพาะอาหารและลำไส้เล็กส่วนต้น ชนิดแผลและแผลถลอกในผู้ป่วยที่ได้รับยาแอสไพรินเป็นร้อยละ 63.5

สรุป: พบความชุกของการเกิดรอยโรคของกระเพาะอาหารและลำไส้เล็กส่วนต้นค่อนข้างสูงในผู้ป่วยที่ได้รับยาแอสไพริน
