Original article

TRENDS OF PEPTIC ULCER DISEASES AND Helicobacter pylori INFECTION IN NORTHERN THAILAND

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Abstract

Background  The decline in global prevalence of Helicobacter pylori (Hp) and peptic ulcer disease (PUD) has been recognized, while the prevalence of non-Hp PUD is increasing. This study aimed to determine the trends of PUD and Hp infection, and exposure to nonsteroid anti-inflammatory drugs and aspirin (NSAIDs/ASA), their association with upper gastrointestinal (UGI) bleeding, and comparison to previous data.

Methods  All PUD patients with complete records of Hp status and NSAIDs/ASA exposure in 2008 were included for analysis of prevalence and their association with UGI bleeding. We compared present data of PUD and Hp infection to previous data of 1992 to show their trends.

Results  A total of 98 cases were included; gastric ulcer (GU) in 55, duodenal ulcer (DU) in 28, and 15 cases of combined ulcers. The Hp infection in each group was 38.18%, 42.86%, and 33.33%, respectively. Hp related ulcers had less UGI bleeding than NSAIDs/ASA related. When compared to previous data, the proportion of DU had decreased, GU and combined ulcers had increased, and the Hp infection rate in all 3 groups had decreased.

Conclusions  While the prevalence of PUD and Hp was decreasing, more NSAIDs/ASA related and non-Hp, non-NSAIDs/ASA related ulcers were diagnosed. NSAIDs/ASA related ulcers have more chances of bleeding.


Keywords: Helicobacter pylori, peptic ulcer disease, NSAIDs/ASA related ulcer

Helicobacter pylori (Hp) infection has been demonstrated as associated with peptic ulcer disease (PUD).\(^{1}\) Hp infection has been found in 73-100% of patients with duodenal ulcer (DU) and 65-100% of those with gastric ulcer (GU).\(^{2,7}\) During this decade, there have been some reports showing a decline in global prevalence of Hp infection and PUD.\(^{8-10}\) This phenomenon also was seen in many Asian countries.\(^{11-14}\) However, non-steroid anti-inflammatory drugs (NSAIDs), which have been used for various rheumatic conditions, and aspirin (ASA) for prevention of thrombotic events in cardiovascular and cerebrovascular diseases, or protection against colorectal cancer, are still prescribed widely by physicians, and easily available as over-the-counter drugs. These medications have been found as major risk factors in non-Hp associated PUD, especially regarding their complications in GU.\(^{15-18}\)

Methods  This was a retrospective observational study of all upper gastrointestinal endoscopic reports from May to August 2008 at the Endoscopic Unit,
Department of Medicine, Faculty of Medicine, Maharaj Nakorn Chiang Mai Hospital, which is a university hospital providing tertiary care as well as referral center in northern Thailand. Patients with peptic ulcer diseases were examined in detail for the presence of Hp infection, and their history of exposure to NSAIDs/ASA was taken from medical records.

Only patients with gastric and duodenal lesions and complete records on either rapid urease test (RUT) or histology staining to identify Hp by Giemsa stain were enrolled for analysis. Those who had malignant gastric or duodenal lesions were excluded from the analysis. The test for Hp infection by RUT was performed by taking one corpus and one antral biopsy for testing with the commercial testing urea kit, using the Pronto Dry test (Gastrex, Warsaw, Poland). Changing color from yellow to pink-red was interpreted as positive RUT for the presence of Hp. Histology with the use of Giemsa stain for Hp infection was based on identification of the bacteria on at least one of the specimens, which was taken from the corpus or antrum. A patient with a positive result either from RUT or histology was diagnosed as Hp positive. Additional biopsies were taken from the ulcer edges or other areas to rule out malignant diseases if endoscopic appearance was unfavorable for benign lesion.

An ulcer was defined as a breach of mucosa >5 mm in depth. Malignant ulcers were differentiated from benign ones by the histologic appearance in the biopsy specimens.

The presentation of upper gastrointestinal (UGI) bleeding from reports on both endoscopic findings of recent stigmata bleeding and medical records of patient history, physical examination and indication for endoscopic examination of each patient were reviewed.

The patients were categorized into 2 groups: UGI bleeding and non-UGI bleeding. There were 57 cases in the UGI bleeding group, who were scheduled for endoscopy to find the causes of bleeding. All were examined within 24 to 48 hours after their presentations. The 41 cases in the non-UGI bleeding group were scheduled for endoscopic examination, due to symptoms other than those for upper gastrointestinal bleeding, namely, dyspeptic symptoms or abdominal pain. The association of Hp infection with NSAIDs/ASA usage was investigated in all of these patients.

This study was compared with our previous data on PUD, which were collected from December 1991 to August 1992, comprising 80 consecutive cases of PUD tested for Hp infection and prevalence trends of Hp infection and PUD. \(^{(19)}\)

**Statistical analysis**

The characteristics of ulcers were presented as descriptive statistics. Fisher’s exact test was used to compare categorical data and odds ratio (OR) with 95% confidence interval (95% CI).

**Results**

A total of 119 patients with upper gastrointestinal ulcerative lesions was endoscopically diagnosed. Five cases of gastric cancer and 2 with lymphoma were identified by histology and excluded from the analysis, leaving 112 cases of benign peptic ulcer diseases. Sixty-three patients were found to have GU (56.25%), 33 DU (29.46%), and 16 combined GU and DU (14.28%).

The data for Hp tests were not complete in 14 cases of PUD patients, and they were excluded from the analysis. Therefore, the 98 remaining cases had complete results of the test for Hp infection, either by RUT or histology, which fulfilled the criteria of inclusion. Seventy-nine cases were tested by RUT, and 26 showed a positive reaction (32.91%); 40 cases had biopsies taken for histologic staining for Hp, and 19 showed Hp organisms on a Giemsa stain (47.50%); and a total of 38 cases from the 98 tested patients were positive for Hp by either RUT or histology stain for Hp (38.78%).

Of the 98 cases analyzed for the presence of Hp infection, by testing with at least one of the two methods, 55 had GU, 28 had DU, and 15 cases were found to have combined ulcers. Positive results for Hp infection were found in 21 of the 55 cases with GU (38.18%), 12 of the 28 cases with DU (42.86%), and 5 of the 15 cases with combined ulcers (33.33%), making a total of 38 positive Hp infection cases in 98 patients (38.78%).

Medical records showed that of 42 patients with a history of NSAIDs/ASA usage in a recent period, 26 were of the 55 GU cases (47.27%), 11 were of the 28 DU cases (39.29%) and 5 were of
the 15 combined ulcer cases (33.33%) (Table 1).

The percentages of patients were then examined in the aspects of \textit{Hp} infection alone, history of NSAIDs/ASA exposure alone, combination of both \textit{Hp} infection and NSAIDs/ASA exposure, and non-\textit{Hp}, non-NSAIDs/ASA exposure, and the following findings were obtained:

Of the 55 GU patients, 9 cases had both \textit{Hp} infection and a history of NSAIDs/ASA usage (16.36%), 12 had only \textit{Hp} infection without a history of NSAIDs/ASA usage (21.82%), 17 had only a history of NSAIDs/ASA usage without \textit{Hp} infection (30.90%), and 17 showed no \textit{Hp} infection and no history of NSAIDs/ASA exposure (30.90%).

In the 28 DU patients, 4 cases had both \textit{Hp} infection and a history of NSAIDs/ASA usage (14.49%), 8 had only \textit{Hp} infection without a history of NSAIDs/ASA usage (28.57%), 7 had only a history of NSAIDs/ASA usage without \textit{Hp} infection (25.00%), and 9 showed no \textit{Hp} infection and no history of NSAIDs/ASA exposure (32.14%).

Of the 15 combined GU & DU patients, there were 5 cases in each of the 3 groups: \textit{Hp} infection alone, NSAIDs/ASA exposure alone, and non-\textit{Hp}, non-NSAIDs/ASA exposure (Table 2).

By grouping the patients into UGI bleeding and non-UGI bleeding, there were 57 UGI bleeding and 41 non-UGI bleeding patients. Of the UGI bleeding patients, 18 had \textit{Hp} infection (31.58%), and 30 had a history of NSAIDs/ASA usage (52.63%). In the non-UGI bleeding patients, 20 cases had \textit{Hp} infection (48.78%), and 12 had a history of NSAIDs/ASA usage. (29.27%). The history of NSAIDs/ASA exposure was significantly associated with the UGI bleeding group (OR 2.69, 95% CI 1.16-6.23), while \textit{Hp} infection was found more in the non-bleeding group (OR 0.49, 95% CI 0.21-1.10) (Table 3). When analysed by grouping the patients into 4 subgroups, using non-\textit{Hp}, non-NSAIDs as a reference, it was found that an NSAIDs/ASA associated ulcer had more tendency towards UGI bleeding than \textit{Hp} associated ulcers. However, a combination of \textit{Hp} infection and exposure of NSAIDs did not show increased risk of UGI bleeding in our series (Table 4).

From our previous data of PUD and \textit{Hp} infection, which were collected from December 1991 to August 1992, we had 80 consecutive cases with PUD and tested for \textit{Hp} infection in every one using both RUT and histologic staining for \textit{Hp} by Giemsa stain. For RUT, the CLO test (Ballard Medical Products, USA.) was used. There were 33 GU (41.25%), 40 DU (50%), and 7 combined ulcers (8.75%). The \textit{Hp} infection was found by

<table>
<thead>
<tr>
<th>Table 1. Patients’ for Hp tests and history of NSAIDs/ASA exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of PUD</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>GU</td>
</tr>
<tr>
<td>DU</td>
</tr>
<tr>
<td>GU + DU</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

<p>| Table 2. Patients’ profile on association of Hp status and NSAIDs/ASA exposure |
|-----------------|--------|-----------------------------|-------------------------------|--------------------------------------|-------------------------------------|</p>
<table>
<thead>
<tr>
<th><strong>No</strong></th>
<th><strong>Hp+/NS+ No (%)</strong></th>
<th><strong>Hp+/NS- No (%)</strong></th>
<th><strong>Hp-/NS+ No (%)</strong></th>
<th><strong>Hp-/NS- No (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>GU</td>
<td>55</td>
<td>9 (16.36)</td>
<td>12 (21.82)</td>
<td>17 (30.9)</td>
</tr>
<tr>
<td>DU</td>
<td>28</td>
<td>4 (14.29)</td>
<td>8 (28.57)</td>
<td>7 (25)</td>
</tr>
<tr>
<td>GU + DU</td>
<td>15</td>
<td>0 (0)</td>
<td>5 (33.33)</td>
<td>5 (33.33)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>98</td>
<td>13 (13.27)</td>
<td>25 (25.51)</td>
<td>29 (29.59)</td>
</tr>
</tbody>
</table>

\textit{Hp+} = positive \textit{Hp} test; \textit{NS+} = exposure to NSAIDs
\textit{Hp-} = negative \textit{Hp} test; \textit{NS-} = non-exposure to NSAIDs
positive results from either RUT or histologic proof of the organisms, and there was \(Hp\) infection in 22 cases of the 33 GU (66.7%), 29 of the 40 DU (72.5%), and 4 of the 7 combined GU & DU (57.2%) (Table 5, 6).

It was noticeable that the proportion of GU and DU in this study changed in the opposite direction, when the proportion of GU significantly increased (41.25% vs 56.12%, \(p = 0.034\)), while that of DU significantly decreased (50.00% vs 28.57%, \(p = 0.012\)) (Table 5). The prevalence of \(Hp\) infection in PUD significantly declined from 68.75% to 38.78% (\(p < 0.001\)) during this period. Also the prevalence of \(Hp\) infection in GU declined from 66.7% to 38.18%, and that in DU from 72.5% to 42.86% (Table 6).

**Table 3.** UGI bleeding vs non-bleeding on \(Hp\) status and history of NSAIDs exposure

<table>
<thead>
<tr>
<th>Status</th>
<th>UGIB (57 patients)</th>
<th>Non-UGIB (41 patients)</th>
<th>OR (95% CI)</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS+</td>
<td>30 (52.63)</td>
<td>12 (29.27)</td>
<td>2.69 (1.16-6.23)</td>
<td>0.024</td>
</tr>
<tr>
<td>(Hp)+</td>
<td>18 (31.58)</td>
<td>20 (48.78)</td>
<td>0.49 (0.21-1.10)</td>
<td>0.097</td>
</tr>
</tbody>
</table>

**Table 4.** Risk of UGI bleeding in different status of \(Hp\) infection and NSAIDs/ASA exposure

<table>
<thead>
<tr>
<th>Status (No)</th>
<th>OR</th>
<th>SE</th>
<th>(p)-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Hp)-ns- (31)</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>(Hp)+ns- (25)</td>
<td>0.41</td>
<td>0.22</td>
<td>0.10</td>
<td>0.14-1.20</td>
</tr>
<tr>
<td>(Hp)-ns+ (29)</td>
<td>1.90</td>
<td>1.05</td>
<td>0.25</td>
<td>0.64-5.60</td>
</tr>
<tr>
<td>(Hp)+ns+ (13)</td>
<td>1.63</td>
<td>1.14</td>
<td>0.50</td>
<td>0.41-6.44</td>
</tr>
</tbody>
</table>

**Table 5.** Comparison of PUD prevalences in 1992 vs 2008

<table>
<thead>
<tr>
<th>Status</th>
<th>1992 No (%)</th>
<th>2008 No (%)</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GU</td>
<td>33 (41.25)</td>
<td>55 (56.12)</td>
<td>0.034</td>
</tr>
<tr>
<td>DU</td>
<td>40 (50)</td>
<td>28 (28.57)</td>
<td>0.012</td>
</tr>
<tr>
<td>GU+DU</td>
<td>7 (8.75)</td>
<td>15 (15.31)</td>
<td>0.137</td>
</tr>
<tr>
<td>Total</td>
<td>80 (100)</td>
<td>98 (100)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

**Table 6.** Comparison of \(Hp\) prevalences in 1992 vs 2008

<table>
<thead>
<tr>
<th>Status ((Hp)+/total (%))</th>
<th>1992</th>
<th>2008</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GU</td>
<td>22/33 (66.7)</td>
<td>21/55 (38.18)</td>
<td>0.015</td>
</tr>
<tr>
<td>DU</td>
<td>29/40 (72.5)</td>
<td>12/28 (42.86)</td>
<td>0.023</td>
</tr>
<tr>
<td>GU+ DU</td>
<td>4/7 (57.2)</td>
<td>5/15 (33.33)</td>
<td>0.376</td>
</tr>
<tr>
<td>Total</td>
<td>55/80 (68.75)</td>
<td>38/98 (38.78)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Discussion

During the past three decades, the prevalence of PUD has decreased remarkably in the United States, Europe, Australia and Japan.\(^{20-22}\) Many factors have been taken into consideration regarding this phenomenon, for example, the rapid change in the pattern of PUD is more likely due to changes in environmental factors rather than those in the gene of an affected patient.\(^{23}\) The decline in \(Hp\) infection prevalence during this decade may be due to the global trend of improved socioeconomic status. One study from Japan showed that the decline of \(Hp\) infection was as much as 20% between 1986 and 1994,\(^{24}\) while another study from South Korea showed that the prevalence of infection in young children was inversely related to the socioeconomic class of their family,\(^{25}\) and a study from Italy showed that the prevalence of \(Hp\) infection was higher in rural areas when compared to that in industrial ones.\(^{26}\) Besides socioeconomic status or environmental issues, part of the reasons for this decline might be increased awareness of \(Hp\) eradication from the “test and treat” strategy used by both general practitioners and specialists,\(^{27}\) and also the effectiveness of organism eradication by antibiotics combined with proton pump inhibitors\(^{28-29}\) as well as the low re-infection rate of \(Hp.\)\(^{30}\) All these reasons have led to the decrease of \(Hp\) infection and low ulcer recurrence in patients, which in turn might be reflected by decreased peptic ulcer prevalence related \(Hp\) infection.

The data from this study and the previous period also gave results that showed a significant
Prevalences of PUD and *Hp*, NSAIDs/ASA exposure

In conclusion, our studies from 2 periods showed the trends of decline in PUD and *Hp* infection, which were in accordance with the global incidence. At the same time, we found more NSAIDs/ASA associated cases and more non-*Hp*, non-ASA/ASA associated ulcers, as well as NSAIDs/ASA related PUD having a greater percentage of UGI bleeding. We believe that effective eradication of *Hp* infection and more thoughtful decision making in prescribing NSAIDs/ASA to patients would reduce the prevalence of PUD in these entities. However, for non-*Hp*, non-ASA/ASA related PUD, the prevalence would not decrease, and we need to know more about the natural history of this entity of ulcer before we can have effective management of it, which may be different from that used in *Hp* or NSAIDs/ASA associated ulcers.

References

8. el-Serag HB, Sonnenberg A. Opposing time
แนวโน้มของอุบัติการณ์โรคแผลในกระเพาะอาหารและลำไส้เล็กส่วนต้น
gบการคิดแข็ง Helicobacter pylori ในภาคเหนือ

องอาจ ไพรสมหาราจ, ว.พ., พิษณุ, พิเศษพงษา, พ.บ., สิทธิ์หงส์ทรงเกียรติ, พ.บ.
ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

บทคัดย่อ
บทคัดย่อ อุบัติการณ์ของแผลในทางเดินอาหารส่วนต้นและการคิดแข็ง Helicobacter pylori หรือ H. pylori (Hp) มีแนวโน้มลดลงทั่วโลก ในขณะเดียวกันอุบัติการณ์ของแผลจากการใช้ยาต้านการอักเสบที่ไม่ใช่สแตียรอยด์ มีแนวโน้มที่จะลดลงตามลำดับ ส่วนการคิดแข็งหลังจากที่ผู้วิจัยได้สืบค้นแนวโน้มของอุบัติการณ์ดังกล่าวรวมไปถึงแนวโน้มการมีเลือดออกจากแผลในทางเดินอาหารส่วนต้นในแต่ละกรณี

วิธีการ ทำการวิเคราะห์ข้อมูลของแผลในทางเดินอาหารส่วนต้นในช่วงเดือนพฤษภาคม ถึงเดือนสิงหาคม 2551 และเปรียบเทียบข้อมูลเดิมที่ทำเมื่อเดือนธันวาคม 2534 ถึงเดือนสิงหาคม 2535

ผลการศึกษา ความสัมพันธ์กับการคิดแข็ง H. pylori ใน GU, DU, combined ulcers ร้อยละ 38.18, 42.86 และร้อยละ 33.33 ตามลำดับ แผลจากการคิดแข็ง H. pylori มีลักษณะข้อมูลกว่าแผลส่วนใหญ่ที่เกิดจาก NSAIDs/ASA เมื่อเปรียบเทียบกับข้อมูลแต่ละกรณี การคิดแข็ง H. pylori ในพื้นที่DU ลดลงแต่พบ DU และ combined ulcers กลับเพิ่มขึ้น การคิดแข็ง H. pylori ลดลงที่ 3 กลุ่ม

สรุป อุบัติการณ์ของแผลในทางเดินอาหารส่วนต้นสัมพันธ์กับการคิดแข็ง H. pylori นอกจากนี้ผลก็ยังแสดงถึงผลการใช้ NSAIDs/ASA และแผลที่ไม่สัมพันธ์กับปัจจัยที่สงสัยมีอัตราส่วนเพิ่มขึ้น โดยที่สัมพันธ์กับการใช้ NSAIDs/ASA มีอุบัติการณ์คล้ายคลึงกันกับแผลในกลุ่มคิดแข็ง H. pylori เชียงใหม่


Keywords: เชื้อ Helicobacter pylori โรคแผล แผลกระเพาะอาหารและลำไส้เล็กส่วนต้น แผลจากการใช้ยาต้านการอักเสบที่ไม่ใช่สแตียรอยด์