Evolution in the epidemiology of non-variceal upper digestive hemorrhage from 1985 to 2006

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ABSTRACT

Objectives: to describe changes occurred in the characteristics of patients suffering from non-variceal upper gastrointestinal bleeding, and in this condition's epidemiology.

Methods: a prospective study was carried out to examine the occurrence and causes of non-variceal upper digestive bleeding in the corresponding health department at Virgen de las Nieves Hospital in Granada, Spain. In this study three periods of time were compared. Group 1 (1985): 284 patients; group 2 (1996): 259 patients; and group 3 (2006) 291 patients.

Results: in group 1 the incidence was 71/100,000 inhabitants; in group 2, 64/100,000; and in group 3, 66/100,000. Mean age in 1985 was 57.4; in 1996, 59.6; and in 2006, 62.38. In all groups a majority of cases were men (75.4, 69.5, and 72.2%, respectively). Major causes included duodenal ulcer (1: 40.5%; 2: 43.2%; 3: 40.5%), gastric ulcer (1: 24.3%; 2: 30%; 3: 18.9%); LAMG (1: 53.3%; 2: 43.2%; 3: 9.6%); neoplasia (1: 1.7%; 2: 1.9%; 3: 5.2%), and vascular injuries (1: 0.5%; 2: 1.5%; 3: 9.3%). The death rate was 2.5% in 1985; 1.5% in 1996; and 1% in 2006.

Conclusions: a significant increase in mean age over the years was detected. The most frequent cause of hemorrhage was duodenal ulcer followed by gastric ulcer. Of significance is an increase in the proportion of neoplasias above of vascular injuries in the later group as opposed to the earlier one. We found no significant difference in mortality between groups.

Key words: Epidemiology. Peptic ulcer haemorrhage. Duodenal ulcer. Incidence.
on the characteristics of patients with non-variceal upper hemorrhage, as well as on its incidence and causes.

Among these drugs the impact of proton pump inhibitors should be highlighted, as they have brought about a decrease in rebleeding rates (2,3), and reduced bleeding in patients with a high risk of upper gastrointestinal hemorrhage and in those undergoing treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) (4-6).

Helicobacter pylori eradication also proved effective for the reduction of non-variceal UGIB (7).

Endoscopic hemostatic treatment is currently the treatment of choice for upper gastrointestinal bleeding of peptic origin, because it significantly reduces rebleeding and surgery rates (8).

Therefore, if we now apply these treatments incidence, rebleeding, and surgery rates should be smaller nowadays.

In a study on upper gastrointestinal bleeding, Rockall et al. (9), using a multivariate analysis, significantly and independently related the mortality rate of this condition to: age, previous medical comorbidity, and endoscopy findings; they formulated a predictive system for mortality that was validated by other authors (10).

If population ageing is a fact, and with an increased presence of medical comorbidity, the mortality rate should have increased according to the above criteria.

In our study we will describe the changes occurred in the characteristics of patients who suffered from non-variceal upper gastrointestinal bleeding during the period from 1985 to 2006 in a third-level hospital.

MATERIAL AND METHODS

We did a prospective observational study in which we analyzed cases of nonvariceal gastrointestinal bleeding treated in Virgen de las Nieves Hospital (Granada) during three periods, each of one year’s duration, from 1985. Virgen de las Nieves Hospital has a reference population of 439,032 inhabitants; in 1996 it had 401,735 inhabitants; and in 1985, 398,950.

The first study was carried out from January 1st, 1985 to December 31st, 1985 in 284 patients. The second study took place from January 1st to December 31st, 1996 in 251 patients. The third study took place from January 1st to December 31st, 2006 in 291 patients. All patients suffered from non-variceal gastrointestinal bleeding.

We included in the study all patients diagnosed with nonvariceal gastrointestinal bleeding who were looked after by the Gastroenterology Department at Virgen de las Nieves Hospital, who had been treated with a therapeutic and/or diagnostic endoscope (according to the presence of endoscopists), and whose cause was not due to esophageal or gastric varices, nor was a consequence of portal high blood pressure. Therefore, patients not receiving endoscopy or whose digestive hemorrhage was caused by portal high blood pressure (esophageal or gastric varices, portal hypertensive gastropathy) were excluded from the study, and their information was not recorded.

Demographic and clinical data were collected in the same way for the three periods of time analyzed. Data consists of: Demographic data, symptoms of digestive hemorrhage present during the episode (hematemesis as the vomiting of hematic contents, and melena as the expulsion through the rectum of blood remains). Previously present medical comorbidities, drugs used, endoscopic diagnosis including the cause and signs of recent bleeding, endoscopic treatment undertaken, surgery, and mortality. All these data were collected with the knowledge and consent of patients.

Severe digestive hemorrhage was defined as the presence of hemodynamic shock signs in the physical exam, including a systolic blood pressure lower than 100 mmHg and more than 100 heart beats per minute; moderate digestive hemorrhage was defined as a blood pressure over 100 mmHg and more than 100 heart beats a minute; and mild digestive hemorrhage was diagnosed if blood pressure was over 100 mmHg with fewer than 100 heart beats a minute.

Endoscopic results were classified according to Forrest’s classification system (11): Forrest Ia = active arterial bleeding; Forrest Ib = oozing bleeding; Forrest IIa = no bleeding visible vessel; Forrest IIb = adhered red blood clot; Forrest IIc = black blood clot; Forrest III = clean base.

Statistical analysis

The results of quantitative variables were expressed as mathematical averages. Qualitative variables are expressed as percentages.

Continuous variables were compared by using a t test, or an ANOVA test for independent variables. For qualitative variables we used the $\chi^2$ test. These tests were carried out using the SPSS 15.0 program.

RESULTS

The incidence of peptic gastrointestinal bleeding was 71 cases per 100,000 inhabitants in 1985; 64 in 1996; and 66 in 2006.

Mean age in the different groups was: 1985 (57.45 ± 17.09 years); 1996 (59.6 ± 15.45 years); and 2006 (68.28 ± 15.18 years). We found no significant differences between the first two groups, while the latter shows an older age in a significant way with respect to the two previous groups.

By analyzing by age groups, as expressed in figure 1, significant statistical differences were noted. These differences are due to an increase in patients over 70 in group 3, a greater proportion of patients between 30 and
50 years in groups 2 and 3, and more patients under 30 in group 1.

The characteristics of the patients analyzed are listed in Table I. We may see that the male:female ratio remains stable. There are differences regarding medical comorbidities, and a greater proportion of these may be seen in the latter group (Table I).

We observe a lower use of NSAIDs in the latter group as compared to the other two during the two weeks before the acute event (group 1: 45.7%; group 2: 47%; group 3: 33.6%) (Table I).

Table II lists nonvariceal UGIB presentation forms. We find that severe hemorrhage is proportionally more relevant in group 2. Hematemesis was more common in the 1985 group versus the other two groups. Presentation in the form of melena has remained stable.

Endoscopic results have varied throughout the series, and what has to be highlighted is a greater proportion of Forrest III lesions in the latter series.

Given the quantity of exiting etiologies we analyzed the incidence of the most frequent ones, including these in a common group (duodenal ulcer, gastric ulcer, non-specific mucosal abnormalities, and the rest of injuries): Group 1: 115 patients with duodenal ulcer, 69 with gastric ulcer, 43 erosive gastritis, and 57 with other causes; group 2: 112 patients with duodenal ulcer, 78 gastric ulcers, 23 with non-specific mucosal abnormalities, and 46 with other causes; group 3: 118, 22, 28, and 90, respectively (Fig. 2).

The test is of statistical significance given the increase in gastric ulcers in the 1996 group, the greater proportion of non-specific mucosal abnormalities found in the 1985 group, and the great increase of patients whose cause we included in the other causes category.

There were no differences in the proportion of duodenal ulcers in the 3 groups, this also being the most frequent cause of nonvariceal upper gastrointestinal bleeding in the study.

### Table I. Characteristics of patients suffering from upper gastrointestinal bleeding in the different studies

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1985 (%)</th>
<th>1996 (%)</th>
<th>2006 (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 70 years old</td>
<td>71.1</td>
<td>67.2</td>
<td>57.7</td>
<td>0.002</td>
</tr>
<tr>
<td>&gt; 70 years old</td>
<td>28.9</td>
<td>32.8</td>
<td>42.3</td>
<td>0.356</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>24.6</td>
<td>30.1</td>
<td>27.8</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>75.4</td>
<td>69.9</td>
<td>72.2</td>
<td></td>
</tr>
<tr>
<td>Comorbidity</td>
<td>45.8</td>
<td>44.4</td>
<td>65.3</td>
<td>0.000</td>
</tr>
<tr>
<td>Main nonsteroidal antiinflammatory taken</td>
<td>Aspirin = 69%</td>
<td>Aspirin = 46.7%</td>
<td>Ibuprofen = 49%</td>
<td>0.002</td>
</tr>
<tr>
<td>Consumption of oral anticoagulants</td>
<td>0%</td>
<td>4.5%</td>
<td>13.7%</td>
<td>0.000</td>
</tr>
<tr>
<td>Consumption of proton pump inhibitors</td>
<td>0%</td>
<td>4%</td>
<td>33.7%</td>
<td>0.000</td>
</tr>
</tbody>
</table>

### Table II. Characteristics of upper gastrointestinal bleeding in the three series under study

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1985 (%)</th>
<th>1996 (%)</th>
<th>2006 (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>71.8%</td>
<td>60.8%</td>
<td>78%</td>
<td>0.000</td>
</tr>
<tr>
<td>Moderate</td>
<td>23.2%</td>
<td>27.8%</td>
<td>15.8%</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>4.9%</td>
<td>12%</td>
<td>6.2%</td>
<td></td>
</tr>
<tr>
<td>Presentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematemesis</td>
<td>64.4%</td>
<td>52.5%</td>
<td>50.9%</td>
<td>0.002</td>
</tr>
<tr>
<td>Melena</td>
<td>76.1%</td>
<td>81.1%</td>
<td>74.8%</td>
<td>0.187</td>
</tr>
<tr>
<td>Forrest</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8.8%</td>
<td>17.4%</td>
<td>14.1%</td>
<td>0.000</td>
</tr>
<tr>
<td>II</td>
<td>73.9%</td>
<td>61%</td>
<td>34.4%</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>17.3%</td>
<td>21.6%</td>
<td>51.5%</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>2.5%</td>
<td>1.5%</td>
<td>1%</td>
<td>0.400</td>
</tr>
<tr>
<td>Surgical treatment carried out</td>
<td>13.4%</td>
<td>5%</td>
<td>5.8%</td>
<td>0.000</td>
</tr>
</tbody>
</table>
Mortality rate in group 1 is 2.5%; in group 2: 1.5%; and in group 3: 1%. We see no significant differences between groups.

DISCUSSION

In a similar way to the study carried out by Van Leerdman (12), we can observe a steady increase in age in our series.

In general, the treatment of upper gastrointestinal bleeding has improved because of endoscopic therapy as well as the use of proton pump inhibitors, which increase gastric pH acid in a more efficient way, thus facilitating the healing of the underlying cause. However, mortality remains the same, which is thought to be due to increased age and comorbidities in patients (12-16).

Age is a factor in the evolution of upper gastrointestinal bleeding, as accepted by a majority of authors. Severe upper digestive hemorrhage appears more frequently in elderly people, who often have more medical comorbidities: Cardio-respiratory, renal, and/or vascular conditions that usually decompensate in the severe group (9,10,16-19).

So, the greatest number of deaths does not result from digestive hemorrhage as such but from decompensation of underlying conditions, and postoperative complications, which are more common in this group of patients (10,14-18).

In our study 44% suffered from chronic illness in 1996, and 63% in 2006, similar to other studies (19-21). Also, in another study done in our country, which was recently published, an increase in chronic pathology was found for hospitalized patients (22).

Therefore, improved treatment of upper gastrointestinal bleeding has compensated increasing death rates as a result of older age in our patients.

In our series duodenal ulcer is the first cause of hemorrhage with: 40.5, 43.2, 40.5%, in each of our series. This pathology is most frequent in a majority of published series (9,12,19-22). However, Boonpneganee et al. (1), who used the CORI database, found that gastroduodenal peptic ulcer only accounted for 20.6%, which means a much lower proportion versus other series; furthermore, gastric ulcers are more frequent than duodenal ulcers (11.4 vs. 9.2%). This trend reported by an American study (1) was also noted in the study by Garrido et al. (20), although the main cause of upper gastrointestinal bleeding was still duodenal ulcer followed by gastric ulcer.

After duodenal ulcer and gastric ulcer, the next main cause was severe injury and nonspecific gastric mucosal abnormalities. This is consistent with most other studies (12,13,19-24), except that by Boonpneganee (1), who considers that peptic ulcer is given a too great importance as a cause of upper gastrointestinal bleeding.

In this section we must note that some gastric injuries are difficult to identify as erosions or ulcers as endoscopy might not accurately read lesion depth. Therefore, there is some subjectivity in categorizing these injuries. With lower percentages, other causes noted include: Mallory-Weiss syndrome, esophagitis, malignancy (fundamentally gastric), mouth ulcers, anastomotic ulcers, and vascular lesions.

We must point out the huge increase in vascular lesions that accounted for 9.3% in the last series, while in the first and second series it was 1 and 1.5%, respectively. Also an increase in malignancies: 5.2 versus 1.7% in 1985, and 1.9% in 1996.

The other causes remained stable in the three series. We must point out that this increase was not found in other similar studies (13,21-24). Perhaps the use of new technologies in endoscopy is bringing about more accurate diagnoses.

Among the different types of endoscopic treatments the most widely used option in our field is injection. Although different variables have been evaluated for this treatment, a significant difference in death rates and rebleeding has not been found; what has been found is a decrease in surgical procedures (25).

This decrease in surgery rates has caused a corresponding decrease in the death rate this treatment produces.

In the first series proton pump inhibitors were not used; they were used in the second and in high dose in the third one. These drugs have proved more efficient than the H_{2} antagonists and placebo in decreasing surgery needs and rebleeding but not so regarding mortality (26-28). Various tests have shown that high-dose proton pump inhibitors, first in bolus and then in perfusion for the first 72 hours of endoscopic treatment, causes a significant reduction in rebleding and surgery needs (2,26-28). These changes in treatment have resulted in a progressive decrease in surgery needs and death rates.

We consider that better patient management through the use of drugs such as proton pump inhibitors and endoscopic treatment have compensated for the risk of increased age and medical comorbidity, which have increased over time.
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