Changes in the etiology, outcome, and characteristics of patients with acute gastrointestinal bleeding between 1999 and 2005

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RESUMEN

Objetivos: analizar la evolución, a lo largo del periodo 1999-2005, de las siguientes variables de los pacientes ingresados por hemorragia digestiva (HD) en una Unidad de Sangrantes: etiología, patología de base, consumo de AINE/anticoagulación y mortalidad.

Material y métodos: durante el periodo 1999-2005 se ha estudiado la evolución de las siguientes causas de HD que requirieron ingreso en la Unidad de Sangrantes: úlcus duodenal (UD), úlcus gástrico (UG), hipertensión portal (HPT) y otros. De igual forma se ha analizado la evolución en el porcentaje de enfermos ingresados con patología de base, consumo de fármacos AINE/anticoagulantes y mortalidad.

Resultados: se han incluido 1.611 pacientes en el estudio con una edad media de 60,45 años (59,7-61,2), 76,41% hombres (74,3-78,5). La UD fue responsable del 22,20% de episodios (20,2-24,3), la UG del 18,40% (16,6-20,4) y la HPT del 33,60% (31,3-36,0).

De forma global realizaban tratamiento con AINE el 34,5% (32,6-37,3), anticoagulación el 7,1% (6,0-8,6), presentaban patología de base el 72,6% (70,4-74,8) y la mortalidad global fue del 6,27% (5,16-7,59). A lo largo del periodo estudiado se constató un aumento de los pacientes con patología de base (p < 0,02) y un descenso en los ingresos por UD (p < 0,04), permaneciendo estables el resto de variables estudiadas.

Conclusiones: la UD y UG junto con la HPT suponen el 75% de los ingresos de la Unidad de Sangrantes. A lo largo de los últimos 7 años se constata un aumento de los casos debido a UD y un aumento de pacientes con patología de base, mientras la mortalidad global se mantiene estable.


ABSTRACT

Objectives: to analyze the evolution of the following variables in patients admitted to a Blood Unit for gastrointestinal bleeding throughout 1999-2005: etiology, comorbid diseases, use of NSAIDs/anticoagulants, and mortality.

Material and methods: we analyzed the evolution of the following causes of GIB that required admission to the Blood Unit from 1999 to 2005: duodenal ulcer (DU), gastric ulcer (GU), portal hypertension (PHT), and others. We also analyzed changes in the percentage of patients admitted with comorbid disease, use of NSAIDs/anticoagulants, and mortality.

Results: 1,611 patients with a mean age of 60.45 years (59.7-61.2) were included in this study; 76.41% were males (74.3-78.5). DU was the cause of bleeding in 22.20% of cases (20.2-24.3), GU in 18.40% (16.6-20.4), and PHT in 33.60% of cases (31.3-36.0).

In all, 34.5% (32.6-37.3) of patients were taking NSAIDs, 7.1% (6.0-8.6) were receiving anticoagulant therapy, 72.6% (70.4-74.8) presented with comorbid disease, and overall mortality was 6.27% (5.16-7.59). Throughout the 1999-2005 period there was an increase in the number of patients with comorbid diseases (p < 0.02), and a decrease in cases of DU (p < 0.04), without significant differences in the remaining variables.

Conclusions: DU, GU and PHT account for three quarters of admissions to our Blood Unit. Over the last seven years, there has been a decrease in cases due to DU, and an increase in patients with comorbid disease; overall mortality rates have remained stable.

Key words: Etiology. Epidemiology. Gastrointestinal bleeding. Gastroroduodenal ulcer. Variceal bleeding.
sources (1). Traditionally, it has been classified according to its upper or lower origin (proximal or distal to Treitz’s angle), and according to its etiology as variceal bleeding (PHT) or non-variceal bleeding (the main cause of which is gastroduodenal ulcer). The method of diagnosis, treatment, and prognosis are different for these etiologies (2).

Due to advances in the medical field both overall and particularly in gastroenterology, a decreased incidence and improved prognosis for GIB would be expected over recent years; however, increasingly older patients with numerous pathologies are admitted to hospital for GIB, and therefore no significant change in these parameters may be seen (3). Helicobacter pylori eradication, a high incidence of viral hepatitis, and alcohol consumption are increasing the percentage of variceal bleeding versus gastroduodenal ulcer (4).

An analysis of trends regarding the etiology and risk factors linked to poorer prognoses in patients with GIB over recent years will enable the implementation of specific prophylactic measures focused on decreasing its incidence and improving patient outcomes (5).

This study evaluates the etiology, characteristics, and outcomes regarding patients admitted to the Blood Unit of a tertiary referral hospital due to severe GIB.

PATIENTS AND METHODS

We carried out a study of all patients admitted to the Blood Unit at Virgen del Rocío Hospital (a tertiary referral hospital), Seville, for both upper and lower gastrointestinal bleeding during the period from 1999 to 2005. This hospital serves a population of 735,973 inhabitants. Included in the study were patients requiring transfusions who presented with hemodynamic instability or whose characteristics suggested a persistent or recurrent hemorrhage.

In all cases patient details were recorded, including sex and age upon admittance; personal history of tobacco and alcohol use (tobacco use being defined as the smoking of more than 10 cigarettes/day, and alcohol use as the regular consumption of more than 80 g of alcohol/day for males and 40 g/day for females). A history of the use of aspirin, other NSAIDs, or oral anticoagulants was taken into account when clearly reflected in the medical history by patients or their family members.

The presence of comorbid diseases in any vital system or organ (cardiovascular, pulmonary, renal, etc.) was also evaluated.

With regard to type of hemorrhage, this was classified as: upper gastrointestinal bleeding (originating between the upper esophageal sphincter and Treitz’s angle) or lower gastrointestinal bleeding (from Treitz’s angle to the anal margin). We also evaluated the form of clinical presentation—hematemesis, melena, hematochezia or rectorrhagia, in addition to the patient’s hemodynamic status, defined as stable when the following criteria were fulfilled: systolic blood pressure higher than 100 mmHg, heart rate lower than 100 beats/minute, no changes to blood pressure and heart rate following orthostatism, no clinical evidence of peripheral hypoperfusion and diuresis exceeding 30 ml/h; and hemodynamic instability when two or more of the following criteria were met: systolic blood pressure lower than 100 mmHg, heart rate higher than 100 systoles/minute, clinical evidence of peripheral hypoperfusion, and significant changes in blood pressure and heart rate following orthostatism.

The etiology of upper gastrointestinal bleeding was recorded as follows: DU, GU, Mallory-Weiss, PHT, upper gastrointestinal bleeding (UGIB) of unknown origin, and other; lower gastrointestinal bleeding was classified according to its etiology as follows: diverticular disease, angiodysplasia, lower gastrointestinal bleeding (LGB) of unknown origin, and other.

The evolution of patients was classified as: a) favorable: in cases with no evidence of new external bleeding episodes, stable hemodynamic status, and no decreases in hematocrit; b) recurrent hemorrhage: if the need for fluid infusion exceeded 1,000 ml/h within 48 hours of onset to maintain hemodynamic stability, or when there was a decrease of at least 7 points in hematocrit in association with “new melena” or new episodes of hematemesis or rectorrhagia. From the third day on, bleeding was considered recurrent when new episodes of external hemorrhaging occurred; and c) patient outcome.

Statistical study

Several quantitative and qualitative variables were included, expressed as means or percentage, respectively, with 95% confidence intervals. A single-factor ANOVA was performed to compare changes in variables throughout the years included in the study. Statistical significance was defined at p < 0.05. The statistical analysis was carried out using the SPSS 12 program.

RESULTS

During the 1999-2005 period 1,611 patients admitted to the Blood Unit, Department of Gastroenterology, Virgen del Rocío Hospital, Seville, were included in this study. Of these 76.41% were males (74.3-78.5) and 23.59% were females (21.4-25.8), with a mean age of 60.45 ± 15.59 years (59.7-61.2).

Table I shows the general characteristics of all patients in the sample with regard to history, form of presentation, etiologic diagnosis; it must be pointed out that 36.70% corresponded to patients with a history of alcohol use, and 34.5% to subjects previously treated with NSAIDs. Gastroduodenal ulcers were the cause in 40.60% of patients requiring hospital admission (18.40% had GU and 22.20% had DU); hemorrhages due to PHT were seen in...
33.60% of cases. Both etiologies together constitute three quarters of all admissions to the Blood Unit.

Table II shows that 59.4% of patients had hemodynamic instability and 72.63% had a comorbid disease; there was an overall mortality rate of 6.27%, and this was significantly higher in cases of variceal bleeding compared to gastroduodenal ulcers (p < 0.01).

The ANOVA test showed a lower incidence of hemorrhage from DU throughout the period studied, in addition to an increasingly greater percentage of patients with comorbid diseases (diagrams 3 and 4), and a greater proportion of both lower and upper hemorrhages of unknown origin (diagram 5). In contrast, no differences were found throughout the study in the incidence of hemorrhage from GU or PHT (p = NS).

No differences were found throughout the study in clinical presentation, presence of hemodynamic instability, treatment with NSAIDs or anticoagulants, and mortality.

Table I. General characteristics of the sample (n = 1,611)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>95% IC</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. General information</td>
<td></td>
<td></td>
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<tr>
<td>Age (years)</td>
<td>60.45</td>
<td>59.7-61.2</td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>76.41</td>
<td>74.3-78.5</td>
<td></td>
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<tr>
<td>Tobacco use (%)</td>
<td>26.70</td>
<td>24.6-28.9</td>
<td></td>
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<tr>
<td>Alcohol use (%)</td>
<td>36.70</td>
<td>34.3-39.1</td>
<td></td>
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<tr>
<td>Prior treatment with NSAIDs (%)</td>
<td>34.50</td>
<td>32.6-37.3</td>
<td></td>
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<tr>
<td>T with anticoagulants (%)</td>
<td>7.10</td>
<td>6.0-8.6</td>
<td></td>
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<tr>
<td>B. Clinical presentation of hemorrhage</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hematemesis (%)</td>
<td>50.22</td>
<td>47.8-52.7</td>
<td></td>
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<tr>
<td>Melena (%)</td>
<td>53.88</td>
<td>51.4-56.3</td>
<td></td>
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<tr>
<td>Rectorrhaga (%)</td>
<td>13.70</td>
<td>12.0-15.5</td>
<td></td>
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<tr>
<td>Haematochezia (%)</td>
<td>2.60</td>
<td>1.9-3.5</td>
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<tr>
<td>C. Etiologic diagnosis</td>
<td></td>
<td></td>
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<tr>
<td>Gastric ulcer (%)</td>
<td>18.40</td>
<td>16.6-20.4</td>
<td></td>
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<tr>
<td>Duodenal ulcer (%)</td>
<td>22.20</td>
<td>20.2-24.3</td>
<td></td>
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<tr>
<td>Mallory-Weiss (%)</td>
<td>5.00</td>
<td>4.0-6.30</td>
<td></td>
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<tr>
<td>Angiodysplasia (%)</td>
<td>1.60</td>
<td>1.0-2.30</td>
<td></td>
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<tr>
<td>Portal hypertension (%)</td>
<td>33.60</td>
<td>31.3-36.0</td>
<td></td>
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<tr>
<td>Diverticulosis (%)</td>
<td>3.60</td>
<td>2.8-4.70</td>
<td></td>
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<tr>
<td>UGIB of unknown origin (%)</td>
<td>1.70</td>
<td>1.1-2.20</td>
<td></td>
</tr>
<tr>
<td>LGIB of unknown origin (%)</td>
<td>3.30</td>
<td>2.5-4.30</td>
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<tr>
<td>Other (%)</td>
<td>10.70</td>
<td>9.4-12.5</td>
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</table>

\( T \): treatment; NSAIDs: non-steroidal anti-inflammatories; UGIB: upper gastrointestinal bleeding; LGIB: lower gastrointestinal bleeding.

Table II. General characteristics of the sample (n = 1,611)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>95% IC</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamic instability (%)</td>
<td>59.40</td>
<td>56.96-61.81</td>
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<tr>
<td>Comorbid disease (%)</td>
<td>72.62</td>
<td>70.36-74.78</td>
<td></td>
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<tr>
<td>Overall mortality rate (%)</td>
<td>6.27</td>
<td>5.16-7.39</td>
<td></td>
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<tr>
<td>PHT mortality rate (%)</td>
<td>10.43</td>
<td>8.91-12.02</td>
<td></td>
</tr>
<tr>
<td>Mortality due to DU (%)</td>
<td>3.04</td>
<td>2.51-3.73</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Mortality due to GU (%)</td>
<td>3.86</td>
<td>3.15-4.61</td>
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</tbody>
</table>

PHT: hemorrhage due to portal hypertension; DU: hemorrhage due to duodenal ulcer; GU: hemorrhage due to gastric ulcer.

DISCUSSION

There is an incidence of 50-150 cases a year per 100,000 inhabitants for lower gastrointestinal bleeding (6); peptic ulcer causes 60-70% of cases, followed by hemorrhage due to esophageal-gastric varices (1,6).
At our Blood Unit, DU hemorrhages correspond to 22.20% of admissions, and GU hemorrhages correspond to 18.40%. Peptic ulcers account for 40.6% of all admissions, and this figure is slightly lower than that reported some years ago. This decrease is the result of an increasingly lower incidence of GIB from DU.

In the late 1980s and early 1990s no decrease in the number of hospital admissions due to bleeding ulcers was reported (2,7); however, over the last 10 years, and as a result of an increased administration of proton-pump inhibitors (linked to a lower costs), in addition to Helicobacter pylori eradication, which prevents ulcer recurrence and complications, there has been a decrease in the incidence of peptic ulcers as a cause of gastrointestinal bleeding (8). By way of example, in a recent study of 7,822 patients with upper gastrointestinal bleeding, peptic ulcer only corresponded to 20.6% of cases (9).

The two most significant causes of peptic ulcer and associated complications are Helicobacter pylori infection and the use of NSAIDs (10). The treatment and subsequent eradication of this infection in young patients is changing the profile of patients with active ulcer and associated complications (11), favoring anticoagulated patients who are users of aspirin/NSAIDs, and who are generally elderly patients with comorbid diseases (12).

In our study, 34.5% of patients were taking NSAIDs and 7.1% were receiving anticoagulant treatment. In addition, over the years we have recorded an increase in patients with comorbid disease, who are commonly elderly people usually with various associated illnesses that require several drugs. This would explain, at least in part, why there has been no significant decrease in mortality rates from ulcer-related hemorrhages over recent decades, despite significant advances in clinical treatment, endoscopy, and pharmacology (3).

In contrast, mortality from acute hemorrhage by esophageal varices has considerably decreased over the last two decades, from approximately 40% in the 1980s (13) to below 20% at present (14). This decrease is partly due to improved acute hemorrhage management, in addition to a better understanding of the natural history and physiopathology regarding the formation, progression, and rupture of varices, which allow interventional pharmacology, endoscopy, and radiology treatments to be applied (15). Currently, hepatocellular carcinoma leads to the greatest number of deaths in patients with cirrhosis, followed by GIB (16); however, although mortality rates have decreased, this is not the case with incidence over recent years, which has remained stable or even increased, and is the cause of high rates of morbidity, in addition to being an important source of healthcare resource utilization.

A recent multicenter epidemiologic study carried out in France during the period 1996-2000 reported that cases of variceal bleeding were as frequent as hemorrhages due to peptic ulcers, and there was a significant decrease in mortality rates (11.1% in 2000) (17). In our study, hemorrhage from cirrhotic PHT corresponded to one third of the total number of patients admitted to the Unit, with an average mortality rate of 10.43%, which has remained stable throughout the period studied.

Helicobacter pylori eradication has decreased the incidence and complications of DU. However, alcohol intake (declared by the World Health Organization as the third cause of disability in the Western world (18), and a frequent cause of hospitalization) (19), and the epidemic of chronic hepatitis C (beginning in the 1960s and reaching its peak in the mid-1980s), the consequences of which are now and will continue to be evident for the next two decades (20), make it unlikely that there will be a decrease in the incidence of variceal bleeding over the coming years.

In the majority of patients with gastrointestinal bleeding the origin of hemorrhage is identified using conventional diagnostic tests. Nevertheless, in 5% of cases, as in our study, bleeding persists and escapes diagnosis by these methods; this is called a hemorrhage of unknown origin (21).

Although an isolated study does not find differences with regard to length of hospital stay, transfusion requirements, need for surgery, and prognosis of these patients as compared to other causes of hemorrhage (22), a majority of authors agree that the management and treatment of these patients is usually complicated, requiring multiple transfusions and hospital stays (23). The explanation for this may be due to the fact that most injuries leading to gastrointestinal bleeding of unknown origin are located in the small intestine (23), an inaccessible area for the conventional endoscopic treatment that has managed to
decrease the rate of persistent hemorrhage. Furthermore, we are usually dealing with elderly patients, many of whom are receiving anticoagulant treatment, which may explain admissions for recurrent hemorrhage (21,22).

Currently, as compared to studies carried out 10-15 years ago (24), the profile of a patient admitted to our Blood Unit rather corresponds to that of someone with a comorbid disease and on several drugs (anticoagulants, NSAIDs, etc.), or with cirrhosis and hemorrhage from PHT, with a clear decrease in the number of young patients with duodenal ulcers. We hope that in the near future double-balloon enteroscopy will contribute to define the etiology, and also to decrease the incidence, of recurrent hemorrhage originating in the small intestine, the latter through appropriate treatment (25).

REFERENCES