Management of bleeding peptic ulcer in France: a national inquiry

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SUMMARY

Aims of the study — To evaluate and compare management practices in France for bleeding peptic ulcers using a national inquiry of university and non-university hospitals.

Method — Responses to questionnaires sent to 812 gastroenterologists, 496 practicing in non-university hospitals and 316 in university hospitals, were compared.

Results — An analysis was possible in 279 (34% response rate) of the questionnaires. Forrest classification was used more frequently in university hospitals (83% vs 60%, P < 0.01). Endoscopic hemostatic therapy was used more frequently in university hospitals for Forrest Ib (92% vs 81%, P = 0.02), IIa (93% vs 73%, P < 0.001), and IIb (58% vs 29%, P < 0.001) ulcers. Injection therapy, mainly epinephrine, was the first-intention treatment for 99% of the responding gastroenterologists. Proportions of clinicians employing hemoclips (27%) or argon plasma coagulation (21%) were similar in both types of practice. Anti-secretory treatment included mainly omeprazole (82%), given intravenously (76%), sometimes as bolus iv doses followed by iv high-dose continuous infusion (15%) with some variations according to the type of hospital. In the event of recurrent or persistent bleeding, surgery was more frequent in non-university hospitals. When rebleeding occurred, a second endoscopic treatment was performed in about one quarter of patients.

Conclusion — In France, management practices for bleeding peptic ulcer vary between university and non-university hospitals.

RÉSUMÉ

Prise en charge des hémorragies digestives ulcéreuses en France en CHU et en CHG : une enquête nationale de pratique

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But — Évaluer et comparer par une enquête déclarative de pratique la prise en charge des hémorragies ulcéreuses dans les hôpitaux généraux et universitaires français.

Méthode — Les réponses de 496 hépato-gastroentérologues exerçant en hôpital général et de 316 exerçant en hôpital universitaire ont été comparées.

Résultats — Deux cent soixante dix-neuf questionnaires étaient analysables (34%). La classification de Forrest était plus utilisée en hôpital universitaire (83 % vs 60 %, P < 0.01). L’hémostase endoscopique était plus souvent pratiquée en hôpital universitaire en cas d’ulcères Forrest I b (92 % vs 81 %, P = 0,02), II a (93 % vs 73 %, P < 0,001) et II b (58 % vs 29 %, P < 0,001). Les injections, avant tout d’adrénaline, étaient la première modalité thérapeutique dans 99 % des cas. L’utilisation des clips (27 %) et de la coagulation au plasma argon (21 %) était comparable dans les 2 types de structure. Le traitement antisécrétoire était le plus souvent de l’omeprazole (82 %), principale-ment par voie intraveineuse (76 %) et parfois selon le schéma bolus-perfusion continue (15 %) mais avec des modalités différentes d’utilisation selon les centres. En cas d’hémorragie persistante ou récidivante, un traitement chirurgical était plus souvent réalisé dans les hôpitaux généraux. En cas de récidive hémorragique un nouveau traitement endoscopique était proposé environ une fois sur 4.

Conclusion — La prise en charge des hémorragies ulcéreuses en France est différente en hôpital général et en hôpital universitaire.

Introduction

Bleeding peptic ulcer (BPU) disease is the leading cause of upper gastrointestinal bleeding. In France, one-third of all upper gastrointestinal bleeding episodes are considered to arise for BPU with an estimated incidence of about 25,000 episodes per year [1]. Mortality remains high, estimated at about 15% in the most recent reports [1, 2]. In 1999, the French Society of Gastrointesti- nal Endoscopy (SFED) published guidelines for the management of BPU [3]. In France, nine out of ten patients with BPU are treated in public hospitals but no data concerning current practices are available [4]. The purpose of our work was to 1) study management practices for BPU in French public hospitals; 2) compare practices between university hospitals and non-university hospitals.

Patients and methods

A questionnaire was developed using the usual methodology for clinical practice inquiries [5]. The questions concerned the different steps of management procedures for upper gastrointestinal bleeding. Yes-no or multiple choice questions were used. The items were divided into four categories: 1) organization of management practices; 2) conditions of the first endoscopic procedure; 3) treatment modalities; 4) type of hospital, its organization, and medical personnel. The target population was defined from the national registries of hepatogastroenterologists maintained by the ANGH (Association Nationale des Hépato-gastroentérolo- gues des hôpitaux non universitaires) and the SNFGE (Société Nationale Française de Gastro-entérologie) and from phone conversations with the secretaries of the university hospital units to establish the list of qualified practitioners (senior hospital physicians, non-territorialized senior physicians). The questionnaire was tested before the inquiry with five hospital

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This work was supported by a grant from SFED-AstraZeneca.
physicians performing emergency gastrointestinal endoscopy procedures. The questionnaire was then sent by mail, at the end of 2001, to 812 hepatogastroenterologists, 496 practicing in 211 non-university general hospitals and 316 practicing in 54 university hospitals (106 in 20 centers of the Public Parisian Hospitals [AP-HP] and 210 in 34 teaching centers of 25 University Hospitals). The practitioners were expected to respond within two months. The practitioners were not contacted again if no response was received.

The chi-square test was used for qualitative variables and Student’s t test or a non-parametric test as appropriate for quantitative variables. The physician and not the hospital was the analysis unit. The significance threshold was set at P < 0.05. Certain items could not be analyzed due to insufficient sample size.

Results

An analyzable questionnaire was returned by 269 gastroenterologists (34% response rate), 191 practicing in non-university hospitals and 88 in 40 university hospitals (38% vs 28%, P < 0.001).

Organization of management practices

Patients were more frequently hospitalized in gastroenterology units and in specialized sectors in university hospitals (43.2% vs 27.7%, P = 0.016). One-third of university hospitals had a specialized sector for this type of patient. In non-university hospitals, 61.3% of patients were hospitalized in a unit other than a gastroenterology or intensive care unit. Endoscopy was performed by a senior operator for 64.5% of patients (67% in non-university hospitals and 63% in university hospitals). The senior operator had 10.88 ° 5.54 years experience in university hospitals and 16.15 ° 5.79 in non-university hospitals (P = 0.011). A 24-h endoscopy service was available in 84.9% of the hospitals with no difference by type of hospital. A gastroenterologist was on call for emergency procedures in 82.1% and 77.3% of the non-university and university hospitals respectively while emergency endoscopists were on duty permanently in only the university hospitals (14.8% vs 0%, P < 0.001).

Conditions of the first endoscopic procedure (table I)

The first endoscopic procedure was performed within the first six hours of the bleeding episode in 28% of patients and within 24 h in 96%. For 83.2%, sedation was not used. General anesthesia was given in 8.2% of patients and controlled or non-controlled sedation in 8.6%. Gastric aspiration was employed in 21.5% of patients with hematemesis, in 2.5% of patients with melana, and systematically in 23.7% of cases. The procedure was conducted without prior aspiration in 40.1% of patients. An erythromycin infusion was administered in 21.9% of patients, with a 250 mg dose for half of them and in association with gastric aspiration in 36.1%. The emergency procedure was performed in an endoscopy room with video-endoscopy for 78.5% of patients. When performed elsewhere, optic equipment was used for two-thirds of patients. An assistant was present for 97.8% of the procedures (an endoscopy nurse for 29%, available personnel for 69%). The operative conditions were not different between university and non-university hospitals.

ABBREVIATIONS :
BPU : bleeding peptic ulcers
SFED : Société Française d’Endoscopie Digestive (French Society of Gastrointestinal Endoscopy)

Table I. – Modalities of emergency endoscopy for non variceal upper gastrointestinal bleeding in all the hospitals.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without gastric inspiration</td>
<td>40 %</td>
</tr>
<tr>
<td>Erythromycin infusion</td>
<td>22 %</td>
</tr>
<tr>
<td>Endoscopy within 24 hours</td>
<td>96 %</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>8 %</td>
</tr>
<tr>
<td>Performed by a senior operator</td>
<td>64 %</td>
</tr>
<tr>
<td>In an endoscopy room</td>
<td>78 %</td>
</tr>
<tr>
<td>With video-endoscopy</td>
<td>85 %</td>
</tr>
<tr>
<td>With an assistant</td>
<td>98 %</td>
</tr>
</tbody>
</table>

Treatment modalities

A prognostic score (e.g., Baylor, Rockall) was not used for classification in 94% of patients. The Forrest classification was used in 67% of patients and more frequently in university hospitals (83% vs 60%, P < 0.01). An endoscopic hemostatic treatment was delivered in 98%, 84%, 79%, 38%, 2%, and 1% of patients with Forrest grade Ia, Ib, Ila, IIb, and III ulcers, respectively. Endoscopic treatment was performed significantly more often in university hospitals for diffuse oozing bleeding, visible non-hemorrhagic vessels, and adherent clots (figure 1). Clot mobilization was attempted more often in non-university hospitals (87% vs 65%, P < 0.01). Hemostatic injections were attempted in 99% of patients using diluted epinephrine (63%), saline solution (14%), polidocanol (8%), ethanol (5.4%), other agents (2.5%) or a combination of agents (1.4%). Other techniques employed were hemoclip (27%), argon plasma coagulation (21%), bipolar electrocoagulation (9%), thermocoagulation (5%) and Nd Yag laser (0.4%). Epinephrine injection was used more often in university hospitals (86% vs 51%, P < 0.001) and polidocanol in non-university hospitals (11% vs 2%, P < 0.02) (figure 2). A combination was used for 47% of patients, generally injections and hemoclip (34% of the combination treatments), injections and argon plasma coagulation (21%), or injections and bipolar electrocoagulation (11%). Use of thermal or mechanical hemostatic techniques was not significantly different between university and non-university hospitals.

Antisecretory medications were administered in association with the endoscopic treatment in 99% of patients. Omeprazole was generally used (82%), mainly by intravenous infusion (76%) and occasionally with a bolus-continuous infusion scheme (15%). Omeprazole was used more often than other proton pump inhibitors in general hospitals (88% vs 67%, P < 0.001). Omeprazole followed by intravenous infusion was more frequent in university hospitals (34% vs 9%, P < 0.001) where the mean dose of omeprazole was higher (84.51 ° 8.88 mg/d vs 64.02 ° 2.68 mg/d, P = 0.03) (figure 3). If bleeding persisted, surgical treatment was undertaken more often in general hospitals (60% vs 43%, P = 0.02). Surgical treatment was also employed for recurrent bleeding more often in general hospitals (51% vs 31%, P = 0.001); 27% of the physicians proposed a new endoscopic treatment (32% and 25% in university and non-university hospitals, P = NS). When overt bleeding did not recur, a new endoscopic procedure was performed within 72 hours in 43% of patients. When a second procedure was performed, discovery of a visible non-hemorrhagic vessel did not lead to a new endoscopic treatment in 40% of patients. The same hemo-
static treatment used initially was applied again in nine out of ten patients.

At the time of endoscopy, 55.2% of the physicians performed gastric biopsies to detect Helicobacter pylori infection; a rapid urease test was used by 18.3%. Serological tests for Helicobacter pylori were preferred by 28% of physicians. An eradication treatment was instituted for 83.2% of patients after the bleeding episode was controlled. Eradication was proposed for 92% of patients. A repeat endoscopy was planned for 50.5% of patients. No significant difference was found between university and non-university practitioners concerning management of Helicobacter pylori infection.

Discussion

This is the first clinical inquiry conducted in France concerning management practices for BPU. High prevalence and persistent gravity of BPU seem to justify our inquiry. The study was based on the physicians’ statements and did not focus on objective measurements of clinical practices and results. This approach led to several biases: imperfectly representative sample since the response rate was 34%, absence of information concerning the patients and the characteristic features of the health care centers, particularly the number of beds and number of patients treated.

Despite these limitations, our results provide interesting informations. The initial endoscopic procedure was performed within the first 24 hours in nearly all patients, in line with reports showing the importance of early endoscopy for prognosis [6]. Most endoscopic procedures for upper gastrointestinal bleeding were performed without general anesthesia. Sedation controlled by an anesthesiologist and general anesthesia were exceptional. Use of sedation without proper control by an anesthesiologist, an unacceptable practice according to the current French regulations, was very rare. Since endoscopy for gastrointestinal bleeding is a long difficult procedure, we considered that the specialist societies, namely the SFED and the SFAR, should promote more widespread use of anesthesia for emergency procedures. At the time of this inquiry, erythromycin was not widely used in France for this indication, the two trials demonstrating its usefulness for emergency upper endoscopic procedures being published in 2002 [7, 8]. Use of erythromycin, which does not appear to have any inconvenience, can be expected to become routine practice. Lavage-aspiration, which was not often used even in case of hematemesis, will undoubtedly be used even less in the future. The Baylor [9] and Rockall [10] scores, which are widely used in Great Britain, are not commonly employed in France despite several publications which have demonstrated their prognostic value. The fact that these scoring systems are “relatively” complex cannot, alone, explain this situation. A recent French publication demonstrated that diffusion of practice guidelines...
including the Rockall score can contribute to improved prognosis of upper gastrointestinal bleeding [11]. Widespread, though not universal (67%), use of the Forrest classification, particularly in non-university hospitals where it was used significantly less often, was a rather unexpected finding. This is an old system published in 1975 and is known to be operator-dependent [12]. It is however useful for management of BPU, as correct use pertains to indications of hemostatic treatment [6] or even type of endoscopic treatment [13]. Moreover, a detailed description of lesions observed (active or non-active bleeding, visible non-hemorrhagic vessel ...) can be used to choose endoscopic treatment without determining the Forrest classification. The results of the current study and observations of daily practice suggest that some physicians are not fully informed about this classification system. A point which might be improved during future training.

Regarding indications for hemostatic treatment, nearly all spurting BPU (98%) were treated endoscopically, while management of oozing BPU varied significantly between university and non-university hospitals (treatment in 92% and 81% of patients respectively). According to the literature where the distinction between spurting and oozing BPU is made, the risk of rebleeding is much lower for oozing bleeding. For oozing BPU, the risk of persistent bleeding or recurrence is approximately 10% [14]. For this reason, certain authors consider that endoscopic treatment offers little or no benefit for patients with oozing bleeding, suggesting that endoscopic treatment is not warranted for these patients [14]. This difference in attitude, expressed by more "active" intervention in university hospitals than in non-university hospitals, was also found for patients with a visible non-hemorrhagic vessel (treatment in 58% and 29% of patients, respectively). The risk of rebleeding for patients with a visible non-hemorrhagic vessel or an adherent clot who do not undergo endoscopic treatment is about 50% and 20% respectively [6]. Combining endoscopic treatment with medical treatment for patients with visible non-hemorrhagic vessels significantly reduces the risk of recurrence compared with medical treatment alone [15]. For adherent clots, endoscopic treatment [16, 17] and high-dose proton pump inhibitors administered intravenously [17] both significantly reduce the risk of rebleeding. The longer experience of the non-university hospital senior physicians who responded to the questionnaire (16 years versus 12 years for university hospital physicians) and different recruitment practices (more seriously ill patients being referred to university hospitals) might explain in part this difference.

Injections were clearly the preferred treatment modality at the time of the inquiry. A large number of publications have demonstrated that epinephrine injections, which have proven efficacy and no risk of morbidity, are a simple-to-use low-cost method generally considered as the gold standard [6]. It was recently suggested that high-dose epinephrine (> 10 mL) could be significantly more effective in terms of recurrence than the usual doses [18]. Sclerosing agents are used much less often, but were nevertheless employed more often in non-university hospitals (11% vs 2%, P < 0.001). There is no satisfactory explanation for this observation. Use of sclerosing agents, particularly at a high dose, has been incriminated as a cause of rare but sometimes serious local complications [6]. Most of the reported trials have not demonstrated any superiority of the epinephrine-sclerosing agent combination over epinephrine alone [6]. Bipolar electrocoagulation and thermoregulation, widely used in other countries, appeared as marginal options in our inquiry. Combinations of hemostatic methods with different modes of action were used for about half of patients, the predominant combinations being injections plus hemoclips or argon plasma coagulation. There is no real proof of the therapeutic superiority of combinations except for patients with spurting bleeding [19]. The use of hemoclips and argon plasma coagulation is widespread but the literature provides conflicting data concerning hemoclips [20, 21], and is more favorable for argon plasma coagulation which can be associated with epinephrine injections [22, 23].

The use of proton pump inhibitors, mainly omeprazole, in combination with endoscopic treatment is common practice in France for BPU. Intravenous infusion is preferred. The bolus plus continuous infusion scheme is not infrequent and is in line with data in the literature demonstrating that high-dose proton pump inhibitors administered intravenously have a synergetic effect with endoscopic treatment and reduce the risk of rebleeding for Forrest I and IIa ulcers [24].

Conservative surgery was not an exceptional option for persistent or recurrent bleeding. The surgical option was more frequent in non-university hospitals for persistent bleeding. A second endoscopic treatment was rarely proposed in either type of hospital (27%). These data contrast with those from a randomized trial which demonstrated that definitive hemostasis can be achieved with a second endoscopic procedure in the event of recurrence after a first procedure in the majority of patients and that this can be achieved without increasing mortality or risking higher surgical morbidity [25].

Regarding tests for identification of Helicobacter pylori infection and treatment, the results of the current study were in agreement with data in the literature, particularly concerning treatment chronology after the hemorrhagic episode. Helicobacter pylori infection increases the risk of mid- and long-term rebleeding, but does not appear to modify the risk of early rebleeding [26].

The only study comparable with ours is a publication from The Netherlands reported in 2000 [27]. The main differences in the results with our study concern the high response rate of the Dutch physicians (73% response rate with 90 analyzable questionnaires), the much higher frequency of the epinephrine-polidocanol combination (60%), use of H2 receptor antagonist in one quarter of patients, and the frequency of second procedures for rebleeding (76%). It is interesting to note that in The Netherlands where BPU is managed either by gastroenterologists or internists performing endoscopic procedures, the gastroenterologists were more “active” in their interventions for Forrest Ib, IIa and IIb ulcers. An observation also made in our inquiry. The use of the Forrest classification was also similar in the Dutch inquiry (61%) where injections were used as the first intention treatment for 93% of patients.

In conclusion, our study, which is the first inquiry of this type conducted in France, shows that management practices for BPU vary between university and non-university hospitals. The differences probably arise from the different types of institutional organization and patients recruitment as well as experience among the physicians who responded to the questionnaire. Nevertheless, management practices in France are largely in agreement with the SFED recommendations. More widespread access to anesthesia for emergency endoscopy as well as improved operator training and more uniform management practices for BPU could be beneficial. Further studies based on objective criteria instead of subjective statements are necessary to evaluate management practices for this frequent and serious disease.

REFERENCES


