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Endoscopic treatment of high-risk bleeding ulcers: success, rebleeding and mortality

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ABSTRACT

Introduction and aims. Endoscopic treatment of peptic ulcers with high-risk stigmata has been probed. The rates of recurrent bleeding, need for emergent surgery and death are related to Forrest Classification, Blatchford's modified risk score and the kind of endoscopic treatment used (monotherapy *vs.* dual). The aims of the present study were to report the success of endoscopic therapy in the reduction of the rate of initial success, recurrent bleeding, the need for surgery, and the mortality rate for patients with bleeding peptic ulcer and high-risk stigmata. **Patients and methods.** From a retrospective view, patients seen from September 2004 to March 2007 who had peptic ulcers Forrest Ia, Ib, IIa and/or IIb were included. **Results.** Fifty-six patients were included (mean [SD] age 57.3 ± 16.6 years). The success rate was 91%, whilst the rest of the patients required immediate surgery. Recurrent bleeding was presented in 14 (27%) patients and eight (14.2%) required emergency surgery. The mortality rate was 3.6%. No factors were associated with the risk of failure to initial treatment, recurrent bleeding or need for surgery. The use of monotherapy by endoscopy was associated with the mortality. The variable "fellow alone" was not associated with any kind of outcome. **Conclusion.** Complication rate is similar to previous reports of general hospitals, but is higher than those of referral centers. Endoscopic monotherapy is associated with a major mortality risk.

Key words. Peptic ulcer. Endoscopic Hemostasis. Hemorrhage. Treatment Failure. Mortality.

Tratamiento endoscópico de las úlceras de alto riesgo: éxito, resangrado y mortalidad

RESUMEN

Introducción y objetivos. El tratamiento endoscópico ha probado ser eficaz en las úlceras pépticas con estigmas de alto riesgo. Las tasas de recurrencia de sangrado, necesidad de cirugía y muerte están relacionadas con la clasificación de Forrest, el puntaje del Score modificado de Blatchford y el tipo de tratamiento utilizado (único vs. *doble). El objetivo del estudio fue reportar los resultados del tratamiento endoscópico (tasa de recurrencia de sangrado, necesidad de cirugía y mortalidad) en nuestro medio. Pacientes y métodos. Se evaluaron de manera retrospectiva los pacientes que acudieron de septiembre 2004 a marzo de 2007. Se incluyeron pacientes con úlceras clasificadas como de alto riesgo (Forrest Ia, Ib, IIa, IIb). Resultados. 56 pacientes fueron incluidos (27 mujeres y 29 hombres; edad media (DE) 57.3 ± 16.6 años). El control en la primera sesión se logró en 91% de los pacientes, el resto de pacientes requirieron de cirugía inmediata. En 14 pacientes (27%) se documentó recurrencia de sangrado y ocho (14.2%) pacientes requirieron tratamiento quirúrgico urgente. La mortalidad en el grupo fue de 3.6%. No se identificaron factores asociados al éxito inicial, recurrencia de sangrado o necesidad de cirugía urgente. La aplicación de monoterapia endoscópica está asociada con el desenlace de mortalidad. No se encontró asociación de alguno de los desenlaces evaluados y los procedimientos realizados por médicos residentes. Conclusión. La tasa de complicaciones en nuestro instituto es similar a lo reportado por otros centros de atención general de países de primer mundo; sin embargo es más alta que la reportada por centros de referencia. El uso de monoterapia endoscópica se asocia a una mayor mortalidad.*

Palabras clave. Úlcera péptica. Hemostasia endoscópica. Hemorragia. Falla al tratamiento. Mortalidad.

INTRODUCTION

There is no doubt that endoscopic treatment of peptic ulcer hemorrhage is superior to conservative treatment, with a significant reduction in recurrent bleeding, emergency surgery and death.[1,2] Endoscopic methods for hemostasis include injection therapy, thermal coagulation, and mechanical therapy with hemoclips and bands. The success rate expected with endoscopic therapy (ET) is 95%.[3] The frequency of recurrent bleeding in referral centers has been reported in less than 15% of patients.[4] Previous studies have shown that dual ET (DET) is better than epinephrine injection alone, but not different from any other single ET (thermal or mechanical).[5] However, epinephrine injection is still among the most popular ET because of its safety, low cost, and it is application easiness.

The aim of this study was to report the experience of ET in the initial success, rate of recurrent bleeding, the need for surgery, and death rate in patients with bleeding peptic ulcer and/or high-risk stigmata for recurrent bleeding. The second aim was to determine the frequency of each treatment modality (DET *vs.* monotherapy).

PATIENTS AND METHODS

We retrospectively reviewed the electronic and paper-based records of patients with high-risk bleeding ulcers (HRBU) whom underwent an endoscopy at the Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán" from September 2004 to March 2007. For this study, HRBU was defined as patients with hemorrhage from peptic ulcer disease (gastric or duodenal) with major bleeding stigmata, defined by groups according to Forrest's classification:[6] Ia (spurting hemorrhage), Ib (oozing hemorrhage), IIa (nonbleeding visible vessel), and IIb (adherent clot). Monotherapy was defined as epinephrine injection alone on a 1:10 000 dilution. Dual therapy was considered when, besides epinephrine injection, an extra ET method was used (heat probe, argon-plasma coagulation, hemoclips). Patients with haematemesis and those who were haemodynamically unstable underwent an endoscopy after initial resuscitation. In all patients, according to institutional politics, informed consent was obtained before the procedure. A regular diagnostic endoscope was initially used (GIF-100, GIF-130, GIF-140 or GIF-160, Olympus, Japan) and therapeutic modality (monotherapy or dual) was assigned according with physician criteria. Aside from epinephrine injection, ET was performed with heat probe coagulation, Argon plasma coagulation or Hemoclips (Olympus, Japan). All conscious patients were sedated with midazolam, phentanyl and/or propofol.

Initial endoscopic haemostasis

In Forrest Ia and Ib ulcers, initial success was accomplished when endoscopic haemostasis was reached within the procedure. In Forrest IIa and IIb ulcers, initial success was accomplished when ET was applied without immediate bleeding.

Recurrent bleeding

Recurrent bleeding was clinically defined as the passage of haematemesis or melena, or both, coupled with the development of shock or decrease in hemoglobin concentration by at least 2 g/dL after initial stabilization of 24 hours or aspiration of fresh blood from nasogastric tube.[3,5] Bleeding was confirmed by endoscopy or surgery in all cases.

The Forrest's classification, clinical, laboratory, and demographic characteristics were recorded, modified Blatchford Score Risk, the initial endoscopic technique for haemostasis, rebleeding, requirement for surgery, blood transfusion, and mortality during the first 30 days after the procedure.

Statistical Analysis

Results are expressed as means and $\pm$ SD. Comparison of quantitative data were performed using the Student's t-test or Mann-Whitney U test, according with variable distribution. The differences between proportions of categoric data were obtained by the Fisher exact test when the number of expected subjects was less than 5, and by the Chi-square test otherwise. A P-value < 0.05 was considered statistically significant. All statistical analyses were conducted using the statistics program SPSS/PC version12.0 (Chicago, IL, USA).

RESULTS

During the study period, 56 patients with upper gastrointestinal bleeding due to peptic ulcer were admitted to our hospital. Twenty-seven women (48.2%) and twenty-nine men (51.8%) were included, with a mean age of 57.3 $\pm$ 16.6 years. Clinical, demographic and laboratory characteristics are shown in table 1. Duodenum was the most common localization, and Forrest IIb was the most frequent grade

(Figure 1). A total of 31 (55.3%) patients received proton pump inhibitors (PPI) before the event; 25 (44.6%) patients had previous peptic ulcer disease (according to paper based records); and 14 (25%) patients were positive to histological examination for *H. pylori* infection. The mean number of endoscopic procedures by patient was 2 (range 1-4). Twenty-four (42.9%) patients received single ET and thirty-two (57.1%) patients underwent dual therapy (Figure 2). Mean epinephrine volume injected was 15 ± 6.6 milliliters.

Initial success for endoscopic haemostasis was achieved in 51 patients (91%). Primary haemostasis
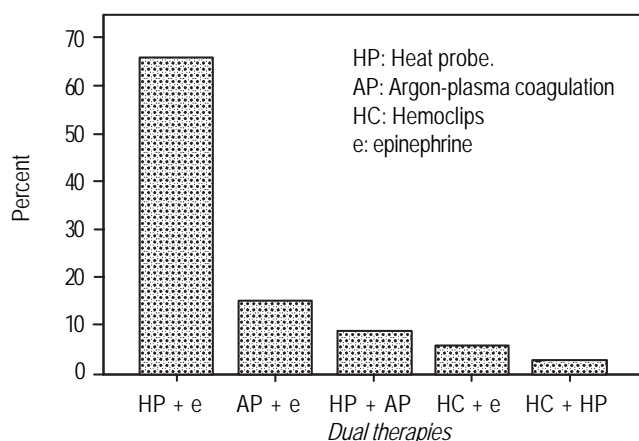

Figure 2. Dual therapies.

Table 1. Clinical and demographic characteristics of patients (n = 56).

Variable	n (%)
Age, *y*[*]	57.3 ± 16.6
Female	27 (48.2)
Hemoglobin, *g/dL*[*]	9.5 ± 2.5
INR[*, †]	1.3 ± 0.7
NSAID[‡], *yes*	15 (26.8)
Antiplatelet agents, *yes*	12 (21.4)
Oral anticoagulation, *yes*	7 (12.5)
Endoscopic treatment, *single*	24 (42.9)
Shock, *yes*	12 (21.4)
Comorbilities	
Hypertension	19 (34)
Diabetes mellitus	17 (30.3)
CKD[§]	9 (16)
Cancer	9 (16)
Cirrhosis	6 (10.7)
Stroke(history)	5 (8.9)
Autoimmune disease	5 (8.9)
Heart disease	3 (5.3)

[*] Expressed in mean (SD). [†] International Normalized Ratio. [‡] Non-Steroid anti-inflammatory drugs. [§] Chronic kidney disease.
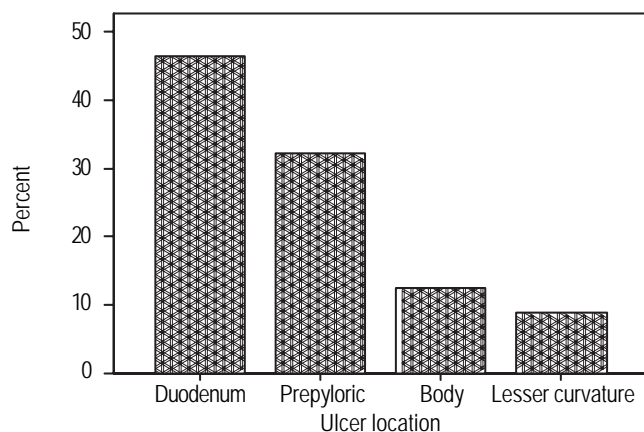

Figure 1. Frequencies of ulcer location.

was not possible in five (9%) patients whom went directly to surgery. Two of them subsequently died (between five and twenty days after surgery). Recurrent bleeding was documented in 14/51 (27.4%) patients, with a median time to bleeding recurrence of 5 (range 1-30) days. Beside the five patients that required surgery due to failure to initial success; three patients underwent emergency surgery of recurrent bleeding. During 30 days of follow up, mortality was 19.6% (11 patients), although only in two patients was the cause of death directly related to ulcer bleeding (3.6%). No statistical differences between patients with and without any endpoint were found (Table 2).

No differences were found according to different types of endoscopic treatment. Table 3 displays the outcomes, frequency of monotherapy and procedures by fellows. No ET (mechanical or thermal) beside epinephrine was used as monotherapy.

DISCUSSION

This report represents the first data regarding endoscopic therapy and HRBU from our center and, to the best of our knowledge, from any other Mexican or Latin American center. This is an important world-wide topic and information from other Latin American centers will be useful to improve the quality and increase survival in these kinds of patients. Our results are similar to some reports on recurrent bleeding, emergency surgery, and mortality rates,[5] but are still slightly higher in respect to other foreign referral centers.[4] Increased complication rates could be explained by the higher punctuation of severity in Blatchford's modified Risk Score[7] present in our patients (82.1% have 2 or more points); since monotherapy, ulcer location, sub-groups of Forrest's classification, symptoms,

Table 2. Differences between included patients according to presence/absence of outcomes.

Variable	Presence n (%)	Absence n (%)	p value
Failure to initial treatment			
Age, *years**	51 (34-73)	58 (21-85)	0.46
Female, *yes*	1 (20)	26 (51)	0.19
mBRS >1[†], *yes*	4 (80)	42 (82.4)	1
Forrest Ia/Ib, *yes*	2 (40)	9 (17.6)	0.25
Duodenum, *yes*	2 (40)	24 (47)	0.56
H. pylori, *yes*	0 (0)	14 (27)	0.22
Procedure by fellow	1 (20)	6 (12)	0.5
Recurrent bleeding			
Age, *years**	60 (32-80)	57 (21-85)	0.46
Female, *yes*	5 (35.7)	22 (52)	0.36
mBRS >1[†], *yes*	13 (93)	33 (79)	0.21
Forrest Ia/Ib, *yes*	5 (36)	6 (14.3)	0.09
Duodenum, *yes*	8 (57)	18 (43)	0.37
H. pylori, *yes*	5 (35.7)	9 (21)	0.23
Procedure by fellow	2 (14)	5 (12)	0.56
Requirement for surgery			
Age, *years**	57 (32-75)	57.5 (21-85)	0.63
Female, *yes*	2 (25)	25 (52)	0.15
mBRS >1[†], *yes*	7 (87)	39 (81)	0.56
Forrest Ia/Ib, *yes*	3 (37.5)	8 (16.7)	0.18
Duodenum, *yes*	4 (50)	22 (46)	0.56
H. pylori, *yes*	0 (0)	14 (29)	0.08
Procedure by fellow	1 (12.5)	6 (12.5)	0.68
Death			
Age, *years**	54 (21-85)	58 (25-82)	0.44
Female, *yes*	4 (36.4)	23 (51)	0.50
mBRS >1[†], *yes*	9 (82)	37 (82)	0.63
Forrest Ia/Ib, *yes*	3 (27)	8 (19)	0.36
Duodenum, *yes*	5 (45.5)	21 (47)	1
H. pylori, *yes*	1 (9)	13 (29)	0.16
Procedure by fellow	0 (0)	7 (15.6)	0.19

* Expressed in median and range. [†] Modified Blatchford Score Risk.

Table 3. Differences according to different types of endoscopic treatment (monotherapy *vs.* dual).

Variable	Monotherapy, n = 24 n (%)	Dual therapy, n = 32 n (%)	p value
Initial endoscopic haemostasis	22 (92)	29 (90.6)	1
Rebleeding	7 (29.1)	7 (21.8)	0.5
Requirement for surgery	3 (12.5)	5 (15.6)	1
Transfusion (units, median, range)	0 (0-3)	1 (0-6)	0.17
Mortality	8 (33.3)	3 (9.4)	0.04
Epinephrine volume (mL, mean, SD)	15.3 ± 5.2	15.1 ± 7.6	0.91
Procedures by fellow (n = 7)	4 (57)	3 (43)	0.69

or age were not predictive factors for reebleding or need of surgery in our research.

Some interesting points that we found in this study were: 1) although dual ET has been proved to be the best treatment for HRBU[5,8] almost half of our patients received endoscopic monotherapy, 2) the variable fellow alone *vs.* fellow + staff physician was not a factor of endpoint and, 3) the low prevalence

of *H. pylori* on a high risk population such as Mexican one.

Nowadays, dual therapy in endoscopy is the most accepted treatment due to HRBU. This modality has shown to be better when compared to epinephrine injection alone for reducing further bleeding, the need for emergency surgery and mortality.[5,8-10] According to our results, there was no correlation between recurrent hemorrhage and need for emergency surgery with the use of monotherapy *vs.* dual ET. We consider that this finding is due to the reduced sample number and do not reflect the best feasible results with single ET, compared to other worldwide centers (same phenomena with Forrest classification). Mortality in our population was in agreement with other previous reports.

The numbers of procedures carried out by fellows alone were few, and this small number limits comparison on this feature. However, according to these results, it seems likely that there are no implications if the procedure is performed solely by a fellow. No differences with the endpoint (rate of initial success, recurrent bleeding, the need for surgery, and death rate) were found.

Regarding *H. pylori* infection, compared with previous reports in Mexican population,[11] the prevalence in our group of patients was low. A possible explanation for this finding is that the diagnostic methods used were different. In a work made by Torres, *et al.*[11] the diagnostic tool used for *H. pylori* infection was a serologic testing using ELISA method for detection of IgG antibodies. Another important factor is that in only 30 of our patients a tissue sample for *H. pylori* evaluation was obtained; so the prevalence considering this fact is higher (14/30; 46.6%), and is consistent with previous reports.[11,12] Another possible explanation is the previous administration of *H. pylori* eradication treatment; unfortunately this information was not available.

Limitations of our work are the sample number and the retrolective collection of data. However, this is the only information available as to evaluate therapeutic issues in upper non-variceal gastrointestinal bleeding. Future prospective studies are necessary to confirm these results.

In conclusion, the rates of complications in our institute are higher than in other referral centers. The use of epinephrine injection alone, age, symptom of presentation or the procedure made by a fellow alone are not related factors of initial success, recurrent bleeding, or need of emergency surgery. Our results suggest that mortality rate may be influenced by the use of dual ET.

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