Research article/Raziskovalni prispevek

PEPTIC ULCER HEMORRHAGE: COMPARISON OF EFFICACY OF TWO METHODS OF ENDOSCOPIC HEMOSTASIS – A PROSPECTIVE STUDY*

KRVAVEČA PEPTIČNA RAZJEDA: PRIMERJAVA UČINKOVITOSTI DVEH METOD ENDOSKOPSKE HEMOSTAZE – PROSPEKTIVNA RAZISKAVA

Pavel Skok[1], Marija Skok[2]

[1] Dep. of Gastroenterology and Endoscopy, Clinical Department of Internal Medicine, General Hospital Maribor, Ljubljanska ulica 5, 2000 Maribor

[2] Health Centre Dr. A. Drolc Maribor, Ul. Talcev 5, 2000 Maribor

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Key words: *peptic ulcer; hemorrhage; endoscopic hemostasis; argon plasma coagulation; injection sclerotherapy; prospective study*

Abstract – Background. *Interventional endoscopy has largely reduced mortality in patients with peptic ulcer hemorrhage.*

Study aims. *To evaluate the efficacy and safety of endoscopic hemostasis with argon plasma coagulation and injection sclerotherapy in bleeding peptic ulcer and determine the mortality of patients in a prospective, controlled study.*

Patients and methods. *The study includes 100 patients with peptic ulcer hemorrhage (male 63, female 37, av. age 57.1 years, SD ± 16, span 26–80; gastric ulcer 50 patients, duodenal ulcer 50 patients) in the period between 1 Jan. 1999 and 15 May 2000 treated in our institution. The bleeding activity was determined according to Forrest classification. Fifty patients were randomized to receive argon plasma coagulation (ARCO 2000 Electro Surgery unit, group A) and in fifty patients injection sclerotherapy (sclerosing with diluted adrenalin 1:10,000 plus polidocanol 1%, group B) was performed. The groups did not differ with respect to age, sex, site, severity of bleeding, use of NSAID and additional diseases.*

Results. *Clinically and endoscopically diagnosed reebleding occured in 7/50 patients (14%) in group A and in 9/50 patients (18%) in group B; p = 0.78. The majority of reebleding occured within 48 hours after endoscopic hemostasis, group A 4/7 (57.1%), group B 7/9 (77.7%), p = 0.74. Repeated endoscopic hemostasis did not prove successful in 8 patients (group A 3/50, 6%, group B 5/50, 10%), p = 0.71. Seven patients were treated operatively. The total mortality rate was 9% (9/100 patients, group A 4/50, 8%, group B 5/50, 10%), p > 0.05. Only one patient died due to peptic ulcer hemorrhage, other 8 patients died due to concomitant diseases.*

Conclusions. *Argon plasma coagulation seems to be an effective and safe alternative to injection sclerotherapy and other hemostatic modalities in peptic ulcer hemorrhage.*

Ključne besede: *peptična razjeda; krvavitev; endoskopska hemostaza; argonska plazemska koagulacija; injekcijsko sklerozacijsko zdravljenje; prospektivna raziskava*

Izvleček – Izhodišča. *Akutne krvavitve iz zgornje prebavne cevi sodijo med pogosta nujna stanja, s katerimi se srečujemo v urgentni medicini in gastroenterologiji. Peptična razjeda je najpomembnejši vir krvavitev. V Sloveniji je letna incidenca krvaveče peptične razjede 118 bolnikov/100.000 prebivalcev. Bolezen je povezana s pomembno umrljivostjo, še zlasti pri starejših bolnikih s pridruženimi obolenji. Po podatkih iz literature so endoskopske hemostatske metode in zdravljenje v usmerjenih intenzivnih enotah vplivale na zmanjšanje umrljivosti pri teh bolnikih v zadnjem obdobju.*

Namen raziskave. *Namen raziskave je bil ovrednotiti učinkovitost in varnost argonske plazemske koagulacije v primerjavi z injekcijskim sklerozacijskim zdravljenjem pri krvaveči peptični razjedi in ugotoviti umrljivost teh bolnikov v prospektivni, kontrolirani raziskavi.*

Bolniki in metode. *Raziskava vključuje 100 bolnikov s krvavečo peptično razjedo, 63 moških in 37 žensk, povprečne starosti 57,1 leta, SD ± 16 let, v razponu od 26–80 let. Med njimi je bilo 50 bolnikov z želodčno razjedo in 50 bolnikov z razjedo dvanajstnika, zdravljenih zaradi krvavitve v naši ustanovi v obdobju od 1.januarja 1999 do 15. maja 2000. Vsi bolniki so prvič zakrvaveli zaradi razjede. Ob nujni endoskopski preiskavi je bila aktivnost krvaveče razjede ocenjena v skladu z Forrestovo klasifikacijo. Po randomizaciji smo pri 50 bolnikih opravili endoskopsko hemostazo z argonsko plazemsko koagulacijo (instrument ARCO 2000, skupina A), pri 50 bolnikih pa injekcijsko sklerozacijsko zdravljenje (z razredčenim adrenalinom v razmerju 1:10.000 in 1% polidokanolom, skupina B). Bolnike smo zdravili v enoti internistične intenzivne medicine, kjer so bili hemodinamsko nadzorovani. Prejemali so simptomatsko zdravljenje, vključno s transfuzijami. Skupini bolnikov se nista pomembneje razlikovali glede na starost, spol, aktivnost krvavitve, uporabo nesteroidnih protivnetnih zdravil in pogostost pridruženih obolenj.*

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Rezultati. *Klinično in endoskopsko smo potrdili ponovitev krvavitve pri 7/50 bolnikov (14%) v skupini A in pri 9/50 bolnikih pri skupini B (18%), p = 0,78. Večina ponovitev krvavitev je bila v prvih 48 urah po endoskopski hemostazi, v skupini A 4/7 (57,1%), v skupini B 7/9 (77,7%), p = 0,74. S ponovljeno endoskopsko hemostazo nismo bili učinkoviti pri 8 bolnikih (skupina A 3/50, 6%, skupina B 5/50, 10%), p = 0,71. Zaradi neuspešne endoskopske hemostaze smo 7 bolnikov zdravili operativno. Skupna umrljivost vseh naših bolnikov je bila 9% (9/100 bolnikov, skupina A 4/50, 8%, skupina B 5/50, 10%), p > 0,05. Samo en bolnik je umrl zaradi krvaveče peptične razjede, ostalih 8 bolnikov pa zaradi pridruženih bolezni.*

Zaključki. *Argonska plazemska koagulacija sodi med učinkovite, varne in cenovno dostopne metode endoskopske hemostaze pri akutnih krvavitvah iz prebavne cevi. Rezultati raziskave potrjujejo, da je učinkovitost te metode pri krvaveči peptični razjedi primerljiva z injekcijskim zdravljenjem, ki je v Sloveniji med najpogosteje uporabljenimi tehnikami hemostaze. Umrljivost bolnikov s krvavečo peptično razjedo je praviloma odvisna od pridruženih obolenj, ki vplivajo na razvoj zapletov in neuspešnost endoskopskega in/ali operativnega zdravljenja.*

Introduction

Acute upper gastrointestinal hemorrhage is a frequent emergency encountered in family practice, urgent medicine and gastroenterology (1–3). This condition usually necessitates hospital admission, often to an intensive care unit (ICU) for fluid and blood resuscitation, hemodynamic monitoring and urgent endoscopy. The most frequent causes of severe hemorrhage are complications due to peptic ulcers of stomach or duodenum and hemorrhagic, erosive mucosal changes of the upper digestive tract (4, 5). Helicobacter pylori infection and nonsteroidal antiinflammatory drugs (NSAIDs) account for the majority of benign ulcerations (5). The importance of NSAIDs as a major cause of peptic ulcer bleeding may decline in the future, because the new class of NSAIDs, selective cyclooxigenase-2 (COX-2) inhibitors, holds a great deal of promise in terms of reduced gastrointestinal toxicity. Various statistics have confirmed that 20% of all peptic ulcer patients have at least one incident of hemorrhage in their life. In Slovenia, the incidence of peptic ulcer hemorrhage is 118/100,000 inhabitants, with a significant mortality (5). At all ages the incidence is higher in males, except in the age group over 80 years.

Emergency endoscopy is the most effective diagnostic and therapeutic method in peptic ulcer hemorrhage (6–10). This treatment modality has considerably reduced the number of emergency operations, length of hospital stay and mortality (4, 5, 7, 9). Different endoscopic techniques including electrocoagulation, laser therapy, thermal probes, mechanical devices, injection of fibrin/thrombin glue or injection of adrenaline with or without a sclerosant or dessicant score a similar therapeutic success in peptic ulcer bleeding, but recurrences of hemorrhage and the development of hemorrhagic shock still represent alarming problems (3, 5, 6, 9–11). Argon plasma coagulation (APC) is a special procedure of contact-free electrocoagulation in which energy is transmitted to the tissue through ionized and therefore conductive argon gas (i.e. argon plasma) (11–19). APC through a flexible endoscope provides a new technique for thermal devitalization or blood coagulation which was introduced by Grund et al. in Tübingen already in 1991 (11, 12).

The main objectives of this prospective study conducted at our institution were to evaluate the efficacy and safety of APC in comparison with injection sclerotherapy (IS) in bleeding peptic ulcer and to evaluate the mortality of these patients.

Patients and methods

The study includes 100 patients with an emergency hospital admission due to peptic ulcer hemorrhage (male 63, female 37, av. age 57.1 years, SD ± 16, span 26–80; gastric ulcer 50 pts, duodenal ulcer 50 pts) in the period between 1 January 1999 and 15 May 2000. The study was approved in 1998 by the Medical Ethics Committee of the Republic of Slovenia *(No. 90/09/98; The influence of Helicobacter pylori eradication on development of reflux disease of the esophagus in patients with bleeding peptic ulcer)* and carried out in accordance with the principles of the Helsinki – Tokyo Declaration and the Code of Ethics of Slovene health workers. At our institution all patients with gastrointestinal hemorrhage are treated at the Department of the Internal Medicine where the only endoscopy unit is located, situated directly next to the Intensive Care Unit (ICU). The organization of work ensures the 24-hour presence of the endoscopy team. In all cases urgent endoscopic investigations of the upper digestive tract were carried out to determine the origin of hemorrhage within two hours after admission. Prior to the procedure, each patient was acquainted with the aim of the investigation and he gave his written consent to the endoscopic procedure. As premedication prior to the procedure, butylscopolamine 20 mg/ml (Buscopan, Boehringer Ingelheim, Germany) was administered in the iv. form, as well as local anesthesia with 1% lidocaine spray (Xylocain, Astra), usually 1–2 insufflations. All investigations were carried out with an Olympus GIF Q20 and GIF Q30 device (Olympus GmbH, Hamburg) and the EVIS (Endoscopic Video Information System, CLV U20) with OTV-F3 OES TV system (Olympus Optical, Hamburg GmbH). Vigorous washing with the USW-1 water pump (Olympus Optical, Hamburg GmbH) was performed to remove adherent clots from the ulcer floor to better inspect the ulcer base. The bleeding activity was determined according to Forrest classification. In all patients endoscopic hemostasis was performed. During interventional endoscopy patients were randomly allocated to either of

two groups by using sealed envelopes which has been distributed to endoscopists. Fifty patients were randomized (group A) to receive Argon Plasma Coagulation (APC), and in fifty patients (group B) injection sclerotherapy (IS) was performed. The groups did not differ with respect to age, sex, site and severity of bleeding, additional diseases or use of nonsteroidal anti-inflammatory drugs (NSAIDs). APC was performed with ARCO 2000 Electro Surgery unit (Söring Ltd, Quickborn, Germany; the angle of the probe app. 45° in relation to tissue surface, distance from tissue app. 10 mm, power settings: 70 W, gas flow 2 l/min, using Argon gas of 99.99% purity). During endoscopic hemostasis, APC was first performed around the bleeding source and if the vessel was visible, also the vessel was coagulated. IS was performed with diluted adrenalin 1:10,000 and 1% polidocanol (Sclerovein® preparation, Resinag AG, Schwyz). Injection treatment consisted of diluted adrenaline which was administered in aliquots of 1 ml close to the bleeding site (up to 6 ml) until the hemorrhage stopped. Subsequently up to 3 ml of polidocanol were injected closely around the bleeding lesion. After endoscopic control of bleeding, patients were admitted to the ICU. Blood pressure and heart rate were continously monitored. Each patient received 40 mg omeprazole iv. (Losec® preparation, Astra, Södertälje, Sweden), which was followed by oral treatment with 20 mg omeprazole twice daily after 3 days. Conventional supportive therapy including intravenous fluids and transfusions were given as required. Transfusion of packed red cells was administered in order to maintain the hemoglobin level at approximately 95–100 g/l. In cases of clinically evident reebleding (hemodynamic instability: systolic pressure < 100 mm Hg, heart rate > 100 beats/min, hematemesis or bloody aspirates after clear lavages from nasogastric tube, passage of melena with a fall of hemoglobin level of 20 g/l or an inadequate increase in hemoglobin after transfusion) the patients were reendoscoped and the same hemostatic modality was repeated. In cases of second reebleding surgery was recommended to the attending physician in the ICU. Each patient received another endoscopy four days later for Helicobacter pylori detection, biopsies were taken from antrum and corpus, rapid urease test (Jatrox®-H. p.-Test, C. H. R Heim Arzneimittel GmbH, Darmstadt, Germany) was performed and histological examination in case of gastric ulcers to exclude malignancy. If Helicobacter pylori infection was confirmed, recommended antibiotic treatment (metronidazol 400 mg twice daily, claritromycin 500 twice daily for the period of 7 days) was combined with proton pump inhibitor, omeprazol twice daily. Ulcer healing and Helicobacter pylori eradication (rapid urease test and histologic examination) was registered 4 weeks after introduction the eradication therapy. If first line eradication therapy failed, treatment was given according to the antibiogramm.

The minimum observation time for the 91 patients who survived the bleeding or operation connected to hemorrhage was 12 month. During the follow-up period patients were managed as outpatients. One year after inclusion in the study, 84 patients (84/91, 92.3%, group A: 42/46 patients, 91.3%, group B: 42/45 patients, 93.3%) came to the gastroenterologic OPD for a follow-up endoscopic investigation. Seven patients refused the investigation.

Statistical analysis. The data were analyzed statistically using the program SPSS for Windows (Version 8.0, SPSS Inc., 1989–1997). The statistical data were expressed as arithmetic mean and standard deviation. The Mann-Whitney U-test was used for the analysis of nonparametric quantitative data and the interaction of categorical data was determined with χ^2 test. Conclusions were reached at a risk under 5% ($p < 0.05$).

Results

One hundred patients with active bleeding or stigmata of recent bleeding from peptic ulcer were included in this study: 25 patients with spurting arterial bleeding (F1a), 25 patients with oozing bleeding (F1b), 25 patients with visible vessel in the ulcer (F2a) and 25 patients with adherent clot in the ulcer (F2b). Patient characteristics are summarized in table 1. All patients included in the study had their first episode of peptic ulcer hemorrhage. After initial endoscopic hemostasis, clinically and endoscopically diagnosed reebleding occured in 7/50 patients (14%) in group A and in 9/50 patients (18%) in group B, $p > 0.05$. The reebleding rates of ulcers with different Forrest criteria are listed in table 2. If only clinically diagnosed episodes were considered, the rate of recurrent hemorrhage compared well between groups A and B, with 8% (4/50) and 10% (5/50), $p > 0.05$. The majority of reebleding occured within 48 hours, group A 4/7 (57.1%), group B 7/9 (77.7%). Reebleding ulcers were not significantly larger than ulcers without further hemorrhage (1.55 cm vs. 1.45 cm, respectively). The transfusion requirements were greater in group A (1116 ± 216 ml vs. 1044 ± 144 ml, $p = 0.05$). Repeated endoscopic hemostasis did not prove successful in 8 patients (group A 3/50, 6%, group B 5/50, 10%), $p > 0.05$. After repeated endoscopic interventions (21 in all, average 2.6, group A: 8 endoscopic interventions in three patients, group B: 13 endoscopic interventions in five patients), seven patients were treated operatively. One patient refused operative treatment. Apart from the bleeding peptic ulcer, every patient had at least one coexisting disease. In three patients, the cause of hemorrhage was a gastric ulcer and in four duodenal ulcer. Regarding the type of operation, 4 patients were treated with gastric resection according to the Billroth II method, three by hemostatic suturing. During the postoperative period three patients died (3/6, 50%, group A one patient, group B two patients). Comparison of the outcome for patients in both groups is listed in table 3. The total mortality rate was 9% (9/100 patients), group A 8% (4/50), group B 10% (5/50), $p > 0.05$. Only one patient (1/100 patients, 1%) who refused operative treatment died directly due to peptic ulcer bleeding, other 8 patients (8/100) patients, 8%, died due to concomitant diseases, three among them (3/100 patients, 3%) after emergency surgery. Causes of death included: respiratory failure (2 patients), heart failure (2 patient), cerebral ischemia (1 patient); among patients after surgery: multiorgan failure (1 patient), heart failure (1 patient), pulmonary embolism (1 patient).

At control endoscopic investigation, which was carried out four weeks after introduction of eradication therapy, peptic ulcer healing was confirmed in 42/46 patients, 91.3%, in group A and in 39/45 patients, 86.7% in group B, $p > 0.05$. H. pylori eradication treatment was efficient in 29/32 patients, 90.6% in group A (two patients with Helicobacter pylori infection died, one after surgery, the other during hospitalisation) and in 29/33 patients, 87.9% in group B (two patients with Helicobacter pylori infection died after surgery), $p > 0.05$. The results of the follow-up endoscopic investigation, one year after inclusion in the study, are summarized in table 4. None of these 91 patients were treated for repeated hemorrhage during this period.

Discussion

Significant advances have been made in understanding the pathophysiology and management of peptic ulcer bleeding, including improvements in endoscopic techniques, advances in resuscitative measures and development of more potent pharmacologic drugs (1, 2). The diagnosis and treatment of

Table 1. *Patients characteristics.*

Razpr. 1. *Značilnosti bolnikov.*

	Group A (APC) Skupina A (APK)	Group B (IS) Skupina B (IS)	P value P vrednost
Number of patients Število bolnikov	50	50	
Age (years, SD) Starost (leta, SD)	56.7 ± 14.5	57.8 ± 14	ns (nz)
Sex (male/female) Spol (moški/ženske)	32/18	31/19	
Additional disease (%) Pridružene bolezni (%)	46	48	ns (nz)
NSAID (%) NSAR	32	30	ns (nz)
H. pylori (%)	68	70	ns (nz)
gastric ulcer želodčna razjeda	64	64	
dudenal ulcer razjeda dvanajstnika	72	76	
Hemoglobin (g/l) Hemoglobin	103 ± 22	105 ± 20	ns (nz)
Ulcer location Lokalizacija razjede			
Gastric Želodec	25	25	
Duodenal Dvanajstnik	25	25	
Ulcer size (mm, SD) Velikost razjede (mm, SD)	13 ± 3	13 ± 4	ns (nz)
Forrest classification Forrestova klasifikacija			
1a	12	12	
1b	13	12	
2a	12	13	
2b	13	13	

ns – not significant
nz – statistično neznačilno

Table 2. *Reebleding rate of ulcers with different Forrest criteria.*

Razpr. 2. *Ponovitve krvavitev pri različnih razjedah glede na Forrestove kriterije.*

Forrest classification Forrestova klasifikacija	Group A (N, %) Skupina A (štev., %)	Group B (N, %) Skupina B (štev., %)	P value P vrednost
1a – spurting arterial bleeding brizgajoča arterijska krvavitev	2/12 (16.7)	2/12 (16.7)	ns (nz)
1b – oozing arterial bleeding mezeča arterijska krvavitev	1/13 (7.7)	3/12 (25)	ns (nz)
2a – visible vessel in the ulcer viden krn žile v dnu razjede	2/12 (16.7)	2/13 (15.4)	ns (nz)
2b – adherent clot in the ulcer krvni strdek v dnu razjede	2/13 (15.4)	2/13 (15.4)	ns (nz)
Av. reebleding rate (%) Povprečna ponovitev krvavitve (%)	14%	18%	p = 0.78

ns – not significant
nz – statistično neznačilno

Table 3. *Comparison of the outcome for patients in both groups.*

Razpr. 3. *Primerjava učinkovitosti zdravljenja bolnikov v obeh skupinah.*

	Group A (N, %) Skupina A (štev., %)	Group B (N, %) Skupina B (štev., %)	P value P vrednost
Failure of endoscopic hemostasis Neuspešna endoskopska hemostaza	3/50 (6)	5/50 (10)	ns (nz)
Surgery Operativno zdravljenje	3/50 (6)	4/50 (8)*	ns (nz)
Mortality – after surgery Umrli – po op. posegu	1/3 (33.3)	2/4 (50)	ns (nz)
Total Skupaj	4/50 (8)	5/50 (10)	ns (nz)

ns – not significant
nz – statistično neznačilno
* – one patient refused operative treatment
bolnik je odklonil operativno zdravljenje

Table 4. *The results of follow-up endoscopic investigations in 84 patients one year after inclusion in the study (seven patients refused endoscopy).*

Razpr. 4. *Rezultati kontrolne endoskopske preiskave pri 84 bolnikih leto dni po vključitvi v raziskavo (sedem bolnikov je preiskavo zavrnilo).*

	Group A (N, %) Skupina A (štev., %)	Group B (N, %) Skupina B (štev., %)	P value P vrednost
Number of patients Število bolnikov	42/46 (91.3)	42/45 (93.3)	ns (nz)
Peptic ulcer (recurrence) Ponovitev peptične razjede			
gastric želodčna	–	–	
duodenal [1] dvanajstnika	1/42 (2.4)	1/42 (2.4)	ns(nz)
Peptic ulcer bleeding Krvaveča peptična razjeda	–	–	
H. pylori (re)infection Ponovna okužba s H. pylori			
gastric ulcer [2] želodčna razjeda	1/42 (2.4)	–	ns (nz)
duodenal ulcer [3] razjeda dvanajstnika	1/42 (2.4)	2/42 (4.8)	ns (nz)

[1] Both patients were using preparations of acetilsalycilic acid in the last week before endoscopic investigation and were H. pylori negative.
Oba bolnika sta uporabljala pripravke acetilsalicilne kisline v zadnjem tednu pred endoskopijo, okužbe s H. pylori nismo potrdili.

[2] The patient had H. pylori infection at inclusion at the study.
Bolnik je imel okužbo s H. pylori ob vključitvi v raziskavo.

[3] The patient from group A had H. pylori infection at inclusion at the study, from group B one patient had also H. pylori at inclusion at the study.
Bolnik iz skupine A je imel okužbo s H. pylori ob vključitvi v raziskavo, iz skupine B pa je imel okužbo s H. pylori ob vključitvi v raziskavo samo en bolnik.

peptic ulcer hemorrhage remains one of the most challenging and potentially rewarding parts of interventional endoscopy (3–10). In addition, emergency endoscopy can be useful in predicting which patients are at higher risk for reebleding. Although peptic ulcer bleeding is self limited in approximately 80% of cases, in the other 20% of patients who have continued bleeding or reebleding during a hospitalisation, mortality rates may be as high as 30% (1, 4, 5). In the last twenty years, numerous effective methods of endoscopic hemostasis were developed, making it possible to arrest most hemorrhages from the peptic ulcer which did not stop spontaneously (1, 3, 4, 8, 9). During the last ten years, a large number of clinical trials have established that different modalities of injection therapy *(fibrin glue, thrombin, sclerosing agents, ethanol, cyanoacrylate, cyanoacrylate glue, adrenaline)*, thermal methods *(electrocoagulation with monopolar or bipolar probe, heater probe, laser photocoagulation, microwave)* and mechanical methods *(hemoclips, rubber band ligation, endo-*

loop, endoscopic sewing) control active bleeding from peptic ulceration and decrease the risk of rebleeding (3, 6, 8, 9, 17–20). Their success is similar, to a great extent the success depends on personal training, experience of the investigator and the quality of instruments for interventional endoscopy (3, 6). Injection therapy is widely used, because effective hemostasis can be accomplished with injection of various solutions, including vasoconstrictors such as adrenaline, sclerosants such as 1% polidocanol, ethanolamine, hypertonic saline and 98% alcohol (3, 4). In Slovenia, sclerotherapy with polidocanol is the method which has been used most frequently in the last fifteen years (1–3). This method is still considered effective, safe and economical. In clinical trials the amount of sclerosants is usually limited, because of the risk of ulcer extension or perforation with larger volumes of injection. Serious complications of endoscopic sclerotherapy are unusual and only sporadicaly reported: extensive necrosis of gastric mucosa, gastric ulcer, cholestasis and duodenal hematoma (3, 4, 8, 9). Potential adverse effects of injecting adrenaline include systemic absorption, which is rarely clinically significant (3).

APC is a recently introduced treatment in gastrointestinal endoscopy. This coagulation method is a special procedure which transfers high-frequency current to tissue in a non-contact manner via ionized and therefore conductive argon gas (i. e. argon plasma) (11–17). The argon gas is ionised in the high-frequency electric field between the electrode of the applicator and the tissue. This method of endoscopic hemostasis was introduced in our department in 1998 and replaced the use of Nd-Yag laser in different hemorrhagic lesions and gastrointestinal tumors (17). Argon is a colour- and odourless, non toxic, inert gas. It illuminates in ionised conditions, which makes the use of the high-frequent alternating current under visual-endoscopic control possible. In the past, this method has been successfully used for hemostasis and devitalisation in open surgery. Liver transplant surgeons use a similar device to treat the bleeding surface of the diaphragm and the liver following blunt dissection. Over the last decade this method was also introduced into laparoscopic surgery (11, 12). The development of special probes, which can be handled via flexible endoscopes, has made this method applicable for interventional endoscopy as well. From the beginning, APC was used for the treatment of benign and malignant tumors of the gastrointestinal tract and endoscopic hemostasis in hemorrhagic lesions (11, 12, 17–19). APC is becoming increasingly popular also for treatment of Barrett's esophagus. The method proved to be highly effective and easily used. The advantages of this technique are particularly evident in difficult hemostasis situations, i. e. over large surface areas, profuse hemorrhaging, in instances of difficult localization or critical wall characteristics (11, 12, 17). Due to shallow penetration depth, this method reduces damage to adjacent or submucosal tissues and also reduces the risk of perforation (1, 12, 15, 19). Depending on instrument settings, power settings, argon gas flow and the type of application (axial, radial, retrograde), the penetration depths remains between 0.5 and 3 mm and is therefore particularly suitable for endoscopic hemostasis also in the duodenum and thin-walled colon (11, 12). According to the results published, APC is suitable in angiodysplasia, watermelon stomach, radiation proctitis, bleeding peptic ulcers, obstructed stents, multiple polyps and residues after polypectomy or mucosectomy (12, 17–19). When compared with laser treatment, APC has a better advantage-risk ratio. Ease of learning, low cost and mobility of the equipment are additional arguments for choosing APC rather than laser. However, the extensive gas production and related painful distension of the intestinal wall and risk of perforation must not be underestimated. The results of our study indicate that APC is a safe and effective alternative of endoscopic hemostasis in peptic ulcer hemorrhage. No perforations, uncontrollable bleeding or other serious complications were seen in treatment of any of this patients. Although no significant differences in efficacy were found comparing two hemostatic methods, in the group of patients treated with APC, lower rebleeding rates and lower mortality were observed. Another advantage of this method compared to IS might be that repetition is harmless. In our patients no serious complications developed after retreatment. The results of our trial also confirmed that only one patient (1%) died directly due to peptic ulcer bleeding, other seven patients died due to concomitant diseases.

There is no doubt, that due to development of interventional endoscopy and hemostatic therapy, allowing a successful arrest of hemorrhage in as many as 90–97%, the mortality from peptic ulcer hemorrhage has decreased (4, 6, 18–25). The association between continued or recurrent bleeding and high mortality in patients with peptic ulcer hemorrhage has been already recognized in the past. According to various authors, the mortality rate is still 5–14% (4, 5, 18–20). In our group of patients it was 9%. There are several clinical and endoscopic risk factors (different risk scoring systems: APACHE – ***A**cute **P**hysiology **a**nd **C**hronic **H**ealth **E**valuation scoring system,* Rockall *risk scoring system,* ASA – ***A**merican **S**ociety of **A**naesthesiology classification,* Baylor *bleeding score*) that have been suggested as predictive of an adverse outcome in these patients (1, 4, 5, 17, 18, 24–26). Development of clinical predictive scoring systems has the potential to provide rational and scientifically based criteria for diagnostic and management decisions such as triage to an ICU, repeated attempts of endosopic hemostasis, elective versus emergency surgery and early discharge from ICU (19, 27, 28). The demographics of patients with peptic ulcer hemorrhage suggest that this population is older and includes many patients with significant medical conditions which increase mortality (3, 4, 6, 21, 26). Reebleding is considered one of the most important risk factors for mortality and occurs in 10–30% of those successfully treated, although there is still considerable disagreement about what the most important prognostic factors are (1, 5, 6, 26–30). Many factors independently predict the risk of rebleeding. According to some authors, the activity of bleeding at the time of evaluation is a key prognostic factor (1, 19, 24, 27, 31–35). The risk of reebleding from gastric or duodenal ulcers can be estimated on the basis of endoscopic signs and different other criteria (36–41). Endoscopic stigmata of recent bleeding – including the presence of an active spurting vessel, a visible vessel or a fresh clot – are predictors of an increased risk of bleeding. Ulcers on the proximal lesser curve of the stomach and on the posterior surface of duodenum generally have a higher chance of rebleeding because of their proximity to the left gastric and gastroduodenal arteries (42, 43). Patients with bleeding gastric ulcer develop recurrent hemorrhage more often than do those with bleeding duodenal ulcer. Other important independent predictors of rebleeding are mainly shock at admission, age older than 65 years, ulcer size (diameter greater than 2 cm) and comorbidity (36, 38, 39).

In treating a patient with peptic ulcer hemorrhage, it is vital to strive for definitive endoscopic hemostasis. If continued bleeding cannot be stopped, a timely decision regarding other therapeutic options must be made (30, 38–40). Minimally invasive surgery, as well as radiological techniques, particulary arterial embolisation, are valid alternatives to repeated attempts of endoscopic hemostasis (43). A surgeon should be notified immediately after interventional endoscopy if endoscopic hemostasis was unsuccessful or if an ulcer at high risk of rebleeding was diagnosed. The combination of endoscopic stigmata and clinical risk factors should guide our punctual clinical decisions and increase the accuracy of predicting individual risk in patients with peptic ulcer hemorrhage (34,

39, 44–49). Optimization of diagnostic and therapeutic management may help decrease the mortality from peptic ulcer bleeding in the future (50, 51).

Conclusions

During the past twenty years, endoscopy has developed as the modality of choice for determining diagnosis, prognosis and therapy for peptic ulcer bleeding. Clinical trials have confirmed that different methods of endoscopic hemostasis including injection therapy, thermal coagulation, hemoclips and other modalities are effective in decreasing bleeding from this type of gastrointestinal hemorrhagic lesion. The method used for the individual patient depends on available resources and the experience of the endoscopist. Argon plasma coagulation seems to be an effective and safe alternative to other hemostatic modalities in peptic ulcer hemorrhage. No serious complications were related to application of this hemostatic method in our study. Further prospective studies should be directed towards refining our understanding of which ulcers will rebleed and why, and optimizing therapy on selected high-risk patients to improve their outcome.

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