

Clinical researches

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GASTRIC MUCOSAL MICROCIRCULATION IN PATIENTS WITH DUODENAL PEPTIC ULCER AGAINST THE BACKGROUND OF ERADICATION THERAPY

Jafar Akermi, Y. A. Andreeva

Zaporizhzhya Medical Academy of Postgraduate Education, Ukraine

The article presents the results of investigation of gastric mucosal microcirculation with the help of laser-Doppler flowmetry in acute phase of duodenal ulcer during 7 and 14-day eradication therapy. The study enabled to obtain some data on effectiveness of the two therapeutic eradication regimens as well as their impact on gastric mucosal microcirculation in the process of ulcer defects healing.

KEY WORDS: microcirculation, peptic ulcer, duodenum, eradication therapy

СТАН МІКРОЦИРКУЛЯЦІЇ СЛИЗОВОЇ ОБОЛОНКИ ШЛУНКА У ХВОРИХ НА ВИРАЗКОВУ ХВОРОБУ ДВАНАДЦЯТИПАЛОЇ КИШКИ НА ФОНІ ЕРАДИКАЦІЙНОЇ ТЕРАПІЇ

Жаафар Акермі, Я. О. Андреева

ДЗ «Запорізька медична академія післядипломної освіти МОЗ України», Україна

У статті наведені результати дослідження мікроциркуляції слизової оболонки шлунку методом лазерної доплерівської флуометрії в гостру фазу виразкової хвороби дванадцятипалої кишки, на тлі 7 і 14-денної ерадикаційної терапії. Отримано дані про ефективність двох схем ерадикаційної терапії, вплив різних схем на стан мікроциркуляції слизової оболонки шлунку на тлі загоєння виразкового дефекту.

КЛЮЧОВІ СЛОВА: мікроциркуляція, виразкова хвороба, дванадцятипала кишка, ерадикаційна терапія

СОСТОЯНИЕ МИКРОЦИРКУЛЯЦИИ СЛИЗИСТОЙ ЖЕЛУДКА У БОЛЬНЫХ С ЯЗВЕННОЙ БОЛЕЗНЬЮ ДВЕНАДЦАТИПЕРСТНОЙ КИШКИ НА ФОНЕ СТАНДАРТНОЙ ЭРАДИКАЦИОННОЙ ТЕРАПИИ

Жаафар Акермі, Я. А. Андреева

ГЗ «Запорожская медицинская академия последипломного образования МОЗ Украины», Украина

В статье приведены результаты исследования микроциркуляции слизистой оболочки желудка методом лазерной доплеровской флуометрии в острую фазу язвенной болезни двенадцатиперстной кишки, на фоне 7 и 14-дневной эрадикационной терапии. Получены данные об эффективности двух эрадикационных схем терапии, влияние различных схем на состояние микроциркуляции слизистой желудка на фоне заживления язвенного дефекта.

КЛЮЧЕВЫЕ СЛОВА: микроциркуляция, язвенная болезнь, двенадцатиперстная кишка, эрадикационная терапия

Gastric and duodenal peptic ulcer (PU) is one of the major problems of contemporary clinical medicine. Despite successful implementation of diverse *Helicobacter pylori* (*H. pylori*) eradication therapies, PU is still among leading diseases of digestive system [1,

2]. In accordance with classical views, the processes of ulcerogenesis, chronization of arisen ulcers and their recurrence are closely associated with insufficient blood supply to gastroduodenal zone, hemodynamic disturbances in abdominal cavity vessels as well as in micro-

circulation in stomach wall, and, therefore, in injured tissues trophism [3–5]. All intensive processes in mucosa, including its rehabilitation, physiologic and reparative regeneration of epithelial and glandular cells, can be supported by adequate regional blood supply only [6–10]. The assumption that vascular injury (as a fact of ultimate injury in ulcerogenesis) is directly induced by bacterial chemotactic products and is one of the mechanisms of injury as well as the target of realized by *H. pylori* factors, renewed interest in investigation of regional blood flow in mucosa of gastroduodenal zone [11–13]. However, there is still a need for complete and conclusive conception of pathogenetic significance of microcirculation disturbances in injured tissues and its association with *H. pylori* infection.

The aim of the study was to investigate characteristics of gastric mucosa in patients with duodenal PU treated with standard triple eradication therapy.

MATERIALS AND METHODS

For the aims of this study we examined 68 patients with common and complicated clinical courses of chronic duodenal PU. 35 of the patients were male and 33 female. Age of the patients ranged 22–64 years (mean age $43,2 \pm 6,3$ years). The control group consisted of 25 preventively examined practically healthy middle-aged people. The groups were comparable in age ($48,47 \pm 0,82$ years) and gender (12 males and 13 females) composition. Patients with *H. pylori* positive duodenal PU were enrolled.

All the patients underwent esophagogastroduodenoscopy (EGDS) with gastric mucosa biopsy of ulcer defect area. The examination was conducted twice with 1 month's interval.

Regional perfusion was studied using laser-Doppler flowmetry (LDF) (LAKK – 02, SPE «Lazma», Russia). Mucosal microcirculation was examined with cavitory sensor inserted through bioptic canal of Gastroduodenoscope into stomach and duodenal lumen. In course of the study were registered and evaluated: arithmetical mean of microcirculation (M), measured in (pf.sb.), standard deviation fluctuation range of blood supply from M (SD) measured in (pf.sb.), coefficient of variation (K_v), index of microcirculation effectiveness (IME). The examination was conducted in acute phase during ulcer defect scarring (phase of red and

white scar) 1–3 month after remission of acute conditions.

After initial examination all the patients with *H. pylori*-associated duodenal PU were divided into two groups. Group I was formed by 34 patients, who underwent first-line eradication therapy for 7 days. Group II included 34 patients with duodenal PU, who underwent first-line 14-day eradication therapy. The therapy included a proton pump inhibitor — rabeprazole (20 mg twice daily) and 2 antibacterial agents: clarithromycin (500 mg twice daily), amoxicillin (1 g twice daily, for 7 or 14 days), pre- and probiotics (Maastricht-4, 2010) [10, 14]. Effectiveness of treatment was evaluated regarding reduction of duodenal PU clinical signs, indices of frequency of HP eradication (the results of validated laboratory monoclonal *H. pylori* stool antigen test in 4 weeks) and scarring of ulcer defect (phase of red scar in 4 weeks and phase of white scar in 12 weeks) after the therapy [1, 15, 16].

Mathematical treatment of the results was carried out using statistical package of programs «STATISTICA» 6.0. Normality of index distribution was checked using Kolmogorov-Smirnov criterion. For statistical estimate of results parametric criteria were used — mean value (M) and standard deviation (sd). Reliability of differences between samples was assessed using Wilcoxon-Mann-Whitney criteria. Estimation of correlation between pairs of independent signs marked in a numerical scale was done using Spearman's rank correlation coefficient (r). Significance of correlation coefficients was assessed comparing the estimated coefficients with the critical ones. Differences were considered significant at $P < 0,05$ level.

RESULTS AND DISCUSSION

Estimation of effectiveness of the *H. pylori* eradication was conducted 4 weeks onwards the therapy (Maastricht-4, 2011). The data obtained are shown in Fig. 1.

Eradication by 7-day therapy was reached in 72,3 % of the cases (24 patients). 14-day therapy appeared to be more effective as eradication rate made up 92,4 % in group II (32 patients). The data obtained match the results, cited in Consensus Maastricht-4 (2010) [1, 10, 17–19].

Additionally, 14-day anti-*Helicobacter* therapy regimen was followed by development of side effects in 33,4 % of the patients.

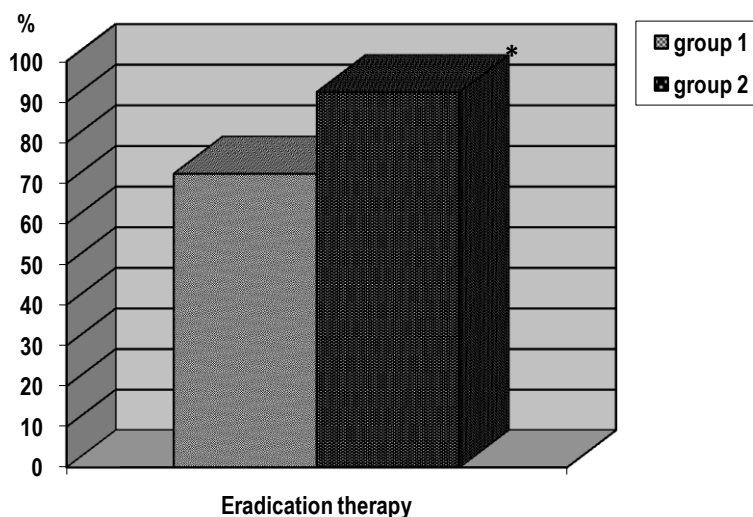


Fig. 1. H. pylori eradication rate in the groups of patients (%)

Comment:

* — differences between the groups are reliable (P < 0,05)

That was the reason for cessation of the therapy in some of the patients. In most cases the patients experienced general weakness (21,4 %), liquid stool (7,8 %), giddiness and headache (11,3 %), abdominal distension and rumbling (8,6 %), nausea (11,4 %). By 7-day

anti-Helicobacter therapeutic regimen insignificant side effects were observed in 18 % of the patients with duodenal PU.

The data obtained by LDF 1 month onwards the therapy indicated improvement of microcirculation during ulcer defect scarring (table 1).

Table 1

Dynamics of microcirculation indices in patients with duodenal PU one month onwards the therapy (M ± sd)

| Region | Index | Control group (n = 25) | Duodenal PU, acute phase (n = 68) | Duodenal PU (n = 68) | |
|---------------|--------------------|------------------------|-----------------------------------|----------------------|---------------------------|
| | | | | Group I (n = 34) | Group II (n = 34) |
| Fundal region | M (pf.sb.) | 6,1 ± 0,15 | 9,22 ± 0,15 | 8,22 ± 0,35* | 7,69 ± 0,21* ^o |
| | SD (pf.sp.) | 0,66 ± 0,02 | 0,32 ± 0,02 | 0,36 ± 0,03 | 0,42 ± 0,07* |
| | K _v (%) | 10,9 ± 0,2 | 4,9 ± 0,3 | 6,41 ± 0,5* | 7,52 ± 0,2* ^o |
| | IME | 1,95 ± 0,14 | 1,62 ± 0,14 | 1,67 ± 0,01 | 1,82 ± 0,02* ^o |
| Antral region | M (pf.sb.) | 5,9 ± 0,08 | 4,2 ± 0,08 | 5,24 ± 0,09* | 5,52 ± 0,04* ^o |
| | SD (pf.sb.) | 0,58 ± 0,05 | 0,33 ± 0,05 | 0,38 ± 0,1 | 0,46 ± 0,12* |
| | K _v (%) | 9,8 ± 0,4 | 8,67 ± 0,4 | 9,03 ± 0,4 | 9,19 ± 0,23* |
| | IME | 2,2 ± 0,19 | 1,3 ± 0,19 | 1,68 ± 0,09* | 1,85 ± 0,12* ^o |

Comment:

* — differences from indices in acute phase are significant (P < 0,05);

^o — differences from indices of group I are significant (P < 0,05)

As it can be seen from the given data, positive dynamics was observed one month onwards the therapy in the both groups, realized in the form of significant decrease of M and increase of SD, IME и K_v. In patients of group I we attested positive changes in the form of significant decrease of M in antral region in combination with increase in this index in fundal region. The decrease of M was not significant and had a character of a tendency. It should be noted that the lowest frequency of HP eradication was observed in this group.

Correlation analysis between these indices has shown negative correlation of mean force (r = -0,24, P < 0,05). In the patients of group II the rate of decrease in index M in fundal region and increase in antral region was higher compared with the rate before the treatment in this group of patients (P < 0,05). This index was significantly increased compared to the indices before the treatment (by 13 %, P < 0,05), and to group I (by 18 %, P < 0,05). The was also noticed increase in SD by 14 % compared to the original (P < 0,05), IME by 22 %

($P < 0,05$) and K_V by 17 % ($P < 0,05$). Hence, a tendency towards normalization of microcirculation indices 1 was noticed in all the patients month onwards the therapy. The most evident changes were recorded in patients of group II.

3 month onwards the therapy in all the patients with duodenal PU was recorded significant decrease of microcirculation index in an-

tral region, increase in SD, K_V and IME in fundal region ($P < 0,05$). Additionally, in group II no significant differences were recorded in most of the indices of gastric mucosal microcirculation compared to the control measures. In patients of group I reduction of K_V in fundal region and IME in antral region retained ($P > 0,05$) (Table 2).

Table 2

**Dynamics of indexes of microcirculation in patients with duodenal PU
3 month onwards the therapy ($M \pm sd$)**

| Region | Index | Control group (n = 25) | Duodenal PU, acute phase (n = 68) | Duodenal PU (n = 68) | |
|------------------|--------------|---------------------------|---|----------------------|----------------------|
| | | | | Group I (n = 34) | Group II (n = 34) |
| Fundal region | M (pf.sb.) | 6,1 ± 0,15 | 9,22 ± 0,15 | 7,31 ± 0,35* | 6,24 ± 0,21° |
| | CKO (pf.sb.) | 0,66 ± 0,02 | 0,32 ± 0,02 | 0,56 ± 0,03 | 0,58 ± 0,07 |
| | K_V (%) | 10,9 ± 0,2 | 4,9 ± 0,3 | 7,32 ± 0,5* | 8,32 ± 0,2° |
| | IME | 1,95 ± 0,14 | 1,62 ± 0,14 | 1,74 ± 0,01* | 1,82 ± 0,02° |
| Antral region | M (pf.sb.) | 5,9 ± 0,08 | 4,2 ± 0,08 | 5,24 ± 0,09* | 5,52 ± 0,04 |
| | CKO (pf.sb.) | 0,58 ± 0,05 | 0,33 ± 0,05 | 0,42 ± 0,1* | 0,46 ± 0,12° |
| | K_V (%) | 9,8 ± 0,4 | 8,67 ± 0,4 | 9,03 ± 0,4* | 9,19 ± 0,23 |
| | IME | 2,2 ± 0,19 | 1,3 ± 0,19 | 1,68 ± 0,09 | 1,85 ± 0,12° |

Comment:

* — differences from indices in acute phase are significant ($P < 0,05$);

° — differences from indices of group I are significant ($P < 0,05$)

As it can be seen from the data, the most evident alterations were also fixed in group II in 3 month. Mean square deviation of microcirculation index in patients of group II in fundal region decreased by 34 % in compassion to the indices before the treatment ($P < 0,05$), in antral region it increased by 47 % ($P < 0,05$). This index was not significantly different from the control, but different from the index in group I ($P < 0,05$). SD in fundal and antral regions increased to $0,63 \pm 0,06$ and $0,58 \pm 0,09$ pf.sb. correspondingly and was not significantly different from the indices of the control group ($P < 0,05$). Significant differences were noticed only between indices of the control group and group II ($P < 0,05$). Index of variation K_V also increased $9,1 \pm 0,4$ %. That was significantly different from indices of group I ($P < 0,05$). Significant differences in IME of the control group, group I and II were also recorded 3 month after the therapy, in contrast to corresponding measures in 1 month ($P < 0,05$).

The conducted analysis enabled to establish strong dependency of alterations in state of gastric mucosal microcirculation on duration of anti-Helicobacter therapy and its efficacy. 14-day eradication regimen has proved to be more effective in patients with duodenal PU, how-

ever, more often followed by side-effects. Besides, disturbances in gastric mucosal microcirculation persisted 3 months onwards the conducted 7-day eradication therapy. More evident alterations in gastric mucosal microcirculation state have been recorded in patients who underwent 14-day therapy. 3 month onwards the therapy most of the indices were not different from the control measures. The mentioned differences in effectiveness of the regimens may be associated with different rate of H. pylori eradication after the treatment and different duration of proton pump inhibitors intake.

CONCLUSIONS

Having compared two standard regimens of eradication therapy we established that 14-day triple regimen is more effective for H.pylori eradication and correction of disturbances in gastric mucosal microcirculation in patients with duodenal PU than the 7-day regimen.

PERSPECTIVES OF FURTHER RESEARCH

Further investigation of gastric mucosal microcirculation in different phases of PU course by application of different therapeutic regimens, as well as study of influence of original microcirculation state on the effectiveness of

eradication therapy, will help to increase efficiency of therapeutic measures and reduce the frequency of relapses and complications after PU.

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