CHARACTERISTICS OF CHANGES IN PROTECTIVE MECHANISMSIN THE GASTRIC MUCOSAL TISSUE IN APPLYING ANTIULCER ANTIBACTERIAL THERAPY

Pulatova N.I.

Tashkent Medical Academy, Tashkent, e-mail: nargizahon13@yahoo.com

In an experimental model of gastric ulcers in rats it is found thatantibacterial drugs have a multidirectional effect on the state of the gastric mucosal barrier. Metronidazole and furazolidone suppress, yet tetracycline, and amoxicillin have no effect on the synthesis of mucosal barrier. One of the reasons of this is the inhibitory effect of metronidazole and furazolidone on the enzyme activity of the MOS. Tetracycline, and amoxicillin have no effect on the enzyme activity of the MOS.

Keywords: gastric ulcers, gastric mucosal, furazolidone, metronidazole, amoxicillin, tetracycline

Peptic ulcer disease is a disease of multifactorial origin, however, now in its etiopathogenesis of major importance is given for the infectious agent-Helicobacter pylori (H.pylori). Numerous clinical studies carried out in our country and abroad, have demonstrated the efficacy of H.pylori therapy in the treatment of peptic ulcer. However, at present, no one can dispute the fact that only a minority of patients infected with H.pylori become ill with a stomach ulcer, which supports the postulate of the comprehensiveness of the pathogenesis of peptic ulcer disease. Therefore, successful treatment can only be achieved by exposing to all the major factors of the pathogenesisat the same time. Unfortunately, up to now, all of the studies were devoted to the study of the effectiveness of the anti-ulcer therapy for eradication of H.pylori. In view of the above, the particular interest is shown to studying the effect of H. pylori products on condition of protective mechanisms in the gastroduodenal area.

The purpose of the research. To study the features of changes of some protective mechanisms in the mucosal tissue of the stomach in the application of anti-ulcer antibiotics.

Materials and methods of research

The studies were conducted in seven groups of animals. There were 6 animals in each group. Model of experimental ulcers (EU) prepared by the method of V.A. Vertelkin in the modification of Losev I.A. et al. [1]. After modeling the animals were divided into the following groups: 1-gr. intact, 2-gr. animals with experimental ulcer, 3-gr. EU + H2O (without treatment), 4-gr. EU + metronidazole, 5-gr. EU + tetracycline, 6-gr. EU + furazolidone, 7-gr. EU + amoxicillin. The drugs which we used were administered orally in the form of aqueous suspension for 10 days at the following doses: metronidazole 50 mg/kg, tetracycline 10 mg/kg, furazolidone 100 mg/kg and 40 mg amoxicillin/kg.

State mucosal barrier was studied by determining the content of the carbohydrate fraction of insoluble glycoproteins (IGP) in the mucosal tissue of the stomach. The sialic acid content was determined by the method of Linevik L.I. [2] Fucose content was determined by the method of Rabinovich P.D. [3]. Monooxygenase system state (MOS) in the mucosal tissue of the stomach was assessed by the activity of NADPH-cytochrome-c-reductase and aminopyrine-N-demethylase [4, 5].

Results of research and their discussion

Results of research on the effect of antibiotics on the content of fractions IGP in the mucosal tissue of the stomach in experimental ulcer are presented in Table 1.

Table 1

Effectof antibiotics on the content of the fractions IGP in the mucosal tissue of the stomach in experimental ulcer.

Animal group	Sialicacid, mcg/ml	Fucose, mg/ml
1. Intact	3,44 ± 0,17	5,66 ± 0,25
2. Experimentalulcer (EU)	1,52 ± 0,11*	1,89 ± 0,12*
3. EU + H_2O	1,74 ± 0,18*	2,11 ± 0,19*
4. EU + Metronidazole	0,71 ± 0,07*@	0,92 ± 0,08*@
5. EU + Tetracycline	1,92 ± 0,12*	2,47 ± 0,17*
6. EU + Furazolidone	0,52 ± 0,05*@	0,78 ± 0,07*@
7. EU + Amoxicillin	1,90 ± 0,14*	2,32 ± 0,16*

N o t e : * $p < 0,05$ on the index of intact group;
@ $P < 0,05$ on the index of group without treatment.

As seen from the shown results in experimental ulcer the content of the IGPissignificantly reduced as well asits fractions in the mucosal tissue of the stomach. In particular, a decrease was observed in sialic acid content for 2, 3 times, and fucose in 3 times. In the group without treatment, this alteration did not change.

It was observed that there was an adverse effect of metronidazole and furazolidone on gastric mucosal barrier. In the groups of animals treated with tetracycline, and amoxicillin, some tendency was observed to an increase in the synthesis of mucosal barrier, but the content of the fractions IGP in these groups did not differ significantly from that of the group with no treatment.

The results of the research carried on the effect of antibiotics at standard schemes of antiulcer therapy on the activity of enzymes MOS in the mucosal tissue in experimental gastric ulcer were demonstrated in Table 2.

Table 2

Effect of antibiotics standard schemes antiulcer therapy on the activity of enzymes of the monooxygenase system in the mucosal tissue of the stomach in experimental ulcer

Animal group	Amidopyrine-N-demethylase (nmol HCOH/min/mg)	NADPH-cytochrome c reductase (nmol/min/mg)
1. Intact	1,72 ± 0,098	17,48 ± 0,94
2. Experimental ulcer (EU)	0,88 ± 0,071*	7,30 ± 0,64*
3. EU + H_2O	0,95 ± 0,068*	7,88 ± 0,45*
4. EU + Metronidazole	0,40 ± 0,033*@	4,21 ± 0,18*@
5. EU + Tetracycline	1,04 ± 0,088*	8,12 ± 0,39*
6. EU + Furazolidone	0,52 ± 0,048*@	4,40 ± 0,31*@
7. EU + Amoxicillin	0,89 ± 0,059*@	7,35 ± 0,34*

N o t e : * $p < 0,05$ on the index of intact group;
@ $P < 0,05$ on the index of group without treatment.

As can be seen from the data in experimental ulcer, activity of aminopyrine-N-demethylaseis reduced for almost twiceand 2, 4 times the activity of NADPH-cytochrome-c-reductase. In the group without treatment, reduction of enzyme activity was the same. As for the efficacy of the data clearly shows that metronidazole and furazolidone have an inhibitory effect on the enzyme activity of the MOS, and tetracycline, and amoxicillin have no effect on their activity. In the group with metronidazole activity ofaminopyrine-N-demethylase was decreased by 57,9%, while in the group with furazolidone by 45,3%. Reduced activity of NADPH-cytochrome-c-reductase in both groups was almost identical (46,4 and 44,2% respectively).

It has been found that among the factors of «protection» in the development of ulcer genesis the special role is played by protective mucus barrier, over 95% of which consists of the IGP. In the synthesis of the IGPof carbohydrate componentsand proteinsMOS enzymes are involved. In turn, changes in the activity of MOS enzymes depend on other factors of aggression, such as reducing the synthesis of NO, increasing the rate of lipid peroxidation and etc.

Our results in monotherapy and in combination therapy are consistent with the allegations and Belov IM [6], which says that triple and quadruple therapyschemes which include omeprazole, metronidazole and furazolidone have quite an active eradication and antisecretory action, however, they have a negative effect on the mechanism of cytoprotection. A similar view is shared by other authors [13].

Unfortunately, we have not found the literature regarding the effectiveness of the influence of amoxicillin, metronidazole and tetracycline under monotherapy for the protective mucus barrier of gastro duodenal area.

Our results on the effect of antibiotics on the state of the enzymes MOS faithfully confirm the special role of this system in the synthesis of mucosal barrier and suggests that one of the reasons for the negative effect of metronidazole and furazolidone on the synthesis of gastric mucosal barrier is their inhibitory effect on the enzymes of the MOS.

We set up that amoxicillin and tetracycline do not affect the activity of enzymes MOS, which is consistent with the data by Yakubov A.V. [21].

Conclusions

1. Antibacterial drugs have a multidirectional effect on the state of the gastric mucosal barrier. Metronidazole and furazolidone suppress, yet tetracycline, and amoxicillin have no effect on the synthesis of mucosal barrier.

2. One of the reasons of this is the inhibitory effect of metronidazole and furazolidone on the enzyme activity of the MOS. Tetracycline, and amoxicillin have no effect on the enzyme activity of the MOS.

References

1. Losev I.A., Kuznetsova I.N. Influence holenopotentsiruyuschih funds for repair processes in the injured gastric mucosa in rats // Exper. and clinical. pharmokol. – Moscow, 1992. – № 5. – P. 15–17.

2. Linevik L.I. Sialic acids // Success of biological chemistry. – M., 1962. – Vol. 4. – P. 199.

3. Rabinovich P.D., Lilyushkin P.V. Biological oxidation and the basic functions of the stomach in patients with peptic ulcer // Therapist archive. – 1979. – № 11. – P. 103–105.

4. Popov R. Determinations on pirmidonovat N-demethylase in cherniyadrobnaplhove // Exper. med. – 1973. – Vol. 12. – № 3. – P. 130–135.

5. Williams C.H., Kamin H. Microsomal triphosphopyridine nucleotide – cetochrome – reductase of liver // J. Biol. Chem. – 1951. – P. 587–237–595.

6. Belov I.M., Belova O.L. Pharmacotherapeutic efficacy of antisecretory and eradication schemes in the treatment of peptic ulcer disease, associated with Helicobacter pylori // Clinical Pharmacology in Russia: achievements and prospects. Proceedings of the conference.Moscow, 2004, 9–10 September. – P. 23–25.

7. Canons A.V., Brain S.I., Lizvan M.A. etc. The morphology of the surface and atrophic gastritis with eradication Helicobacter pylori // Archives of Pathology. – Moscow, 2005. – № 3, Vol. 67. – P. 17–20.

8. Cooke C.E., Sklar G.E., Nappi J.M. Possible pharmacokinetic interaction with guanidine: ciprofloxacin or metronidazole? // Ann. Pharmacother. – 1996. – Apr; Vol. 30 (4). – P. 364–366.

9. Yakubov A.V., Pattahova M.H. The influence of the components and some schemes antiulcer therapy on the content and the enzyme activity of the monooxygenase system in the mucosal tissue of the stomach in experimental ulcer // Medicines case. Medical business. – Kiev, 2009. – № 3–4. – P. 86–90.