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FEATURES OF CHANGES IN THE GASTRIC MUCOSAL PROTECTIVE BARRIER DURING COMBINED ADMINISTRATION OF INDOMETHACIN WITH ENALAPRIL, OMEPRAZOLE, AND FAMOTIDINE

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D.Z. Abdusamatova
Tashkent State Medical University, Department of Clinical Pharmacology

Abstract

As is well known, the relationship between the acid-peptic factor and the condition of the gastric protective barrier plays a crucial role in the mechanisms of damage to the gastroduodenal mucosa. It has been established that NSAID-induced gastropathies are invariably accompanied by increased acid-peptic aggression and impaired protective properties of the gastroduodenal mucosal barrier. Therefore, the treatment of NSAID-induced gastropathies should be aimed both at suppressing acid-peptic aggression and at stimulating protective mechanisms. Unfortunately, the issue of enhancing the protective properties of the mucosal barrier remains unresolved. The use of synthetic prostaglandins for this purpose is still insufficiently studied, while their high cost and frequent adverse effects often limit their clinical application. Considerable progress has been achieved in suppressing acid-peptic aggression through the use of H2-histamine receptor antagonists and proton pump inhibitors. However, their efficacy has mainly been investigated from the standpoint of acid suppression, whereas their effects on the gastric mucosal protective barrier remain inadequately studied.

In view of the above, the aim of the present study was to investigate the characteristics of changes in the gastric mucosal protective barrier during the combined administration of indomethacin with enalapril, omeprazole, and famotidine.

Materials and Methods

Experimental studies were performed on 42 adult male albino rats of mixed strain weighing 150–200 g. The animals were divided into seven groups:

1. Intact healthy controls;
2. Indomethacin (2.5 mg/kg);
3. Indomethacin + enalapril (10 mg/kg);
4. Indomethacin + omeprazole (50 mg/kg);
5. Indomethacin + famotidine (100 mg/kg);

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6. Indomethacin + enalapril + omeprazole (same doses);
7. Indomethacin + enalapril + famotidine (same doses).

Each group consisted of six animals. All drugs were administered orally (*per os*) for 10 consecutive days. The condition of the gastric mucosal barrier was evaluated by determining carbohydrate and protein fractions of insoluble glycoproteins (IGPs). Sialic acid content was measured using the method of L.I. Linevik; fucose content was determined according to the method proposed by P.D. Rabinovich et al.; hexose content was assessed using the method of A. Gottschalk; and total protein content was determined according to the method of O.H. Lowry et al.

Results and Discussion

The results of the study investigating the effects of enalapril, omeprazole, famotidine, and their combinations on the content of insoluble glycoprotein fractions in the gastric mucosa of rats treated with indomethacin are presented in Table 1.

Table 1.

Effects of Enalapril, Omeprazole, Famotidine, and Their Combinations on Insoluble Glycoprotein Fractions in the Gastric Mucosa of Rats Receiving Indomethacin

Experimental Groups	Sialic Acids (μg/mL suspension)	Fucose (mg/mL suspension)	Hexoses (μg/mL suspension)	Total Protein (mg/mL suspension)
1. Intact control	2.56 ± 0.153	4.38 ± 0.223	30.22 ± 1.37	11.69 ± 0.882
2. Indomethacin	1.08 ± 0.076	2.09 ± 0.142	28.58 ± 1.62	10.58 ± 0.802
3. Indomethacin + Enalapril	2.11 ± 0.115*	3.76 ± 0.176*	28.38 ± 1.72	11.41 ± 0.985
4. Indomethacin + Omeprazole	0.931 ± 0.075	1.43 ± 0.136*	24.13 ± 1.84	8.76 ± 0.801
5. Indomethacin + Famotidine	1.96 ± 0.163*	3.56 ± 0.246*	28.43 ± 2.59	11.02 ± 0.898
6. Indomethacin + Enalapril + Omeprazole	1.62 ± 0.16*a	2.68 ± 0.318a	25.01 ± 1.29	10.08 ± 0.768
7. Indomethacin + Enalapril + Famotidine	2.42 ± 0.126	3.94 ± 0.125*	31.06 ± 1.56	10.49 ± 0.852

Note:

- $p < 0.05$ vs. the indomethacin group;
- a – $p < 0.05$ vs. the enalapril group.

As shown in the table, enalapril stimulated the synthesis of insoluble glycoproteins. In this group, the content of sialic acids increased by 95.3%, while fucose levels increased by 79.9% compared with the indomethacin monotherapy group.

Omeprazole inhibited the synthesis of insoluble glycoproteins. A tendency toward decreased levels of sialic acids, hexoses, and total protein was observed. The reduction in fucose content reached statistical significance, amounting to 31.6%.

Famotidine demonstrated a stimulatory effect on insoluble glycoprotein synthesis. Treatment resulted in an 81.5% increase in sialic acid content and a 70.3% increase in fucose levels.

The combined administration of enalapril and omeprazole appeared to be inappropriate. Although increases in sialic acid and fucose levels were observed, these values were significantly lower than those recorded in animals treated with enalapril alone.

The most favorable results were obtained with the combination of enalapril and famotidine. In this group, the stimulatory effects on sialic acid and fucose content were preserved.

It is well established that sialic acids and fucose play a critical role in the proper functioning of insoluble glycoproteins. These carbohydrate components provide elasticity and viscosity to the mucosal barrier. The findings obtained in the indomethacin-treated group suggest that gastric mucosal barrier injury develops as a consequence of reduced insoluble glycoprotein synthesis and functional insufficiency associated with alterations in their rheological properties. According to the literature, the detrimental effect of indomethacin on the mucosal barrier is primarily attributed to cyclooxygenase (COX) inhibition, suppression of prostaglandin synthesis, and subsequent impairment of microcirculation. We believe that this mechanism is not the only one involved. One possible additional mechanism may be dysfunction of the L-arginine–nitric oxide (NO) regulatory system, which serves as a universal trigger for interconnected pathogenetic pathways leading to cellular injury.

With regard to enalapril, the literature provides convincing evidence of its ulcer-healing effects. These effects are generally attributed to stimulation of prostaglandin synthesis. We suggest that this represents only one of the mechanisms underlying its beneficial action, which may also result from its corrective influence on the NO-generating system.

According to Yakubov A.V., triple therapy consisting of omeprazole, metronidazole, and clarithromycin significantly reduces the content of insoluble

glycoproteins in the gastric mucosa of animals with experimental ulcers. The author suggested that this adverse effect is associated with the inhibitory actions of omeprazole and clarithromycin. Our findings regarding the effects of omeprazole on insoluble glycoprotein synthesis are consistent with these observations. We believe that the therapeutic efficacy of proton pump inhibitors, including omeprazole, in peptic ulcer disease is largely attributable to suppression of acid-peptic aggression. This may explain the contradictory reports concerning the efficacy of omeprazole in NSAID-induced gastropathy.

Our study demonstrated a stimulatory effect of famotidine on insoluble glycoprotein synthesis, despite its weaker antisecretory activity compared with omeprazole. Considering that, unlike peptic ulcer disease, NSAID-induced gastropathy may develop independently of pronounced acid-peptic aggression, this effect may be regarded as particularly valuable. Other investigators have also reported beneficial effects of famotidine on the gastric mucosal barrier. Jia X. et al. found that the H2-histamine receptor antagonist famotidine alters the composition of gastric mucus. Similar conclusions have been reported by H.T. Debas and colleagues. These authors suggest that the cytoprotective effect of famotidine is associated with improved mucosal microcirculation.

Conclusions

1. One of the mechanisms underlying indomethacin-induced gastric mucosal injury is disruption of the qualitative composition of insoluble glycoproteins within the mucosal barrier, accompanied by decreased levels of sialic acids and fucose.

2. The preventive efficacy of enalapril and famotidine is associated with stimulation of insoluble glycoprotein synthesis and improvement of their qualitative composition. In contrast, omeprazole suppresses insoluble glycoprotein synthesis. For correction of gastric mucosal barrier synthesis disorders in indomethacin-induced gastropathy, the combined use of enalapril and famotidine appears to be the most effective therapeutic approach.

REFERENCES:

1. Lowry O.H., Rosebrough N.J., Farr A.L., Randall R.J. Protein measurement with the folin phenol reagent. J Biol Chem. 1951;193(1):265–275.

2. Gottschalk A. Glycoproteins. Amsterdam: Elsevier; 1969. P. 228–331.

3. Linevik L.I. Advances in Biological Chemistry. Moscow; 1962. Vol. 4. 193 p.

4. Rabinovich P.D., Milyushkin P.V. Biological oxidation and basic gastric functions in peptic ulcer disease. Terapevticheskii Arkhiv. 1979;(11):103–105.

5. Vatier J., Poitevin C., Mignoum K. Sialic acid as a marker of gastric mucus glycoprotein proteolysis. Gastroenterol Clin Biol. 1985;9(12):108–110.

6. Khamraev A.A. Helicobacter pylori infection and gastric mucosal barrier protection. Doctoral dissertation. Tashkent; 2005.

7. Yakubov A.V., Khamraev A.A. Influence of triple therapy on insoluble gastric glycoproteins. Conference proceedings. Tashkent; 2005:218–219.

8. Lazebnik L.B., et al. NSAID-induced gastroenteropathies: prevention and treatment guidelines. Experimental and Clinical Gastroenterology. 2024;235(3):7–32.

9. Bakulin I.G., et al. Rebamipide: thirty years of clinical use. Terapevticheskii Arkhiv. 2024;96(12):1217–1222.

10. Jia X., He Y., Li L., Xu D. Pharmacological targeting of gastric mucosal barrier. Frontiers in Pharmacology. 2023;14:1091530.

11. Yamate S., et al. Continuous co-prescription of rebamipide prevents upper gastrointestinal bleeding in NSAID users. PLOS ONE. 2024.

12. Garegnani L., et al. Proton pump inhibitors for prevention of NSAID-induced ulcers. Cochrane Database Syst Rev. 2025;5: CD014585.