

Comparative Study of the Influence of Lesbochole, Misoprostol and Mucagen on the Gastric Mucous Barrier in Indometacin Gastropathy

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Abstract In an experiment in order to establish the mechanism of the gastroprotective action of Lesbochol, its effect on the content of the main components of the gastric mucosal barrier in gastropathy induced by indomethacin was studied. It has been established that the formation of gastropathy under the influence of indomethacin is accompanied by a decrease in protective mechanisms manifested in a decrease in insoluble glycoproteins. The cytoprotectors misoprostol and mukagen have a stimulating effect on the content of glycoproteins in the gastric mucosal barrier. Lesbochol has the same type of stimulatory effect as misoprostol and mucogen, and in terms of its pharmacological activity, it is similar to misoprostol and does not yield to mucogen.

Keywords Gastropathy, Gastric mucosal barrier, Gastroprotectors, Soluble and insoluble glycoproteins

1. Introduction

Treatment of gastropathy of various origins, as well as peptic ulcer (PU) of the stomach, despite the development and implementation of new drugs and treatment regimens, is one of the urgent problems, the significance of which is determined by the frequent development of this pathology, the resulting complications and, first of all, gastric bleeding peritonitis, sometimes with a fatal outcome [1,2,3].

The solution to this problem is largely determined by the assessment of the state and elimination of violations of the relationship between the aggressive and protective factors in the gastric mucosa [4,5].

It is considered important to additionally use drugs together with proton pump inhibitors to protect the gastric mucosa with a different mechanism of action, aimed at increasing the resistance of the mucosa to adverse effects [6]. In this regard, a new compound is of particular interest, which is a mixture of extracts of medicinal plants *Hypericum scabrum*, *Ziziphora pedicellata*, *Mediasia macrophylla*, *Glycyrrhiza glabra* conditionally called "Lesbochol", since it has a distinct effect in the prevention of gastropathy induced by indomethacin, alcohol and stress [7,8,9]. Although Lesbochol quite clearly suppresses the development of

gastropathy when exposed to pathogenic factors, its cytoprotective properties remain unexplored. This template, created in MS Word 2003 and saved as "Word 2003 – doc" for the PC, provides authors with most of the formatting specifications needed for preparing electronic versions of their papers. All standard paper components have been specified for three reasons: 1) ease of use when formatting individual papers, 2) automatic compliance to electronic requirements that facilitate the concurrent or later production of electronic products, and 3) Margins, column widths, line spacing, and type styles are built-in; examples of the type styles are provided throughout this document. Some components, such as multi-leveled equations, graphics, and tables are not prescribed, although the various table text styles are provided. The formatter will need to create these components, incorporating the applicable criteria that follow. Use the styles, fonts and point sizes as defined in this template, but do not change or redefine them in any way as this will lead to unpredictable results. You will not need to remember shortcut keys. Just a mouse-click at one of the menu options will give you the style that you want.

2. Materials and Methods

Experimental studies were carried out on mature male rats with an initial weight of 165-185 g. Five groups of animals were composed, six in each. One day and 2 hours before the reproduction of the gastropathy model, the ani-

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mals of the first, second and third groups were intragastrically injected with drugs in doses: Misoprostol - 0.2 mg/kg, Lesbochol - 50 mg/kg, Mucogen (rebamipide) - 100 mg/kg, and the fourth equivolume amount of water (control). The fifth group consisted of healthy animals and served as a control to all the rest (intact). The destruction of the gastric mucosa was reproduced by a single intragastric administration of a non-steroidal anti-inflammatory drug (NSAID) - indomethacin at a dose of 60 mg/kg in saline [10,11]. When playing "indomethacin" ulcers, rats were deprived of food 24 hours before exposure to the ulcerogen.

We studied the content of soluble and insoluble glycoproteins, as well as protein in the gastric mucosa. The content of glycoproteins was estimated by the content of its main components - fucose, hexose and total protein [12]. For biochemical studies, 24 hours after the administration of indomethacin, animals under light ether anesthesia were forgotten by simultaneous decapitation. The stomach was removed, cleaned, washed with cold saline, removing the proventriculus, weighed, then the mucous layer was scraped off, weighed and suspended in distilled water in a porcelain mortar at a rate of 30 mg/ml.

The content of fucose (6-deoxyhexose) in the suspension of the gastric mucosa was determined by the method of P.D. Rabinovich [13]. The method is based on obtaining furfural and its derivatives (methyl-4-hydroxymethylfurfural) from sugars by boiling in a solution of concentrated sulfuric acid. The results were expressed in mg/ml suspension.

The content of hexoses was determined by the method of Gottschalk [14]. When determining hexoses, the total number of hexoses associated with the protein is determined. The method is based on the interaction of nitrogen-free sugars with orcin and sulfuric acid to form a pink color. The optical density of the samples was measured on a spectrophotometer at a wavelength of 560 nm. The results were expressed in $\mu\text{g/ml}$ suspension.

The total protein content was determined spectrophotometrically (reagent kits from CYPRESS Diagnostics, Belgium) on a BA-88A biochemical analyzer (Mindray, Chi-na).

The results of the studies were subjected to statistical

processing using the Biostat 2009 software package with an assessment of the significance of the characteristics $M \pm m$ and differences in the considered samples according to the Student's t-test. Differences in the compared groups were considered significant at a significance level of 95% ($p < 0.05$).

3. Results and Discussion

The results of experimental studies have shown that under the influence of indomethacin there are distinct changes in the content of the main components of the mucous barrier. So, in control animals in the suspension of the stomach, compared with healthy ones, the content of soluble fucose is reduced by 19.5%, and hexose - by 53.3%. Since the components of the mucosal barrier are glycoproteins, it was of great interest to study the content of total protein. Studies of the content of the latter showed that in control, compared with healthy rats, its content is reduced by 33.0%.

Therefore, indomethacin damage to the stomach in white rats is accompanied by a significant change in the level of fucose, hexose and protein, which is the pathogenetic basis for damage to the gastric mucosa (GM) in this type of gastropathy. This conclusion is also confirmed by the results of the study of these components of the gastric mucosal barrier in the insoluble fraction of the gastric mucosa. As shown, the results of the study of the content of fucose and hexose in the latter are reduced by 26.0 and 47.3%, respectively.

Thus, gastropathy induced by indomethacin is accompanied by a decrease in the content of fucose, hexose and protein in both soluble and insoluble fractions of gastric mucosa homogenates, which is one of the important links in the pathogenesis of the development of destructive changes in the gastric mucosa indicated by NSAIDs.

Prostaglandins, including misoprostol, have a pronounced gastroprotective activity [15,16]. Indeed, the data in Table 1 shows that the preventive use of misoprostol leads to a decrease in the damaging effect of indomethacin, which manifests itself in a decrease in the degree of fucose and hexose deficiency not only in the soluble fraction, but also in the insoluble fraction of the gastric mucosa.

Table 1. Study of the effect of mesoprostol, mucogen and lesbochol on the content of glycoproteins and total protein in the gastric mucosa of rats with indomethacin damage ($M \pm m$, $n=6$)

Performance Groups	Soluble glycoproteins		Insoluble glycoproteins		Total protein (mg/ml)
	Fucose, Mg/g tissue	Hexose, $\mu\text{g/g}$ tissue	Fucose, Mg/g tissue	Hexose, $\mu\text{g/g}$ tissue	
Intact	13,76 \pm 0,38	99,18 \pm 6,06	4,16 \pm 0,12	4,16 \pm 0,12	91,33 \pm 2,83
Control	11,07 \pm 0,26*	46,28 \pm 3,80*	3,08 \pm 0,15*	3,08 \pm 0,15*	61,18 \pm 4,38*
Misoprostol + indomethacin	11,98 \pm 0,97	64,80 \pm 4,81*#	3,35 \pm 0,23	3,35 \pm 0,23	70,43 \pm 3,29*
Mucogen + indomethacin	18,05 \pm 1,21*#	89,87 \pm 6,84#	3,82 \pm 0,17#	3,82 \pm 0,17#	83,81 \pm 5,63#
Lesbochol + Indomethacin	17,51 \pm 1,50#	87,25 \pm 6,36#	3,77 \pm 0,26	3,77 \pm 0,26	76,68 \pm 4,69*

Note: * - significant difference in relation to intact, # - significant difference in relation to control animals ($P < 0.05$).

In comparison with this, we noted a higher degree of changes in the group of animals treated with mucogen. Thus, the level of fucose in the soluble fraction increased by 63.0% compared to the control, and hexose by 94.2%. We revealed somewhat less pronounced changes in the insoluble fraction: the content of fucose increased by 24.0%, and hexose - by 37.7%. It is noteworthy that such an effect of mucogen was accompanied by an increase in total protein by 36.9%, which once again confirms the glycoprotein nature of the mucous barrier components. From the data of Table 1, it can be seen that in animals treated with Lesbochol, the studied indicators of the mucous barrier increase compared with the control, not inferior in value to the data of the group of animals treated with mucogen. So, in the soluble fraction of glycoproteins, the content of fucose and hexose increased by 58.2 and 88.5%, and in the insoluble fraction: by 22.4 and 34.8%, respectively, compared with the control. It should be noted that there were no statistically significant differences compared with the group of animals treated with Lesbochol and mucogen, which allows us to consider their pharmacological activity equivalent in correcting violations of the mucous barrier components in destructive erosive damage to the gastric mucosa induced by indomethacin. In our opinion, these data most likely indicate the main pathogenetic links of the gastroprotective action of the studied drugs. In terms of their pharmacological activity, the latter can be put in the following order to increase their activity: mucogen > lesbochol > misoprostol.

4. Conclusions

1. The formation of gastropathy under the influence of indomethacin is accompanied by a decrease in protective mechanisms manifested in a decrease in insoluble glycoproteins.
2. Cytoprotectors misoprostol and mukagen have a stimulating effect on the content of glycoproteins of the gastric mucosal barrier.
3. Lesbochol has the same type of stimulant effect as misoprostol and mucogen, and in terms of its pharmacological activity, it is similar to misoprostol and does not yield to mucogen.

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