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**ORIGINAL ARTICLE** **OPEN ACCESS**

# Oxidative Stress and Anaerobic Glycolysis Status in Gastric Mucosa during Treatment of Experimental Ulcer with Second-Line Three-Component Regimens

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**ABSTRACT**

*The objective of this study was to examine the state of oxidative stress and anaerobic glycolysis in the gastric mucosa during the treatment of experimental ulcers with second-line three-component regimens. In studied the effect of triple therapy with omeprazole, amoxicillin, furazolidone found that, these drugs increase the processes of anaerobic glycolysis, indicating a worsening microcirculatory disorder in the mucosal tissue of the stomach. As a result of the effect of accelerating the rate of lipid peroxidation. In terms of correction of the broken process of anaerobic glycolysis and lipid peroxidation appropriate to use triple therapy with omeprazole, amoxicillin, tetracycline in the treatment of peptic ulcer.*
*Key words: experimental ulcer, lipid peroxidation, anaerobic glycolysis, treatment.*

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## INTRODUCTION

*Helicobacter pylori* infection is widely recognized as the primary cause of gastric ulcers. However, the pathogenesis of ulcers is multifaceted, necessitating the exploration of additional factors contributing to mucosal damage. Alterations in microcirculation and hypoxia in the gastric and duodenal mucosa have been identified as significant factors exacerbating peroxidation processes in cellular and subcellular structures. Consequently, these events may lead to compromised resilience of the gastro-duodenal mucosa. While some research has focused on the effects of first-line therapeutic regimens on peroxidation and anaerobic glycolysis, the influence of second-line regimens remains inadequately understood [10]. Consequently, investigating the impact of second-line anti-Helicobacter therapy on oxidative stress levels is of particular interest.

The objective of this study was to examine the state of oxidative stress and anaerobic glycolysis in the gastric mucosa during the treatment of experimental ulcers with second-line three-component regimens.

## Material and Methods

Experimental Design and Animal Subjects: The study was conducted on 30 male white rats of a mixed population, with body weights ranging from 150 to 190 grams. The experimental ulcer model (EU) was induced using the V.A. Vertelkin method, as modified by I.A. Losev et al. [5]. The animals were divided into five groups, each comprising 6 rats: Group 1 - intact group without ulcer induction; Group 2 - rats with experimental ulcers; Group 3 - EU + H2O (untreated); Group 4 - EU + omeprazole + amoxicillin + tetracycline; Group 5 - EU + omeprazole + amoxicillin + furazolidone. The selected medications were administered orally as aqueous suspensions over 10 days. The triple therapy regimens were recommended by the Fourth Moscow Agreement, adopted by the X Congress of Gastroenterologists on March 5, 2010 [6].

Assessment of Lipid Peroxidation: The status of lipid peroxidation in the gastric mucosa was evaluated by determining the content of malondialdehyde (MDA) and the rate of peroxidation of lipids (POL). The content of MDA in the supernatant of the mucosal suspension was determined using the method described by L.I. Andreeva et al. [1]. The rate of initiated lipid peroxidation in membrane microsomal fraction suspensions was determined using the method developed by Yu.A. Vladimirov and A.I. Archakov [2].

Evaluation of Anaerobic Glycolysis: The status of anaerobic glycolysis was assessed by measuring the content of lactic acid, determined using the method described by I.S. Balokhovsky *et al*. [3].

## RESULTS AND DISCUSSION

As shown by our studies, with an experimental ulcer, the intensity of LPO processes increases significantly (Table). A decrease in the LPO rate was observed, which was accompanied by the accumulation of the final product, MDA. The content of MDA increased by 92.5%, NADPH-dependent LPO increased by 121.8%, and lactic acid increased by 2.5 times. In animals without treatment, the content of products and the rate of lipid peroxidation remained almost unchanged, and the content of lactic acid decreased insignificantly (>0.05).

A prooxidant effect was observed during triple therapy with omeprazole, amoxicillin, and furazolidone. The increase in the content of MDA and the rate of NADPH and ascorbate-dependent LPO in this group was significantly higher than in the group without treatment. In this group, the content of lactic acid significantly increased by 27.9%.

Triple therapy consisting of omeprazole, amoxicillin, and tetracycline had an antioxidant effect. In this group, the content of MDA significantly decreased by 27.9%, the rate of NADPH-dependent LPO decreased by 27.3%, ascorbate-dependent by 21.5%, and lactic acid decreased by 25.7%.

Our conducted research revealed notable insights regarding the impact of experimental ulcers on the intensity of peroxidation processes (Table). We observed a reduction in the rate of peroxidation of lipids (POL), accompanied by the accumulation of the end product, malondialdehyde (MDA). Specifically, MDA content increased by 92.5%, NADPH-dependent POL increased by 121.8%, and lactic acid increased by 2.5-fold. In the untreated group, the content of peroxidation products and the rate of POL remained largely unchanged, while lactic acid content decreased insignificantly (>0.05).

A pro-oxidant effect was observed with triple therapy involving omeprazole, amoxicillin, and furazolidone. The elevation in MDA content and the rates of NADPH and ascorbate-dependent POL in this group were significantly higher compared to the untreated group. Additionally, lactic acid content increased by 27.9% in this group.

Conversely, the triple therapy regimen comprising omeprazole, amoxicillin, and tetracycline exhibited an antioxidant effect. In this group, MDA content significantly decreased by 27.9%, NADPH-dependent POL reduced by 27.3%, ascorbate-dependent POL decreased by 21.5%, and lactic acid content diminished by 25.7%.

These findings underscore the complex interplay between oxidative stress and the chosen therapeutic interventions. The pro-oxidant effects observed in the group receiving furazolidone-containing therapy may be attributed to the intricate interactions between the therapeutic agents, possibly leading to increased oxidative stress markers. On the other hand, the observed reduction in oxidative stress markers in the group treated with omeprazole, amoxicillin, and tetracycline signifies their potential antioxidant properties. These effects might arise from the individual or synergistic actions of these agents on the redox balance within the gastric mucosa.

**Table 1: Influence of Standard Second-Line Therapy Regimens on Peroxidation of Lipids (POL) Indices and Lactic Acid Content in Gastric Mucosal Tissue.**

| Groupings of Animals | Peroxidation of Lipids (POL) Products and Rate | | | Lactic acid nmol/mg protein |
|---|---|---|---|---|
| | MDA nmol/min/mg | NADPH-Dependent POL nmol/min/mg | Ascorbate-Dependent POL nmol/min/mg | |
| 1. Intact Group | 1,74±0,06 | 0,64±0,02 | 0,52±0,04 | 0,114±0,01 |
| 2. EU | 3,35±0,15 * | 1,42±0,10 * | 1,18±0,10 * | 0,285±0,013* |
| 3. EU + $H_2O$ | 3,12±0,12 | 1,36±0,06 | 1,21±0,08 | 0,269±0,013 |
| 4. EU+O+A+T | 2,25±0,09* | 0,99±0,05* | 0,95±0,04* | 6,19±0,29* |
| 5. EU+O+A+F | 3,92±0,06* | 1,78±0,05* | 1,72±0,04* | 2,64±0,19* |

Note: @ p<0.05 of the no-treatment group

O-omeprazole, A-amoxicillin, T-tetracycline, F-furazolidone.

In our investigations, a pronounced pro-oxidant effect was observed with the therapy regimen consisting of omeprazole, amoxicillin, and furazolidone. This effect is likely attributed to the action of furazolidone. P.G. Starozhuk *et al*. [7] reported that furazolidone exerts inhibitory effects on the activity of antioxidant enzymes, which detrimentally impacts the elimination of reactive oxygen species.

The antioxidant effect of the triple therapy with omeprazole, amoxicillin, and tetracycline is presumably due to the inertness of these components on microcirculation and consequently on anaerobic glycolysis processes. This assumption is supported by the results of studies by E.V. Zhuravel [4], who, when investigating the impact of tetracycline and amoxicillin on lipid peroxidation in the liver, found that these drugs do not affect the content of malondialdehyde at therapeutic doses.

## CONCLUSION

In conclusion, our study highlights the dynamic relationship between oxidative stress and different therapeutic regimens in the context of experimental ulcers. The observed pro-oxidant and antioxidant effects of specific triple therapy combinations emphasize the necessity of tailoring therapeutic approaches to mitigate oxidative damage while considering the intricate mechanisms underlying these interactions. Further studies are warranted to elucidate the exact mechanisms through which these therapeutic agents modulate oxidative stress pathways and to determine the most efficacious treatment strategies for managing experimental ulcers.

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