

## THE EFFECTIVENESS OF THE USE OF MACROLIDE ANTIBIOTIC IN INFECTIOUS DISEASES

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### ABSTRACT

Modern principles of treatment involve the frequent use of antibiotics in infectious diseases. One of the most considered antibiotics is the macrolide group. It is these drugs that have relatively few side effects, while at the same time preventing the development of a significant number of dangerous microorganisms and intracellular parasites. A significant disadvantage of macrolide antibiotics is the resistance to their action by many bacteria. This article investigates the preventive effectiveness of three types of macrolide antibiotics in infectious diseases and dysbiosis in the example of laboratory animals. Observations were carried out on four similar groups of laboratory animals, which received erythromycin, azithromycin, and midecamycin as prophylactic drugs. The fourth group was a control group that did not receive any treatment. According to the results of the study, a conclusion was made about the effectiveness of the drugs used. In infectious diseases, the final effectiveness of erythromycin was 60%, azithromycin - 80%, and midecamycin - 55%. In dysbiosis, the efficacy of erythromycin and azithromycin was 100%, and of midecamycin - 90%. The use of macrolide antibiotics for preventive purposes also significantly reduced mortality rates, which in the control were 35% for infectious diseases and 10% for dysbiosis.

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### Introduction

Macrolide antibacterial drugs are one of the safest groups of antibiotics [1-4]. They have a bacteriostatic effect, that is, they do not kill the bacteria themselves, but prevent their reproduction [5]. The human body, which does not have serious diseases, can deal with them by itself. Therefore, these drugs have relatively few side effects. Macrolide antibiotics act mainly on streptococci and staphylococci, but also cope well with intracellular parasites such as chlamydia, mycoplasma, legionella, etc. [6-8].

The first drug from this group, which was synthesized in 1952, was named erythromycin [9]. Now many bacteria are insensitive to it, so it is impractical to take it in the form of tablets [10]. However, it has a good effect when applied topically, for example, as erythromycin ointment [11].

The most commonly used macrolide drugs include:

14-membered: erythromycin, clarithromycin, roxithromycin

15-membered (azalides): azithromycin

16-membered: spiramycin, josamycin, midecamycin.

Macrolide antibiotics are used to treat bacterial infections of the respiratory tract, ENT organs, skin and soft tissues, genital area, kidneys, and urinary system [12-14]. Simply put, the indications for the use of these antibiotics are the same as for

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antibacterial drugs of the penicillin group [15]. And therefore they are most often used in those patients who, for one reason or another, cannot be treated with other forms of treatment (most often due to allergic reactions). Macrolides are much less likely to cause intolerance than other antibiotics [11]. They do not have a harmful effect on the liver, kidneys, and nervous system, and do not cause photosensitization. However, like all antibacterial agents, they can affect the microflora, causing various dyspeptic disorders and candidiasis [16]. It is also worth noting the recently growing resistance to antibiotics of this group in Russia [17, 18]. This can be explained by the widespread use of these drugs, also in the form of self-medication.

#### *Erythromycin*

A bacteriostatic antibiotic from the group of macrolides reversibly binds to the 50S subunit of ribosomes, which disrupts the formation of peptide bonds between amino acid molecules and blocks the synthesis of proteins of microorganisms (does not affect the synthesis of nucleic acids). When used in high doses, depending on the type of pathogen, it may exhibit a bactericidal effect.

Sensitive microorganisms include those whose growth is delayed at an antibiotic concentration of less than 0.5 mg/l, moderately sensitive – 1-6 mg/l, and resistant – 6-8 mg/l [19, 20].

The spectrum of action includes:

Gram-positive microorganisms: *Staphylococcus* spp., producing and not producing penicillinase, including *Staphylococcus aureus*; *Streptococcus* spp. (including *Streptococcus pneumoniae*, *Streptococcus pyogenes*), alpha-hemolytic streptococcus (Viridans group), *Bacillus anthracis*, *Corynebacterium diphtheriae*, *Corynebacterium minutissimum*;

Gram-negative microorganisms: *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Campylobacter jejuni*, *Bordetella pertussis*. *Brucella* spp., *Legionella* spp. including *Legionella pneumophila* and other microorganisms: *Mycoplasma* spp. (including *Mycoplasma pneumoniae*), *Chlamydia* spp. (including *Chlamydia trachomatis*), *Treponema* spp., *Rickettsia* spp., *Entamoeba histolytica*, *Listeria monocytogenes*. Gram-negative rods are resistant to the drug: *Escherichia coli*, *Pseudomonas aeruginosa*, as well as *Shigella* spp., *Salmonella* spp., *Bacteroides fragilis*, *Enterobacter* spp., etc. [21].

The maximum concentration is attained 20 minutes after intravenous administration. The bond with plasma proteins is 70-90%. Bioavailability – 30-65%. It is distributed unevenly in the body. It accumulates in large quantities in the liver, spleen, and kidneys. It penetrates well into the tissues of the lungs, lymph nodes, middle ear exudate, prostate secret, semen, pleural cavity, and ascitic and synovial fluids [22]. It penetrates poorly through the blood-brain barrier, into the cerebrospinal fluid (the concentration is 10% of the concentration of the drug in blood plasma). Inflammatory processes of the brain increases the permeability of in the brain membranes to erythromycin [23].

#### *Azithromycin*

Azithromycin is a broad-spectrum bacteriostatic antibiotic from the group of azalide macrolides. It has a wide spectrum of antimicrobial action. The mechanism of action of azithromycin is associated with the suppression of microbial cell protein synthesis. Binding to the 50S subunit of the ribosome, it inhibits peptidyltransferase at the translation stage and suppresses protein synthesis, slowing down the growth and reproduction of bacteria. In high concentrations, it has a bactericidal effect.

It has activity against several gram-positive, gram-negative, anaerobic, intracellular, and other microorganisms [24]. Microorganisms may initially be resistant to the action of an antibiotic or may acquire resistance to it [25]. After oral administration, azithromycin is well absorbed and quickly distributed in the body. Penetrates through cell membranes (effective in infections caused by intracellular pathogens). It is transported by phagocytes to the site of infection, where it is released in the presence of bacteria [26].

It easily passes the histohematic barriers and enters tissues. The concentration in tissues and cells is 10-50 times higher than in plasma, and in the focus of infection – 24-34% more than in healthy tissues [27].

#### *Midecamycin*

Disrupts the synthesis of microbial proteins at the ribosome level by binding to the 50S subunit of bacterial ribosomes and inhibiting the translocation process. It penetrates cells and creates a high intracellular concentration [22].

It has a bacteriostatic effect, and in high concentration, it has a bactericidal effect against pathogens of diphtheria and whooping cough, as well as pneumococci [28].

It shows high activity against gram-positive cocci (staphylococci, streptococci).

Midekamycin also shows high activity against chlamydia, leptospira, treponema, mycoplasma, and toxoplasma [29].

## Materials and Methods

This scientific work investigates the effectiveness of the preventive action of various types of macrolide antibiotics on laboratory animals in infectious diseases and dysbiosis. In addition, a study of the long-term use of azithromycin on some blood parameters is being conducted.

To study the physiological and biochemical changes in the body of laboratory animals, blood was taken from blood vessels, in which the content of erythrocytes and leukocytes was examined on the Culter Count particle counter (France), hemoglobin was measured with a Sali hemometer, and the hemoglobin cyanide method, the complementary activity of blood serum was

calculated according to the generally accepted method [30-33]. To characterize the clinical condition of the animals, body temperature was measured (rectally), pulse and respiratory rate, and the nature of nasal secretions and feces were determined.

## Results and Discussion

### *Preventive Efficacy of Macrolide Antibiotics in Infectious Diseases*

80 piglets aged 2-3 months took part in the experiment. Before the experiment, the piglets were clinically healthy and had standard characteristics in weight and size. Piglets were divided into 4 groups of 20 individuals according to the principle of analogs. Group 1 received the drug erythromycin for the prevention of an infectious disease, group 2 received the drug azithromycin, group 3 received the drug midecamycin, and group 4 (control) did not receive any drug (**Table 1**).

It was found that the use of erythromycin prevented the occurrence of salmonellosis in 85% of cases, the occurrence of colibacteriosis – in 90% of cases, and the occurrence of pasteurellosis – in 70% of cases. The total effectiveness of the drug was 60%. The mortality rate was 5%.

**Table 1.** Comparative effectiveness of macrolide antibiotics in the prevention of infectious diseases

Animal groups	Group 1 (erythromycin)	Group 2 (azithromycin)	Group 3 (midecamycin)	Control
Number of animals at the beginning of the experiment	20	20	20	20
Average piglet body weight at the beginning of the experiment (kg)	15.4	16.2	15.2	15.8
Average piglet body weight at the end of the experiment (kg)	21.8	23.8	21.4	21.3
Average daily weight gain (g)	228	271	221	196
Got sick with <b>salmonellosis</b> , individuals	3	1	4	6
Got sick with salmonellosis, %	15	5	20	30
Died of salmonellosis, individuals	0	0	1	3
Died of salmonellosis, %	0	0	5	15
Got sick with <b>colibacteriosis</b> , individuals	2	2	3	6
Got sick with colibacteriosis, %	10	10	15	30
Died of colibacteriosis, individuals	0	0	0	2
Died of colibacteriosis, %	0	0	0	10
Got sick with <b>pasteurellosis</b> , individuals	6	3	4	8
Got sick with pasteurellosis, %	30	15	20	40
Died from pasteurellosis, individuals	1	0	1	2
Died from pasteurellosis, %	5	0	5	0
There are healthy animals left at the end of the experiment	12	16	11	3

The use of azithromycin prevented the occurrence of salmonellosis in 95% of cases, the occurrence of colibacteriosis – in 90% of cases, and the occurrence of pasteurellosis – in 85% of cases. The total effectiveness of the drug was 80%.

The use of midecamycin prevented the occurrence of salmonellosis in 80% of cases, the occurrence of colibacteriosis – in 85% of cases, and the occurrence of pasteurellosis – in 80% of cases. The total effectiveness of the drug was 55%. The mortality rate of piglets was 10%.

When no drugs were used during the epidemic of infectious diseases, only 15% of piglets remained uninfected. The mortality rate was 35%.

Morbidity and mortality of animals were taken into account for 28 days. Laboratory animals were examined and diagnosed with the disease. The results of the conducted studies indicate a relatively high efficacy of macrolide antibiotics (from 55 to 80%) with a morbidity rate of 85% in the control.

The results of the conducted studies indicate a relatively high preventive efficacy of azithromycin (80%) compared to erythromycin (60%) and midecamycin (55%).

### *Preventive Efficacy of Macrolide Antibiotics in Dysbiosis*

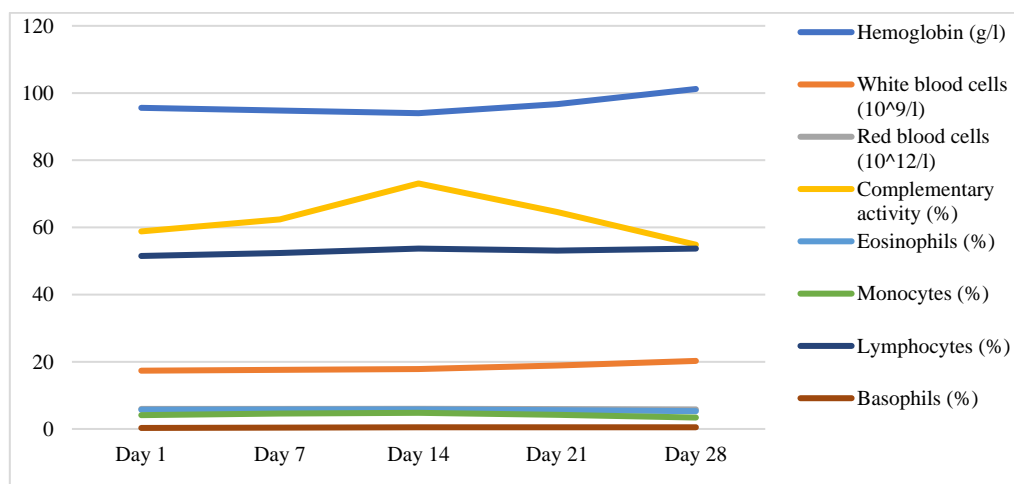
The preventive efficacy of macrolide antibiotics in dysbiosis was studied. 55 piglets aged 2-3 months took part in the experiment. Initially, the piglets were in a pen where dysbiosis developed. Dysbiotic piglets were isolated, and healthy-looking piglets were divided into 4 groups of 10 individuals according to the principle of analogs. Group 1 received erythromycin as a prophylaxis of dysbiosis, group 2 received azithromycin, group 3 received midecamycin, (all were single dosages) group 4 (control) did not receive any drug. The observation of piglets of the control and experimental groups lasted 3 weeks. The results obtained (**Table 2**) indicate a sufficiently high effectiveness of macrolide antibiotics in the prevention of dysbiosis.

**Table 2.** Results of the study of the effectiveness of macrolide antibiotics in dysbiosis

Animal groups	Group 1 (erythromycin)	Group 2 (azithromycin)	Group 3 (midecamycin)	Control
Number of animals at the beginning of the experiment	10	10	10	10
Got sick with dysbiosis, individuals	0	0	1	4
Got sick with dysbiosis, %	0	0	10	40
Died of dysbiosis, individuals	0	0	0	1
Died of dysbiosis, %	0	0	0	10

Out of 10 piglets in the control group, 4 piglets were infected with dysbiosis, and one of them died. When using a macrolide antibiotic, one piglet out of 30 was infected (who was given midecamycin). The effectiveness of erythromycin and azithromycin was 100%. The effectiveness of midecamycin was 90%. The mortality rate when using a macrolide antibiotic was 0%. Thus, a single injection of a macrolide antibiotic prevents the occurrence of dysbiosis if the disease is suspected.

*The effect of Long-Term Use of Macrolide Antibiotic on Blood Parameters*



**Figure 1.** The effect of long-term administration of azithromycin on the dynamics of piglet blood parameters

**Figure 1** shows the dynamics of some blood parameters of piglets who were given the drug azithromycin for a long time. Blood tests were performed on the 1st, 7th, 14th, 21<sup>st</sup>, and 28th days of the experiment. The results showed that by day 14, the animals had an increase in complementary activity and the number of red blood cells, and by day 28, hemoglobin. However, in general, all the studied indicators remained within the normal range.

**Conclusion**

The conducted studies have shown the high preventive efficacy of macrolide antibiotics in infectious diseases and dysbiosis. The most effective of the studied drugs is azithromycin. The use of azithromycin prevented the occurrence of salmonellosis in 95% of cases, the occurrence of colibacteriosis – in 90% of cases, and the occurrence of pasteurellosis – in 85% of cases. The final effectiveness of the drug in infectious diseases was 80%. The effectiveness of azithromycin in piglet dysbiosis was 100%. The mortality rate of laboratory animals was 0%.

The drug erythromycin proved to be less effective. The use of erythromycin prevented the occurrence of salmonellosis in 85% of cases, the occurrence of colibacteriosis – in 90% of cases, and the occurrence of pasteurellosis – in 70% of cases. The final effectiveness of erythromycin in infectious diseases was 60%. The mortality rate was 5%. The effectiveness of erythromycin in piglet dysbiosis was 100%.

The least effective of the studied drugs was midecamycin. The use of midecamycin prevented the occurrence of salmonellosis in 80% of cases, the occurrence of colibacteriosis – in 85% of cases, and the occurrence of pasteurellosis – in 80% of cases. The final effectiveness of midecamycin in infectious diseases was 55%. The mortality rate of piglets was 10%. The effectiveness of midecamycin in dysbiosis was 90%.

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**Ethics statement:** The protocol for experiments with laboratory animals complied with the requirements of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes.

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