Artykuł przeglądowy ***Review***

Problem of coccidiosis in broiler chickens and laying hens: Selected control methods and alternative solutions

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Summary

In industrial poultry production, especially in broiler chickens, coccidiosis, caused by *Eimeria* protozoa parasites in the digestive tract, continues to be a serious health and economic problem. In economic terms, the losses are mainly caused by the costs of prevention and treatment, as well as the reduced weight gain and reduced condition of the birds. Currently, the prophylactic program of this disease unit is mainly based on the use of chemotherapeutics. Another way to control coccidiosis is active immunoprophylaxis, based on the vaccination of chickens for fattening, and passive immunoprophylaxis, based on vaccination of the parent flock. An alternative, effective way to reduce the negative effects of protozoan infestation by *Eimeria* may be the use of herbs and their extracts, pre- and probiotics and betaine.

Keywords: broiler chickens, coccidiostats, immunoprophylaxis, herbs, pre- and probiotics

Coccidiosis is considered to be one of the most important diseases in poultry farming. The disease is a parasitosis caused by protozoa belonging to the genus *Eimeria* (*Phylum Apicomplexa*) parasitizing the gastrointestinal tract (24). Chickens (*Gallus gallus*) are exposed to invasion by seven species of coccidia: *E. acervulina*, *E. maxima*, *E. necatrix*, *E. tenella*, *E. brunetti*, *E. mitis* and *E. praecox*. The first five mentioned above are considered pathogenic species, while *E. mitis* and *E. praecox* are classified as non-pathogenic (25). However, numerous data indicate that these species significantly affect the profitability of breeding.

Lowering production economics is associated with a poorer feed conversion ratio, causing lower body weight gain. Coccidiosis may also occur in a clinical form with diarrhoea, often bloody, and increased animal mortality (5). One of the major problems of current poultry production is the relatively frequent occurrence of coccidiosis in the environment of birds. This disease worldwide annually generates losses of up to 3 billion dollars (9).

Pathogenesis and development cycle of coccidia

Pathogenic species of coccidia are characterized by high specificity in locations within the digestive tract of the host. *E. acervulina* colonizes in the duodenal area, *E. maxima* and *E. necatrix* parasitize in the small intestine, *E. brunetti* do so in the caecum and rectum, while *E. tenella* attacks the caecum (10). One of the main clinical symptoms of *E. tenella* infection is a change in the colour of the stool, which may initially be red or yellow, and subsequently dark-brown with often the addition of blood. Protozoa of this species cause several anatomopathological changes in the caecum, such as distension and haemorrhagic mucositis. In the case of infection with *E. brunetti* and *E. necatrix*, the stool becomes brown-pink or a brown liquid, foamy with high cohesiveness. The protozoa of *E. brunetti* cause inflammation of the large intestine, the steak, the initial segment of the caecum and the iliac intestine. Such inflammation is fibrinous (29). *E. necatrix* causes specific clinical symptoms such as intensive intestinal distension. Moreover, the intestine becomes raspberry or blue-red coloured. Additionally, necrotic-hemorrhagic inflammation of the mucosa of the small intestine is observed (14).

Eimeria protozoa are characterized by a single-host (monoxenic) development cycle. The parasitic form is oocysts, which enter the external environment with the stool and under favourable conditions (presence of oxygen, proper humidity and temperature), undergo the process of sporogony (meiotic process). Finally, four sporocysts are formed with two sporozoites in each of them (1). The oocyst in this form (sporulated) is ingested by the host. The sheath surrounding the oocyst is digested by the trypsin, which results in the release of sporozoites that rapidly colonize the intestinal epithelial cells. These cells transform sporozoites into first-generation schizonts, which, after numerous divisions, form merozoites. Merozoites penetrating successive cells of the intestinal epithelium transform into second-generation schizonts (schizont II). The subsequent divisions of schizont II lead to the formation of second-generation merozoites (merozoites II). The second generation of merozoites enters the subsequent enterocytes and divides in them, gives rise to third-generation schizonts or gametocytes (macrogametes and microgametes). The formation of gametocytes initiates sexual reproduction. The stage of fertilization of the macrogamete by the microgamete launches the formation of a zygote, which then becomes an oocyst surrounded by the sheath. The development cycle is closed when the oocyst is released to the external environment, where it is exceptionally resistant to unfavorable conditions and most commonly used disinfectants. Due to the enormous reproductive potential of the *Eimeria* protozoa, poultry coccidiosis is considered as a very common disease. One invasive oocyst in *E. maxima* is reported to give rise to 12,000 oocysts, while in the case of *E. tenella*, this figure is potentially 400,000 (7, 23, 25).

Tab. 1. Types of coccidiostats and their characteristics

Characteristic	Type of coccidiostat	
	ionophore	chemical
Origin	fermentation product of bacteria *Streptomyces* spp. and *Acinomadura* spp.	synthetic compound
Mechanism of action	disruption of the transport of ions Na^+, K^+, Ca^{2+}, Mg^{2+} through the cell membrane of the parasite, preventing its development	various
Type of action against *Eimeria* spp.	coccidiostatic	coccidiostatic and/or coccidiocidal
Advantages	possible development of natural resistance to coccidiosis, slow resistance generation	low toxicity
Approved as feed additives in the EU countries	lazalocide*, maduramicin (chickens, turkeys), monensin, narasin (chickens), salinomycin* (rabbits, chickens), semduramycin (chickens)	decoquinate, nicarbazine** (chickens), diclazuril*, halofuginone* (chickens, turkeys), robenidine* (chickens, turkeys, rabbits)
Approved as veterinary medicines in EU countries		decoquinate (cattle, sheep), diclazuril (sheep), halofuginone (cattle), klazuril (pigeons), toltrazuril (pigs, cattle, turkeys, chickens)

Explanations: * also chickens reared for laying, ** allowed only in combination with narasin (trade name: Maxiban)

Chemoprophylaxis of coccidiosis

Nowadays, the cheapest and most frequently used method of coccidiosis prophylactic is feed supplementation with chemotherapeutic agents during fattening, but prior to the pre-slaughter grace period. Commonly used coccidiostats are divided into two groups: ionophores (often used) and chemical. Selected characteristics of both groups and the scope of their application are presented in Table 1.

In Poland, the method of using coccidiostats and the conditions for their approval are regulated by European Union (Regulation EC No 1831/2003) (32) and national legal acts (Regulation WE No 1831/2003) (33). In the EU countries, coccidiostats (as feed additives) are found in 86% of all complete feed starter/grower mixtures for broiler chickens and 97% of all for turkeys (35). According to the European Commission, there are currently no alternative methods of preventing coccidiosis that would provide a similar level of protection (34). Classification of coccidiostats as feed additives, however, has caused difficulties in controlling their trade and supervision related to their safe and proper utilization.

Appointed in 2002, the European Food Safety Authority (EFSA) has introduced regulations for the control and evaluation of generally applicable coccidiostats (27). Due to the resistance of *Eimeria* spp. to coccidiostats, their addition to feed should follow a rotating or interchangeable coccidiostatic program (8). The exchange program involves the use of a different coccidiostat in the starter feed (usually a chemical coccidiostat) and another in the grower feed (ionophore coccidiostat). The rotation program is based on the fact that one coccidiostat is usually administered for a period of three production cycles, and then it is replaced with another, belonging to a different group than the one used previously (14).

Immunoprophylaxis of coccidiosis

An alternative to chemoprophylaxis is immunoprophylaxis. Recently, against poultry coccidiosis the following live vaccines have become available: attenuated, resistant to ionophore coccidiostats, for *in ovo* application, subunit and fully virulent. Their use on a global scale is limited due to the significant production costs. Symptoms similar to a mild course of coccidiosis are often observed after vaccination. This has a negative effect on the microbiological status of the gut, leading to a deterioration in production rates (28). The effectiveness of live vaccines against this disease depends on the selection of an appropriate vaccination technique. It is reported that comparable good results are achieved by applying the vaccine as a gel or spray, although better stability is achieved through a gel carrier (37). The first vaccines against coccidiosis were live, non-attenuated and fully virulent. This group includes vaccines for broiler chickens, for instance, CocciVac®-B, Immucox® C1, as well as ADVENT®, and vaccines intended for laying hens and breeding flocks such as CocciVac®-D and Immucox® C2. Live vaccines with fully pathogenic coccidia are not registered in Poland (13).

Currently, in the European Union the most commonly administered vaccines against coccidiosis are live attenuated. This group includes Hipracox® Broilers, Livacox® T and Supercox® – vaccines intended for broiler chickens; Eimerivac® Plus and Immuner® Gel-Coc – which are specified for all production groups of hens; and Livacox® Q or Paracox®-8 – vaccines intended for breeding flocks and laying hen commercial flocks. These vaccines contain different numbers of sporulated oocysts that have previously been attenuated. Attenuation involves parasitizing the protozoan on chicken embryos or selecting strains with a limited development cycle (12). The selection of strains with a shortened life cycle is faster and consequently leads to more stable anti-coccidia strains. The process of shortening the life cycle of *Eimeria* spp. is to get rid of the last generation of schizonts, which leads to a reduction in the number of progeny oocysts. Still, however, the strong immunogenicity of the strain is maintained (5). The next discussed groups of live vaccines are those containing live strains insensitive to ionophore coccidiostats (Nobilis® COX-ATM preparation) and vaccines for *in ovo* application (Inovocox® agent). When using the aforementioned vaccines, it is possible to administer ionophore preparations to chickens during the first three or four weeks of rearing (the time when the birds develop immunity). This process protects them fully against coccidiosis for the entire period of their maintenance. Additionally, in the case of preparations used *in ovo*, it is possible to vaccinate chickens before the end of the incubation period (4).

Subunit vaccines have a completely different effect than live vaccines. Recombinant protein (DNA) techniques are harnessed for producing this type of vaccine (19). The production process is related to having detailed knowledge of the genetic differences among *Eimeria* spp., the coccidial life cycle and specific antigens present at various stages of the parasite's development (38). The use of subunit vaccines is not very common. They still require research. Currently, there is only one vaccine of this type (CoxAbic®) used in breeding chickens in the world. This contains *E. maxima* gametocyte antigens (39).

Alternative solutions

Herbs and their extracts, plant substances. In the prevention of coccidiosis, herbs and preparations based on plants are becoming more and more popular. The substances they contain are believed to have antibacterial, antifungal, antiviral and immunostimulatory properties (15). For example, research data indicate that mugwort (*Artemisia annua*) reduces the invasion of *Eimeria* spp. Indeed, it has been experimentally shown that leaves of this plant administered as dried in the amount of 5% of food dose significantly alleviated intestinal lesions in chickens infected with *E. tenella* oocytes (36). Another herb with a strong antibacterial effect is oregano (*Origanum vulgare*). The addition of an extract from this plant, rich in quarkol and thymol, has a positive effect on production rates, and also contributes to an increase in the number of oocytes excreted, while reducing the degree of intestinal damage (6). In the period of coccidiosis, the processes of lipid oxidation of the intestinal mucosa are intensified. Violet tulbagia (*Tulbaghia violacea*), a phytogenic feed additive, has been shown to protect lipids in the feeding of chickens against oxidative damage (31). Strong antioxidant properties, inhibiting the development of coccidiosis, are also attributed to the proanthocyanidin that is found in grape seed extract (40) and green tea extract (17). Prophylaxis of coccidiosis can also be based on the use of plants with immunostimulating properties. Echinacea purpurea (*Echinacea purpurea*), which increases body weight and reduces intestinal lesions caused by coccidiosis, contributes to the greater effectiveness of preventive vaccination (3). It has also been shown that yucca (*Yucca schidigera*) extract added to the diet of uninfected, vaccinated chickens increases the length of the intestinal villi and improves production rates (2). Japanese plum (*Prunus salicina*) (21) and extracts from some fungi (20) also exhibit immunumodulatory activity.

During coccidiosis, intestinal epithelial cells can become osmotic destabilized as a result of stress caused by dehydration. Betaine (a glycine derivative) has a beneficial effect on maintaining the osmotic balance of cells. Betaine added to the feed in the amount of 0.15% in combination with salinomycin in a dose of 66 ppm reduces the invasion of *E. tenella* and *E. acervuilina*, decreases bird mortality and improves their body weight (36). What is more, betaine added to the feed of chickens infected with *E. acervulina* has been found to have a positive influence on the activity of cells of the immune system by increasing the production of nitric oxide by macrophages and heterophiles (36).

Probiotics and prebiotics. Probiotics are preparations containing desired intestinal microflora, including

Lactobacillus casei, *L. bulgaricus*, or *Bifidobacterium bifidum* and *B. longum* (18). These can be applied in the prevention of coccidiosis in the form of live bacteria, yeast or spores as they stimulate the microbiological balance in the intestines (36). In experiments, the use of a preparation at a dose of 1 or 10 g/kg of feed that includes cultures of *Pediococcus acidilactici* and *Sacharomyces boulardi*, resulted in a reduction in the amount of *E. tenella* and *E. acervulina* oocysts excreted in the faeces. This was accompanied with a simultaneous increase in the production of specific antibodies against coccidia (22). In another work, the presence of *Lactobacilus* bacteria in feed probiotics lowered the level of oocysts in the faeces and increased the numbers of CD3, CD4, CD8 lymphocytes and IL-2 interleukin in the intestines of birds infected with *E. acervulina* (11).

Prebiotics do not contain microorganisms, but do contain a nutrient that supports the growth and development of specific desired intestinal microflora. These products are mainly based on mono-oligosaccharides (MOS), which are obtained from the cell walls of the yeast *Saccharomyces ceravisiae* (16). Preparations based on MOS support the growth of lactic acid bacteria and protect the intestinal epithelium against the adhesion of pathogenic microorganisms. The results of several studies, based on the use of MOS in the prophylaxis of coccidiosis, indicate a reduction in changes caused by *E. maxima* or *E. acervulina* (26).

It should be emphasized that coccidiosis in the modern poultry industry is still the cause of high economic losses. Despite many years of research, the cheapest and so far most effective method of combating coccidiosis is adding coccidiostats to the feed. An alternative and, what is important, an effective way to limit the negative effects of *Eimeria* protozoa can be the use of herbs and their extracts, pre- and probiotics, as well as betaine. Chemotherapy-free poultry production based on alternative methods meets the expectations of modern consumers. Regarding consumer requirements and new legal regulations concerning the use of coccidiostats in poultry farming, it is necessary to introduce new methods of preventing or/and treatment of coccidiosis based on products of natural origin.

In Poland, the need for such action results from the „Declaration of the Polish poultry industry on the rational use of antimicrobial veterinary medicinal products in poultry farming and breeding" developed by experts from the National Poultry Council-Chamber of Commerce (KRD-IG). This assumes a reduction by 2025 of the use of antibiotics, including coccidiostats to an amount not greater than 50 mg/PCU (Advice, 2020). It should be emphasized that under the European Green Deal program, Polish and EU regulations provide for a 50% reduction in the use of antimicrobial agents in poultry production by 2030.

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