Chapter

Nutrition and Poultry Coccidiosis: Causes, Consequences and Current Strategies to Modulate the Disease

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Abstract

Eimeria spp. are parasites specialized in invade and replicate in the intestine, causing coccidiosis, an enteric disease of major economic importance worldwide. The disease causes losses in production and high morbidity ranging from bloody enteritis, with high mortality, to being subclinical silent but affecting feed intake and efficiency. However, intestinal lesions of the infection vary, depending on the species of coccidia. The most important *Eimeria* species in poultry are: *E. tenella, E. acervulina, E. maxima, E. necatrix, E. mitis, E. praecox* and *E. brunetti*. All those species affect different anatomic sites of the intestine. Thus, they alter the homeostasis of the host reducing nutrient absorption and utilization. Nutritional factors are key players in several steps of the coccidiosis disease. Firstly, as a susceptibility or protection factor, secondly, during the process of infection and pathogenesis, and thirdly, in the recovery and compensatory growth of the bird. Otherwise, coccidiosis also triggers immune response in the intestine. To counter these complicated effects, there are nutritional strategies (including formulation of key amino acids, vitamins, short and medium chain fatty acids, prebiotics, enzymes, among others) that can be utilized to reduce the infection, alleviate the signs, and boost the compensatory growth after infection. This chapter review the impacts of coccidiosis in nutrition and discuss about of strategies to mitigate these risks.

Keywords: *Eimeria* infection, amino acids, digestibility, nutrient absorption, compensatory growth, immune response

1. Introduction

Coccidiosis is a worldwide disease caused by the Apicomplexa protozoa of Genus *Eimeria* [1]. This parasitic disease causes economic losses in poultry industry due to malabsorption, reduced weight gain (explained by a reduced feed intake and as well as nutrient absorption), increased mortality and the use of anticoccidial drugs and vaccines [2, 3] and remains as a major issue for poultry producers in a large number of countries including USA [4], costing for the global poultry industry over 3 billion dollars annually [5, 6]. However, subclinical coccidiosis (Coccidiasis) is more costly to producers than clinical coccidiosis because of impairment on FCR (Feed Conversion Ratio) and decreasing in BWG (Body Weight Gain), slightly resistance of anticoccidials as well as the difficultness in the diagnostic [6, 7]. The infection with *Eimeria* begins when the bird ingests sporulated oocyst, and the sporozoite replication occurs in the intestinal cells generating damage in the mucosa [8]. The infection is normally caused because of mixture of *Eimeria* species. Each species develops in different regions of the intestine and they can cause mild to severe grades of lesions [9]. There are several *Eimeria* species that infect chickens, but the most important are *E. maxima, E. acervulina* and *E. tenella* [3]. The infection process is very fast, from 4 to 7 days, depending on the species [9]. Previous studies reported that a coccidia challenge resulted in 29.5, 24.7, 18.8, and 96.2% reductions in the apparent ileal digestibility of DM, N, starch, and fat, respectively. Interestingly, the negative effects of coccidia challenge on fat digestibility suggested complex mechanisms involved [10]. The strategies to reduce the impact of poultry coccidiosis including the use of anticoccidial drugs, vaccination programs and immunomodulators (e.g., nutritional strategies and functional ingredients including phytobiotics and probiotics).

2. Coccidiosis and nutrition

From the nutritional standpoint, *E. acervulina* and *E. maxima* are the most influential species because of the strategic anatomical location being in duodenum (affecting the release of pancreatic juices) and jejunum intestine (nutrient absorption) respectively. *E. acervulina* and *E. maxima* significantly reduces the water consumption and feed intake simultaneously during acute coccidiosis, however the ratio of water intake to feed intake did not differ between chicks with coccidiosis and healthy birds. Hence, nutritional deficiencies and impaired nutrient absorption can occur following feed and water intake restrictions [11, 12].

Nutritional factors are key players in several steps of the coccidiosis disease. Firstly, as a susceptibility or protection component, secondly, during the process of infection and pathogenesis, and thirdly, in the recovery and compensatory growth of the bird.

Based on that, there are some facts pointing out that the presence of intestinal lesion scores correlates with decreases in average daily gain (ADG), energy consumption, retained energy and feed efficiency. Increments in maintenance is also reported while also seeing increase in excreted energy as well as reduced digestibility in most of the dietary nutrients [10]. The activation of immune response also occurs and requiring use of nutrients that cannot be addressed to the conversion of nutrients into meat, the key goal of broiler production. Therefore, it is paramount to figure out that any level of *Eimeria* infection is causing an evident, but difficult to estimate, loss in performance.

The use of good quality ingredients would aid in nutrients losses during infection and might help to reduce the potential secondary health issues. Nutrient dense diets during infection may be used to counteract performance losses and to enhance compensatory growth phase.

3. Malabsorption of nutrients

A reduction in apparent ileal digestibility of some nutrients including nitrogen, starch and fats in challenged birds with *Eimeria* has been reported [10]. As expected, coccidia challenged reduced starch, fat, and amino acids (AA) digestibility. Of these nutrients, fat digestibility was recognized as the most affected by the level of intestinal lesion [10]. Besides, an estimation of the intestinal damage and its impact on fat and AA digestibility was done. For each unit of impairment in total lesion score, digestibility was decreased by 16% and 3.8% respectively [10].

The first sign seen in birds which are infected with *Eimeria* is loss of pigmentation. In some countries, the coloring of the skin of broilers is an important factor when consumers choose the bird that they want to buy, as they directly associate yellowness or even goldenness with high quality, freshness, and country chickens [13, 14]. The extra cost for to achieve the level of desired pigmentation is high being between 8 to 10 percent of the total feed cost. Carotenoids are fat soluble and a loss of digestible energy specially of fats also affects its absorption in plasma. Besides, it is absorbed through the ciliary epithelium of the midgut and, for this take properly, a process of enzymatic hydrolysis of the xanthophylls, present in the diet in the form of fatty acid esters, must occur. During coccidia challenges, there is a decreasing up to 88% in serum levels of lutein. Some species of *Eimeria* cause desquamation and shortening of the villi of the intestinal mucosa and infects the sites of greatest pigment absorption in the intestine of birds [15].

The optimum pH of gastrointestinal tract is crucial for the action of digestive enzymes. However, coccidiosis infection has been responsible of causing malabsorption of nutrients which is related with the alteration of pH and morphological alteration including flattened villi and elongated [16]. The intestinal content was significantly lower in pH in birds after 5–9 days post infection of *E. acervulina, E. mivati, E. maxima, E. necatrix* and *E. brunetti* than in uninoculated control birds causing the impairment in absorption of nutrients [17]. Consequently, *Eimeria*-induced pH reductions likely impact nutrient digestion and absorption in the intestinal lumen. Also, pancreatic and mucosal brush border enzyme activity is affected at the tissue of infection, whereas brush border enzyme activity may be altered in uninfected intestinal regions compensating for losses in nutrient recovery [18]. Decreased activities of digestive enzymes located on the upper half of the villi, such as disaccharidases, indicate a damaged brush border with a decreased digestive absorptive capacity [16].

4. *Eimeria* infection and protein, amino acids and vitamin dietary levels

Nutritionists and parasitologists have argued for a long time the relation between coccidiosis and dietary protein levels. Early studies showed that chickens fed with high crude protein levels (between 20.5 to 22%) and high-vitamin A and B diets (40% more vitamin A, and about 20% more vitamin B of the requirements respectively) compared with low-protein (between 14.5 to 15.5%) and low-vitamin diet and exposed to equal numbers of *E. tenella* oocysts, had a consistently lower excretion of oocysts after 5 days of exposure and less than half the peak of oocyst shedding on day 7 post infection. Mortality percentage was 5% in the high-protein and high-vitamin A diet, compared to 23% in the low-protein and low-vitamin A diet. However, on the fifth and sixth day, the results were completely the opposite, suggesting that a high amount of protein and vitamin on the feed are overcoming the damage of acute coccidiosis. Nonetheless, during a chronic state of the disease, high levels of dietary proteins, caused an impairment of birds health [19]. As a shortcoming of this study, the effect of protein was not separated from the effects of vitamins.

Britton et al. (1964) showed the interaction between dietary protein levels and coccidiosis varying from 0 to 30% in intervals of 5% [20]. They found a significant reduction of mortality rate and in intestinal lesion score with 0 and 5% of dietary protein levels compared with 10 to 30%. In addition, the chickens fed with high amount of dietary protein showed more signs of coccidiosis such as blood in droppings and lethargy during first week of the challenge.

Furthermore, there is a relationship between the amount of dietary crude protein, trypsin activity and susceptibility to coccidiosis infection. To assess that, an experiment was conducted with chicks fed with diets varying protein levels (5, 20 and 30%) and its impact in intestinal trypsin activity. They found low levels of trypsin in 5% of protein fed compared with 20 and 30% protein [20]. A possible explanation is supported by the fact that when the birds are fed with high dietary protein levels, the production of trypsin and bile salts also increases as well. Thus, trypsin is one of the most important gastrointestinal enzymes for excystation of sporocysts from oocysts [21, 22]. The effect of trypsin intestinal levels and coccidia infection was also evidenced by others studies where chicks pancreatic ducts were ligated and there was no infection after orally challenge with *Eimeria* sporulated oocyst [23, 24].

At this regard, a study was conducted to determine the effect of feeding raw soybean containing 20.3 mg of trypsin inhibitor (TI) per g versus soybean meal of 2.2 TI mg/g in corn-soybean base diets in chickens on the risk to infection with 5 different species of *Eimeria* [25]. The key role of trypsin during excystation step in the coccidia cycle and its effect on the susceptibility of *Eimeria* infection was confirmed.

However, the continuous feeding of raw soybean in corn-soybean base diets also extremely developed weight depression and pancreatic hypertrophy, counteracting the positive effects of raw soybean on coccidiosis [25].

On the contrary, a high level of dietary protein was reported as a protection factor against *E. tenella* and *E. acervulina* infection. In contrast, mortality rate in *E. tenella* and the oocyst shedding in *E. acervulina* increase by feeding a diet with a 24% of crude protein. It has been also showed an improvement in the growth curve of chicks between 8 to 14 days post infection as compared with the first seven days post-infection and suggesting that compensatory growth can occur [26]. It would be appearing that the utilization of the maximum potential of compensatory growth requires highest levels in dietary protein or dense diets although more evidence is needed because most of the studies are only performed only seven days post infection disregarding the upcoming phases of broiler growth.

Adverse alterations of coccidiosis on key anatomical specific areas of the intestine such as the jejunum may affect protein digestibility. A compromised reduction in protein digestibility, using appearance of 14C in the blood of chicks fed labeled protein from cholera algae, was observed during an acute phase infection of *E. necatrix*-infected birds (jejunum) versus non-infected birds. Similarly, protein digestibility was not severe impaired in other species of *Eimeria* including *E. acervulina* and *E. brunetti* during the acute phase suggesting that duodenum, ileum, cecum, and colon were less important in protein digestion and absorption areas than jejunum. During the recovery period, a higher protein and absorption was observed above the absorption rates for uninfected birds [27].

Persia et al. (2006) reported a reduced performance, nitrogen-corrected apparent metabolizable energy (AMEn), and a total tract apparent amino acid digestibility (averaging of 12 percentage units for Thr, Val, Ile, Lys and Arg) with *E. acervulina* infection in birds inoculated with 5.0×10^5 sporulated oocyst in a time and dose response manner which was greater for acute versus chronic infections [28]. Ingredients such as fish meal and prebiotics mitigated the negative effects of coccidiosis lesions on cross bred chicks [28].

Parker et al. (2007) showed a decreased apparent total tract amino acid digestibility (ATTD, 8.4 percentage units) using *Eimeria*-vaccinated broilers challenged with a blend of *Eimeria* species compared with non-infected birds, being the branch chain amino acids (BCAA), and Thr and Cys the most affected [29]. Amerah and Ravindram (2015) showed that ATTD was most impacted for Ala, Cys, Ile, and Thr in broilers inoculated with a blend of sporulated *Eimeria* (1.8×10^5, 6×10^3, and 1.8×10^4 *E. acervulina, E. maxima*, and *E. tenella* oocysts, respectively), showing a reduction of 13.4 percentage units in body weight gain (BWG) for all amino acids [10].

The effect of dietary protein on performance characteristics of vaccinated broilers subjected to clinical coccidiosis challenge has been examined. Lee et al. (2011) assessed the effect of dietary protein on the feed varying from 20 to 24% in coccidia-vaccinated chickens at the first day on broilers and subsequently challenged with different species and concentration of *Eimeria* (*E. acervulina* 6 x 10^5, *E. maxima* 4 x 10^5, and *E. tenella* 2 x 10^5) isolated from the field [30]. At day 21, an improvement in BWG and feed efficiency when increase dietary protein concentration regardless of vaccination status was found. However, vaccinated birds had a statistical trend to impair BWG and feed conversion ratio when was compared with non-vaccinated chicks before inoculation. After the *Eimeria* challenge (day 21 of age) and 0-to-6-day post infection, chicks fed with 24 percent crude protein diet had the highest feed efficiency. In the vaccinated group, birds fed the 24% crude protein diet had lower intestinal lesion scores than birds fed the 20% crude protein diet. No effects on compensatory growth were determined because of the end of trial at 6-day post inoculation [30].

Supplementation of some synthetic amino acids and their role in protection to coccidiosis infection are hypothesized that may overcome lesions in vaccinated birds. In this regard, Mussini et al. (2012) assessed the response of coccidiosis-vaccinated broilers to different levels of dietary glutamine (Glu, 0.5, 0.75, or 1%) during the immunity acquisition phases up to 28 days of age on performance and yield meat [31]. When dietary Glu was increased, BWG also increased concomitantly, regardless of the level of supplementation. On the age of 42 days, this observation was evidenced. Meat yield results did not show any effect with the Glu addition, however, a statistically trend ($P = 0.07$) in breast meat yield was observed. It is tempting to speculate, that Glu might be aiding to avoid muscle protein catabolism as well as supporting gastrointestinal and local immune system in the intestine.

In low protein diets, certain amino acids such as Gly, Ser and Pro have been supplemented by using gelatin as a source of conditionally essential amino acids to test their impact on compensatory growth in *Eimeria*-vaccinated broilers over a full grow-out period of 8 weeks. It was demonstrated that these amino acids improved performance because of their role in maintaining the mucosal barrier integrity [32].

The role of Thr (structural and prevalent amino acid of mucin) during broiler coccidiosis is controversial. Wils-Plotz (2013) showed a positive effect on growth performance when Thr was supplemented at 25% higher than dietary requirement. Nevertheless, Kidd et al. (2003) did not find any interaction between *E. acervulina* challenge and Thr supplementation meaning that broiler Thr dietary requirements are not increased during a mild infection of *E. acervulina* [33].

Arg supplementation has been hypothesized that play a key role on innate and humoral immune response during an Eimeria infection. Similarly, alleviate oxidative stress, improve antioxidant capacity, and attenuate the intestinal mucosa disruption. Thus, it might potentially increasing vaccine effectiveness and/or improve the responsiveness to field infections. An experiment varying different dietary levels of Arg and Vit E on the immune response against *Eimeria* challenge at day 14th of age with a field blend of *Eimeria* oocysts showed that heterophil and monocyte oxidative burst was improved with the concomitant inclusion of Arg and Vit E above the NRC requirements as well as serum levels of IgG and IgM [34]. In a recent publication, the effects of varying levels of Arg was measured in broilers challenged with a mix of *Eimeria* showing a promissory result where the levels ranging from 1.24 to 1.44 improving overall growth, intestinal integrity, and morphology [35].

Rochell et al. (2016) evaluated growth performance, ATTD, and plasma concentrations of amino acids, carotenoids, and α1-acid glycoprotein, an acute-phase reactants, in broilers from hatch to 21 d and inoculated with graded doses of *E. acervulina* oocysts [13]. BWG and feed efficiency dropped linearly when the doses of *E. acervulina* increased. Except for Trp and Gly, ATTD values decreased linearly or quadratically for all amino acids, relative to uninfected animals, by an average of 2.6 percentage units for birds inoculated with 1.0×10^6 oocysts.

Methionine (Met) is the first limiting amino acid in corn and soybean meal broiler diets that plays a major role in protein metabolism and has been highlighted as a crucial requirement for the immune system [36] and antioxidant defense system [37].

The impact of three dietary Met levels (0.45%, 0.56% and 0.68%) on alleviation of coccidia negative effects in broilers under various anticoccidial vaccination programs was examined in broilers from 22 to 42 d of age treated or vaccinated against coccidia after inoculation of *E. tenella* (5×10^4 sporulated oocyst) [38]. Dietary Met levels from 0.45 to 0.56% and 0.68% improved BWG and feed conversion ratio of broilers medicated against coccidia. However, dietary Met levels did not improve performance in vaccinated birds suggesting that Met levels could be benefiting the growth outcome in medicated chickens regardless on vaccinated chickens.

Two different Met sources and dietary levels of supplementation (non-supplemented, free Met and dipeptide Met) in coccidia challenged birds were examined on performance, gene expression related with immune responsiveness, antioxidant system and amino acid transport in Broiler diets [39]. No interaction between challenge and diet effects was found. However, BWG and feed conversion were improved (12.5 higher and 11.8% lower respectively) when free Met was supplemented compared to the non-supplemented birds. They also reported strong statistical differences comparing non-challenged versus challenged treatments for feed intake, BWG and feed conversion ratio. Coccidia challenge led higher amounts of oxidative substances in the jejunum of chickens 6 d post infection and decreased the gene expression of some amino acid transporters and immune response genes such as peptide transporter 1, toll-like receptor 5, interleukin-2 and occluding. Interferon gamma gene expression was also found increased [39].

5. How would nutrition help coccidiosis?

If producers are using coccidiosis vaccines, special diets could be designed to avoid peaks in oocyst production including the use of Glutamine [31].

The use of good quality ingredients is critical. High digestible feed ingredients where the nutrients are more available, the birds would have more probability to retain nutrients [40]. Also, to know the origin of feedstuffs avoiding the intake of pathogen microorganisms to the flock is crucial. Both microbiology and digestibility quality can aid in nutrients losses during infection and help reduce potential secondary health issues including necrotic enteritis, salmonellosis among others [41, 42].

Low protein diets may decrease the probability of infection but would affect BWG [25]. Thus, decreasing the amount of dietary protein it is not practical strategy. On the contrary, nutrient dense diets during infection may help with performance losses. However, excess of nutrients needs to be avoided on the lumen which may provide a substrate for entero-pathogens (i.e., surplus of protein in the hindgut for *Clostridium perfringens* proliferation) [43, 44].

The use of natural compounds including phytogenics and probiotics and beyond traditional strategies (ionophores and synthetics) have been considered to control coccidiosis challenges in the field or to reduce its severity [45, 46]. Phytobiotics have shown effectiveness against *Eimeria* (*in-vitro* and *in vivo*) and indirect positive outcomes related with boosting immune system and improving microbiota functions [45, 47]. Furthermore, phytobiotics affects fecal oocyst excretion and decrease intestinal lesion score exerting a direct effect on the parasite itself and altering its life cycle in the host [48, 49]. Anticoccidial effects of individual plants, plant extracts, and unidentified commercial plant-derived feed additives have been reviewed elsewhere [45, 49] but many of these studies were conducted using unknown blends and therefore repeatability and further investigation of physiologic pathways is scarce. Saponins by virtue of their surfactant properties have anti protozoal activity and they have membranolytic properties, they complex with cholesterol in protozoal membranes, causing cell lysis [50]. Saponins have shown immunomodulatory effects in broiler chickens challenged with a mix of *Eimeria* as evidenced by lymphocyte outcomes, changes in intestinal structure and alterations in cecal and duodenal inflammatory gene expression [51].

Feeding Probiotics as a replacement of traditional anticoccidials in the diet of broiler chickens might alleviate the impact of the disease and suggesting a coccidiostatic effect against *E. tenella*. One explanation is that probiotics aid to maintain intestinal health and integrity, act as an competitive exclusion principle and decrease the risk of coccidiosis [52]. It was also demonstrated a reduction in oocyst shedding of probiotics compared with Lasalocid. However, the role of feed supplementation of probiotics in performance did not show any improvement when was compared with Lasalocid [53].

An interesting study showed the positive effects of combine essential oils and vitamin D in vaccinated birds with coccidian oocyst of *E. maxima and E. tenella* [54]. An improvement in BWG and decreasing in FCR were observed when the essential oils and Vit D were supplemented compared with the non-vaccinated and non-treated birds. Furthermore, ATTD of dry matter tended to increase with the supplementation as well as an improvement in *Lactobacillus* counts.

6. Conclusions

Although coccidiosis has been the topic of a huge of research over the last decades, is still the major health issue on poultry industry and crucial questions remain answered. There are strategies to reduce or prevent the infection as well as to boost the compensatory growth after infection phase. In antibiotic free systems (ABF) coccidiosis control is requiring multifaceted approach. Nowadays, the strategy to control coccidiosis would not rely just only in coccidia vaccines or anticoccidials. Dietary interventions including protein and amino acids supplementations above the requirements may alleviate performance and immunological impairments in both vaccinated and/or unvaccinated broilers. Nonetheless, it varies according to characteristics of *Eimeria*, type of challenge, health status and environmental issues. Some studies are not considering long term effects such as compensatory growth and vaccines responsiveness during two or three consecutive flocks which may affect the parasite life cycle and immune response status. Nutritional requirements during coccidia infection can be improved by estimating the exact amount of dietary protein and amino acids required for a variety of intestinal functions (such as protein turnover, mucus production, and epithelial cells replacement, among others) and local immune supporting responses such as gut-associated lymphoid tissue. However, this type of information is scarce and further studies are needed to determine the exact role of each nutrient and their impact on performance and health in different production scenarios.

Conflict of interest

The authors declare no conflict of interest.

Author details

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