Chapter 77

Efficacy of Vaccination against *Eimeria* spp. in poultry

https://doi.org/10.56238/methofocusinterv1-077

Gilberto Chiantelli Ferreira

Rodrigo Pereira Cassiano

Bruna Matarucco Sampaio Beretta

Rodrigo Antonio Fernandes

Katia Denise Sa

ABSTRACT
Eimeriosis represents a considerable challenge faced by the global poultry industry due to the damage it causes. Three species of Eimeria in chickens, in this case, E. acervulina, E.max and E. tenella have the potential to affect the occurrence and extent of resistance to anticoccidial drugs and future vaccines. Thus, it is clear that vaccination against avian eimeriosis has an important role in maintaining biosafety and productivity in poultry breeding, since in addition to providing the immunization of animals, it helps in increasing the therapeutic efficiency of anticoccidial drugs. In this study, we investigated the effectiveness of vaccination against eimeriosis in broiler birds. In total, 589 articles were compiled in research databases and scientific publications. As a filter to avoid duplication between works, 62 articles were obtained. Of these, in only five did we observe a very high degree of recommendation for the use of DNA vaccination, which was considered more effective in preventing eimeriosis, with a lower degree of side effects.

Keywords: Eimeriosis, poultry, vaccination.

1 INTRODUCTION

Protozoa of the phylum Apicomplexa of the genus Eimeria infect cells of the intestinal epithelium of many hosts (Kim et al., 2013) and the disease is called eimeriosis (Fatoba & Adeleke, 2018). For the poultry industry, it is a major commercial problem (Sharman, Smith, Wallach, & Katrib, 2010) and for many years, means of disease prevention and control have been used, in addition to prophylactic actions with specific anticoccidial drugs (Noack, Chapman , & Selzer, 2019).

Brazil produced 13 thousand tons of chicken meat in 2020, according to the Brazilian Association of Animal Protein (ABPA, 2021), of which 31% was destined for exports and 69% for the domestic market. Exports generated an income of US$ 4.23 million for the Brazilian agroindustry, showing an increase of 3% since the last drop in exports that occurred in 2018. did not affect economic growth. In relation to the world market, Brazil occupies the third place, the first position was occupied by the United States of America, with 20.24 thousand tons followed by China with 14.60 thousand tons in 2020 (EMBRAPA, 2020).

The world chicken herd is estimated at approximately 21 billion and approximately 90 billion kilograms of meat and chickens producing 1.1 trillion eggs each year worldwide (www.fao.org/faostat/en).

Infection by Eimeria spp. causes death and low productivity including inefficient feed utilization, poor weight gain and reduced egg production of infected hens (Shirley MW, Lillehoj HS. 2012). Large-scale, long-term use of anticoccidial drugs has been effective in controlling coccidiosis for decades, but this has led to the inevitable development of parasite resistance to almost all anticoccidial drugs, as well as concerns about drug residues in poultry meat. when a period of drug withdrawal is not strictly observed (Peek HW, Landman WJM. 2011). In lieu of drug control, vaccination with virulent (e.g. Coccivac and Immucox) or attenuated (e.g. Paracox and Livacox) vaccines is one of the most efficient methods for protecting breeder and layer flocks against infection by Eimeria, and vaccination is low risk to public health (Chapman HD, Barta JR, Blake D, Gruber A, Jenkins M, Smith NC, Suo X, Tomley FM. 2013).

Immunization is a practical alternative to chemotherapy for controlling coccidiosis. However, most current commercial vaccines consisting of live attenuated or non-attenuated coccidian oocysts are expensive and difficult to manufacture on a large scale. In addition, live vaccines carry a risk of vaccine pathogenicity, potential reversion to virulence, and outbreak of coccidiosis (Del Cacho et al., 2016; Williams, 2002).

The most common species described in the literature that affect birds are Eimeria acervulina, Eimeria maxima, Eimeria necatrix, Eimeria tenella and Eimeria brunetti. These species can cause intestinal lesions that consequently result in reduced weight gain and mortality (McDonald & Shirley, 2009). The use of drugs as a tool for controlling coccidia was the main strategy used over the years, also recognizing the existence of resistance to commonly used drugs (Williams, 2002). In addition, the consequences of using these drugs along the food chain are of concern, as residues are detected in food (Clark et al., 2012).

Immunization in broilers against coccidiosis infection can be provoked by the ingestion of coccidian oocysts of the genus Eimeria (Gazoni et al., 2020) and commercial vaccines against Eimeria have been available since the 1950s (Blake, Pastor-Fernández, Nolan, & Tomley, 2017). However, in recent years, the poultry industry has relied mainly on anticoccidial drugs (Price & Barta, 2010) and synthetic chemicals (Peek & Landman, 2011), to control this parasitic disease. In view of the greater resistance of Eimeriosis to anticoccidial drugs (Chang, Yang, Muthamilselvan, & Yang, 2016) and the growing consumer demand for animals raised free of antibiotics, vaccines against coccidiosis are increasingly used in the poultry industries (M. Song et al., 2020).

DNA vaccines have been suggested as a promising alternative strategy against coccidiosis without the disadvantages associated with chemoprophylaxis and live vaccines (Blake and Tomley, 2014; Pereira et al., 2014; Song et al., 2015). The immunization procedure of the DNA vaccine encoding the Eimeria protein inducing effective protection has been studied (Xu et al., 2008). A practical vaccine against coccidiosis should provide stable protection across different flocks, as well as lasting protection covering the entire production cycle of chickens.

Vaccines are undoubtedly the best and most efficient alternative for immunization, but their high cost makes their use difficult in broiler chicken creations in Brazil. In this literature review, we investigated the efficacy of vaccination against eimeriosis in broiler chickens.

2 MATERIAL AND METHODS

Bibliographic search in databases

A systematic review of the literature on the Regional Portal of the VHL, Pubmed, Virtual Library of CAPES and Google Scholar was carried out, using some filters such as the period of publication between 2015 and 2020 and standardized keywords to index the research: Eimeria, Vaccination and Chicken. Obtaining the articles included the English and Portuguese languages, published in the last five years and excluding review studies and duplicate texts. The pre-selection was initially performed by analyzing the titles relevant to the purpose of the review, reading the abstract and, subsequently, being selected by reading the full text.

The selected articles were evaluated by the authors according to the criteria of the Oxford Center for Evidence-Based Medicine (MBE) and thus, the maximum (1) and minimum (5) level of evidence was considered.

Classification of Article studies

A value called the quality score (0-5) for randomized studies, publications with a value ≥ 3 being considered of good quality (Jadad et al., 1996). The degree of recommendation of the vaccinations applied in each article is classified as A, B, C and D, with grade A being good evidence to support the recommendation, grade B reasonable evidence and grade C insufficient evidence (against or in favor), the grade D discarded the recommendation (Burns, Rohrich, & Chung, 2015).

The variables of interest were: type of study, level of evidence, point on the Jadad scale, evaluation of the clinical trial, the amount of specimen treated and the percentage of broilers with more than 50% improvement and side effects.

In total there were 589 articles, searched in the regional Portal of the VHL, Pubmed, virtual library of CAPES and Scielo, which resulted in 98,104, 384 and three articles respectively. The Mendeley tool was used and a total of 62 articles were obtained, filtering duplicity between works. After that, the types of vaccine were verified, the relevance of the articles referring to the filters and if the articles reported the tests of a new vaccine, as well as their resistance and their respective efficacy.

3 RESULTS AND DISCUSSION

The results were shown in two tables. Table 1 refers to the summary of studies on the efficacy of vaccination against eimeriosis in birds and Table 2 refers to the level of evidence and degree of recommendation on the vaccinations used.

Table 1. Compilation of studies on the efficacy of vaccination in chickens against eimeriosis, according to the scale JADDAD et al., 1996.

References	Sakamoto *et al.* (2014)	Liu *et al.* (2018)	Lin *et al.* (2017)	*Song et al*. (2017)
Kind of study	Série de casos	Série de casos	Série de casos	Série de casos
Escala JADDAD *et al.*, 1996)	3	2	3	2
Disease	Eimeriose	Eimeriose	Eimeriose	Eimeriose
Type of vaccine??	Vacinação	Vacinação	Vacinação	Vacinação
Total Vaccinated Patients	30	30	20	????
Side effects	*	*	*	*
Conclusion	Eficaz	Eficaz	Eficaz	Eficaz

Tabela 2. Nível de evidência e grau de recomendação da vacinação em Aves com eimeriose.

Variable	Results
Disease	Emeriose
Treatment	Vaccination
Number of studies	5
Level of evidence	A
Grade of recommendation	I

From 2014 to 2020, nine articles were selected and none of them obtained an evidence level above 4 (Burns et al., 2015), relying only on case series, case reports and in vivo experimental studies (Tables 1 and 2020). two). This shows that there is a lack of more reliable studies on this subject. However, in all articles it was found that vaccination or the method of immunization against eimeriosis is mostly effective against E.tenella, E. maxima and E. acervulina, and therefore, for the control of this disease, which generated a degree of recommendation level 1 of the selected articles, as shown in Table 2.

The vaccine with the Em14-3-3 antigen can notably lessen jejunal lesions and body weight loss, with a reduction in the elimination rate of protozoan oocysts, as well as producing an anticoccidial index. In the test of the groups immunized with the antigen Em14-3-3 and pVAX1-14-3-3, when compared to the negative controls ($P < 0.05$), it demonstrated that it could be used as a promising candidate against the antigen of E. maxima (Wang et al., 2017).

In a comparative investigation of the effect of isolated glutamine, and associated with acidic glutamine and yeast along with vaccination against coccidiosis, the performance and morphometry of the small intestine of broiler chickens was observed, and it was found that the group fed with glutamine presented better recovery of intestinal mucosal epithelial losses compared to controls (Sakamoto, Faria, Nakagi, & Murakami, 2014). Thus, it was noted that this type of feed supplementation can be a strategy to improve the development of chickens subjected to vaccine stress (Liu et al., 2018).

Molecular cloning, purification and vaccination efficacy showed a new vaccine candidate for eimeriosis in broiler chickens, elongation factor-1a (EF-1a). With two subcutaneous immunizations one week apart with recombinant EF-1α protein expressed by E. coli (r) EF-1α plasmid and evaluated for protection against infections caused by E. tenella or E. maxima. Chickens vaccinated with rEF-1α exhibited increased body weight gain, lower production of fecal oocysts, and higher serum levels of anti-EF-1α

antibodies after challenge infection with E. tenella or E. maxima compared to non-immunized controls. Thus, EF-1α vaccination may represent a new approach to induce cross-protective immunity against avian coccidiosis (Lin et al., 2017).

The Pvax1.0-ta4-yl-2 DNA vaccine was intramuscularly inoculated into two-week-old chickens in order to investigate the duration of their immune protection and showed potential to be developed as an effective vaccine against coccidiosis in general (X. Song, Zhao, Xu, Yan, & Li, 2017).

4 CONCLUSION

Through meta-analysis of multiple controlled studies analyzed in this work, we conclude that DNA vaccination is considered more effective in preventing eimeriosis in broiler chickens, with a lower degree of side effects.

REFERENCES

Abbas, R. Z., Iqbal, Z., Blake, D., Khan, M. N., & Saleemi, M. K. (2011). Anticoccidial drug resistance in fowl coccidia: The state of play revisited. *World's Poultry Science Journal*. https://doi.org/10.1017/S004393391100033X

Blake, D. P., Pastor-Fernández, I., Nolan, M. J., & Tomley, F. M. (2017). Recombinant anticoccidial vaccines - a cup half full? *Infection, Genetics and Evolution*. https://doi.org/10.1016/j.meegid.2017.10.009

Blake DP, Clark EL, Macdonald SE, Thenmozhi V, Kundu K, Garg R, Jatau ID, Ayoade S, Kawahara F, Moftah A, Reid AJ, Adebambo AO, Zapatai RA, Rao ASRS, Thangaraj K, Banerjee PS, Dhinakar-Raj G, Raman M, Tomley FM. 2015. Population, genetic, and antigenic diversity of the apicomplexan Eimeria tenella and their relevance to vaccine development. *Proc Natl Acad SciUSA* 112:E5343–E5350. https://doi.org/10.1073/pnas.1506468112.

Burns, P., Rohrich, R., & Chung, K. (2015). EU Alpine Space Programme, Project AlpBC (Capitalising knowledge on Alpine Building Culture by performing regional smart planning and consultancy strategies for sustainable development), 2012-2015. *Plastic and reconstructive Surgery*, *128*(1), 305–310. https://doi.org/10.1097/PRS.0b013e318219c171.The

Chang, C. L. T., Yang, C. Y., Muthamilselvan, T., & Yang, W. C. (2016). Field trial of medicinal plant, Bidens pilosa, against eimeriosis in broilers. *Scientific Reports*. https://doi.org/10.1038/srep24692

Chapman HD. 1997. Biochemical, genetic and applied aspects of drug resistance in Eimeria parasites of the fowl. *Avian Pathol* 26:221–244. https://doi.org/10.1080/03079459708419208.

Chapman HD, Barta JR, Blake D, Gruber A, Jenkins M, Smith NC, Suo X, Tomley FM. 2013. A selective review of advances in coccidiosis research. *Adv Parasitol* 83:93–171. https://doi.org/10.1016/B978-0-12-407705-8.00002-1.

Clark, J. D., Oakes, R. D., Redhead, K., Crouch, C. F., Francis, M. J., Tomley, F. M., & Blake, D. P. (2012). Eimeria species parasites as novel vaccine delivery vectors: Anti-Campylobacter jejuni protective immunity induced by Eimeria tenella-delivered CjaA. *Vaccine*, *30*(16), 2683–2688. https://doi.org/10.1016/j.vaccine.2012.02.002

Del Cacho, E., Gallego, M., Lillehoj, H.S., Quilez, J., Lillehoj, E.P., Sánchez-Acedo, C., 2016. Induction of protective immunity against experimental Eimeria tenella infection using serum exosomes. *Vet. Parasitol*. 224, 1-6.

Fatoba, A. J., & Adeleke, M. A. (2018). Diagnosis and control of chicken coccidiosis: a recent update. *Journal of Parasitic Diseases*. https://doi.org/10.1007/s12639-018-1048-1

Gazoni, F. L., Adorno, F. C., Matte, F., Alves, A. J., Campagnoni, I. D. P., Urbano, T., … da Silva, A. S. (2020). Correlation between intestinal health and coccidiosis prevalence in broilers in Brazilian agroindustries. *Parasitology International*. https://doi.org/10.1016/j.parint.2019.102027

Jadad, A. R., Moore, R. A., Carroll, D., Jenkinson, C., Reynolds, D. J. M., Gavaghan, D. J., & McQuay, H. J. (1996). Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials*, *17*(1), 1–12. https://doi.org/10.1016/0197-2456(95)00134-4

Kim, D. K., Lillehoj, H. S., Lee, S. H., Jang, S. I., Lillehoj, E. P., & Bravo, D. (2013). Dietary Curcuma longa enhances resistance against Eimeria maxima and Eimeria tenella infections in chickens. *Poultry Science*. https://doi.org/10.3382/ps.2013-03095

Lin, R. Q., Lillehoj, H. S., Lee, S. K., Oh, S., Panebra, A., & Lillehoj, E. P. (2017). Vaccination with Eimeria tenella elongation factor-1α recombinant protein induces protective immunity against E. tenella and E. maxima infections. *Veterinary Parasitology*, *243*, 79–84. https://doi.org/10.1016/j.vetpar.2017.06.003

Liu, J., Liu, L., Li, L., Tian, D., Li, W., Xu, L., … Song, X. (2018). Protective immunity induced by Eimeria common antigen 14-3-3 against Eimeria tenella, Eimeria acervulina and Eimeria maxima 11 Medical and Health Sciences 1107 Immunology. *BMC Veterinary Research*, *14*(1), 1–11. https://doi.org/10.1186/s12917-018-1665-z

McDonald, V., & Shirley, M. W. (2009). Past and future: Vaccination against Eimeria. *Parasitology*. https://doi.org/10.1017/S0031182009006349

Noack, S., Chapman, H. D., & Selzer, P. M. (2019). Anticoccidial drugs of the livestock industry. *Parasitology Research*. https://doi.org/10.1007/s00436-019-06343-5

Peek, H. W., & Landman, W. J. M. (2011). Coccidiosis in poultry: Anticoccidial products, vaccines and other prevention strategies. *Veterinary Quarterly*. https://doi.org/10.1080/01652176.2011.605247

Price, K. R., & Barta, J. R. (2010). Immunological control of coccidiosis in poultry. *SURG Journal*. https://doi.org/10.21083/surg.v4i1.1100

Sakamoto, M. I., Faria, D. E., Nakagi, V. S., & Murakami, A. E. (2014). Sources of trophic action on performance and intestinal morphometry of broiler chickens vaccinated against coccidiosis. *Revista Brasileira de Ciencia Avicola*, *16*(4), 389–396. https://doi.org/10.1590/1516-635x1604389-396

Sharman, P. A., Smith, N. C., Wallach, M. G., & Katrib, M. (2010). Chasing the golden egg: Vaccination against poultry coccidiosis. *Parasite Immunology*. https://doi.org/10.1111/j.1365-3024.2010.01209.x

Shirley MW, Smith AL, Tomley FM. 2005. The biology of avian Eimeria with an emphasis on their control by vaccination. *Adv Parasitol* 60: 285–330. https://doi.org/10.1016/S0065-308X(05)60005-X.

Shirley MW, Lillehoj HS. 2012. The long view: a selective review of 40 years of coccidiosis research. *Avian Pathol* 41:111–121. https://doi.org/10.1080/03079457.2012.666338.

Song, M., Lin, X., Zhao, J., Wang, X., Jiao, H., Li, H., Lin, H. (2020). High frequency vaccination-induced immune stress reduces bone strength with the involvement of activated osteoclastogenesis in layer pullets. *Poultry Science*. https://doi.org/10.1016/j.psj.2019.12.023

Song, X., Zhao, X., Xu, L., Yan, R., & Li, X. (2017). Immune protection duration and efficacy stability of DNA vaccine encoding Eimeria tenella TA4 and chicken IL-2 against coccidiosis. *Research in Veterinary Science*, *111*, 31–35. https://doi.org/10.1016/j.rvsc.2016.11.012

Wang, H., Ni, X., Qing, X., Liu, L., Lai, J., Khalique, A., Zeng, D. (2017). Probiotic enhanced intestinal immunity in broilers against subclinical necrotic enteritis. *Frontiers in Immunology*. https://doi.org/10.3389/fimmu.2017.01592

Williams, R. B. (2002). Fifty Years of Anticoccidial Vaccines for Poultry (1952–2002). *Avian Diseases*. https://doi.org/10.1637/0005-2086(2002)046[0775:fyoavf] 2.0.co;2

Xu, Q., Song, X., Xu, L., Yan, R., Shah, M.A., Li, X., 2008. Vaccination of chickens with a chimeric DNA vaccine encoding Eimeria tenella TA4 and chicken IL-2 induces protective immunity against coccidiosis. *Vet. Parasitol*. 156, 319-323.