

Experimental research on therapeutic value as coccidiostatics of Toltrazuril and Diclazuril in chicken eimeriosis

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INTRODUCTION

The experimental researches regarding the therapeutical and prophylactic efficiency of Toltrazuril and Diclazuril coccidiostatics in chicken eimeriosis have revealed the following:

Toltrazuril, administered once in dose of 1 ml/l of water to the group II had a good efficiency, the survival rate being 100%. Nevertheless, a high rate of oocysts elimination was observed (mean value: 59,027 OPG). The chickens belonging to this group which were sacrificed for control examinations showed lesions of fibrinous and hyperplastic enteritis.

The average weight gain in this group was higher than in group I, but lower than in group III and IV.

The coccidiostatic index in this group was 63.94, greater than the one of group I but smaller than the index of group III.

The coccidiostatic performance rate was 220.56, inferior to the one of group III.

The therapeutical and prophylactic efficiency value of Diclazuril administered in food in 200 mg/kg doses during the entire experimental period in group III was very good, the survival rate being 100% and the oocyst eliminations averaging 920 OPG.

The average weight gain in this group was higher than the one observed in groups I and II but smaller than the one of group IV.

The coccidiostatic index was 96.19, greater than the ones of groups I and II, while the

coccidiostatic performance rate was 331.91, which is much higher than the one observed in group II.

At the control sacrifices performed in this group no lesions were detected.

Due to the wide spreading of avian eimeriosis throughout the world, in every breeding system real control programs have developed (2, 3, 4).

During the last years the use of two anticoccidian medicines within the administration program of SHUTTLE has become completely accepted. In this plan a strong medicine in the beginning followed by an inoforus is used (3).

The extension of chimioprofilactical methods in eimeriosis may lead to the appearance of lines resistant to eimeria, phenomenon which appears, probably on genetic basis. Lately they have tried to thwart the chimioresistance by alternating the medicines in two programmes, one called "feed-back" and the other one called "rotation".

In the present paper, experimental researches were carried out to test the antieimerial efficiency of Toltrazuril (Bayer) and Diclazuril (Janssen) coccidiostatics in chicken eimeriosis.

MATERIAL AND METHODS

The experimental researches were carried out in the Laboratory and the Clinic of Parasitic Diseases of the Faculty of Veterinary Medicine, Cluj-Napoca, on 40 chickens, aged 10 days, experimentally infested. The chickens received the standard fodder, without the addition of coccidiostatic, during the whole experiment.

The chickens were grouped into 4 groups of 10 chickens each and they were kept isolated, in order to avoid spontaneous infestations.

Group I - was used as infested witness. The chickens were given 50,000 infestant oocysts/chickens/day for two days. The group was not treated during the experiment.

Group II - was infested the same way as group I. Three hours after infestation, the treatment with Toltrazuril, in one administration, in dose of 1 ml/l of water started.

Group III - was infested the same way as group I. Three hours after infestation the Diclazuril treatment started, in dose of 200 mg/kg fodder, and it was performed during the whole experiment.

Group IV - was used as uninfested witness.

The infestant material was obtained through prelevation from caecal and intestinal content from several intestinal mass with characteristic lesions and verified for the presence and the density of oocysts. The coprocultures were harvested for sporulation in solution of potassium bycromat 2%. The conditions were of laboratory and before administration, the oocysts were repeatedly washed and deposited and then they were administered individually. Before administration, the density was established through counting with the McMaster method.

The density of the infestant material was of 40,000 oocysts/ml of concentrate. The structure of eimerial populations in the infestant material was the following:

- *E. tenella*: 60%
- *E. maxima*: 10%
- *E. acervulina*: 10%
- *E. necatrix*: 5%
- *E. brunetti*: 5%
- *E. mitis*: 2.5%
- *E. praecox*: 7.5%.

There was plenty of fodder and water for each group and the temperature was of 28°C in the first days, then of 22°C.

In order to verify the anticoccidian, prophylactico-therapeutical efficiency, the tolerance and any adverse reaction during the experiment, there were established the following:

1. The body weight of each group through repeated weighing starting with day 0 and then at a 3 day interval.
2. Mortality dynamics in each group.
3. The marks of faeces aspect varying from 0 to 4; 0 - normal aspect; 4 - hemorrhagical faeces; 1-3 intermediar aspects.
4. Lesional score established on corpses and on chickens sacrificed from each group at the end of experiment. The marks depending on lesion intensivity will be the following: 0 - no lesion; 4 - intense, hemorrhagical lesions.
5. The fodder consumption during the experiment and the weight gain in each group.
6. The eimerial infestation intensivity during disease evolution outlined through coproscopy using the McMaster and Willis methods.
7. Specifying through micro-measurements and oocyst harvests the species of *Eimeria*.
8. Other aspects: water consumption, fodder, behaviour, clinical state of the groups.
9. The coccidiostatic index (C.I.) was established using the following formula:

$$C.I. = M.S. + P.S. - 15 (M.F. + M.L.)$$

M.S. - the average of weight gain during the pursued interval

P.S. - percentage of survival in the final day compared to the first day

M.F. - the average mark of faeces in each group (0-4)

M.L. - the average mark of lesions (0-4)

10. Percentage of coccidiostatic performance (P.P.)

$$P.P. = \frac{\text{index of chicken group infested and treated}}{\text{index of chicken group uninfested and untreated}} \times 100$$

RESULTS

As concerns the average weight gain, group IV, uninfested and untreated, registered the biggest value, followed by group III, treated with Diclazuril and by group II treated with Toltrazuril. The lowest weight gain was registered in group I, uninfested and untreated (Table 1).

The first clinical signs appeared in group I on the 6th day p.i.: inapetency, polydipsy, diarrheic or hemorrhagic faeces. Diarrheic faeces appeared a day before the clinical signs did. In 10 faeces samples, 8 were watery, diarrheic and on the clinical sign apparition day in 10 faeces samples, 8 were hemorrhagic.

The next clinical signs appeared 9 days after infestation in group II treated with Toltrazuril. In 2 chickens there was noticed deviation, inapetency, polydipsy, watery faeces in the beginning and then hemorrhagic faeces. Hemorrhagic faeces elimination stopped on day 12 and the clinical stage of the chickens improved.

In group II the percentage of diarrheic faeces was high until the end of the experiment but hemorrhagic faeces did not appear any more.

In group III no clinical signs or blood diarrhea appeared during the whole experiment.

Mortality index was registered to be the highest in the infested and untreated group while in the treated groups and in the witness group there was no case of mortality. First corpses in group I appeared on day 7 after infestation and they were 5. Then, on day 8, 3 more corpses appeared and on day 9, another one.

Morphopathological examinations allowed us to establish the lesional table and the way of evolution of the disease (1). 9 corpses were necropsied from group I, which was infested and untreated. The result of the necropsic exam is given in table 2.

Oocysts eliminations dynamics was characterised by important differences in the infested groups (Table 3, Fig. 1, 2, 3). While in group I, infested and untreated, the eliminations started on day 5 reaching the peak on day 8, in group II eliminations started on day 7 and they were high during the experiment.

In group III, eliminations started on day 8 and they were low during the experiment.

In group I, oocyst elimination ranged between 1,200-120,000 OPG, in group II between 1,800-137,000 OPG, while in group III they ranged between 300-1,600 OPG.

Eimeria population structure was identified during the experiment in the three infested groups, following the percentage of eliminated oocysts and the specific structure of *Eimeria* populations (Tables 4, 5).

Water consumption was higher in the first days after infestations in group I and it was about 490 ml/day, while in the other groups it was about 450 ml/day.

In order to check the prophylactico-therapeutical effect of the products that were used, there have been made control slaughters on the last day of the experiment. One chicken in group I and two chickens from group II and III, respectively were slaughtered (Table 6).

The coccidiostatic index (I.C.) and coccidiostatic performance was calculated on the basis of the formulas already described (Table 7).

Table 1
Weight value of experimental groups during the experiment (g/group)

| Group | Day 0 | Day 3 | Day 6 | Day 10 | Day 13 | Day 17 |
|-------|-------|-------|-------|--------|--------|--------|
| I | 741 | 755 | 890 | - | - | - |
| II | 783 | 860 | 930 | 1,160 | 1,330 | 1,535 |
| III | 779 | 865 | 963 | 1,236 | 1,437 | 1,662 |
| IV | 792 | 885 | 990 | 1,325 | 1,640 | 1,880 |

Table 2
Lesional table in chicken eimeriosis in witness untreated group

| No. | Group | Lesion location | Lesion name | Lesion Mark |
|-----|-------|------------------------|--|-------------|
| 1 | I | cecum, colon | catarrhal-hemorrhagic typhlocolitis | 4 |
| 2 | I | cecum, colon cloaca | catarrhal-hemorrhagic typhlocolitis, hemorrhagic cloacitis | 4 |
| 3 | I | cecum | fibrinous typhlitis | 3 |
| 4 | I | cecum, colon | hemorrhagic-necrotic typhlitis, catarrhal colitis | 4 |
| 5 | I | cecum | hemorrhagic-necrotic typhlitis | 4 |
| 6 | I | cecum, colon | catarrhal-fibrinous typhlocolitis | 3 |
| 7 | I | cecum | catarrhal typhlitis | 2 |
| 8 | I | small intestine, cecum | catarrhal hemorrhagic enteritis | 4 |
| 9 | I | duoden, jejunum, cecum | catarrhal duodeno-jejunitis, fibrinous typhlitis | 3 |

Table 3
The average of *Eimeria* oocyst coproelimination intensity in experimental chicken groups

| Group | Period (day) | Intensity (OPG) |
|-------|--------------|-----------------|
| I | 11 | 21,354 |
| II | 11 | 59,027 |
| III | 5 | 920 |
| IV | - | - |

Table 4
Specific structure of *Eimeria* populations in the infested groups at the beginning of the experiment

| Group | <i>E. tenella</i> | <i>E. maxima</i> | <i>E. acervulina</i> | <i>E. necatrix</i> | <i>E. brunetti</i> | <i>E. mitis</i> |
|-------|-------------------|------------------|----------------------|--------------------|--------------------|-----------------|
| I | 55 | 20 | 8 | 3 | 10 | 4 |
| II | - | - | - | - | - | - |
| III | - | - | - | - | - | - |

Table 5
Specific structure of *Eimeria* populations in the infested groups on day 14 of the experiment

| Group | <i>E. tenella</i> | <i>E. maxima</i> | <i>E. acervulina</i> | <i>E. necatrix</i> | <i>E. brunetti</i> | <i>E. mitis</i> | <i>E. sp.</i> |
|-------|-------------------|------------------|----------------------|--------------------|--------------------|-----------------|---------------|
| I | 43 | 24 | 14 | 9 | 3 | 2 | 5 |
| II | 54 | 20 | 15 | 6 | 2 | 3 | - |
| III | 1 | 8 | 1 | - | - | - | - |

Table 6
The results of the control necropsic exam at the end of the experiment

| No. | Group | Lesion location | Lesion name | Lesion mark |
|-----|-------|------------------------|--|-------------|
| 1 | I | duoden, jejunum, cecum | hyperplastic duodeno-jejunitis, hyperplastic fibrinous typhlitis | 2 |
| 2 | II | small intestine, cecum | hyperplastic enteritis, hyperplastic fibrinous typhlitis | 2 |
| 3 | II | duoden, jejunum, cecum | hyperplastic duodeno-jejunitis, fibrinous typhlitis | 2 |
| 4 | III | - | - | - |
| 5 | III | - | - | - |

Table 7
Cocciostatic index and performance percentage for Toltrazuril and Diclazuril in chickens

| Group | Quality | Initial number of chickens | Final number of chickens | Period (days) | Average gain (g/chicken) | Survivors % |
|---------------------------|----------------------|----------------------------|--------------------------|---------------|--------------------------|-------------|
| 1. Witness | infested untreated | 10 | 1 | 17 | 2.48 | 10 |
| 2. Prevention Toltrazuril | infested treated | 10 | 10 | 17 | 4.42 | 100 |
| 3. Prevention Diclazuril | infested treated | 10 | 10 | 17 | 5.19 | 100 |
| 4. Witness | uninfested untreated | 10 | 10 | 17 | 6.4 | 100 |

Table 7.a

| No. | Group | The average of grades | | I.C. | P.P. |
|-----|------------------------|-----------------------|---------|-------|--------|
| | | faeces | lesions | | |
| 1 | Witness | 1.4 | 3.5 | 28.98 | - |
| 2 | Prevention Toltrazuril | 1.5 | 1.2 | 63.92 | 220.56 |
| 3 | Prevention Diclazuril | 0.6 | 0 | 96.19 | 331.91 |
| 4 | Witness | 0 | 0 | 106.4 | - |

DISCUSSIONS

In the beginning of 1970 the compounds of relation class with uracil were discovered to have a potentially large efficiency spectrum against chick eimeriosis and the class was rediscovered in 1980 and it was a part of the following products: Toltrazuril, Diclazuril, Clazuril (3, 7, 8).

Toltrazuril is indicated as best level at 25 ppm, in water, in infected chicks. This product proves an excellent use in treatment of animals where the infection signs have already appeared. The disadvantage of this product is the fast resistance apparition and a long period of recovering

caused by the slow elimination of the residues (3, 8).

On the basis of the researches we carried out, this product proves to be efficient as there are no mortality cases but there are lesions in control slaughtered chickens and the oocyst release was considered to be high. Toltrazuril administration at the apparition of the first clinical signs proved to be most efficient related to prophylactic treatment of chickens aged 2 weeks (7).

For Diclazuril, the best level of use is at 1 ppm, although cocciostatic activity is registered even at 0.5 ppm. Activity spectrum was declared on the basis of the experiments made on all avian

eimerian species. The effect on eimerian species is varied. *E. tenella* is more sensitive to Diclazuril in all stages, while *E. maxima* is destroyed only in sexual phase. For this reason the conventional efficiency test based upon weight gain and lesion apparition does not show Diclazuril efficiency against *E. maxima*. Medicine resistance was discovered hard in *E. tenella*, *E. maxima* and *E. acervulina* (3, 10).

The results we obtained revealed the efficiency of Diclazuril as oocyst release was low and no lesion was found in the control slaughters and the average weight gain in the group treated with this product was superior to the one in Toltrazuril treated group.

CONCLUSIONS

Experimental researches concerning prophylactico-therapeutic efficiency of Toltrazuril (Bayer) and Diclazuril (Janssen) coccidiostatics in chickens revealed the following:

1. Toltrazuril, administered in dose of 1 ml/l water in only one administration, had a good prophylactico-therapeutical efficiency. The surviving percentage was of 100% but there was a high rate of oocyst elimination, the average value was of 59,027 OPG. In control slaughtered chickens there were fibrinous and hiperplastic enteritis lesions.

The weight gain was higher in this group than in group I, but lower than in group III and IV.

Coccidiostatic index in this group was 63.94, higher than in group I but lower than in group III.

The performance percentage of this coccidiostatic was 220.56, lower than in group III.

2. The prophylactico-therapeutic value of Diclazuril, administered during the whole experiment in dose of 200 mg/kg fodder, had very good efficiency, the surviving percentage was of 100% and the oocyst release averaged 920 OPG.

Weight gain was higher in this group than in groups I and II, but lower than in group IV.

Coccidiostatic index was of 96.19, higher than in group I and II and the performance percentage of the coccidiostatic was of 331.91, much higher than in group II.

In control slaughters made in this group there was no lesion.

REZUMAT

Cercetări experimentale privind valoarea terapeutică a coccidiostaticelor Toltrazuril și Diclazuril în eimerioză la puii de găină

Coccidiostaticul Toltrazuril (Bayer), administrat în doză de 1 ml/l apă, o singură dată, a avut o eficacitate bună. Procentajul supraviețuitorilor a fost de 100%, dar s-a observat un nivel ridicat al eliminării de oochisturi, valoarea medie fiind de 59.027 OPG. Puii martor sacrificați prezentau leziuni fibrinoase și de enterită hiperplastică.

În cazul produsului Diclazuril (Janssen), administrat pe tot parcursul experimentului în doză de 200 mg/kg hrană, eficacitatea a fost foarte bună, procentajul supraviețuitorilor fiind de 100%, iar eliminarea de oochisturi a înregistrat o medie de 920 OPG.

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