LEVAMISOLE-INDUCED RESISTANCE TO RAILLIETINA TETRAGONA INFECTION IN YOUNG CHICKS

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Abstract


The repeated pre-treatment with levamisole (L-tetramisole) was found to induce significant resistance to Raillietina tetragona infection in 7 day old chicks. A total of 6 twice weekly oral doses of 2.5 mg/kg reduced the parasitic burden from 40% in primarily infected controls (n = 10) to 13% in levamisole-treated chicks (n = 10). Resistance to R. tetragona was also observed in reinfected chicks (n = 9) when the initial infection was subsequently treated with niclosamide (Yomesan, 100 mg/kg). In this respect, the parasitic burden was reduced to 20%. In addition, a further reduction to 8.8% of the parasitic burden was obtained in reinfected chicks (n = 9) when they were also treated with levamisole at 6 twice weekly doses of 2.5 mg before challenge. The increased resistance of the young chicks to R. tetragona infection and/or reinfection was attributed to the immunomodulatory action of levamisole.

Raillietina tetragona (cestode), chicks, Levamisole, resistance.

The imidazole compound levamisole (L-tetramisole) has enjoyed considerable interest in veterinary medicine due to its broad spectrum anthelmintic activity and non-specific immunomodulatory effect (Abdel Salam 1986). The latter property was initially discovered by Renoux and Renoux (1971) and further substantiated by numerous investigations and reports (Janssen 1976; Symoens and Roseenthal 1977; Renoux 1978; Brunner and Muscoplat 1980; Guerreiro 1980; Mullgahy and Quinn 1986). However, the use of levamisole in poultry was still limited to its anthelmintic efficacy against certain parasitic nematodes including Ascaridia, Capillaria and Heterakis spp. (Clarkson and Beg 1970; Altaif 1972; Pankavish et al. 1973). The modulatory effect of levamisole upon the avian immune system has not been apparently investigated and the present report, therefore, describes the effect of levamisole pre-treatment on the susceptibility to Raillietina tetragona infection in young chicks. The parasite belongs to the cestode group which does not normally respond to the chemotherapeutic action of the drug.
Materials and Methods

Birds: Newly-hatched White Leghorn chicks were purchased from commercial farms (Almasara Co. Ltd, Khartoum North) and raised on standard grower diet with free access to water. The chicks were kept for one week before experiments commenced.

Drugs: Levamisole (Nilverm, ICI solution containing 7.5% W/V L-tetramisole) Niclosamide (Yomesan 500 mg tablets, Bayer). Levamisole was further diluted to 1:10 in water. Niclosamide was also dissolved in water and both drugs were administered orally.

Infective material: Cysticercoids of *R. tetragona* were recovered from naturally-infected ants (*Pachycondyla sennaarensis*) collected from soil in the neighbouring farms. The required number of cysticercoids was suspended in saline and transferred into gelatinous capsule for oral administration.

Experimental design: Two complementary experiments were performed on the effect of levamisole against primary infection and reinfection with the homologous cestode.

Experiment 1: (Primary infection)

Twenty chicks were divided into two equal groups (A & B). The first group (A) was pre-treated with 2.5 mg/kg levamisole twice weekly for three weeks. Group B was left without treatment for the same period of time. Both groups were then infected with *R. tetragona* (15 cysticercoids/chick) and killed two weeks post infection (see Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>Infective dose (cysticercoids)</th>
<th>No. of worms recovered at necropsy per individual chick</th>
<th>Total No.</th>
<th>Group mean (± SD)</th>
<th>% Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>A - Levamisole treated</td>
<td>15</td>
<td>2,1,2,1,2,3,2,3,1,3</td>
<td>20</td>
<td>2.0±0.82</td>
<td>13.3%</td>
</tr>
<tr>
<td>(n = 10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B - Untreated controls</td>
<td>15</td>
<td>4,8,9,8,5,6,4,3,7,6</td>
<td>60</td>
<td>6.0±2.0</td>
<td>40%</td>
</tr>
<tr>
<td>(n = 10)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Experiment 2: (Reinfection)

Three equal groups of chicks (A₁, B₁ & B₂) were used. Each group was composed of 9 chicks of the same age (7-day old). Groups B₁ and B₂ were initially infected with 20 cysticercoids per chick and subsequently treated with niclosamide (100 mg/kg) a week after. Both groups were then reinfected with the same number of cysticercoids and killed after another two weeks (Table 2). However, group B₂ chicks were first pre-treated with levamisole (2.5 mg/kg twice weekly) for 3 weeks before reinfection. On the other hand, group A₁ chicks were used as primarily infected controls (i.e infected with 20† cysticercoids each and killed two weeks post - infection for comparison).
### Table 2
Experimental design and results of experiment 2 (Reinfection)

<table>
<thead>
<tr>
<th>Group</th>
<th>Infective dose (cysticercoids)</th>
<th>No. of worms recovered at necropsy per individual chick</th>
<th>Total No.</th>
<th>Group mean (± SD)</th>
<th>% Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A_1$</td>
<td>Primarily infected (n=9)</td>
<td>12,9,11,9,7,8,12,10,8</td>
<td>86</td>
<td>9.6±1.81</td>
<td>47.8%</td>
</tr>
<tr>
<td>$B_1$</td>
<td>Reinfected (treated with niclosamide) (n=9)</td>
<td>4,6,2,4,3,5,4,5,3</td>
<td>36</td>
<td>4.0±1.22</td>
<td>20%</td>
</tr>
<tr>
<td>$B_2$</td>
<td>Reinfected (treated with levamisole niclosamide) (n=9)</td>
<td>2,1,1,2,3,1,1,3,2</td>
<td>16</td>
<td>1.8±0.83</td>
<td>8.8%</td>
</tr>
</tbody>
</table>

**Worm recovery**

The whole intestines were immediately removed at necropsy and opened into plastic dishes containing normal saline. The content was evacuated and the recovered worms were collected and preserved in Roudabush solution. They were then identified under light microscope and counted individually. Student's t-test was employed for the statistical evaluation of the results.

**Results**

The results of tapeworm recovery in primary infection and reinfection with *R. tetragona* in chicks are also shown in tables 1 and 2.

**Primary infection (Table 1):**

The mean parasitic burden in levamisole-treated chicks (group $A_1$) was significantly lower ($P < 0.001$) than in untreated controls (group $B_1$). The mean percentage tapeworm recovery was reduced from 40% in the control group to 13% in levamisole treated chicks.

**Reinfection (Table 2):**

The total worm burden in the reinfected groups ($B_1$ and $B_2$) was significantly lower ($P < 0.001$) than in primarily infected chicks (group $A_1$). The overall percentage tapeworm
recovery was reduced to 20% in the reinfected chicks (group B₁) without levamisole treatment. However, a further reduction to 8.8% of the overall percentage tapeworm recovery was obtained by levamisole treatment in reinfected chicks (group B₂).

The results of the present work have generally indicated that the pretreatment of young chicks with repeated doses of levamisole (2.5 mg/kg twice weekly for three weeks) increased their resistance to *R. tetragona* infection as judged by the significant reduction of worm recovery (Table 1). The result was probably due to the immunomodulatory action of levamisole, since the drug was not found to have any anthelmintic efficacy against tapeworms (Thienpont et al. 1966; Janssens 1976). Although the modulatory effect of levamisole upon the mammalian immune system is now well recognized (Muleahy and Quinn 1986), however, the exact mechanisms by which the drug can exert its immunological effects are not fully understood. Nevertheless, the drug was suggested to enhance the lymphocyte proliferative responses, increase lymphokin production and promote macrophage function (phagocytosis) (Aibrahim et al. 1977). In addition, the drug was found to be more effective in young hosts (Janssens 1976) and in those with hypofunctional T-lymphocytes (Guerrero 1980). In the present report, the chicks were used as young as 7-day old and that would probably account for the relative success of the drug in inducing significant immune protection against the parasite (*R. tetragona*).

Acquired resistance to homologous reinfection with cestode parasites has been previously reported (Health et al. 1979). In the present work, a significant resistance to reinfection with *R. tetragona* was also observed in young chicks (Table 2). The results, therefore, indicate that chicks are capable of developing acquired resistance to homologous reinfection with the cestode parasites. Such resistance was probably due to the antigenic stimulation caused by the destruction and disintegration of the dead parasite of the previous infection as a result of niclosamide treatment. Resistance to reinfection was also enhanced by levamisole pre-treatment (Table 2).

It is finally concluded that the routine use of levamisole in poultry management is highly beneficial in terms of its broad-spectrum anthelmintic activity and non-specific immunomodulation.
Acknowledgement

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Levamisolem indukována resistence
k infekci Raillietina tetragona u kuřat

Opakovaná premedikace levamisolem (L-tetramisole) vedle k signifikantní resistenci vůči infekci Raillietina tetragona u 7denních kuřat. Celkem 6 orálních dávek po 2,5 mg.kg⁻¹ zredukovalo 40% parazitární invazi u primárně infikovaných kontrol (n = 10) na 13 % u kuřat ošetřených levamisolem. Resistance vůči R. tetragona byla také pozorována u reinfikovaných kuřat (n = 9), když byla počáteční infekce léčena niclosamidem (Yomesan, 100 mg.kg⁻¹). V tomto případě byla parazitární invaze zredukována na 20 %. Další redukce na 8,8 % nastala u reinfikovaných kuřat (n = 9), která byla také ošetřena levamisolem za použití 6 dávek po 2,5 mg 2 x týdně před čelenží. Zvýšená resistance kuřat k infekci R. tetragona a reinfekci je přisuzována imunomodulačnímu účinku levamisolu.

Индуктированная левамисолом резистентность
к инфекции Raillietina tetragona у цыплят

Повторная премедикация левамисолом (L-tetramisole) вылилась в значимую резистентность к инфекции Raillietina tetragona у цыплят в возрасте 7 суток. В итоге 6 оральных доз по 2,5 мг.кг⁻¹ редуцировало 40% паразитарную инвазию у первичных инфицированных контрольных групп (n=10) в случае 13% цыплят, принимающих левамисол. Резистентность к R. tetragona наблюдали также у инфицированных цыплят (n=9), когда начальную инфекцию лечили никлоксамидом (emesan, 100 мг.кг⁻¹). В данном случае паразитарную инвазию редуцировали до 20%. Последующая редукция до 8,8% имела место у повторно инфицированных цыплят (n=9), принимающих левамисол.
в 6 дозах по 2,5 мг два раза в неделю перед введение лек- жированием. Повышение регенеративной функции к ин- фекции R. tetragona и реинфекции связывается с иммуно- модуляционным воздействием левамизола.

References


