EFFECT OF FIBRONOL AND DELTAMETHRIN VERSUS IVERMECTIN IN CONTROLLING CTENOCEPHALIDES CANIS INFESTATING GOATS

By
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Abstract

A total of 15 goats were randomly divided into five groups (n=3): control (no treatment), deltamethrin (5mg/kg), fipronil (10mg/kg), ivermectin (0.2mg/kg), and deltamethrin & fipronil. Fleas were counted at 0-, 2-, and 6-weeks post-treatment Blood samples were collected at the same time points of (deltamethrin & fipronil) to determine hemato-biochemical parameters such as Red blood cells (RBC), White blood cells (WBC), Hemoglobin (Hb), Hematocrit (Hct), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Total protein (TP), Albumin (Alb), Globulin (Glo), Cholesterol (Chol), Creatinine (Cr), Urea (Urea), and Glucose (Glu). Physiological performance was assessed by rectal temperature, skin temperature, respiration rate and pulse rate. The results showed that combination therapy had the highest efficacy against flea infestation compared to ivermectin treatment or the control group. The combination therapy also improved hemato-biochemical parameters such as RBC, HGB, HCT, and T3 compared to the control group or ivermectin treatment. The combined therapy significantly decreased ALT, AST or Cortisol compared to the control group or single treatments.

Key words: Ctenocephalides canis, Goat, Deltamethrin, Fipronil, Ivermectin, Hematology.

Introduction

Livestock is the main source of energy, food, raw materials, and compost for crops, particularly the dairy industry, have risen as an important economic source and a trademark for the agri-business in dairy, meat, and many other products (Gizaw et al, 2020).

Ctenocephalides canis is the commonest flea species on goats, leading to various health issues such as skin irritation, dermatitis, and anemia even in man (El Okbi et al, 1991). So, there was a need for flea control with safe, effective, and friendly measure (Gutiérrez et al, 2014). Combined therapy with multiple active ingredients was suggested as a potential alternative to flea control measures with enhance efficacy without resistance development (Krieger et al, 2005). Deltamethrin is a synthetic pyrethroid insecticide acts by disrupting the nervous system of insects, highly effective against fleas and ticks, but with adverse effects on animal health as hypersensitivity reactions and neurotoxicity (Diaz et al, 2005).

Fipronil is a phenyl-pyrazole insecticide acts by disrupting insects' nervous system by inhibition of γ amino-butyric acid (GABA) receptors in fleas and ticks, but associated with adverse effects on animal health such as hypersensitivity reactions and neurotoxicity (Alvarez et al, 2004).

Ivermectin is an avermectin macrocyclic lactone that acts by disrupting parasites nervous system by inhibiting Glutamate-gated chloride channels (Campbell, 2012). It has high efficacy against gastrointestinal nematodes (Salem et al, 2021), bancroftian filariasis circulating MF (Hassan et al, 2001), Leishmania promastigotes (Rasheid and Morsy, 1998), scabies (Elmogy et al, 1999), mites and ticks (Morsy and Haridy, 2000), Chrysomya bezziana infesting child teeth (Sharma and Hedge, 2010), and human lice (Ahmad et al, 2014), but with minimal one on fleas (Beugnet et al, 2005).

Efficacy of selamectin and fipronil-(s)-methoprene against cat fleas showed significantly impacted larval and adult emergence, with
fipronil-(s)-methoprene with greater larval reduction and the emerging adult in 6th week (Dryden et al, 2007).

This study aimed to evaluate efficacy of combined therapy against *Ctenocephalides canis* infesting goats and to assess the impact on hematological and physiological parameters.

**Materials and Methods**

The study was carried out from May 10 to July 10, 2023, on a farm in the El-Kharga Oasis, New Valley Governorate located in the Western Tropical Egyptian Desert.

Parasitological study: A total of 15 goats aged 2-3 years with a body weight of 17-25 kg were housed in semi-open sheds and randomly divided into five groups of 3 goats each: G1: control, G2: deltamethrin (5mg/kg) treated, G3: fipronil (10 mg/kg) treated, G4: ivermectin (0.2mg/kg) treated and G5: deltamethrin & fipronil treated. Fleas were counted at 0-, 2-, & 6-weeks post-treatment. Animal was placed on its back and the fleas were counted on the least haired parts- abdomen, udder, perineal area, and medial side of thighs. Interpretation was level 0: no fleas; level 1: 1-2 fleas (very weak infestation); level 2: 3-6 fleas (weak infestation), level 3: 7-10 fleas (moderate infestation), level 4: 11-15 fleas (high infestation); and level 5: 16 or more = severe infestation (Nizamov, 2023). Identification of flea species was done (Lewis, 1967).

Therapy administrations: 1- Goats were dipped in a 5% Deltamethrin solution (3-acino-3-phenoxybenzyl (1R,3R)-3-(2-2 Dimethylcyclopropano carboxylate) 1 cm for each liter for 5-7 minutes according to the manufacturer's instructions. Treatment was repeated after 2 & 6 weeks for a total of 3 dips. 2- Goats were sprayed with a 10% Fipronil solution at a dose of 10 ml/kg body weight. This treatment was repeated after 2 and 6 weeks for a total of 3 sprays. 3- Goats received an intramuscular injection of ivermectin (Ivermectin 1g, Clorsulon 10g) at a dose of 0.2 mg/kg body weight. Treatment was repeated after 2 & 6 weeks for a total of 3 injections.

Blood parameters: Two blood samples were collected from the goats' jugular vein (one for whole blood and second to separate sera).

Hematological parameters: About 2ml of blood was collected in a clean ependorph tube with anticoagulant (EDTA) before watering and feeding during the experimental study. Anti-coagulated blood was analyzed for complete CBC.

Analytical procedures: Second blood sample was without anticoagulant and left to clot, centrifuged at 3000rpm for 10 minutes to separate serum and examined for total proteins, albumin, urea, creatinine, glucose, and total cholesterol. Globulin concentration was computed by subtracted-albumin concentration from TP. Sera enzymatic activities of ALT & AST were also assayed. All chemicals used were of analytical grade.

Physiological parameters: Thermoregulatory responses, RR and PR, were evaluated at day 0, 2 & 6 weak post-treatment before measuring rectal temperature. RR was measured by counting flank movements at 15s and multiplied by 4 to get breaths per minute (Al-Qaisi et al, 2020). RT & temperature were recorded using a digital thermos.

Statistical analysis: Data were computerized and analyzed using SAS v 9.1 and differences among periods were tested using Duncan's Multiple Range Test (Duncan, 1955).

The model used was $Y_{ij} = \mu + A_j + \xi_{ij}$, $Y_{ij} = \text{observation period}$, $\mu = \text{overall mean}$, $A_j = \text{experimental period}$ & $\xi_{ij} = \text{random error}$.

**Results**

Dog flea, *C. canis* infested 100% goats with mean number of control group was significantly (P< 0.05) higher than other groups. Also, Gs 3 & 4 was significantly (P < 0.05) increased the mean number of fleas as compared with Gs 5 & 6 but, without significant differences detected among Gs 2, 3, & 4 or Gs 5 & 6. So, combined therapies gave highest efficacy against flea infestation compared to single ivermectin or control.

Combined therapies decreased significantly (P< 0.05) WBC and MCV as compared with pretreatment. However, total number of RBC,
HGB, & HCT significantly (P< 0.05) increased with both at 6 weeks post-treatment.

Combined therapies didn't significantly affect total protein, albumin, globulin, glucose, total cholesterol, urea-n, and creatinine. But, AST & ALT was significantly (P < 0.05) decreased with both particularly at 6 weeks post-treatment as compared to pre-treatment. Concentration of T3 hormone was significantly (P < 0.05) higher with both at 6 weeks post-treatment than pre-treatment. But, cortisol decreased with combined ones at 2nd & 6th weeks of post treatment as compared to pretreatment.

Deltamethrin and Fipronil showed decrease in heart rate by disrupting fleas’ nervous system causing paralysis and death. Also, chemicals showed indirect effects on goat’s physiology. Both showed decrease in rectal temperature, skin temperature decreased heart rate and rectal temperature.

Details were given in tables (1, 2, 3 & 4) and figures (1 & 2).

**Table 1: Efficacy of combination of therapies against flea infestation**

<table>
<thead>
<tr>
<th>Time per week</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>G5</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>17</td>
<td>13</td>
<td>15</td>
<td>16</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>8</td>
<td>11</td>
<td>15</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>7</td>
<td>13</td>
<td>11</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Fleas (mean)</td>
<td>23.33±3.76</td>
<td>9.33bc±1.86</td>
<td>13.00b±1.13</td>
<td>14.00b±1.53</td>
<td>4.67dc±1.76</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Table 2: Efficacy of a combination of therapies against flea infestation on hematology analysis**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-treatment</th>
<th>2 week post-treatment</th>
<th>6 week post-treatment</th>
<th>SEM</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (10³/µl)</td>
<td>14.18A</td>
<td>13.06B</td>
<td>12.64B</td>
<td>0.23</td>
<td>0.0109</td>
</tr>
<tr>
<td>RBC (10⁶/µl)</td>
<td>6.68H</td>
<td>6.86H</td>
<td>8.09A</td>
<td>0.19</td>
<td>0.0015</td>
</tr>
<tr>
<td>HGB (g/dl)</td>
<td>9.22H</td>
<td>9.78H</td>
<td>11.02A</td>
<td>0.25</td>
<td>0.0041</td>
</tr>
<tr>
<td>HCT %</td>
<td>32.18H</td>
<td>34.72A</td>
<td>36.36A</td>
<td>0.65</td>
<td>0.0229</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>49.66A</td>
<td>46.62AB</td>
<td>44.44B</td>
<td>0.87</td>
<td>0.0449</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>18.42</td>
<td>17.06</td>
<td>16.64</td>
<td>0.43</td>
<td>0.2556</td>
</tr>
<tr>
<td>MCHC (g/dl)</td>
<td>37.10</td>
<td>36.26</td>
<td>35.72</td>
<td>0.40</td>
<td>0.4133</td>
</tr>
</tbody>
</table>

**Table 3: Efficacy of a combination of therapies against flea infestation on blood biochemical parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SEM P-values</th>
<th>2 week post-treatment</th>
<th>6 week post-treatment</th>
<th>SEM P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein (g/l)</td>
<td>7.548</td>
<td>7.574</td>
<td>7.614</td>
<td>0.03</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.608</td>
<td>3.546</td>
<td>3.446</td>
<td>0.08</td>
</tr>
<tr>
<td>Globulin (g/dl)</td>
<td>3.840</td>
<td>3.868</td>
<td>4.088</td>
<td>0.09</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>57.4</td>
<td>58.2</td>
<td>59.6</td>
<td>1.21</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>159.914</td>
<td>172.708</td>
<td>163.532</td>
<td>2.63</td>
</tr>
<tr>
<td>Liver function:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST (U/l)</td>
<td>47.8A</td>
<td>44.6H</td>
<td>42.8H</td>
<td>0.79</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>19.8A</td>
<td>18.2A</td>
<td>16.8H</td>
<td>0.51</td>
</tr>
<tr>
<td>Kidney function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea-N (mg/dl)</td>
<td>26.408</td>
<td>25.51</td>
<td>24.484</td>
<td>0.49</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.807</td>
<td>1.7668</td>
<td>1.6338</td>
<td>0.53</td>
</tr>
</tbody>
</table>

**Table 4: AST, aspartates aminotransferase; ALT, alanine aminotransferase.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SEM P-values</th>
<th>2 Week post-treatment</th>
<th>6 Week post-treatment</th>
<th>SEM P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3 (µg/dl)</td>
<td>1.74A</td>
<td>1.796B</td>
<td>1.98A</td>
<td>0.04</td>
</tr>
<tr>
<td>Cortisol (ng/dl)</td>
<td>15.942A</td>
<td>15.242H</td>
<td>14.972H</td>
<td>0.14</td>
</tr>
</tbody>
</table>

**Discussion**

Phylogenetic models showed cat fleas are capable of infesting a broad diversity of wild mammal species through ecological fitting. Those that use anthropogenic habitats are at highest risk. Dog fleas have been recorded in 31 mammal species that are primarily restricted to certain phylogenetic clades, including canids, felids and murids. It closely resembles at flea, *Ctenocephalides felis* lives on a wider range of animals with more prevalent globally (Clark et al, 2018).

In the present study, combination of fibronol and deltamethrin gave higher efficacy in treating *C. canis* compared to a single ivermectin treatment. This agreed with Al-Hadhrami *et al*.
al. (2021), they found that the synergistic effect of the two compounds. Fibronol, a synthetic pyrethroid, acts as an insecticide by disrupting the fleas' nervous system causing their paralysis and death. Deltamethrin, another synthetic pyrethroid, also targets the fleas' nervous system but, with a longer residual effect (El-Mashad et al, 2020). Ivermectin is a broad ant-helmintic drug (Freedman et al, 1989), as well as insecticidal activities (Morsy et al, 2001). Nevertheless, combined fibronol and deltamethrin gave a more comprehensive and effective control of sheep fleas (Al-Mahrooqi et al, 2019). Combined of deltamethrin and fipronil spraying was effective against sheep fleas under field conditions without significant adverse effects or toxicity with the used dose. This agreed with El-Hefnawy and El-Mahdy (2018); El-Sherif and El-Sherif (2019) and Al-Mashhadani and Al-Bahadly (2019). Besides, ivermectin administration made a farmer aware of adverse reactions and dosing (Smith et al, 2021). Nevertheless, ivermectin is continuing to offer more and more promise to improve global public health by treating a diverse range of diseases, with its unexpected potential as an antibacterial, antiviral and anti-cancer agent being particularly extraordinary (Crump, 2017).

In the present study, morphological identification of fleas by light microscopes was a crucial aspect. The light microscope showed detailed flea morphology to distinguish between different species. Head is characteristic oval form, with distinct lateral margins that taper to posterior end, which allows the flea to easily attacking host's fur and sucks blood. Length of the first genal comb spine is noteworthy located along the head side being particularly long and prominent. Two short, stout bristles located between the post-median and long apical bristles of the hind tibia dorsal margin. The bristles maintain balance and grip on host's fur to support during movement. All these agreed with Yakub et al. (2020).

In the present study, RBC, HGB & HCT significantly (P< 0.05) increased with combined therapy at 6 weeks post-treatment. This agreed with Ajith et al. (2019), who found significant improved of hematological parameters on 21th day post therapy. The decreased in rectal temperature might be caused by flea allergy or transmit bacterial diseases to goats. This agreed with Ezeakacha et al. (2015), they reported that temperature was due to fleas' bites irritation and skin inflammation of host.

**Conclusion**

No doubt, the cat fleas are among the most host-generalist of all indoors ectoparasites. Combined Fibronol and Deltamethrin gave high efficacy in *Ctenocephalides canis* eradication compared to a single ivermectin dose. Fibronol and Deltamethrin improved the hematological and biochemical parameters.

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**Explanation of figure**

Fig. 1: Effects of flea infestation on goats and its control on temperatures

Fig. 2: Effects of flea infestation on goats and its control rates