A COMPARATIVE STUDY OF EFFICIENCY OF DIFFERENT IVERMECTIN MEDICINAL FORMS FOR TREATING HELMINTOSIS IN LIVE- STOCK ANIMALS

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Key words: helmintosis; ivermectin; parasites

A comparative study of efficiency of injection and oral forms of ivermectin has been conducted. The research results indicate that efficiency of drugs with ivermectin against endoparasites is very high and reaches 100%. The exception is Oesophagostomum dentatum, the therapeutic effectiveness against it in some cases was less – from 85% to 95%. The therapeutic effectiveness in experimental groups is 100%; it confirms the complete parasites elimination by “Neoverm” in the doses from 0.2 to 0.3 mg/kg when using it twice and in the dose of 0.3 mg/kg with a single use. The single use of “Neoverm” in the doses lower than 0.3 mg/kg does not provide the complete elimination of parasites. The use of drugs with ivermectin – “Neoverm” and “Intramek” based on a nanoemulsion provides the therapeutic effect even after single administration. In spite of the fact that a single administration of injection drug “Intramek” in the recommended dose of 0.3 mg/kg did not result in the complete elimination of O. dentatum, its efficiency can be considered as rather sufficient compared to the oral drug “Neoverm”. The oral 0.6% ivermectin premix also showed high efficiency against endoparasites, except for O. dentatum. The use of injection and oral drugs with ivermectin – “Neoverm” and “Intramek” based on nanoemulsions is technologically more advantageous for farms than application of the oral premix since these drugs provide a therapeutic effect even after a single administration, while the premix must be given during a week. The therapeutic effectiveness of “Neoverm” and “Intramek” can be considered as equivalent. It is obvious that oral drug “Neoverm” will be beneficial for large livestock and injection “Intramek” – for small farms.

A wide distribution of helminthoses in agriculture of Ukraine requires improvement of the existing antihelmintic drugs and introduction of the new ones from the scientists of veterinary medicine.

One of the high-effective anthelmintics is ivermectin, which possesses the expressed insectoacaricid and antihelmintic action [4, 5]. Ivermectin affects glutamate-sensitive chloric channels and γ-aminobutiric acid receptors of parasites.

Owing to development of a new research area – nanotechnology, a unique possibility of creating new medicinal forms based on micelles, liposomes and submicronic emulsions (nanoemulsions) has appeared [9, 11]. Nanoemulsions are also known as miniemulsions, ultradisperse emulsions and submicronic emulsions. Nanoemulsions are emulsions with an average particle diameter from 10 to 1000 nm [6]. The particle size depends on the quantitative composition of the emulsion and the ratio of active and auxiliary components [8]. Particles may exist in the “oil-in-water” and “water-in-oil” forms where the core of the particle is oil or water, respectively [10].

Based on the nanoemulsion of ivermectin the Ukrainian researchers created “Neoverm” and “Intramek” drugs for oral and parenteral use that are easy-to-use, non-toxic in therapeutic doses and effective against endo- and ectoparasites [3].

The aim of the study was to conduct a comparative study of the therapeutic effectiveness of injection and oral drugs with ivermectin based on nanoemulsions, as well as to determine the minimal effective dose and the required dosage frequency of “Neoverm”.

Materials and Methods

The clinical studies of drugs with ivermectin were conducted at “Agroprodservice” agro-enterprise in the Ternopol region. Three drugs were selected for comparative studies:

- “Neoverm” – a nanoemulsion for oral administration produced by “AT Biopharm” (Kharkiv, Ukraine);
- “Intramek” – a nanoemulsion for injections produced by “AT Biopharm” (Kharkiv, Ukraine);
- “Ivomec” – 0.6% oral ivermectin premix produced by Merital (USA) [7].

The clinical studies of drugs were conducted in the following directions:

- qualitative and quantitative study of helminthic invasion in pigs;
- study of the therapeutic effect when using drugs on animals;
- determination of the minimal effective dose and the required dosage frequency of “Neoverm”.

The coproovoscopic examination of feces was performed by the method of Fulleborn. Counting the number of helmithic eggs in 1 g of feces was performed by Trach method. Feces taken from all animals were examined for the presence of eggs of pulmonary and gastrointestinal nematodes, the intensity of infection was determined by Trach method [1, 2].
The studies for the presence and intensity of invasion were performed in 14 days after treatment.

For the research there were 9 groups of pigs, 20 animals in each group, 5 months old with the body weight of 70-80 kg. Group 1 was the control and received no drugs. The experimental groups 2-9 received drugs with ivermectin in an amount of 0.1-0.3 mg of the active substance (AS) per 1 kg of body weight (Tab. 1).

### Results and Discussion

The results of the qualitative and quantitative study of helminthic invasion are given in Tab. 2. *Ascaris suum, Trichuris suis, Oesophagostomum dentatum, Metastrongylus spp., Strongyloides ransomi* were detected. The invasion intensivity was from 5 to 40 eggs per 1 g of feces.

The results of fecal test coproovoscopy in 14 days after treatment are given in Tab. 3-5. The therapeutic effectiveness of drugs in experimental groups 2-5 is 100%; it indicates the complete para-

### Table 1

| Group No. | The number of animals in the group | The drug used | Dose and drug regimen |
|-----------|-----------------------------------|--------------|-----------------------|
| 1         | 20                                | no           | no (control)          |
| 2         | 20                                | Neoverm      | 0.3 mg AS/1 kg b.w., twice, with 24 h interval |
| 3         | 20                                |             | 0.25 mg AS/1 kg b.w., twice, with 24 h interval |
| 4         | 20                                |             | 0.2 mg AS/1 kg b.w., twice, with 24 h interval |
| 5         | 20                                |             | 0.3 mg AS/1 kg b.w., once |
| 6         | 20                                |             | 0.25 mg AS/1 kg b.w., once |
| 7         | 20                                |             | 0.2 mg AS/1 kg b.w., once |
| 8         | 20                                | 0.6% Ivomec premix | 0.1 mg AS/1 kg b.w., daily, for 7 days |
| 9         | 20                                | Intramek    | 0.3 mg AS/1 kg b.w., once |

### Table 2

| Parasites                  | IE, % | II, eggs per 1g of feces |
|----------------------------|-------|--------------------------|
| *Ascaris suum*             | 90    | 10-40                    |
| *Trichuris suis*           | 45    | 5-20                     |
| *Oesophagostomum dentatum* | 80    | 5-10                     |
| *Metastrongylus spp.*      | 21    | 5-10                     |
| *Strongyloides ransomi*    | 90    | 5-15                     |

### Table 3

| Group No. | Parasites                  | IE, % |
|-----------|----------------------------|-------|
| 2         | *Ascaris suum*             | 100   |
|           | *Trichuris suis*           | 100   |
|           | *Oesophagostomum dentatum* | 100   |
|           | *Metastrongylus spp.*      | 100   |
|           | *Strongyloides ransomi*    | 100   |
| 3         | *Ascaris suum*             | 100   |
|           | *Trichuris suis*           | 100   |
|           | *Oesophagostomum dentatum* | 100   |
|           | *Metastrongylus spp.*      | 100   |
|           | *Strongyloides ransomi*    | 100   |
| 4         | *Ascaris suum*             | 100   |
|           | *Trichuris suis*           | 100   |
|           | *Oesophagostomum dentatum* | 100   |
|           | *Metastrongylus spp.*      | 100   |
|           | *Strongyloides ransomi*    | 100   |
| 5         | *Ascaris suum*             | 100   |
|           | *Trichuris suis*           | 100   |
|           | *Oesophagostomum dentatum* | 100   |
|           | *Metastrongylus spp.*      | 100   |
|           | *Strongyloides ransomi*    | 100   |
| 6         | *Ascaris suum*             | 100   |
|           | *Trichuris suis*           | 100   |
|           | *Oesophagostomum dentatum* | 90    |
|           | *Metastrongylus spp.*      | 100   |
|           | *Strongyloides ransomi*    | 100   |
| 7         | *Ascaris suum*             | 100   |
|           | *Trichuris suis*           | 100   |
|           | *Oesophagostomum dentatum* | 85    |
|           | *Metastrongylus spp.*      | 100   |

### Table 4

| Group No. | Parasites                  | IE, % |
|-----------|----------------------------|-------|
| 9         | *Ascaris suum*             | 100   |
|           | *Trichuris suis*           | 100   |
|           | *Oesophagostomum dentatum* | 95    |
|           | *Metastrongylus spp.*      | 100   |
|           | *Strongyloides ransomi*    | 100   |

### Table 5

| Group No. | Parasites                  | IE, % |
|-----------|----------------------------|-------|
| 8         | *Ascaris suum*             | 100   |
|           | *Trichuris suis*           | 100   |
|           | *Oesophagostomum dentatum* | 95    |
|           | *Metastrongylus spp.*      | 100   |
|           | *Strongyloides ransomi*    | 100   |
sites elimination by “Neoverm” in the doses from 0.2 to 0.3 mg/kg when using it twice and in the dose of 0.3 mg/kg with a single use. The single use of “Neoverm” in the doses lower than 0.3 mg/kg does not provide the complete elimination of parasites (Tab. 3).

In spite of the fact that a single administration of injection drug “Intramek” in the recommended dose of 0.3 mg/kg did not result in the complete elimination of O. dentatum (Tab. 4), its efficiency can be considered as rather sufficient compared to the oral drug “Neoverm”.

The oral 0.6% ivermectin premix also showed high efficiency against endoparasites, except for O. dentatum (Tab. 5).

CONCLUSIONS
The use of injection and oral drugs with ivermectin—“Neoverm” and “Intramek” based on nanoemulsions is technologically more advantageous for farms than application of the oral premix since these drugs provide a therapeutic effect even after a single administration, while the premix must be given during a week [7].

A simple calculation shows that when using the oral premix for the period recommended by the manufacturer (7 days) each animal receives 0.7 mg of the active substance per 1 kg of the body weight, and while using “Neoverm” and “Intramek” only 0.3 mg is administered. It significantly decreases the likelihood of penetration of residual quantities of the active substance in a human food and reduces the cost for treatment of animals.

The therapeutic effectiveness of “Neoverm” and “Intramek” can be considered as equivalent. It is obvious that oral drug “Neoverm” will be beneficial for large livestock and injection “Intramek” – for small farms.

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СРАВНИТЕЛЬНОЕ ИССЛЕДОВАНИЕ ЭФФЕКТИВНОСТИ РАЗЛИЧНЫХ ЛЕКАРСТВЕННЫХ ФОРМ ИВЕРМЕКТИНА ПРИ ЛЕЧЕНИИ ГЕЛЬМИНТОЗОВ СЕЛЬСКОХОЗЯЙСТВЕННЫХ ЖИВОТНЫХ
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Ключевые слова: гельминтоз; ивермектин; паразиты; экстенсэффективность

Проведено сравнительное исследование эффективности инъекционной и пероральной форм ивермектина. Результаты исследования свидетельствуют, что эффективность препаратов ивермектина против эндопаразитов очень высока – 100%. Исключением является Oesophagostomum dentatum. Экстенсэффективность действия препаратов против этого вида паразитов в некоторых случаях несколько меньше – от 85% до 95%. Экстенсэффективность препаратов в опытных группах составляет 100%, что свидетельствует о полном уничтожении паразитов препаратом «Неоверм» в дозах от 0,2 до 0,3 мг/кг при двухкратном применении и в дозе 0,3 мг/кг – при однократном. Однократное использование «Неоверма» в дозах меньше 0,3 мг/кг не обеспечивает уничтожение 100% паразитов. Несмотря на то, что однократное применение инъекционного препарата «Интрамек» в рекомендованной дозе 0,3 мг/кг не привело к полному уничтожению O. dentatum, эффективность препарата можно считать вполне достаточной по сравнению с пероральным препаратом «Неоверм». Пероральный 0,6%-ный премикс ивермектина также показал высокую эффективность против эндопаразитов, за исключением O. dentatum. Применение иекционных и пероральных препаратов ивермектина на основе наноэмульсий «Неоверм» и «Интрамек» технологически более выгодно для хозяйств, чем использование перорального премика, т. к. данные препараты обеспечивают терапевтический эффект даже после однократного применения, а премикс необходимо давать на протяжении недели. Терапевтическую эффективность «Неоверма» и «Интрамека» можно считать эквивалентной. Очевидно, что пероральный препарат «Неоверм» будет выгоден на большом поголовье, а инъекционный «Интрамек» – для небольших хозяйств.