

THE EFFICACY OF FLUBENDAZOLE AGAINST *TRICHINELLA SPIRALIS* IN SWINE

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Summary :

A trial was undertaken to assess the efficacy of flubendazole against experimentally induced trichinellosis in pigs when given mixed with food at different dose rates. At the start of the experiment, 48 pigs were infected with approximately 35,000 larvae of *Trichinella spiralis*, after what the animals were distributed in six groups. The first three groups were used to test the activity of the drug against adult stages. Other three groups served to define the efficacy against muscle larvae. The dose rate of flubendazole varied according to the purpose of the experiment (from 8 mg/kg up to 62 mg/kg). At the end of the trial, the pigs were necropsied and the number of adults and larvae in predilection muscles were determined. At a dose rate of 8 mg/kg flubendazole supplied with food during eight days was 100 % effective against adults. At a dose rate of 31 mg/kg flubendazole administered for 14 days was 72.35 % effective. Treatment with higher dosages of flubendazole (62 mg/kg) resulted in increased efficacy (87.77 %) against the parasites. The biological assay performed with larvae from the muscle samples originating from the pigs treated with 62 mg/kg showed that at least half of the larvae were not infective.

KEY WORDS : *Trichinella spiralis*, pig, flubendazole.

Many compounds have been alleged to be effective against *Trichinella*. Some of them are still used in the treatment of patients but none of them up to now found a significant role in the treatment of pigs. Flubendazole is a broad spectrum anthelmintic which is well tolerated in all animals. The activity of flubendazole against *Trichinella spiralis* in pigs was just preliminary reported by Thienpont & Vanparijs (1980), Vanparijs & Thienpont (1980) and Vanparijs & Thienpont (1984). A more extended study was conducted by Vanparijs *et al.* (1979). The authors found a high activity of this compound against all *Trichinella* stages in rats. The knowledge on efficacy in

pigs still lacks on reliable data obtained on higher number of animals. The aim of this study was to demonstrate the level of activity of flubendazole against adult worms and muscle larvae of *Trichinella spiralis* in pigs in order to define potential for treatment or prevention of trichinellosis in pigs.

MATERIALS AND METHODS

The trial has been conducted on Duroc x Landrace pigs (48 animals), 6 weeks old and weighing about 10 kg. At the start of the trial, all animals were infected with approximately 35,000 muscle larvae *Trichinella spiralis* (MSUS/PO/60/1593, *Trichinella* Reference Centre). Infected pigs were split in six groups, (A, B, C, D, E, F). The first three groups (A, B, C) were fed with medicated food from the 6th day up to 14th day after infection. Group A received the lower dosage rate of flubendazole (8 mg/kg) while the group B the higher one (16 mg/kg). The Group C remained untreated. Other three groups (D, E, F) were fed with medicated food from the day 56 up to the day 70 after infection. The group D was treated with flubendazole at the dose rate of 31 mg/kg. The group E received the higher dosage (62 mg/kg) of the same drug. The group F remained also untreated.

The drug, flubendazole was supplied by Krka, Novo Mesto (BIOVERMIN, original package) and was mixed in commercial food at designed dosage rates (Table I).

ADULT STAGE AND MUSCLE LARVAE RECOVERY PROCEDURE

The intestines were slit lengthwise and incubated for two hours in warm saline. After thorough grinding, muscle samples (20 g) were artificially digested during 45 minutes. All the recovered larvae were immediately counted in order to distinguish viable from non viable or damaged larvae.

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Group	No. pigs per group	Day of first treatment (Days post infection)	Treatment days	Dose rate of flubendazole	Necropsy
A	1/6	6	8	8 mg/kg	15*
B	2/6	6	8	16 mg/kg	15
C	3/6	6	8	no treatment	15
D	4/10	56	14	31 mg/kg	14**
E	5/10	56	14	62 mg/kg	14
F	6/10	56	14	no treatment	14

* days after infection

** days after treatment.

Table I. – Design of the trial.

BIOLOGICAL ASSAY IN MICE

In order to define the infectivity of the larvae from diaphragms of treated animals (pig no. 2/31 mg/kg; pig no. 5/62 mg/kg), further biological assay in mice was also performed. Immediately after counting, approximately 200 larvae were orally administered to five C57 Bl/6J male mice. Thirty days later, mice were killed and their whole carcasses were digested after what the muscle larvae burden was compared to controls. The control mice were infected with the same dose of viable larvae from the tissue of control pigs.

RESULTS

The activity of flubendazole on the development of the adult worms was 100 % when given at 8 mg/kg or 16 mg/kg from day 6 to day 14 after infection. No adult worms were found in intestines when checked at day 14 whereas the corresponding untreated group necropsied at the same day

harboured a high number of adults (mean number per group = 8,200, data not shown). Among pigs fed with lower dose rate of flubendazole, variable findings were noted (Figs 1, 2, 3). The efficacy ranged from 69.80 % up to 74.55 % (in different muscle samples). Samples from pigs treated with 62 mg/kg of flubendazole have significantly higher number of dead larvae than pigs treated at the dosage rate of 31 mg/kg. The efficacy for this dose rate ranged from 86.16 % up to 89.44 %. Statistically significant difference ($p \leq 0.03$) between the two treated groups was also found. Biological assay (infection with larvae originating from pigs treated with 62 mg/kg of flubendazole) performed in mice showed that at least half of the larvae were not infective (Fig. 4). Infection of mice with larvae from pigs treated with 31 mg/kg of flubendazole resulted in higher larvae burden when compared to those infected with larvae from pigs treated with 62 mg/kg of flubendazole. Statistically significant difference ($p \leq 0.0005$) was also noted between two groups of mice infected with larvae from pigs treated with different dosages.

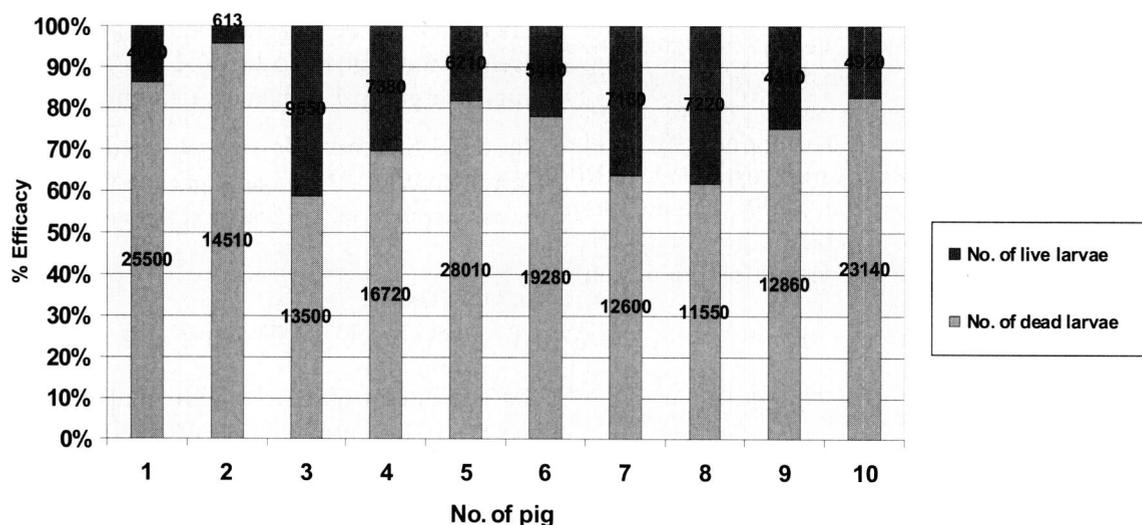


Fig. 1. – Muscle larvae recovery from the diaphragm of pigs treated with 31 mg/kg of flubendazole.

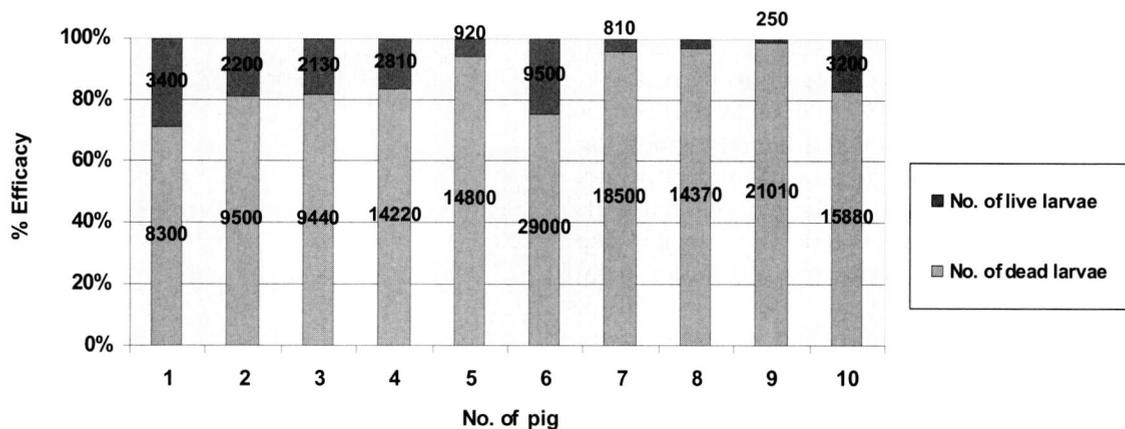


Fig. 2. – Muscle larvae recovery from the diaphragm of pigs treated with 62 mg/kg of flubendazole.

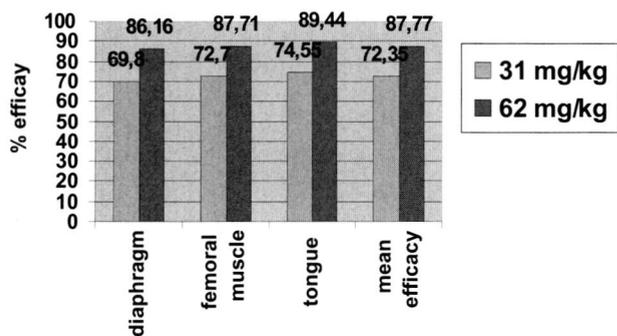


Fig. 3. – Efficacy (%) per group of pigs treated with different dosage of flubendazole.

DISCUSSION

The activity of flubendazole against adult worms was found excellent. In agreement with our results, Vanparijs & Thienpont (1984) also found that the development of larvae into adult worms is completely inhibited with a dose level of 8 mg/kg given for two weeks. Vanparijs *et al.* (1984) indicated

that the adult worms of *Trichinella pseudospiralis* in rats are extremely sensitive to low doses of flubendazole since a dose level of 8 mg/kg, given for seven days, was about 100 % effective. According to the activity against muscle larvae quite variable findings were noted in this study. Among pigs fed with lower dose rate of flubendazole the efficacy ranged from 69.60 % up to 74.55 % (in different muscle samples). Samples from pigs treated with 62 mg/kg of flubendazole have significantly higher number of dead larvae than pigs fed with lower dose rate. The efficacy for this dose rate ranged from 86.16 % up to 89.44 % which is not in perfect accordance with previously published results by Thienpont & Vanparijs (1980). Mentioned authors found that all animals treated during the encysted phase with dose levels of 31 and 62 mg/kg, were completely clean at post-mortem. Even we administered same dosage rates the activity over 90 % was found just in few animals. Though it is hard to be certain it can be assumed that the variable activity could

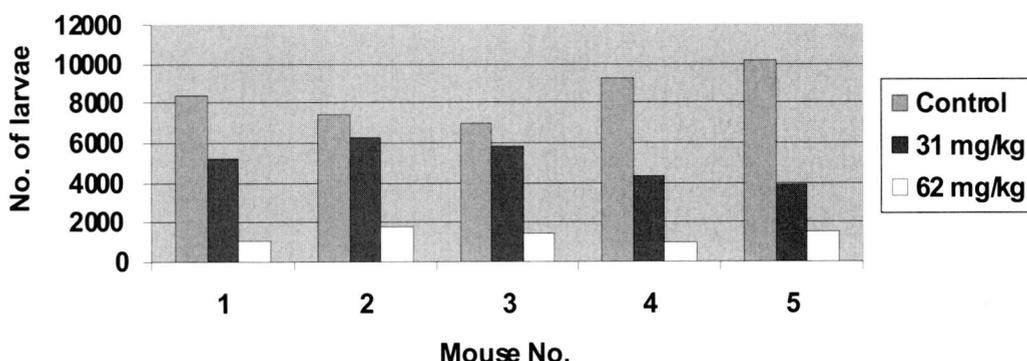


Fig. 4. – Biological assay for infectivity of larvae in C57BI/6J mice.

depend on the amount of ingested medicated food. It has to be stressed that in previous studies authors used a small number of pigs (from two up to five). According to De Nollin *et al.* (1976) flubendazole induces severe morphologic alterations in infected muscle in such a way that shortly after fortnight treatment period, the muscle becomes cleared of the parasite and starts to normalize. Authors found deteriorative changes like degradation of different organs in the parasite including the disappearance of microtubules in the cells of the oesophageal part of the intestine. According to our studies, the biological assay performed in mice showed that at least half of larvae were not infective. At the end it can be concluded that his investigation clearly illustrates that treatment with flubendazole could have some potentials in the control of trichinellosis especially against intestinal stages. Further investigations on the activity of prolonged or continuous treatment with economy feasible dose rates (1-2 mg/kg) will unequivocally define the real potential of the treatment as a preventive measure that could be easily applied in areas of endemic swine trichinellosis.

REFERENCES

- DE NOLLIN S. & BORGERS M. An ultrastructural study on the effects of flubendazole on the encysted phase of *Trichinella spiralis* in the rat, *in: Proceedings of the Fourth International Conference on Trichinellosis*, Kim C.W. & Pawlowski Z.S. (eds), 1976, 445-462.
- THIENPONT D. VANPARIJS O. Prophylactic and curative action of flubendazole against experimental trichinellosis in pigs, *in: Proceedings of the Fifth International Conference on Trichinellosis*, Kim C.W., Ruitenber E.J. & Teppema J.S.D. (eds), 1980, 343-346.
- VANPARIJS O., HERMANS L. & VAN DER FLAES L. Efficacy of flubendazole on *Trichinella pseudospiralis* in rats, *in: Proceedings of the Sixth International Conference on Trichinellosis*. Kim C.W. (ed), 1984, 330-335.
- VANPARIJS O., HERMANS L. & THIENPONT D. Anthelmintic activity of flubendazole against *Trichinella spiralis* in rats. *Veterinary Parasitology*, 1979, 5, 237-242.
- VANPARIJS O. & THIENPONT D. Immunological reactions of pigs experimentally reinfected with *Trichinella spiralis* after treatment with flubendazole, *in: Proceedings of the Fifth International Conference on Trichinellosis*. Kim C.W., Ruitenber E.J. & Teppema J.S.D. (eds), 1980, 347-352.
- VANPARIJS O. & THIENPONT D. Systemic anthelmintic activity of flubendazole, *in: Proceedings International Pig Veterinary Society*, Ghent, Belgium, August, 1984, 27-31, 209.