

## 豚疥癬に対するIvermectinの治療効果

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著者	大場, 茂夫 鳥海, 弘 武石, 昌敬
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## Efficacy of Ivermectin Against Live Mites and Eggs of *Sarcoptes scabiei* in Pigs

Shigeo OHBA, Hiroshi TORIUMI, Masatoshi TAKEISHI, and Ryoji NODA

Department of Veterinary Medicine, College of Agriculture and Veterinary Medicine, Nihon University, 1866 Kameino, Fujisawa, Kanagawa 252, Japan

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**ABSTRACT.** Sows infested with *Sarcoptes scabiei* var. *suis* (ssvs) were treated with 75, 150 and 300 µg/kg of ivermectin by a single subcutaneous injection at the neck region. Compared to the numbers of mites and eggs just before injection, those on post treatment weeks (PTW) 1, 2 and 4 showed significant decreases. Especially at 300 µg/kg, the counts showed almost all mites and eggs were eradicated on PTW 1, manifesting ivermectin to possess potential effect on ssvs without apparent abnormal side effect. Potential mitocidal effect of ivermectin on ssvs was revealed.—**KEY WORDS:** efficacy, ivermectin, pig, *Sarcoptes scabiei*.

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*Sarcoptes scabiei* var. *suis* (ssvs) that predominantly infests earlobes of pig is a prevalent ectoparasite in Japan. They penetrate deep into the skin, induce severe itch and cause stress, resulting in the loss of body weight of the pigs [1, 7]. They usually infest a localized region such as the external acoustic meatus, root of earlobe, around the eyes, limbs, abdominal areas, and dorsal regions, and eventually spread to the whole body. Before the introduction of avermectins, eradication of mites and their eggs with the use of previous insecticides available in the market has been difficult. The avermectins, macrocyclic lactones of microbial origin, elicit broad, nematocidal properties [5, 8] and are being employed extensively in other countries. We first applied ivermectin (22, 23-dihydro avermectin B1) in Japan as an insecticide against these mange mites.

### MATERIALS AND METHODS

**Pigs:** Eighty-five sows, infested with ssvs, were sampled from Kanagawa prefecture.

**Duration:** The experiment lasted from March to May, 1986 (for 2 months).

**Drug, dose and route of administration:**

Ivermectin injection, (Merck & Co., Inc.) containing 1% (W/V) of ivermectin ( $\geq 80\%$  of 22, 23-dihydro avermectin B1a, and  $\geq 20\%$  of 22, 23-dihydro avermectin B1b), formal glycerin 40% (V/V), and added propylene glycol to make the final volume 100%), was used. Vehicle was used as the control agent. Ivermectin was injected subcutaneously (sc) only once at the neck with three different doses, 0.0075 ml/kg (or 75 µg ivermectin/kg), 0.015 ml/kg (or 150 µg ivermectin/kg) and 0.030 ml/kg (or 300 µg ivermectin/kg). Three experimental groups in an increasing order were known as Group 75, (N=23 pigs), Group 150 (N=25) and Group 300 (N=26), respectively. The control group (N=11) was administered at 0.030 ml/kg with the control agent.

**Mite count:** According to the score index of Martineau *et al.* [6], regions (2 cm × 2 cm) around the earlobe, neck and/or limbs with clinical significance of mange exceeding scores of 3 were moistened with mineral oil, and scraped lightly until slight bleeding just before ivermectin treatment, post-treatment week (PTW) 1, 2 and 4. Number of motile (live) and nonmotile mites and eggs were counted under the microscope after the

samples were subjected to 37°C for 10 min. Observation time was 20 sec and only the mites that moved were counted.

*Insecticidal effect:* The effects on ssvs in each group were observed and the decreases in the number of live mites and eggs were calculated using the following formula:

$$\text{Decrease rate(\%)} = (\text{No} - \text{Nt}/\text{No}) \times 100,$$

where No is the number of mites or their eggs just before ivermectin treatment and Nt, the number of mites or their eggs on post-treatment week (PTW) 1, 2 or 4 with ivermectin.

*Statistical analysis:* Decreases of mite and egg counts were compared statistically between 2 of the 4 groups at any one time by

Kruskal-Wallis test and Dunn's multiple comparative evaluation test.

## RESULTS

*Mite count:* Table 1 shows the rate of pigs turning negative for mite infestation in each experimental-herd. The decreases in the treated groups compared to the controls are shown in Table 1 (A). On PTW 1, 2 and 4, the number of mites were decreased with the use of ivermectin when compared with the control. On PTW 1, 2 and 4, G75 showed decreases of 59.1 (13/22), 86.4 (19/22) and 95.5% (21/22), respectively. For G150, the decreases were 70.8 (17/24), 87.5 (21/24) and 100% (24/24), respectively. For G300, 100% were achieved in all pigs on

Table 1. Rates of pigs which turned negative for counts of mites (A) and their eggs (B)

Group	(A) Live mite Post-treatment week(PTW)				(B) Mite egg Post-treatment week(PTW)			
	0	1	2	4	0	1	2	4
Control	0/11 (0.0%)	1/11 (9.1%)	0/11 (0.0%)	0/11 (0.0%)	0/7 (0.0%)	2/7 (28.6%)	3/7 (42.9%)	0/7 (0.0%)
G75 75 µg/kg	0/22 (0.0%)	13/22 (59.1%)	19/22 (86.4%)	21/22 (95.5%)	0/10 (0.0%)	5/10 (50.0%)	8/10 (80.0%)	10/10 (100%)
G150 150 µg/kg	0/24 (0.0%)	17/24 (70.8%)	21/24 (87.5%)	24/24 (100%)	0/10 (0.0%)	9/10 (90.0%)	9/10 (90.0%)	10/10 (100%)
G300 300 µg/kg	0/25 (0.0%)	24/25 (96.0%)	25/25 (100%)	25/25 (100%)	0/14 (0.0%)	13/14 (92.9%)	14/14 (100%)	14/14 (100%)

Fractions and numerals (in parentheses) indicate ratios and percentages of the number of mite-free (A) and egg-free (B) pigs against total number of pigs in each herd, respectively.

Table 2. Average decrease in mite number (A) and egg count (B) expressed in percentages (%) by the use of ivermectin

Group	(A) Live mite Post-treatment week(PTW)			(B) Mite egg Post-treatment week(PTW)		
	1	2	4	1	2	4
Control	-28.8	-84.1	-179.5	-86.1	-105.6	-138.9
G75 75 µg/kg	83.3	99.0	100.0	44.7	97.9	100.0
G150 150 µg/kg	92.8	97.6	100.0	93.5	96.8	100.0
G300 300 µg/kg	100.0	100.0	100.0	98.1	100.0	100.0

G75, G150 and G300 indicate groups administered with 75, 150 and 300 µg/kg (sc), respectively.

PTW 1, 2 and 4.

The decrease rate of mite number (Table 2(A)) showed significant differences ( $p < 0.05$ ) in all 3 groups treated with ivermectin, whereas that of the control group showed a tendency to increase gradually. On PTW 1, 2 and 4 the decreases were 83.3, 99.0 and 100% in G75, 92.8, 97.6 and 100% in G150, and 100% in all specified observation intervals in G300, respectively. When the decrease rates of the 4 groups were compared on the basis of the multiple comparison test at the specified observation intervals, significant differences (near 0) in all groups were seen (Table 3).

As such, on PTW 1, 2 and 4, the decreases in mite number were significant compared with the control groups. Moreover, at all specified observation intervals, a significant dose-response curve was obtained when the control group was taken

as zero ivermectin dose.

*Mite egg count:* Table 1 (B) shows the rate of pigs turning negative for egg count in each experimental-herd. Just before the experiment, mite eggs were confirmed in the control (N=7 pigs), G75 (N=10), G150 (N=10) and G300 (N=14). For the controls on PTW 1, 2 the rates were 28.6% (2/7), 42.9% (3/7), and on PTW 4 there were no decreases. For G75 and G150 on PTW 1, 2 and 4, the rates were 50 (5/10), 80 (8/10) and 100% (10/10), and 90 (9/10) and 100% (10/10), respectively.

For G300 on PTW 1, no decrease in mite egg was seen in one pig, whereas the eggs in the rest were all eradicated (Table 2 (B)). A decrease in mean mite egg number was not seen in the control with slightly increasing tendency. The decreases in the mean egg count on PTW 1, 2 and 4 were 44.7, 97.9 and 100% for G75, 93.5, 96.8 and 100% for

Table 3. Comparison of decrease rate of live mites among the 4 groups by Kruskal-Wallis test and Multiple Comparative Analysis

Time after treatment	Group of pigs	Treatment	No. of pigs	Mean rank	K-W test (df:3)	Multiple comparative
1 week	G1 :Control	(Placebo)	11	11.23	$X^2=36.322$ p=near 0	G1-G2:-3.739*
	G2 :G75	75 $\mu\text{g}/\text{kg}$	22	38.71		G1-G3:-4.667*
	G3 :G150	150 $\mu\text{g}/\text{kg}$	24	45.04		G1-G4:-5.924*
	G4 :G300	300 $\mu\text{g}/\text{kg}$	25	53.88		G2-G3:-1.079 G2-G4:-2.609 G3-G4:-1.554
2 week	G1 :Control	(Placebo)	11	6.00	$X^2=57.457$ p=near 0	G1-G2:-6.318*
	G2 :G75	75 $\mu\text{g}/\text{kg}$	22	45.40		G1-G3:-6.409*
	G3 :G150	150 $\mu\text{g}/\text{kg}$	24	45.40		G1-G4:-7.207*
	G4 :G300	300 $\mu\text{g}/\text{kg}$	25	50.00		G2-G3:-0.002 G2-G4:-0.940 G3-G4:-0.959
4 week	G1 :Control	(Placebo)	11	6.00	$X^2=74.875$ p=near 0	G1-G2:-7.377*
	G2 :G75	75 $\mu\text{g}/\text{kg}$	22	45.90		G1-G3:-7.785*
	G3 :G150	150 $\mu\text{g}/\text{kg}$	24	47.50		G1-G4:-7.834*
	G4 :G300	300 $\mu\text{g}/\text{kg}$	25	47.50		G2-G3:-0.373 G2-G4:-0.377 G3-G4: 0.0

Group 1, 2, 3 and 4 are represented as G1, G2, G3 and G4, respectively.

Asterisk (\*) indicates significant difference ( $p < 0.05$ ).

On PTW 1, 2 and 4, the groups were compared with multiple comparative analysis. The gradual increases in significance for G1-G2, G1-G3 and G1-G4 were indicated. This manifests the mite number was effectively decreased against time in all groups treated with ivermectin, when compared to the controls.

Table 4. Comparison of decrease rate of mite eggs among the 4 groups by Kruskal-Wallis test and Multiple Comparative Analysis

Time after treatment	Group of pigs	Treatment	No. of pigs	Mean rank	K-W test (df:3)	Multiple comparative
1 week	G1	:Control (Placebo)	7	11.57	$X^2=13.516$ $p=0.004$	G1-G2:-1.144
	G2	:G75 75 $\mu\text{g}/\text{kg}$	10	17.00		G1-G3:-2.830
	G3	:G150 150 $\mu\text{g}/\text{kg}$	10	25.00		G1-G4:-3.173*
	G4	:G300 300 $\mu\text{g}/\text{kg}$	14	25.71		G2-G3:-1.858 G2-G4:-2.186 G3-G4:-0.179
2 week	G1	:Control (Placebo)	7	11.93	$X^2=12.566$ $p=0.006$	G1-G2:-2.292
	G2	:G75 75 $\mu\text{g}/\text{kg}$	10	20.80		G1-G3:-2.770
	G3	:G150 150 $\mu\text{g}/\text{kg}$	10	22.65		G1-G4:-3.458*
	G4	:G300 300 $\mu\text{g}/\text{kg}$	14	24.50		G2-G3:-0.527 G2-G4: 1.138 G3-G4:-0.569
4 week	G1	:Control (Placebo)	7	4.00	$X^2=39.546$ $p=\text{near } 0$	G1-G2: 5.296*
	G2	:G75 75 $\mu\text{g}/\text{kg}$	10	24.50		G1-G3:-5.296*
	G3	:G150 150 $\mu\text{g}/\text{kg}$	10	24.50		G1-G4:-5.296*
	G4	:G300 300 $\mu\text{g}/\text{kg}$	14	24.50		G2-G3: 0.0 G2-G4: 0.0 G3-G4: 0.0

Group 1, 2, 3 and 4 are represented as G1, G2, G3 and G4, respectively.

Asterisk (\*) indicates significant difference ( $p < 0.05$ ).

On PTW 1, 2 and 4, the groups were compared with multiple comparative analysis. The gradual increases in significance for G1-G2, G1-G3 and G1-G4 were indicated. This manifests the mite egg number was effectively decreased against time in all groups treated with ivermectin, when compared to the controls.

G150, and 98.1, 100 and 100% G300, respectively.

As shown in Table 4, the 4 groups were compared by the multiple comparative test at the specified observation intervals. At any specified interval, there were significant differences among the 4 groups ( $p=0.004$ , 0.006 and near 0) by Kruskal-Wallis test. On PTW 1 and 2, G300 showed significant decreases in egg count compared with the control. On PTW 4, all the 3 treated groups showed a significant decrease in mite egg count compared with the controls.

From the above findings, treatment with sc ivermectin caused marked decreases in mite number and egg count in ssvs-infested pigs, especially Group G300 showing the most potential effect.

There were no apparent abnormal behaviors with ivermectin administration.

## DISCUSSION

The use of insecticides to erase mites infestation in pigs has been practised for long, but because of deep penetration by mite into earlobes and their excessively fast reproductivity, a small infested region can spread to the whole body within a short period. Therefore, frequent spraying of insecticides has been used but failed to abate the problem. With sc ivermectin of 300  $\mu\text{g}/\text{kg}$ , eradication of ssvs mites has been effective [2, 4, 7]. We experimented with sc administration of ivermectin at 75, 150 and 300  $\mu\text{g}/\text{kg}$  only once at the neck region in ssvs-infested pigs.

Ivermectin administration reduced markedly the number of mites and their eggs, confirming its efficacious effects in eradicating ssvs. The ivermectin dose of 300

$\mu\text{g}/\text{kg}$  was especially potent, advocating thus previous findings [3, 6].

On PTW 1, almost all mites were eradicated, resulting in subsequent decreases in the number of eggs. The economical loss as a result of stress induced by mange mites could be eliminated by the use of ivermectin, especially at a dose of  $300 \mu\text{g}/\text{kg}$  sc within PTW 1. Our results indicated that only 1 dose of  $300 \mu\text{g}/\text{kg}$  sc could control mite infestation and their eggs. Ivermectin therefore is a potential drug to count on in eradicating problems caused by mites.

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#### 要 約

豚疥癬に対する Ivermectin の治療効果：大場茂夫・鳥海 弘・武石昌敬・野田亮二(日本大学農獣医学部) — 豚穿孔ヒゼンダニに罹患している母豚を対象に、体重 kg 当り  $75 \mu\text{g}$ 、 $150 \mu\text{g}$  および  $300 \mu\text{g}$  のイベルメクチンを一回頸部皮下注射し、投薬時、投薬後 1 週目、2 週目および 4 週目に虫体数および虫卵数を算定し、イベルメクチンの豚穿孔ヒゼンダニに対する効果を調べた。イベルメクチン投与の 3 群に对照群に比較して、投薬後顕著に虫体数および虫卵数は減少した。特にイベルメクチン体重 kg 当り  $300 \mu\text{g}$  投与では、投薬後 1 週目よりほぼ完全に虫体および虫卵が認められなくなり、非常に効果のあることが確認された。