EFFECTS OF AMPEROZIDE ON BITING BEHAVIOR AND PERFORMANCE IN RESTRICTED-FED PIGS FOLLOWING REGROUPING1,2

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ABSTRACT

Eight experiments were conducted to determine the effect of a single administration of amperozide on agonistic behavior and growth performance in newly mixed, restricted-fed pigs. Two hundred 12-wk-old pigs were used in a 4-wk trial (Exp. 1) to investigate the effect of amperozide on agonistic behavior and performance. The pigs were assigned to each pen on the basis of body weight and sex, ensuring that pigs in each pen were unacquainted. Each pig was weighed individually on d 3, 7 and 28. Agonistic behavior was quantified by counting bite and slash marks on each pig at 8, 26 and 48 h after penning. An i.m. injection of amperozide immediately before mixing the pigs reduced the physical damage (P < .001) at each time point. There was no evidence of amperozide causing either sedation or motor disturbances. On the average, amperozide treatment improved (P < .001) daily gain in the 4-wk study period by 70 g (17%). In Exp. 2 to 8, 1,648 pigs growing from approximately 20 to 100 kg body weight were used to determine the effect of amperozide on weight gain. Pigs were penned in groups of 9 to 11, randomly assigned to each pen on the basis of sex. Each pig was weighed individually after penning, on d 35 and at slaughter. Untreated control pigs had a poorer growth performance than did amperozide-treated pigs. During the first 5 wk postpenning average daily gain was improved (P < .001) by 90 g (26%) in pigs receiving a single oral administration of amperozide at penning. For the entire growing-finishing period daily gain was improved (P < .05) by 20 g (3.2%). Amperozide treatment did not affect daily gain in restricted-fed, acquainted pigs (Exp. 9). The results indicate that treatment with amperozide is an effective way to minimize the negative growth effects of agonistic behavior and the concomitant social stress following regrouping.

(Key Words: Agonistic Behavior, Growth, Performance, Pigs.)

Introduction

Under commercial pig farming conditions it is necessary at times to move and mix pigs. When previously unacquainted pigs are mixed together they fight while establishing a dominance hierarchy (Meese and Ewbank, 1973). Fighting is known to be a potent activator of the pituitary-adrenal axis (Brain, 1977; Arnone and Dantzer, 1980; Barnett et al., 1981). Moreover, growth and immunity are closely tied to the hormonal mediation of stress reactions (Selye, 1974; Kelley, 1980). In a restricted environment, newly formed pig groups show more aggression than would appear to be necessary for the establishment of a stable dominance hierarchy (Fraser, 1974). In addition, it is argued that in the pig the social stress caused by agonistic encounters following regrouping may increase the feed:gain ratio (Aherne, 1976) and increase the incidence of diseases. There is a need, therefore, to find means of reducing aggression and the concomitant social stress in order to improve animal welfare and productivity.

The objective of this study was to determine the effect of a single dose of a novel drug, amperozide6, on agonistic behavior and growth

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performance following the formation of new pig groups.

Materials and Methods

Nine experiments involving 1,928 pigs were conducted. In Exp. 1 the effect of amperozide on agonistic behavior and performance was investigated. Experiments 2 to 8 were designed to determine the effect of amperozide on average daily gain (ADG) during the entire growing-finishing period. In Exp. 9 the effect of amperozide on ADG in acquainted pigs was measured.

Experiment 1. A total of 200 12-wk-old Swedish Landrace X Yorkshire pigs, weighing 21.4 ± 3.2 kg (x ± SD), were used. The experiment was conducted in an integrated commercial herd. All pigs were obtained from the same weaner unit. Twenty pens were used that provided each of 10 pigs with .7 m² of floor space (solid concrete lying area .5 m²/pig and slatted dunging area .2 m²/pig). The pens were separated by steel rail partitions (bottom half solid, top half tubular).

The pigs were weighed and ear-tagged the day before (d 0) the experiment started. Only pigs without wounds were selected. Pigs were assigned to each pen on the basis of body weight and sex, ensuring that pigs in each pen were of equivalent average body weight and unacquainted (i.e., drawn from 10 different litters). Also, an equal sex ratio was maintained. Pig groups then were allocated randomly to one of the two treatments.

Every pig in each pen was given a single i.m. injection of either 1 mg/kg of amperozide hydrochloride (10 mg/ml solution) or an equivalent volume of saline immediately before being moved from the weaner unit. In a dose-response study (A. Björk, unpublished data), a dose of amperozide of 1 mg/kg i.m. was found to give the maximum duration of antiaggressive activity (i.e., no fighting displayed by the pigs) without side effects. Side effects of higher i.m. doses (> 2 mg/kg) were salivation and vomiting.

Each experimental pen was kept separate during transport from the weaner unit to the growing-finishing unit. Transport took 5 min. Pigs were housed in their experimental pens at about 0900 on d 1 of the experiment. Every 2nd pen contained pigs treated with amperozide; the remaining pens served as controls. The pigs received a dry-meal diet containing olaquindox as a growth promoter at 50 ppm the first 14 d following penning, and at 10 ppm thereafter. The diet composition was 85% barley (hammer milled) and 15% commercial protein/mineral/vitamin concentrate, containing about 12.2 MJ of metabolizable energy (ME)/kg of feed and 15.5% crude protein. All pigs were fed the same way according to a restricted, time-related program with the total daily allowance equally divided between two feedings. All pigs were fed to appetite in the morning on d 1 about 2 h before treatment and moving, and they received .35 kg/pig of feed in the afternoon 6 h after penning. They were offered a total of .7 kg/pig of feed on d 2 and were gradually brought up to 1.0 kg of feed per pig per d over the next 3 d. Pigs then were fed to a program with 1.1 kg, 1.3 kg and 1.4 kg of feed per pig per d during wk 2, 3 and 4, respectively. Pigs had free access to water from nipple waterers located above the trough.

A four-point scoring system was employed to evaluate degree of physical damage. The pig's body was divided into six zones: left and right ear, left and right shoulder and left and right flank. A single well-trained observer noted the score of injuries (bite and slash marks in each zone) for each pig immediately before mixing and at 8, 26 and 48 h after introduction. Only marks easily detectable visually were counted. The following scoring system was used: 0 = no marks, 1 = 1 to 3 marks per zone, 2 = 4 to 6 marks per zone and 3 = more than 6 marks per zone. Analyses were performed on the total of all scores (range 0 to 18).

Each pig was weighed individually between feeding on d 3, 7 and 28.

All calculations of injury scores and weight gains were based on pen as the experimental unit. Student's t-test was used to determine treatment differences. Separate analyses were performed for injury scores obtained at 0, 8, 26 and 48 h, respectively.

Experiment 2 to 8. A total of 1,648 Swedish Landrace X Yorkshire pigs were used. The pigs were obtained at 20 to 25 kg live weight from several feeder pig units and transported (kept together) 4 to 6 h by road to the trial sites. Pigs were fed to appetite before transport.

The experiments were conducted in six different commercial pig fattening units. Pigs were penned in groups of 9 to 11, depending on the housing system used at each separate farm. Pigs were randomly assigned to each pen on the

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7 BAY-O-NOX, Bayer (Sweden) AB.
basis of sex, ensuring that the pens were made up of the same number of castrated males and females in each individual trial. Pigs were not sorted into weight blocks; that is, the average pen weights were similar. A total of 156 pens were involved overall, with up to 27 pens on one individual trial site. The pens provided each pig with .7 m² of floor space (solid concrete lying area and a slatted dung passage area). The pens were separated by steel rail partitions (bottom half solid, top half tubular). A trough (3 m) was set along the front pen wall. The pens were equipped with nipple waterers located above the trough.

The pigs received a restricted dry-meal diet containing either olaquindox⁷ (50 ppm) or avoparcin⁸ (10 ppm) as a growth promoter during the first 14 d following penning, and at 10 ppm for both compounds thereafter. The diet contained 12.1 MJ ME/kg of feed and 15.5% crude protein. All pigs were fed according to the same time-related program with the total daily allowance equally divided between two feedings. All pigs were started the 1st d on .2 kg/pig of feed and over 8 d gradually brought up to 1.0 kg of feed per pig per d. The pigs then were fed to a program with 1.10 kg, 2.15 kg and 2.85 kg of feed per pig per d in wk 2, 8 and 15 with estimated average live weights of 25 kg, 50 kg and 90 kg, respectively.

Every 2nd pen was treated with amperozide; the remaining pens served as untreated controls. Amperozide hydrochloride was supplied as a 1% granule mixed with the first ration offered. Immediately upon penning, the pigs were fed .2 kg/pig of feed top-dressed with amperozide hydrochloride to give an average oral dose of 4 mg/kg body weight. This feed was spread before penning on the floor in front of the trough. No additional amperozide treatment was given.

Each pig was weighed individually about 3 h after the morning feeding the 1st d and between feedings d 7 and 14. The amount of feed consumed in each pen was recorded throughout. All calculations of weight gain were based on the pen as the experimental unit. Average daily gain was analyzed using analysis of variance techniques (BMPD, 1987).

Results

Experiment 1. After a few minutes of exploratory behavior, fierce fighting involving pushing and biting episodes was recorded in the control pigs. There were no fights recorded during the first 6 h following penning in the amperozide-treated group. About 30 min after penning, the amperozide-treated pigs were seen to huddle together and to lie on top of one another. The pig groups stayed in this position for most of the first 6 h. Pigs, however, did not appear to

⁷AVOTAN, Kemi-Intressen AB (Am. Cyanamid).
TABLE 1. EFFECT OF AMPEROZIDE ON INJURY
SCORES (MEAN ± SE) RECORDED 0, 8,
26 AND 48 H AFTER MIXING
(EXPERIMENT 1)

<table>
<thead>
<tr>
<th>Time, h</th>
<th>Control</th>
<th>Amperozide</th>
</tr>
</thead>
</table>
| 0       | .01 ± .01
| 8       | 4.89 ± .28
| 26      | 7.43 ± .35
| 48      | 7.98 ± .36 |

a Injuries scores on range 0 to 18.
b,c Means in the same row with different superscripts differ (P < .001).

be sedated. When an observer entered a pen they quickly got up and moved about normally without motor disturbance.

In the period 30 to 60 min after amperozide treatment, about 10% of the pigs were noted to be showing evidence of nausea, with some vomiting. The act of vomiting did not appear to cause any distress and the affected pig returned to the main group. No other side effect was observed.

The number of bite and slash marks was lower (P < .001) at each time point in the amperozide-treated pigs compared with the controls (Table 1).

The amperozide-treated pigs had gained more weight (P < .001) than the control pigs when weighed on d 3, 7 and 28. The improvements in weight gain were 1.0 kg, 1.3 kg and 2.1 kg, respectively (Table 2). When weighed on d 3 the control pigs had lost on the average .5 kg in body weight.

Experiment 2 to 8. After a few minutes of exploratory behavior following penning, the pigs started to consume the feed spread on the floor.

When first penned, amperozide-treated pigs exhibited aggression. Within 30 min of penning, however, no aggressive behavior was observed among amperozide-treated pigs. After about 1 h they tended to huddle together and lie on top of one another. Very few fights occurred during the 1st day, and no adverse effects of any kind were noticed.

No outbreaks of diarrhea that would have affected performance were observed in either treatment group during any of the experiments. During the experiments a total of 34 pigs died, 17 from the control groups and 17 from the amperozide-treated groups. In all cases deaths were not attributable either to treatment or to any one disease entity.

Although there was a small, but significant, difference between initial weight in the amperozide and control groups, there was no difference in final weight (calculated as 1.39 x carcass weight) between the groups.

Because pigs were fed according to the same program, ADG is appropriate as a measure of growth and efficiency. There were no experiment x treatment interactions for ADG (two-way analysis of variance: ADG 0 to 35 d, F = .33, df = 6/142, P = .90; 0 to slaughter, F = .26, df = 6/142, P = .96), thus data were pooled across trials. On the average, amperozide treatment improved (P < .001) ADG in the first 35 d by 90 g (26%; Table 3). Feed was the same in both groups at 1.16 kg/d. For the entire growing-finishing period, amperozide treatment improved (P < .05) ADG by 20 g (3.2%; Table 3).

Experiment 9. The change in body weight is presented in Table 4. Amperozide treatment did not affect weight gain in restricted-fed, acquainted pigs.

TABLE 2. EFFECT OF AMPEROZIDE ON WEIGHT GAIN (MEAN ± SE)
DURING THE FIRST 4 WK POSTPENNING (EXPERIMENT 1)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Amperozide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial weight, kg</td>
<td>21.4 ± 0</td>
<td>21.4 ± 0</td>
</tr>
<tr>
<td>Weight gaina, kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 – 3 d</td>
<td>−.5 ± .08b</td>
<td>.5 ± .07c</td>
</tr>
<tr>
<td>3 – 7 d</td>
<td>1.7 ± .07d</td>
<td>2.0 ± .07c</td>
</tr>
<tr>
<td>7 – 28 d</td>
<td>10.8 ± .23d</td>
<td>11.6 ± .25e</td>
</tr>
</tbody>
</table>

aPigs were regrouped on d 1.
b,c Means in the same row with different superscripts differ (P < .001).
d,e Means in the same row with different superscripts differ (P < .05).
TABLE 3. EFFECT OF AMPEROZIDE ON AVERAGE DAILY GAIN (MEAN ± SE) DURING THE FIRST 5 WK POSTPENNING AND OVER THE ENTIRE GROWING-FINISHING PERIOD (EXPERIMENT 2 TO 8)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Amperozide</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pigs</td>
<td>814</td>
<td>834</td>
</tr>
<tr>
<td>No. of pens</td>
<td>77</td>
<td>79</td>
</tr>
<tr>
<td>Initial weight, kg</td>
<td>22.5 ± .2a</td>
<td>21.9 ± .2b</td>
</tr>
<tr>
<td>Final weight, kg</td>
<td>103.6 ± .3a</td>
<td>104.2 ± .3a</td>
</tr>
<tr>
<td>ADG, g 0 - 35 d</td>
<td>341 ± 8c</td>
<td>431 ± 7d</td>
</tr>
<tr>
<td>ADG, g 0 - slaughter</td>
<td>630 ± 6a</td>
<td>650 ± 6b</td>
</tr>
</tbody>
</table>

a,b Means in the same row with different superscripts differ (P < .05).

c,d Means in the same row with different superscripts differ (P < .001).

Discussion

Environmental parameters and management practices that may affect the aggressive behavior while hierarchy is being established are not well known (Kelley et al., 1980; Friend et al., 1983). Provision of pens equipped with sanctuary (hide) areas to use for escaping attacks, however, appeared to be a reasonable way to reduce the amount of injury during times of high agonistic activity (McGlone and Curtis, 1985).

Tranquillizers have been tested to reduce aggressive behavior in domestic pigs at penning. Several neuroleptics and anxiolytics have been used. In pigs most neuroleptics and anxiolytics reduce agonistic behavior to a certain degree by sedation (Rehm et al., 1982). The antiaggressive action of sedatives is mainly temporary, lasting only until the sedation ends (Blackshaw, 1981). In a review, Dantzer (1974) concluded that neuroleptic drugs are most successfully employed as premedication or immobilization agents.

The effects of lithium (Li) on aggressive behavior in pigs have been reported (Dantzer and Mormede, 1979; McGlone et al., 1980). The results suggest that because of resulting emesis and reduced feed intake, the use of Li is not an effective means of reducing aggression among unacquainted pigs.

In the search for novel, psychotropic agents it is recently demonstrated (E. Christensson, unpublished data) that amperozide exhibited properties in the rat and mouse suggesting a selective limbic profile of action. Amperozide was shown to possess potent antiaggressive and anticonflict (anxiolytic) effects. For example, amperozide blocked aggression in previously separated male mice pairs and enhanced punished responding in a punished-drinking paradigm in rats. Contrary to classical neuroleptics and anxiolytics it did not cause impairment of motor coordination or sedation, as evidenced by behavioral and receptor binding studies. Thus, amperozide did not induce ataxia and had a low affinity for α-adrenoceptors. This prompted research to explore the use of amperozide as a possible way to reduce fighting when pigs are mixed.

Pharmacokinetic studies of amperozide have been performed in pigs. Amperozide was administered via i.m. and oral routes. After both i.m. and oral administration, the time to reach plasma peak level ranged from 2 to 3 h. The

TABLE 4. EFFECT OF AMPEROZIDE ON AVERAGE DAILY GAIN (MEAN ± SE) IN ACQUAINTED PIGS (EXPERIMENT 9)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Amperozide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial weight, kg</td>
<td>49.3 ± 1.5</td>
<td>48.7 ± .3</td>
</tr>
<tr>
<td>ADG, g</td>
<td>930 ± 140</td>
<td>860 ± 20</td>
</tr>
<tr>
<td>0 - 7 d</td>
<td>770 ± 50</td>
<td>750 ± 60</td>
</tr>
<tr>
<td>7 - 14 d</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
plasma elimination half-life was found to be about 4 h. The total concentration of amperozide, including its metabolites, has been determined in fluids and autopsies from pigs at different times (1 to 30 d) after a single administration of [14C]amperozide. After i.m. injection at 1 mg/kg, the total concentration in muscle, fat and skin was low at all times, with only .01 to .04 µg/g wet tissue remaining after 8 d. The highest residue values were found in eliminating organs. The amounts remaining in liver and kidney after 8 d were about .1 µg/g. Similar patterns were observed to those following i.m. injection and oral administration.

Biting is manifested generally between newly mixed pigs, and biting behavior usually results in injury to other pigs. The aggressive behavior following regrouping normally ceases within about 24 h, and social stability is reached within 24 to 48 h of grouping (Meese and Ewbank, 1973; McGlone, 1986). Preliminary studies showed that the appearance of bite and slash marks in untreated mixed pigs was in accordance with what has been reported earlier on agonistic behavior in respect to both point of time after mixing (McGlone, 1986) and bite targets on the pig body (McGlone, 1985). At 8, 26 and 48 h, injury scores were much lower (P < .001) in the amperozide-treated group than in the controls. Amperozide was found not only to delay the initial violent aggressive outbursts but also to reduce the level of aggression subsequently. Although there was no fighting recorded in the amperozide-treated pigs for the first 6 h after penning, the total injury score from 8 to 48 h did not increase among amperozide-treated pigs more than among untreated mixed pigs. This may suggest that the number of fights among amperozide-treated pigs did not exceed the number among the control pigs in the periods beyond 8 h after penning. Therefore, the amperozide-treated pigs appeared to reach social stability with significantly less aggression and physical damage than the control pigs.

Results of studies on the effects of mixing pigs on weight gain have been contradictory. Dantzer (1970a,b) concluded that moving and mixing negatively affected performance. Aherne (1976) reported that mixing of pigs resulted in a reduction in performance, whereas Sherritt et al. (1974) found no such effect unless other stressors were present. Friend et al. (1983) reported that mixing litters greatly increased agonistic behavior but did not affect long-term performance. McGlone and Curtis (1985) found that regrouping tended to reduce both weight gain and feed efficiency during 7 d postmixing, but not after 21 d. Furthermore, McGlone et al. (1986), using larger pigs, reported that regrouping depressed feed intake and reduced weight gain during the first 7 d following mixing.

In Exp. 1 both control and amperozide-treated pigs were offered and consumed the same amount of feed daily. Nevertheless, control pigs lost weight and were significantly less efficient during several weeks following regrouping than amperozide-treated pigs. In Exp. 9, amperozide did not affect weight gain in acquainted pigs. Consequently, the results of this present study would suggest that, in pig groups of 10, the excessive fighting during establishment of a dominance hierarchy led to a detrimental adaptation process, causing a longer and more adverse effect on feed efficiency, and hence growth performance, than would be expected generally.

In Exp. 2 to 8 the amperozide-treated pigs by d 35 had gained on average 3.2 kg more than the control pigs. This improvement was found mainly to persist through to slaughter (2.6 kg). This can be interpreted as showing that untreated pigs did not display a compensatory response to the performance loss following regrouping when fed on a restricted schedule.

Reported findings suggest that regrouping growing and finishing pigs reduces the rate and efficiency of gain. The cause-and-effect sequences, however, have not been thoroughly analyzed. After weaning of young pigs, Kenworthy and Allen (1966), Kenworthy (1976) and Hampson (1986) reported marked alterations in the small intestinal structure and brush-border enzyme activities associated with a malabsorption syndrome. In other investigations it was suggested that the social stress upon weaning caused several clinical and physiological effects that were prime determinants of the weight depression seen after weaning (Lofstedt, 1986).

In summary, amperozide effectively reduced the agonistic behavior following the formation of a new pig group, thereby resulting in a social stability with minimal fighting and associated physical damage. The antiaggressive action of amperozide did not appear to result from either sedation or motor disturbance, because treated pigs in this study were easy to move and remained responsive to handling procedures. Furthermore, the poor long-term growth
performance demonstrated in the control pigs following mixing and moving was avoided by the amperozide treatment. Research now should proceed to assess in detail the effects of amperozide at regrouping on production and disease in pigs in commercial production.

Literature Cited


