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The effect of ketoprofen on feeding behavior of tail-bitten pigs

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Abstract

No research has been reported on the effect of intramuscular ketoprofen administration on the feeding behavior of tail-bitten pigs. In order to investigate this, a longitudinal, double blind, placebo-controlled field trial was conducted with a total of 77 pigs from a finishing herd. Pigs received either ketoprofen (KET) or a placebo (PLAC) intramuscularly for three days and procaine penicillin for five days after the tail was first observed to be damaged. Pigs were followed from day −2 to day 3 with respect to a noted tail wound. Only new incidence of tail biting was included. Nine to 11 pigs per pen were reared with a single automatic feeder. A transponder attached to the ear of each pig recorded times of entrance and exit to the feeder and feed consumed. To calculate average daily weight gain (ADG), pigs were weighed at days 0, 6 and 13. Time spent at the feeder by visit and on a daily basis, and mean daily intervals between feeder visits per pig were computed in minutes. Daily feeding rate (FR) was calculated from the feeder data (consumed feed (g) / time at the feeder (s)).

Placebo pigs consumed more feed and spent more time at the feeder on day 1 than KET pigs ($P < 0.05$). For all pigs, FR increased from day 1 to day 3 ($P < 0.05$). Feeder visit intervals were longer and frequency lower on day 0 compared with other days ($P < 0.05$). Average feed consumption and time spent at the feeder per day decreased on day 0 and returned to the initial level on day 1 ($P < 0.05$ for both). No effect on ADG was recorded.

Intramuscular administration of ketoprofen induced little change in feeding behavior and had no effect on weight gain. Placebo-treated pigs may have used feed as an analgesic and calming substance to some degree, leading to temporarily increased feed consumption.

Background

Tail biting is a global behavioral problem that impacts finishing pig health. In Finland, about 12 % of slaughtered pigs were affected by acute tail biting [1]. Tail damage leads to inflammation and infection and thereafter problems in the slaughterhouse due to septicemia that causes abscesses around the carcass [2, 3]. As an entity, tail biting compromises pig welfare [1, 4].

The Finnish food safety authority recommends penicillin treatment for affected pigs to suppress infection in the tail [5], but no guidelines or references are available for pain alleviation in the wounded pigs, despite analgesics being able to enhance welfare of the bitten pigs. Tissue trauma was defined as being painful in International Association for the Study of Pain (IASP) [6] taxonomy in 2014. However, pain experienced by individual tail-biting victims has largely been neglected [7].

Bite wounds resemble stab wounds, which are known to induce hyperalgesia in and around the injury site, causing behavioral changes lasting up to two days post trauma, at least in a rodent model [8]. In pigs, pain can still be very difficult to detect and with varying manifestations on feeding behavior in animals of different ages. Farrowed sows expressed reduced feeding for longer when pain was not treated [9]. Piglets undergoing castration showed reduced suckling behavior for several days after the procedure [10] but no differences in weight gain for castrated piglets treated either with NSAID (meloxicam) or placebo were detected [11]. Very little is known about pain in finishing pigs. Earlier studies show that tail-biting victims had lower average daily weight gain (ADG) than non-bitten controls [12]. Feeding behavior can alter from the baseline even weeks before any damage has been detected [13], but whether fluctuations are pain-induced, remains uncertain. Differences in feed

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conversion ratio may also go unnoticed [14] and the problem may go undertreated.

Ketoprofen is a non-steroidal anti-inflammatory drug (NSAID), and can be sold for treating pigs in the EU. It has antipyretic, anti-inflammatory and analgesic effects, and the recommended dose is 3 mg/kg BW [15]. It was shown to be effective in treating lameness in sows [16], and improved feed intake in sows after farrowing [9] and in pigs challenged with *Actinobacillus pleuropneumoniae* [17]. It is well absorbed after intramuscular injection [18].

Our aim was to study the influence of pain alleviation by injectable ketoprofen on the feeding behavior of tail-bitten pigs. We assumed that tail-biting victims experience pain, which can be alleviated by ketoprofen. We hypothesized that ketoprofen-treated pigs recover their feeding behavior faster to a pre-bitten level than placebo-treated ones within the first few days after the tail is wounded.

Methods

The experiment was approved by the ethical committee of Viikki Campus, University of Helsinki (3A/2010) and the Finnish medicines agency (Fimea, vetkl-nro 03/10).

Animals and housing

This was a longitudinal, double blind, placebo-controlled field trial including 77 bitten pigs from a finishing herd of 900 pigs. Pigs selected for the study included gilts (27), boars (20) and barrows (30). Pigs were grouped in 37 pens with 9 to 11 pigs in each. The size of the pens was 16.4 m^2 and they consisted of 2/3 concrete and 1/3 slatted floor. A handful of hay was placed on the floor of each pen every day.

Each pig included in the experiment pig had a transponder attached to the ear. The transponder registered the amount of feed consumed by the pig, and the time of arrival and exit to and from the feeder. Each pen had one automatic feeder (Schauer Machinenfabrik, Austria) with an open rear end and an automatic feed distributor (Spotmix, Ireland) that delivered feed continuously. Feed consisted of barley, oat, wheat, distillers grain feed, calcium carbonate, vegetable oil and fat, soybean meal, wheat bran and mixed molasses. Feed was composed of 14.8 % crude protein, 3.4 % crude fat and 4.2 % crude fiber with a net energy value of 10.5 MJ/kg DM (megajoules per kilogram of dry matter).

Inclusion criteria

The caretakers checked the pigs carefully twice a day and looked for signs of tail biting. Only new incidences with fresh, semi-fresh and slightly dried biting wounds were included in the study. Pigs with gangrenous, black tail tips or crater-like old injuries were excluded from the study and moved to a hospital pen. The biter was also removed from the pen if identified. Pigs treated earlier for tail-biting wounds were also excluded.

Medication

Pigs were randomly allocated in blocks of 6 into two treatment groups receiving intramuscular ketoprofen (Ketovet 100 mg/mL, Richter Pharma, Wels, Austria, KET) 3 mg/kg live weight (n = 36) or placebo (Isotonic sodium chloride, PLAC) (n = 41) isovolymetrically for three consecutive days. All bitten pigs were treated with intramuscular procaine penicillin (Penovet vet 300 000 IU/ml, Boehringer Ingelheim, Copenhagen, Denmark) at a dose of 20 000 IU/kg daily for 5 days. All treatments were begun on the day when the tail was first noted to have been bitten (day 0).

Recordings

Feeder data were collected starting from day −2 with respect to tail biting (day 0) and continued until day 3. Pigs were weighed on days 0, 6 and 13 after initiation of medication. Weighing and medication took place during piggery morning working hours (from 06.00 to 08.00).

Individual time at the feeder per visit and day were calculated from the feeder data and presented in minutes. Mean daily intervals between feeder visits were also calculated. Feeding rate (FR) was computed as the amount of feed consumed in grams divided by time spent at the feeder in seconds. Average daily weight gain (ADG) was calculated from the weighings. Feed conversion rate (FCR) per day was calculated with feed intake in grams divided by daily weight gain.

Statistics

Linear mixed models for repeated measurements were used for analyzing differences between treatments and days for all feeding parameters. In the initial models treatment (KET or PLAC), day (from −2 to 3) and their interactions from day 0 to day 3, during which there was treatment, were added as fixed factors, and pig nested in a group and groups were added as random factors. Group refers to the animals in the pen at the time of the tail-biting outbreak. Weight on day 0 was used as a covariate if significant. Only significant interactions were used in the final models. The normality and homogeneity assumptions of the models were checked with a normal probability plot of residuals and scatter plot of residuals against fitted values. The differences in weights on days 0, 6 and 13 and ADG from day 0 to day 6 and day 6 to day 13 between treatments were tested with *T*-test. The upper limit for a statistically significant effect was set to $P < 0.05$. P-values between 0.05 and 0.1 were considered to be tendencies. All statistical analyses were conducted using PASW Statistics 18.0.1 (IBM Acquires SPSS Inc. 2009). All the results are presented as estimates with standard errors of means (mean ± SEM).

Results

Treatment effect

The pigs weighed between 35.2 kg and 107.0 kg on the day when the first signs of biting were observed (day 0). No treatment effects were detected in intervals between feeder visits, FE, feeder visit frequency, FCR, and weights on days 0, 6 and 13 (Table 1).

Interaction between treatment and time

No differences were detected in ADG between KET and PLAC pigs between days 0 and 6 (1139 ± 59 g vs. 1269 ± 59 g $P = 0.34$ or between days 7 and 13 (KET 831 ± 39 g vs. PLAC 909 ± 47 g $P = 0.44$). Interactions between treatment and time for total time spent at the feeder and average feed consumption per day differed ($P < 0.05$ for all) (Fig. 1).

Time effect

FR increased from day 1, it being highest for all pigs on day 3 ($P < 0.05$). Feeder visit intervals were longer on day 0 than on other days ($P < 0.05$) (Fig. 2). Pigs tended ($P = 0.08$) to have higher FCR on days 2 (2.4 ± 0.1) and 3 (2.3 ± 0.1) than on day 1 (2.2 ± 0.1) from tail biting.

Discussion

Ketoprofen had little effect on feeding behavior of tail-bitten pigs. Contrary to our hypothesis, placebo-treated pigs temporarily increased their feed consumption rather than those treated with ketoprofen during the first day after the onset of tail biting. During the two weeks of weight follow-up, no differences in weight gain were established. Treatment differences were found only in time spent at the feeder and feed consumption, which may indicate that changes in feeding behavioral parameters that we measured in tail-bitten pigs were not caused by inflammatory pain or that pain alleviation was not adequate.

In a single space feeder system such as used here, competition for feeder places is probably high and aggression may occur at the entrance to the feeder, as discussed earlier [19]. Fear of aggression and tail bites can thus potentially cause reluctance to enter the feeder. Tail-bitten pigs may search for cover and comfort to avoid bites. Feeder visit frequency decreased at the day of noted tail wound for all pigs, but after initiation of treatment ketoprofen-treated pigs spent less time at the feeder than placebo-treated ones. The analgesic or anti-inflammatory properties of ketoprofen probably diminished the need of pigs to feed or search for a hiding place. Placebo pigs spent more time at the feeder and consumed more feed, which is in agreement with earlier studies [20]. Intramuscular ketoprofen increases muscle enzyme activities such as creatinine kinase in sows [9] and cattle [21], suggesting that it may irritate tissues. Tissue irritation in the neck region may contribute to the ease of movements of head, and thus eating behaviour, but a major effect on feeding is unlikely. We also found that all victim pigs reduced their feed intake and their feeder visits became sparser prior to the onset. It appears that tail biting does reduce feeding frequency. We established that elevated feeding rate lasted for several days despite visit frequency to the feeder recovering to pre-biting levels. Feed consumption also decreased on the day of a noted tail wound, and increased together with feeding rate.

Not all the factors affecting feeding behavior of tail-biting victims can be influenced by pain alleviation. Tail-bitten pigs have high levels of stress and there are many stressors involved in a tail-biting outbreak [22, 23]. Chronic stress might lead to excess consumption of food and increased obesity, as was reported in humans [24] and rats [25]. However, in pigs, comfort food remains unidentified. Untreated pain at the rump may lead to complicated pain-coping mechanisms. Castrated piglets without pain alleviation showed more pain-induced behaviour, such as resistance movements during surgery and huddling up post surgery, which indicated the need for treatment for pain [26]. On the other hand, in piglets, castration with analgesics demonstrated no changes in suckling behavior or weight gain compared with castration without analgesics [27]. Alterations in behaviors may increase additional pain avoidance and can last for up to four days post-surgery [10, 28]. Therefore we expected that also the pigs with a bitten tail might benefit from pain alleviation for at least three days. Inconsistency between our study and castration studies on piglets may be due to age and drug differences. Finishing

Table 1 Feeding parameters for 77 tail-bitten pigs treated either with ketoprofen or placebo for three days starting on the day when the tail wound was first noted (day 0). Overall data are reported from day −2 to day 3. Results between treatments are presented from day 0 to 3. All results are presented as mean ± SEM

	Overall value from day −2 to 3	Differences between treatments from day 0 to day 3		
Parameter		Ketoprofen	Placebo	P
Intervals between feeder visits (min)	59.6 ± 3.9	58.7 ± 4.8	58.8 ± 4.6	1.0
Feeding efficiency (g/s)	0.5 ± 0.007	0.5 ± 0.03	0.6 ± 0.03	0.5
Average frequency of feeder visits per day	30.7 ± 2.6	33.0 ± 3.2	29.0 ± 3.1	0.3
Average feed conversion ratio	2.3 ± 0.2	2.3 ± 0.2	2.2 ± 0.2	0.6

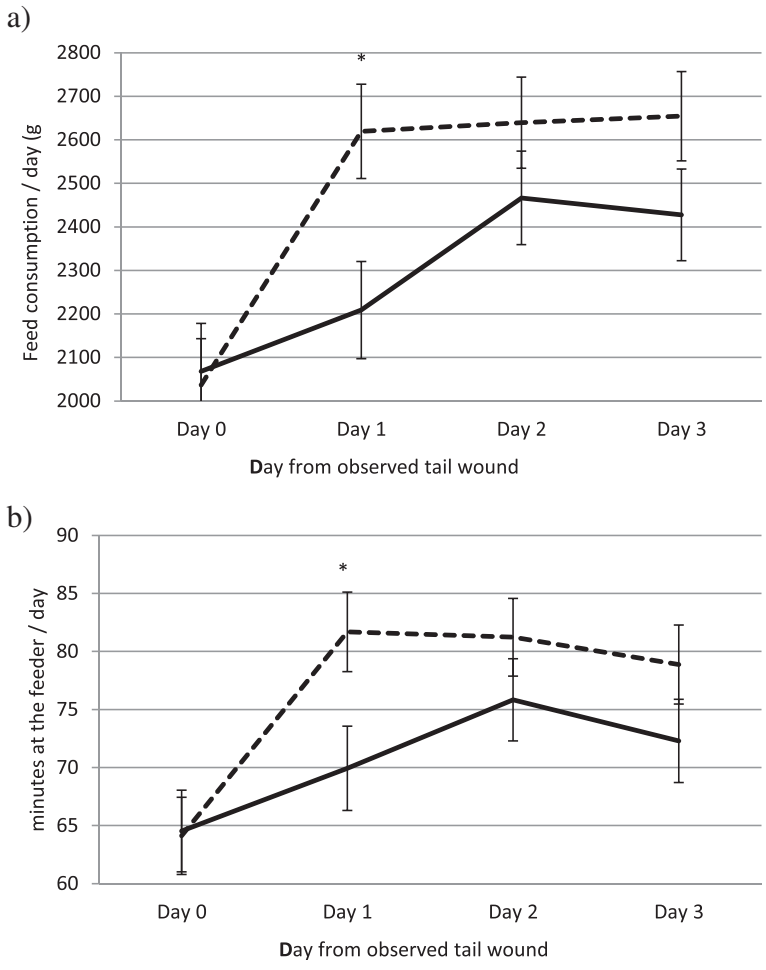

Fig. 1 Seventy-seven tail-bitten pigs were investigated for average feed consumption per day (**a**) and time spent at the feeder per day (**b**). Thirty-six tail-bitten pigs received ketoprofen 3 mg/kg IM (solid line) and 41 pigs placebo (broken line) daily during days 0–2 and followed until day 3 with respect to noted tail wound (day 0). Results are presented as mean ± SEM. *P < 0.05 between treatments at day 1

pigs differ from suckling piglets by size, they are fed differently and their neuronal circuits are more mature, which could have been altered in the early age by a painful stimulus such as castration [29].

The endogenous opioid system is up-regulated in painful situations, but only humans have been reported to react to a placebo similarly as to analgesics [30]. When the opioid system is down-regulated by an antagonist (naloxone), the palatability of food decreases, at least in rats [31]. In pigs such phenomena are unspecified. However, in our study, the temporary increase in feed consumption in placebo-treated tail-bitten pigs may implicate opioid system involvement in feed consumption. In fact, earlier studies demonstrated an opioid-mediated hypoalgesia after feeding in pigs [32]. Rats are also known to eat in order to relieve pain and tend not to stop feeding until pain is tolerable [33]. Even infants are given sucrose as an analgesic during invasive operations [34]. Feed intake may also vary according to the magnitude of the infection. Smaller doses of lipopolysaccharides from *Escherichia coli* – bacterium injected intraperitoneally caused a temporary increase in feed intake whereas very large doses induced anorexia in barrows that was inhibited by pretreatment with indomethacin (NSAID) [20].

Pain coping mechanisms vary among species, and in chicken increased feed intake was found to be one of these behaviors [35]. An interesting finding was that improved feed intake diminished peripheral inflammation in chicken [36]. Tail biting results in a strong inflammation response [3], thus causing peripheral sensitization. Whether pigs benefit from pain coping via feed, as in chicken, remains unknown. In addition, shift in attention is also known to decrease pain in humans [37, 38]. Victim pigs may have used feed not only as an analgesic, but also as a distraction from tail biting.

We found recorded feeding rate or rapid feed intake, "gobbling", of feed immediately after a tail-biting outbreak. This may be a response to increased restlessness

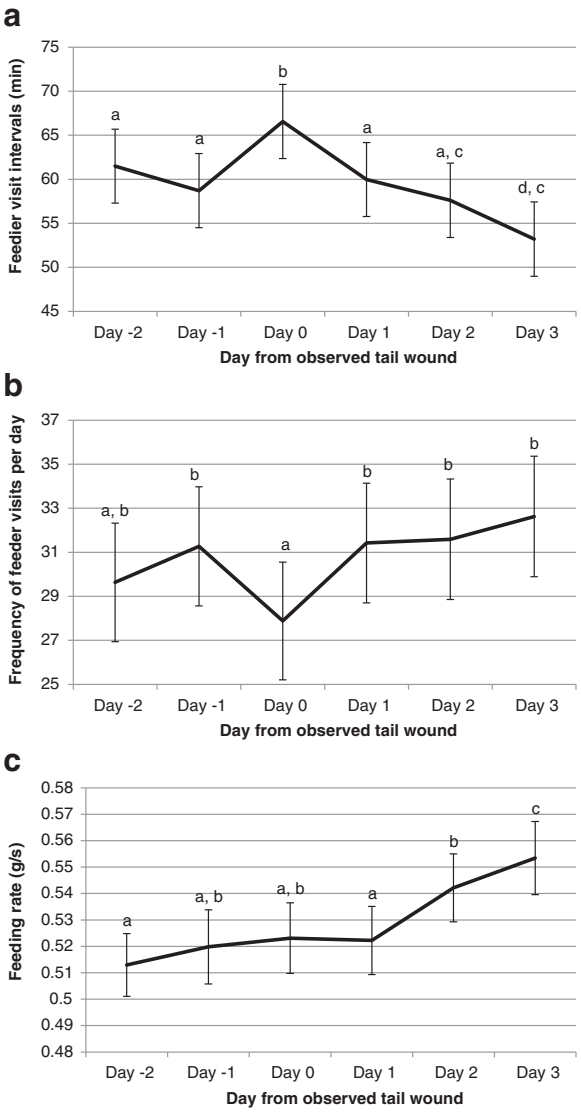

Fig. 2 Seventy-seven (receiving either ketoprofen or placebo IM, pooled data) tail-bitten pigs were followed for average intervals between feeder visits (**a**), frequency of feeder visits per day (**b**) and daily feeding rate (**c**). Follow-up took place at days −2 – 3 with respect to noted tail wound (day 0). Results are presented as mean ± SEM. Time points with different letters indicate $P < 0.05$

[39] where ketoprofen treatment does not work. We were unable to establish whether pigs ate all the feed consumed or whether some of it spilled out of the feeder. Agitation does increase even prior to tail-biting outbreaks in a pen [22] and alterations in feeding behavior can be detected even weeks before the actual onset of tail biting [13]. Tail bites that leave no mark do occur during this time [39]. Ketoprofen could improve the welfare of the pigs in subclinical cases, but we were unable to recognize them. Underlying tail chewing prior to an outbreak may lead the focus of the pigs temporarily away from the feed, since we established how feed consumption decreased a day before a wound was noticed. Additionally, tail biting changes the intestinal morphology and nutrient absorption in pigs [19], which can reduce weight gain. In our study, daily weight gain fell during the final weeks of weighing. The reason for this is not known. One possible explanation is that the need for rapid feed intake dropped after a tail-biting outbreak had settled and the situation in the pen normalized. Alternatively, tail chewing continued to a lesser extent after the major outbreak, influencing feed intake and weight gain. Nevertheless, ketoprofen being a non-steroidal-anti-inflammatory drug, can potentially also

damage the gastric mucosa [40]. Combined with alterations in the intestines, it may disturb normal metabolism and later feeding behavior.

Tail-bitten pigs could also have nutritional deficiencies, such as reduced amino acid levels in their serum [19], but the reason for these was not well identified. Jejunal morphology may alter after tail-biting damage, which can lead to reduced absorption of nutrients and amino acids [19] and poor growth and health.

All the feeding pattern alterations discussed above stabilized within a few days, as occurs for other behaviors, such as restlessness in a pen at the onset of a tail-biting outbreak [41]. Pain behavior associated with tail biting seems to be of a transient nature, but nonetheless trauma to the tail can cause painful neuroma formation at the tail as with tail docking, even in apparently healthy tails [42]. So, the long term pain after tail biting remains incompletely understood.

Conclusions

Intramuscular administration of the non-steroidal anti-inflammatory drug ketoprofen induced little change in feeding behavior and had no effect on weight gain. Placebo-treated pigs may have used feed as an analgesic and calming substance to some degree, leading to temporarily increased feed consumption. Behavioral pain coping mechanisms appear very complex in the described feeder pig rearing system.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors participated on the design of the study. EV, AV and MH carried out the data collection in the piggery. EV and LH carried out the statistical analysis of the data. All authors participated on the interpretation of the results and EV wrote the manuscript, which was read and accepted by all authors.

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