Effect of ketoprofen treatment in the prevention of postpartum dysgalactia syndrome in sows

Het effect van ketoprofenbehandeling ter preventie van het postpartum dysgalactiasyndroom bij zeugen

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ABSTRACT

Postpartum dysgalactia syndrome (PDS) is an economically important condition in sows. The syndrome is characterized by a reduced milk and colostrum production within 12 to 48 hours post partum. The objective of this study was to determine whether preventive treatment with ketoprofen (Ketofen®10%, Merial, Belgium) has a positive effect on the subclinical form of PDS. Sows (n = 39) were randomly divided into two groups: one served as control group whereas the other was treated intramuscularly with ketoprofen within twelve hours after parturition.

During the first 24 hours postpartum, the rectal temperature of the sows decreased (-0.43 ± 0.13 °C) in the ketoprofen group. In the control group, an increase was seen (+0.07 ± 0.02 °C) (P < 0.05). There was no significant effect on back fat loss of the sows, weight gain of the piglets (n = 541) and survival rate.

In conclusion, a single intramuscular administration of ketoprofen to sows shortly after farrowing decreased rectal temperature but did not improve the performance of the piglets.

SAMENVATTING

Het postpartum dysgalactia syndroom (PDS) is een economisch belangrijke aandoening bij zeugen. Het syndroom wordt gekenmerkt door een verlaagde melk- en colostrumproductie binnen de 12 à 48 uur na het werpen van de jongen. Het doel van deze studie was nagaan of een preventieve behandeling met ketoprofen (Ketofen®10%, Merial, België) een positief effect heeft op de subklinische vorm van PDS. De zeugen in de studie (n = 39) werden willekeurig in twee groepen ingedeeld: de ene diende als controlegroep en de andere werd intramusculair behandeld met ketoprofen binnen de twaalf uur na de partus.

Tijdens de eerste 24 uur na de partus daalde de rectale temperatuur van de zeugen (-0,43 ± 0,13 °C) in de ketoprofengroep. In de controlegroep werd een stijging gezien (+0,07 ± 0,02 °C) (P < 0,05). Er werden geen significante verschillen gevonden betreffende spekdikteverlies bij de zeugen, gewichtstoename van de biggen (n = 541) en overleving. Er kan geconcludeerd worden dat een eenmalige intramusculaire injectie met ketoprofen bij zeugen kort na het werpen de rectale temperatuur deed dalen maar geen invloed had op de prestaties van de biggen.

INTRODUCTION

Postpartum disorders, primarily those referred to as postpartum dysgalactia syndrome (PDS), have a major economic impact on pig production worldwide (Bertschinger, 1999). A decrease in colostrum and milk yield (in both quality and quantity) can be observed within 12 to 24 hours after parturition resulting in reduced weight gain and increased piglet mortality (Klopfenstein et al., 2006).

In the literature, many synonyms for PDS are mentioned, such as mastitis-metritis-agalactia complex (Martin et al., 1967), periparturient hypogalactia syndrome (Smith et al., 1992) and coliform mastitis (Gerjets and Kemper, 2009). Yet, information about subclinical forms of PDS is scarce.

Diagnosing PDS is not easy and is mainly based on a combination of increased body temperature of the sow (> 39.4 °C) during the first 12 to 18 hours after parturition and clinical signs in the sow or suck-

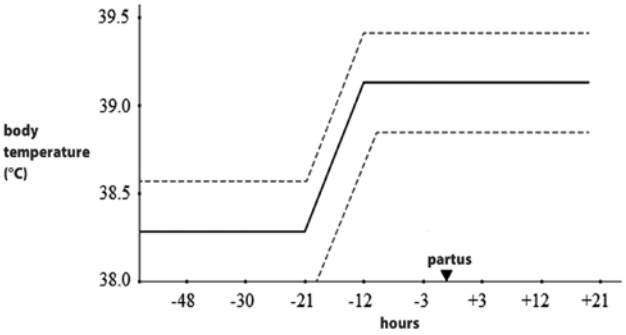

Figure 1. Physiological increase of body temperature of sows around parturition. The space between the dotted lines shows the possible variation between sows (adapted from Martineau et al., 2012).

ling piglets (Bertschinger, 1999; Furniss, 1987). Preferably, a threshold value is used when monitoring the rectal temperature of sows, as they, and especially gilts, may show a physiological increase in body temperature starting from 24 hours before parturition (Martineau et al., 2012) (Figure 1). Clinical signs may be visible in the sow, such as mastitis, constipation, fever and anorexia (Martineau, 2005; Martineau et al., 2012). Although some sows show no clinical symptoms, they have a reduced milk yield (Maes et al., 2010). Piglets may also show clinical signs. Poor body condition and depression can be seen in piglets, with or without diarrhea (Martineau et al., 2012). Furthermore, piglet mortality can be increased and the uniformity of the litter reduced. A general reduced weaning weight and/or a lower number of weaned piglets per year can be observed at herd level (Martineau et al., 2012).

PDS has a complex and multifactorial etiology. Various infectious and non-infectious factors, such as *E. coli* infection or constipation, may be involved in the pathogenesis of PDS (Gerjets and Kemper, 2009; Maes et al., 2010). Symptoms of PDS may occur when one or more of these factors are present, but not all factors are needed for PDS to occur (Martineau et al., 2012). When a herd suffers from PDS-related problems, preventive measures, such as optimal feeding strategies or proper interventions during parturition, are of the utmost importance to minimize problems. However, the identification of these risk factors in a herd is not easy (Messias de Bragança et al., 1998), and proper preventive or therapeutic measures are not always obvious (Maes et al., 2010).

The treatment of a sow with PDS consists of three pillars: 1) treatment with an anti-inflammatory drug, 2) stimulation of milk production and 3) treatment with antibiotics in case of bacterial infection (Martineau et al., 2012). Also her piglets should be treated. Next to that, dehydration of the sow and piglets should be avoided at all times (Klopfenstein et al., 1999), and energy losses of piglets should be reduced. Piglet transfer protocols and climate control may also play a crucial role (Klopfenstein et al., 2006).

Treatment of the sow with non-steroidal, anti-inflammatory drugs (NSAIDs) may be beneficial when used in the clinical form of PDS through the control of postpartum edema, pain and inflammation, as well as via inhibition of the endotoxin responses in the body (Martineau et al., 1992; Gerjets and Kemper, 2009). NSAIDs are already widely used in the preventive treatment of PDS, but the possible effect on the technical performance of the sow and her piglets after preventive administration still needs to be investigated.

The aim of this study was to determine whether a preventive treatment with ketoprofen (Ketofen10%, Merial, Belgium) in sows has an effect on the subclinical form of PDS, by monitoring the rectal temperature and back fat loss of the sow during lactation, the piglet survival rate and the piglet daily weight gain until weaning.

MATERIALS AND METHODS

Study population

The study was performed in a farrow-to-finish breeding herd (Hypor, Belgium) with a history of mild problems in sows around parturition, such as insufficient milk yield, poor feed intake, anorexia and fever (> 39.4 °C), and where no obvious diagnosis could be made and where the cause of the problems was not clear. The herd consisted of two different breeds of sows: Hypor x Pietrain crossings and pure line crossings (Landrace sow x Large white boar). The pure line crossing produced the future Hypor gilts and male fattening pigs. The Hypor x Pietrain produced fattening pigs that left the herd at finishing age, together with the male piglets of the pure line crossings. The herd operated on a three-week batch production system for the sows. Pregnant sows were kept in group with ad libitum feeding from 28 days of gestation, and were moved to the farrowing unit seven days before parturition. The sows were given a fixed amount of feed per day in the postpartum period: on the day of farrowing, 1-2 kg was provided. This amount was gradually increased to approximately 6-7 kg per day per sow on day 10 postpartum. The sows had permanent access to drinking water. During this trial, two successive farrowing groups of sows were monitored. This study took place from January 2013 until March 2013.

Only visually healthy sows with a normal body condition from parity 1 to 8 were included in the trial. In total, 41 sows complied with these criteria in the first farrowing group and 33 in the second farrowing group, which initially led to a total of 74 sows. For practical reasons, only the sows that farrowed between Wednesday and Sunday were maintained in the trial (n=56). Afterwards, 17 sows were excluded from the trial for different reasons: clinical signs of mastitis (n=6), dystocia (n=2), sows, whose piglets after birth were not transferred according to the protocol (see below) (n=2),

treatment by the farmer with other medicinal products, for example in case of lameness or pneumonia (n=7). Consequently, the data of 39 sows were included and subjected to statistical analysis.

EXPERIMENTAL DESIGN

The sows were stratified by parity and breed and then divided randomly into two treatment groups. The first group was not treated and served as control. The sows in the second group were treated within 12 hours after farrowing with ketoprofen (Ketofen 10%, Merial, Belgium) by intramuscular administration using the recommended dosage (1 mg/kg bodyweight). Ketoprofen is an analgesic with an anti-inflammatory and antipyretic activity, belonging to the group arylpropionic acid derivatives of the NSAIDs (FAMHP, 2012). If a sow had finished farrowing, she was treated at 8h AM or PM. When a sow had not farrowed on day 114 of gestation (day 0 of gestation being the date of the second insemination), induction of parturition was applied using an intramuscular administration of prostaglandins F2α (Planate®, MSD Animal Health, Belgium). The sows and piglets were individually identified by ear tags. The piglets received their ear tags before the first weighing (within 12 hours after parturition (D0)). Transfer of piglets between sows of the same treatment group was permitted during the first 48 hours after farrowing. The normal management practices of the herd were maintained during the trial, and intervention was kept to a minimum. All treatments and cases of mortality were recorded.

MEASUREMENTS AND PARAMETERS OF COMPARISON

The number of live-born, stillborn and the body weight of the live born piglets at D0 per sow were noted. The rectal temperature of the sows was measured during farrowing, just before treatment, 12 and 24 hours after treatment and in the morning of day 2 and 3 (T0, Ttr, T12, T24, TD2 and TD3, respectively). Sow back fat levels were measured at three different time points namely 3 days before farrowing, 7 days postpartum and the day before weaning (respectively D-3, D7 and D27). All sows were measured on the same day, e.g. when farrowing took place on Saturday or on Sunday, the sows were measured on Wednesday (3 to 4 days before farrowing (D-3)), on Saturday (6 to 7 days after farrowing (D7)) and on the day before weaning (D27).

The back fat level of the sow was measured using A-mode ultrasound (Renco Lean Meter). The measurement was done at the P2 position (a small handspan behind the last rib and next to the spine) (Maes et al., 2004), both at the left and right sides of the animal. The average of both measurements was used for statistical analysis.

The piglets were individually weighed within 24 hours after birth, on day 7 and on the day before weaning (respectively D0, D7 and D27). An overview of the timing of all measurements is presented in Table 1. The time points were chosen to minimize possible interference with the management practices on the farm.

In case of piglet mortality, the age was recorded and the suspected cause was registered. The survival of the piglets was calculated between D0 and D7, D7 and D27, and between D0 and D27. In each time interval, the percentage of piglets that survived was measured, taking cross-fostering of piglets into account (number of piglets and day of cross-fostering).

STATISTICAL ANALYSIS

The number of live-born piglets, stillborn piglets and the body weight of the piglets at D0 were compared between the control group and ketoprofen group using univariate analysis.

The change in back fat thickness and rectal temperature of the sows during the farrowing period were analyzed with repeated measures analysis of variance. The first back fat measurement and temperature at time of treatment were used, respectively as a covariate in the model. The analysis of these parameters per time interval and the comparison of control and treatment groups at a specific time point were performed via univariate analysis.

The analysis of a possible difference in body weight of the piglets between the two groups was performed with repeated measures analysis of variance. The daily weight gain was calculated from the difference in weight between D0 and D7, D7 and D27, and between D0 and D27. The daily weight gain in the control group and the ketoprofen group was compared for each of these three periods using univariate analysis.

Table 1. Timing of back fat measurement and measurement of rectal temperature in sows and weighing of piglets. D0 corresponds with the day of farrowing.

	D-3	D-2	D-1	D0	D1	D2	D3	D4	D7	D27
Rectal temperature				X X	X X	X	X			
Back fat levels	X								X	X
Piglet weight				X					X	X

Additionally, the weight gain per litter was calculated between D0 and D7, D7 and D27, and between D0 and D27. Piglet mortality was taken into account for this analysis, i.e. standardized weight of the piglets according to the day of mortality.

The piglet survival rate in the two groups was compared at sow level using survival analysis.

SPSS 21.0 was used for the statistical analyses and a p-value <0.05 was considered significant.

RESULTS

Number of live-born piglets, stillborn piglets and body weight of the live-born piglets at D0

The number of live-born piglets, stillborn piglets and the body weight of the live-born piglets at D0 are presented in Table 2.

Rectal temperature of sows

The course of the rectal temperature of the sows is presented in Figure 2. The sows of the ketoprofen group had a higher initial rectal temperature than the sows of the control group. After treatment, the average rectal temperature was lower in the ketoprofen group at all the time points except for TD3. The difference between the two groups was significant between Ttr and T24. The mean rectal temperature of the sows during the first 24 hours postpartum decreased (-0.43 ± 0.13 °C) in the ketoprofen group, whereas a slight increase was seen in the control group (+0.07 ± 0.02 °C) (P < 0.05).

Back fat levels during lactation

The average back fat levels of the sows at different points in time are presented in Table 3. The average decrease in back fat levels for the sows of both groups was 6.5 mm between D-3 and D27. There was no statistical difference between the two groups (P>0.05). Furthermore, the variation in back fat loss was similar in both groups.

Individual piglet weight

Birth weights (kg) were very similar in both groups, i.e. 1.41 ± 0.33 kg (control) and 1.43 ± 0.35 kg (ketoprofen) (P = 0.694). On D7, the average weights in both groups were very similar (P =0.719). In the control group, piglets weighed 2.95 ± 0.63 kg. In the ketoprofen group, the mean weight on D7 was 2.93 ± 0.68 kg. On D27, the average weights were statistically different between the two groups, with respectively 7.23 ± 1.48 kg (control) and 6.91 ± 1.46 kg (P = 0.022). Furthermore, the mean weight gain over the entire suckling period (D0-D27) was statistically significant between the two groups (P<0.05), i. e. 0.221 ± 0.053 (control group) and 0.208 ± 0.054 (ketoprofen).

Piglet weight gain per litter

The piglet weight gain per litter (kg) was very similar in both groups between D0 and D7, respectively 17.3 ± 1.3 kg (control) and 17.6 ± 0.8 kg (ketoprofen) (P = 0.833). Between D7 and D27, the mean weight gain per litter in both groups was also very similar (P = 0.272). The weight gain per litter was 49.0 ± 1.2 kg in the control group, compared to 46.3 ± 2.0 kg in the ketoprofen group. Over the entire suckling period (D0-D27), there was no statistically significant difference in piglet weight gain per litter between the two groups (P = 0.679).

Survival rate of the piglets

There was a tendency towards a higher survival rate in the ketoprofen group, but the difference was not statistically different. The main reasons for piglet mortality were poor vitality ('too weak') (55%), crushing by the sow (40%) and disease (5%).

DISCUSSION

The present study investigated the effect of a single intramuscular treatment with ketoprofen in sows shortly after farrowing on rectal temperature during the first three days postpartum, back fat loss during the lactation period and the performance of the offspring (daily weight gain and survival rate until weaning).

In total, data of 39 sows were included in the analysis. This was less than the original target (50 to 60 sows). The exclusion of sows was due to different

Table 2. Mean ± SD of the number of live-born piglets, stillborn piglets and the weight of the live-born piglets at the day of farrowing (kg), n=20 litters in the control group (C) and n=19 litters in the ketoprofen group (K).

	C (n=264)	K (n=277)	P-value
Live-born	13.0 ± 2.9	13.4 ± 2.6	0.691
Stillborn	0.8 ± 1.0	1.5 ± 1.7	0.123
Body weight at D0 (kg)	1.41 ± 0.33	1.43 ± 0.35	0.694

Table 3. Mean back fat levels (in mm) (± SD) measured at the P2 position in sows (n=39) at different time points (with D0 as day of farrowing) in the control group (C) and the ketoprofen group (K).

Point in time	C (n=20)	K (n=19)	P-value
D-3	19.93 ± 4.77	19.32 ± 3.63	0.653
D7	17.57 ± 6.69	16.84 ± 3.46	0.582
D27	13.38 ± 4.03	12.79 ± 3.28	0.616

reasons, such as clinical mastitis, dystocia, non-compliance with the protocol and treatment by the farmer for various disease conditions.

The conclusion that treatment with ketoprofen reduced rectal temperature between Ttr and T24 was in line with the expectations, given that ketoprofen may exert a measurable effect as early as one hour after administration and that the half-life of the product is 2.24 ± 0.11 hours (mean ± SD) (Anonymous, 2012). Therefore, the increase in rectal temperature around parturition, which may occur physiologically (Martineau et al., 2012) but also pathologically, can be reduced and shortened by the administration of ketoprofen shortly after parturition.

By anti-inflammatory treatment and prevention of the increase of body temperature, sows might have an increased feed intake and higher milk yield. However, the restricted feeding during the lactation period most likely minimized differences between the two groups in the present study. In line with this, the analysis of back fat loss during lactation showed no significant difference between the control and ketoprofen groups.

Very similar birth weights were recorded in both groups ($P > 0.05$). This means that neither group had an advantage in average weight at birth and that the possible effect of treatment could be properly evaluated. The individual piglet weight at D7 was similar in both groups. In contrast, the individual piglet weight at D27 was significantly higher in the control group than in the ketoprofen group. When analyzing litter weight, this difference was not seen. The weight gain per litter can give a better indication of the sow's milk production because there may be differences in the number of piglets per sow.

Piglet mortality was mainly due to a non-infectious cause: lack of vitality and piglets crushed by the sow. Many studies underline the importance of colostrum and milk intake for neonatal piglets (Bertschinger, 1999; Gerjets and Kemper, 2009). Therefore, inadequate colostrum and milk production during the first days after parturition is a major cause of neonatal problems. This leads to poor growth performance of piglets and a higher mortality rate in the farrowing pen (Klopfenstein et al., 2006). In the present study, the highest piglet mortality occurred during the first days of life. This is in agreement with the study of Smith et al. (1992), which demonstrated that most problems occur within 12 to 24 hours after parturition.

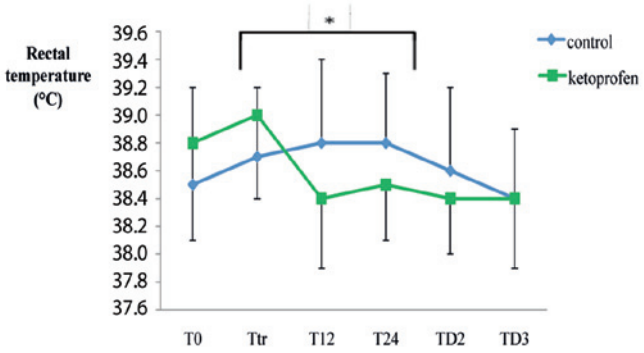

Figure 2. The mean rectal temperature of sows (n=39) (n=20 in the control group and n=19 in the ketoprofen group), measured from the day of farrowing (D0) until three days after farrowing (D3). Error bars indicate the standard deviation. * Significant difference in mean rectal temperature.

CONCLUSION

The present study showed that a single preventive treatment with the NSAID ketoprofen to sows shortly after farrowing decreased the rectal temperature of the sows during the first 24 hours, but did not improve the survival rate and growth of the suckling piglets. Further research, including herds with different feeding strategies and genetic background, is warranted to investigate possible beneficial effects of ketoprofen treatment to sows shortly after parturition.

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Uit het verleden

JULES BORDET

Het bacteriëngeslacht *Bordetella* is vernoemd naar de Belgische arts Jules Bordet (Zinnik, 1870 – Brussel, 1961). Hij werkte vanaf 1894 aan het Parijse 'Pasteur Instituut' en bestudeerde in het bijzonder de fagocytose. Hij stichtte in 1900 het Brusselse 'Institut Pasteur'. Daar ontdekte en beschreef hij dat het effect van immunoglobulines versterkt werd door lichaamseigen plasma-elementen die tegenwoordig bekend staan als "complement". De daaruit ontwikkelde complementbindingsreactie vormde de basis voor het ontstaan van talrijke serologische diagnostische tests.

Bordet en Gengou isoleerden in 1906 een bacterie die zij *Haemophilus pertussis* noemden en aanwezen als veroorzaker van kinkhoest. Nadat gebleken was dat deze soort niet verwant is met de eigenlijke *Haemophilus*, werd de genusnaam *Bordetella* eraan toegekend.

In 1919 ontving Jules Bordet de Nobelprijs voor de Geneeskunde, vooral voor zijn immunologische ontdekkingen. Het Brusselse 'Jules Bordet Instituut' is naar hem genoemd. 'Bordet' is in het Brusselse ook als naam voor een station en een verkeersknooppunt bekend.

Luc Devriese