Research Paper Summary

Evaluating the use of ketoprofen for the treatment of the pain and lameness associated with digital dermatitis in dairy cattle

A randomised, positive controlled, clinical trial

Authors of the published paper:
Konstantina Kasiora[1], Alkiviadis Anagnostopoulos[1], Cherril Bedford[1], TheologiaMenka[1], Matthew Barden[1], Bethany Eloise Griffiths[1], Damien Achard[2], Katherine Timms[3], Vinicius SilvaMachado[4], Amy Coates[1], Georgios Oikonomou[1]

Summary of a paper published online in the Veterinary Record, October 2021
https://doi.org/10.1002/vetr.977

[1]Department of Livestock and One Health,Veterinary and Ecological Sciences, Institute of Infection, University of Liverpool, Liverpool, UK [2]CEVA Animal Health LTD, Libourne, France [3]CEVA Animal Health LTD, Amersham, UK [4]Department of Veterinary Sciences, College of Agricultural Sciences & Natural Resources, Texas Tech University, Lubbock, Texas, USA

How to cite this article: Kasiora K, Anagnostopoulos A, Bedford C,Menka T, Barden M, Griffiths BE, *et al*. Evaluation of the use of ketoprofen for the treatment of digital dermatitis in dairy cattle: A randomised, positive controlled, clinical trial. Vet Rec. 2021;e977. https://doi.org/10.1002/vetr.977

Introduction & Study Objectives

Lameness is one of the most significant problems facing the dairy industry worldwide, having a major impact on cattle welfare, health and production, and leading to substantial economic losses[1]. Lameness has been associated with reduced milk yield[2], mastitis, and infertility[3], yet the mean herd lameness prevalence on UK dairy herds was most recently found to be 31.8%[4].

Digital dermatitis (DD) is one of the most frequently recorded diseases associated with lameness in dairy cattle and has a complex, multifactorial aetiology with spirochetes from 3 families of *Treponema spp* being commonly isolated[5,6]. Despite the steadily increasing introduction of routine preventative measures on farms, the prevalence of digital dermatitis remains high with between 15 and 41% of cows affected[6]. Several regimes are used for the treatment of DD in the UK including the application of a topical antibiotic spray[7], although repeated applications are often required[8].

Whilst it is recognised that some stages of DD are painful, there has been little research to determine the value of including analgesia in the treatment of DD. It has been discussed, but not proven, that the use of NSAIDs alongside topical antibiotic treatment may be justified on welfare and possibly on economic grounds.

The objective of this randomised, positively controlled study was to explore the potential benefits of a single administration of ketoprofen (3mg/kg Ketofen 10% solution for injection: Ceva Animal Health) when treating the pain and lameness associated with active DD lesions.

Study Design

Cows from four dairy herds, already involved in a larger scale study and based in the North West of England and North Wales, were enrolled. Cows at three lactation time points: 1 week post calving (fresh) 50-100 days post calving (early) or 170-200 days post calving (late) were recorded.

At commencement, cows were separated from their group during milking and were mobility scored using the UK Agricultural and Horticultural Development Board (AHDB) 0–3 scale scoring method[9].

The cows were then examined in a foot trimming crush and any lesions recorded. If a DD lesion was found during the examination, it was macroscopically classified using the modified standardised M scoring system[8] (6 levels).

Cows recorded with an active DD lesion (M1, M2 or M4.1 stage) were then enrolled into the study group.

Images showing classical DD lesions M1, M2 and M4.1

M1

M2

M4.1

Eligible cows (those fulfilling the above criteria and not having received any antimicrobial or systemic analgesic treatments in the previous week) were then randomly allocated to the control or treatment group.

The DD lesions were carefully cleaned and dried and then treated with the application of a topical antibiotic spray. Cows in the treatment group also received an intramuscular injection of ketoprofen (3mg/kg Ketofen® 10% solution for injection: Ceva Animal Health).

All enrolled cows were mobility scored again one week later and their farm record data such as calving date, parity and daily milk yield (for both the week before and the week after assessment) were collected (***Table 1***).

		Days in Milk			
Stage of Lactation	**N**	**Mean**	**Min**	**Max**	**Std dev**
Fresh	34	6.56	1	16	2.94
Early	59	85.98	61	107	12.87
Late	65	185.55	170	221	11.91

Table 1: Summary of lactation stage for the study population at enrolment

Results

158 cows were enrolled to the study: 90 received ketoprofen and 68 were in the control group and did not receive ketoprofen. There was no statistical difference between the two groups with respect to parity, days in milk and milk yield at the week before enrolment.

1. Lameness prevalence at enrolment

Lameness prevalence (a mobility score of 2 or 3) was 11.8% in the control group and 14.4% in the treatment group and not statistically different at enrolment (p=0.62) (***Figure 1)***.

When assessing the prevalence of all lesions, it was found that the difference in cases of active M2 stage DD was not statistically different between groups. Likewise, the prevalence of claw horn lesions, such as sole ulcers, sole haemorrhage and white line disease, was very low and not statistically different between the two groups ***(Table 2)***.

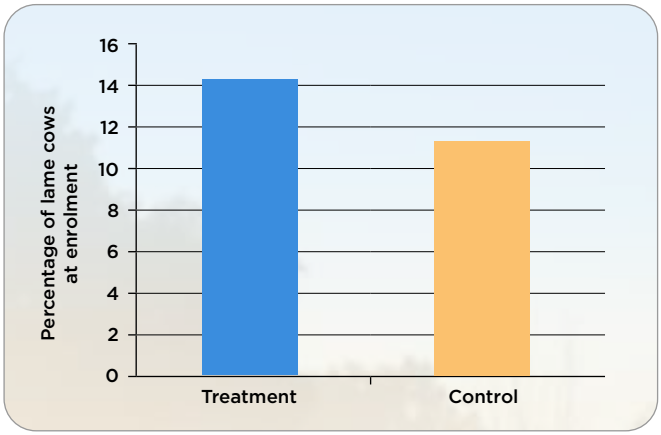


Figure 1: Showing the overall level of lameness (score 2 or 3) in the treatment group *vs*. the control group

Foot Lesions at enrolment	N	% of total
DD stage M2	84	53.16%
DD stage M1 or M4.1	74	46.83%
Sole ulcer	6	3.80%
White line disease	14	8.86%
Sole haemorrhage	3	1.9%

Table 2: Prevalence of foot lesions at enrolment

2. Analysis of whole group lameness prevalence at 2nd evaluation (1 week)

Whole group analysis showed that 12 out of 65 (18.46%) animals in the control group and 10 out of 87 (11.49%) in the treatment group were lame at the second evaluation, this data was not statistically significant (p=0.23) (***Figure 2)***.

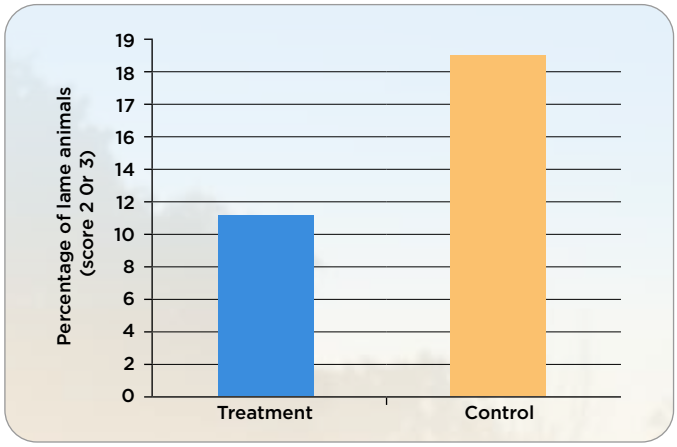


Figure 2: Graph showing the percentage of ALL animals lame after one week in the control *vs.* treatment groups.

As might be expected, the chances of a cow being found lame at the 2nd evaluation were 13.55 times higher if the cow was lame on enrolment.

Interestingly, control animals which received only topical antibiotic treatment were 2.57 times more likely to be lame at the second evaluation compared to those that received one injection of ketofen as well as topical treatment (p=0.103 - not statistically significant).

3. Lameness prevalence of cows assessed as lame at enrolment *w* 2nd evaluation (1 week)

When data was considered only from those cows that were lame at enrolment, those receiving only topical antibiotic treatment at the first evaluation, were 20.2 times more likely to be lame at the 2nd evaluation than those also receiving ketoprofen (p=0.027)*.

Additionally, five out of seven (71.43%) lame animals that were in the control group remained lame (score 2 and 3) a week after treatment whereas four out of 13 (30.77%) lame animals in the treatment group remained lame. This data showed a statistical trend (p=0.08) (***Figure 3)***.

*Statistically significant. Note: low sample size (n=20)

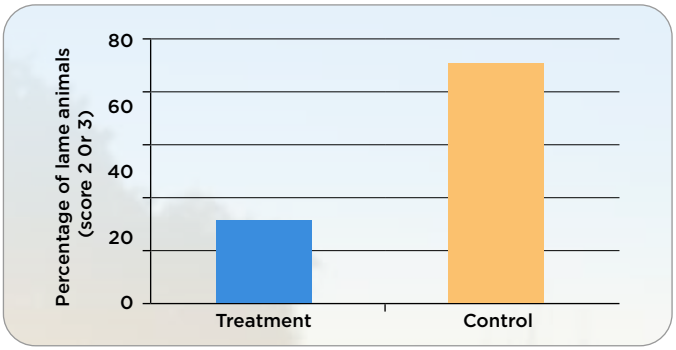
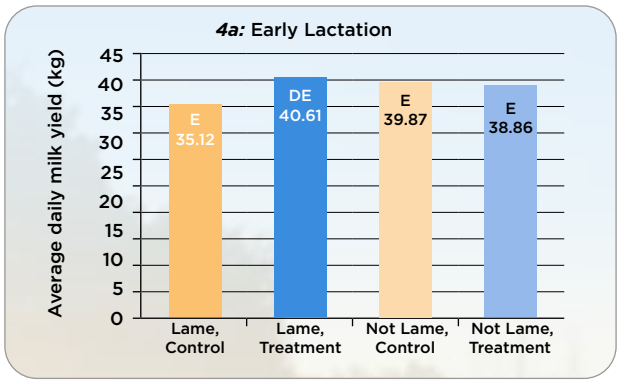


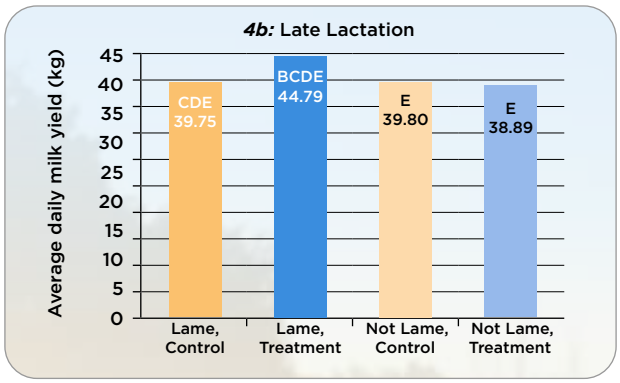
Figure 3: Showing the percentage of cows which remained lame upon the 2nd evaluation (i.e. from the group of animals which were lame upon enrolment).

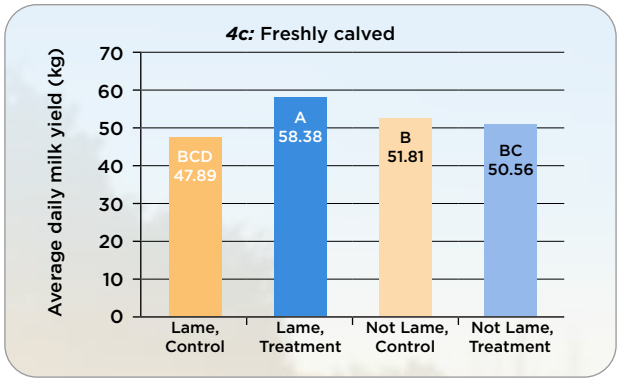
4. Effect on milk yield

Overall, cows in the treatment group produced a higher volume of milk than those in the control group, 45.35kg/day and 42.37kg/day (p<0.01) respectively, for the week following enrolment.

Early and late lactation cows which were lame on day 0 (enrolment) and in the treatment group receiving ketoprofen, produced approximately 5Kg more milk per day of the week after treatment than lame cows in the control group (***Figures 4a*** and ***b***).







Freshly calved cows that were lame at enrolment showed a statistically significant benefit in milk yield if treated with a single injection of ketoprofen compared to the control animals. These cows produced 58.38 (± 1.85) kg milk per day for the week after compared to the control group that produced 47.89 (± 1.81) kg per day (p < 0.05) (**Figure 4c**).

Figure 4: Results from multivariable linear regression model for outcome mean daily milk yield (kg) during the first-week post-enrolment for cows enrolled at different stages of lactation (Fresh (***a***), Early Lactation (***b***) or Late Lactation (***c***)).

Levels within a variable with different letters are statistically significantly different

Conclusions and Discussion

This study demonstrates that administering ketoprofen to cows experiencing the pain and lameness associated with DD, may lead to beneficial effects on their mobility and milk production, especially if animals are visibly lame when treated (score 2 or 3). The study also provides the first evidence of possible welfare and production benefits associated with the use of NSAIDs when treating the pain associated with active DD lesions in lame cows.

In a 2018 expert opinion survey, it was reported that nine out of twelve experts would recommend the use of NSAIDs for the treatment of active DD, but most of them would reserve this for cows with a mobility score of 3[7], although the decision could not be evidence-based as there had been no published study investigating this at the time.

The pain experienced by animals suffering with DD negatively affects their behaviour and productivity[10], both directly and indirectly through a decrease in dry matter intake. Previous studies have shown that lame cattle consume less feed and produce less milk than their non-lame counterparts[11] and the consumption of sufficient amounts of dry matter is particularly important for periparturient animals. If cows develop DD and, even more importantly, become lame in the periparturient period they will suffer production losses, possibly because of reduced dry matter intakes[12]. This could possibly explain why the administration of ketoprofen had such a significant effect on the milk production of lame animals affected with DD, especially those that were freshly calved.

The potential welfare benefits alone should be enough to justify the use of ketoprofen for the management of the pain and lameness associated with DD - but when the possible milk production and economic benefits to the farmer (especially given the fact that administration of ketoprofen does not require a milk withdrawal period in the UK) are also considered, it is more likely such a treatment approach should be adopted.

The addition of ketoprofen to the treatment of the pain and lameness associated with active digital dermatitis lesions may be beneficial for animal welfare and productivity

References

1. Huxley JN. Impact of lameness and claw lesions in cows on health and production. Livestock Sci. 2013;156(1–3):64–70.
2. Amory JR, Barker ZE, Wright JL, Mason SA, Blowey RW, Green LE. Associations between sole ulcer, white line disease and digital dermatitis and the milk yield of 1824 dairy cows on 30 dairy cow farms in England and Wales from February 2003-November 2004. Prev Vet Med. 2008;83(3–4):381–91.
3. Buch LH, Sørensen C, Lassen J, Berg P, Eriksson J-Å, Jakobsen JH, *et al*. Hygiene-related and feed-related hoof diseases show different patterns of genetic correlations to clinical mastitis and female fertility. J Dairy Sci. 2011;94(3):1540–51.
4. Griffiths BE, Grove White D, Oikonomou G. A cross-sectional study into the prevalence of dairy cattle lameness and associated herd-level risk factors in England and Wales. Front Vet Sci. 2018;5:1–8.
5. Evans NJ, Murray RD, Carter SD. Bovine digital dermatitis: current concepts from laboratory to farm. Vet J. 2016;211:3–13.
6. Bell and Vanhoundt 2020 Treatment and control of DD in dairy cattle. In Practice 42(10):554-567
7. Bird KL, Higgins H. Expert opinion on the treatment of individual cattle with digital dermatitis lesions. Cattle Pract. 2018;26(2):143.
8. Berry SL, Read DH, Famula TR, Mongini A, Döpfer D. Longterm observations on the dynamics of bovine digital dermatitis lesions on a California dairy after topical treatment with lincomycin HCl. Vet J. 2012;193(3):654–8.
9. Whay HR, Main DC, Green LE, Webster AJ. Assessment of the welfare of dairy cattle using animal-based measurements: direct observations and investigation of farm records. Vet Rec. 2003;153(7):197–202.
10. Pavlenko A, Bergsten C, Ekesbo I, Kaart T, Aland A, Lidfors L. Influence of digital dermatitis and sole ulcer on dairy cow behaviour and milk production. Animal 2011;5(8):1259–69.
11. Galindo F, Broom DM. The effects of lameness on social and individual behavior of dairy cows. J Appl Anim Welf Sci. 2002;5(3):193–201.
12. Gomez A, Cook NB, Socha MT,Döpfer D. First-lactation performance in cows affected by digital dermatitis during the rearing period. J Dairy Sci. 2015;98(7):4487–98.

Ketofen®

Reduce the pain and lameness associated with digital dermatitis

A recent study[1] concluded that in dairy cows, the addition of Ketofen® to protocols for the treatment of pain and lameness associated with digital dermatitis, could be beneficial for animal welfare and productivity.

#wavegoodbyetopain

Ketofen is part of the cattle NSAID trio from Ceva Animal Health which also includes:

Meloxidyl®
(meloxicam) - the longer duration of action[2] means it is ideally suited for use in beef cattle and calves

Allevinix®
(flunixin) - in cattle, can be given i/v or i/m to suit a range of situations, and is now available in CLAS® vials

[1]Kasiora K, Anagnostopoulos A, Bedford C,Menka T, Barden M, Griffiths BE, *et al*. Evaluation of the use of ketoprofen for the treatment of digital dermatitis in dairy cattle: A randomised, positive controlled, clinical trial. Vet Rec. 2021;e977. https://doi.org/10.1002/vetr.977 [2]Okkinga, K., 1998. Comparative clinical efficacy of a single versus three subcutaneous injections of Meloxicam (Metacam®) as adjunct to antibiotic therapy for the treatment of respiratory diseased calves. Presented at the 20th World Association for Buiatrics Congress, Sydney.

Ketofen® 10% solution for injection for horses, cattle and pigs contains 100 mg ketoprofen per ml. **Meloxidyl® 20 mg/ml** solution for injection for cattle, pigs and horses contains 20 mg meloxicam per ml. **Allevinix®** 50 mg/ml solution for injection for cattle, pigs and horses contains 50 mg flunixin (as meglumine) per ml. **Legal Category for all products:** UK POM-V

Further information is available from the product SPC, data sheet or pack insert.

Prescription decisions are for the person issuing the prescription alone. Use medicines responsibly (www.noah.co.uk/responsible)

Ceva Animal Health Ltd, Explorer House, Mercury Park, Wycombe Lane, Wooburn Green, Bucks.
Tel: 01628 334056 **www.ceva.co.uk**

cevolution
PRACTICAL INNOVATION IN THE MANAGEMENT OF HEALTH

Ceva

KET20-L446-0122-0.5 AUG24