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Analgesic Effect of Meloxicam in Canine Acute Dermatitis – a Pilot Study

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Viking Höglund O. and Frendin J: Analgesic effect of meloxicam in canine acute dermatitis – a pilot study. Acta vet. scand. 2002, 43, 247-252. – A double-blind trial was performed on 12 client-owned dogs suffering from acute and painful dermatitis. Clinically these cases represented pyotraumatic dermatitis and pyotraumatic folliculitis. Six dogs were injected with meloxicam and 6 were given placebo. Signs of pain were recorded on a visual analogue scale before administering the drug. This was repeated over the following 2-3 days. All dogs were treated with cephalexin orally. Six dogs given meloxicam and cephalexin showed an average decrease of pain on day 2 of 28.3%, whereas the 6 dogs given placebo and cephalexin showed an average decrease of pain on day 2 of 8.3%. When compared in the Wilcoxon two-sample test, using change in percent and absolute change, the 2 groups yielded $p = 0.026$ and $p = 0.064$ respectively. These findings indicate that meloxicam has an analgesic effect on acute dermatitis in dogs.

dermatitis; meloxicam; NSAID; analgesic; canine; dogs; pain.

Introduction

The effect of nonsteroidal anti-inflammatory drugs (NSAID) on dermatitis is well known from human trials and research using rats and mice (*Bayerl et al.* 1998, *Snyder* 1975, *Fleischer* 1999). To the best of our knowledge only one study has been published showing whether any of the modern NSAID impact the inflammatory process in acute dermatitis in the canine species (*Kimura & Doi* 1998).

According to data sheets for medicines indicated for usage in humans and animals, meloxicam hinders the accumulation of leukocytes in inflamed skin and other tissues *(Medical Products Agency* 2002). In addition, pruritus is a known side effect of this agent in canines *(Medical Products Agency* 2001) so meloxicam does have some effect in the dermis of canines. The aim of this study was to investigate the analgesic effect of meloxicam on acute dermatitis in the canine species. A second objective was to measure signs of central sensitisation, wind-up, after 3 weeks of treatment and to investigate whether the healing process is impaired when canine dermatitis patients are treated with meloxicam.

Materials and methods

Animals

Twelve client-owned dogs suffering from any kind of moist, and when pinched, painful dermatitis were included in this trial with their owners' consent. Painful dermatitis was defined as a VAS-value beyond 10 millimetres (se below). The cases clinically represented pyotraumatic dermatitis (acute moist dermatitis) and pyotraumatic folliculitis (local pyoderma).

Dogs showing no sign of pain when the affected area was pinched, dogs on current NSAID medication and dogs having suffered previous side effects when treated with meloxicam were excluded from the study. One and the same person made the inclusion and exclusion decisions and conducted all examinations.

Treatment protocol

A randomised, controlled, double-blinded trial was designed. Dogs were divided into 2 groups of 6. Cases representing the 2 different diagnoses were evenly distributed between the 2 groups. All dogs were given antibiotics (cephalexin) at standard dosage. The average dosages of cephalexin of group one (treated) and 2 (control) were 18.8 mg/kg and 19.9 mg/kg respectively, twice daily. Dogs were treated with antibiotics for 20 days. In addition, group one was given meloxicam (Metacam, 5mg/ml, Boehringer Ingelheim Vetmedica GmbH, Binger Straße 173, 55216 Ingelheim am Rhein, Germany), subcutaneously, at standard dosage of 0.2mg/kg on day one, followed by oral treatment (Metacam oral suspension 1.5mg/ml) at standard dosage of 0.1mg/kg for the following one or 2 days, depending on response to treatment.

The control dogs (group 2) were given an injection of saline. On day 2, these control dogs were given oral treatment with ordinary sugar syrup diluted with water. This placebo treatment continued for one or 2 days, depending on response to treatment.

The examining veterinary surgeon and the owners were blinded for treatment. In addition, the results were assessed prior to decoding group identity. The nurse who administered the initial injection followed a randomised double-blinded protocol.

A visual analogue scale (VAS) 0-100 mm was used to record pain. At the first consultation on day 1, the dogs were examined and the affected area was pinched between the thumb and index finger. Signs of pain were observed and scored on the VAS. Painscore was judged by the intensity of physical reactions, such as tail no longer wagging, vocalising, head turning and signs of aggression in response to the applied stress (pinching).

The dogs were re-examined the following day. An obvious change was defined as a minimum decrease of painscore of 10 percent on the VAS. If no obvious improvement was noted on re-examination, the owners were asked to return on the third day.

Follow-up examination

Assessment of treatment was based on telephone interviews and clinical examinations. All owners were interviewed approximately 20 days after initiation of therapy. The procedure for painscore was repeated in 4 of the dogs from group one and 3 from group 2. The skin was inspected and tested for signs of wind-up, i.e. observations were made of the dogs' reactions to

Table 1. Individual data derived from painscore on VAS, day one and two.

	Painscore day 1	Painscore day 2	Decrease of painscore (mm)	Decrease of painscore (%)
Group 1				
Case 1	53,5	42,5	11	20,5
Case 2	15	8,5	6,5	43,3
Case 3	11,5	8,5	3	26,1
Case 4	20	19	1	5
Case 5	30,5	19	11,5	37,7
Case 6	21,5	13,5	8	37,2
Group 2				
Case 7	12,5	12,5	0	0
Case 8	22,5	22	0,5	2,3
Case 9	65	64,5	0,5	0,8
Case 10	15	14	1	6,7
Case 11	33	25	8	24,2
Case 12	25	21	4	16

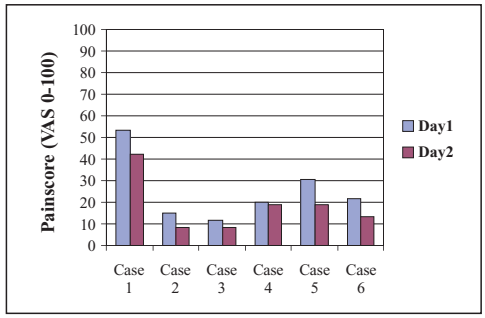

Figure 1. Group 1 (treated). Pain scored on a visual analogue scale (VAS) in 6 dogs with acute dermatitis on day one (blue columns), and day 2 (red columns), approximately 24 h after initiating therapy with meloxicam and cephalexin.

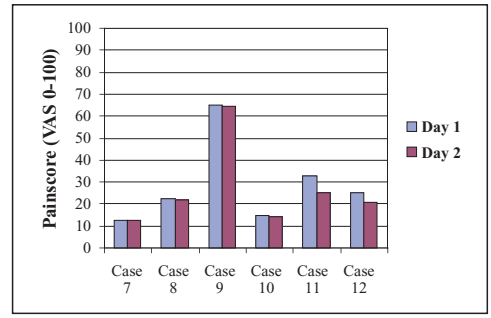

Figure 2. Group 2 (control). Pain scored on a visual analogue scale (VAS) in 6 control dogs with acute dermatitis on day one (blue columns), and day 2 (red columns), approximately 24 h after initiating therapy with saline and cephalexin.

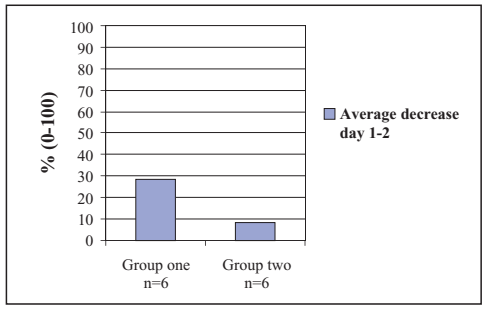

Figure 3. Average decrease in signs of pain scored on VAS from day one to day 2. Change expressed as a percentage. Group 1 was given meloxicam and cephalexin, group 2 was given placebo and cephalexin. Groups compared in Wilcoxon two-sample test p = 0.026.

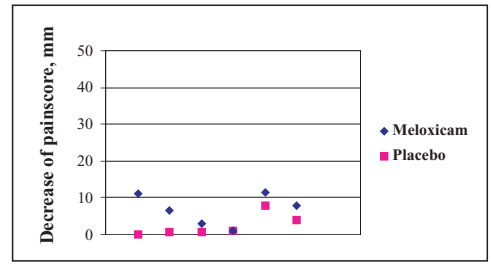

Figure 4. Groups 1 and 2. Decrease of painscore on VAS from day one to day 2. Absolute decreases shown in millimetres. Each individual's change is displayed. Groups compared in Wilcoxon two-sample test p = 0.064.

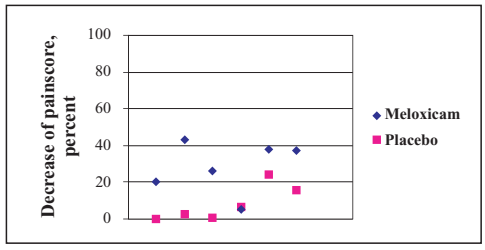

Figure 5. Groups 1 and 2. Decrease of painscore on VAS from day one to day 2. Relative decreases shown in percent. Each individual's change is displayed. Groups compared in Wilcoxon two-sample test p = 0.026.

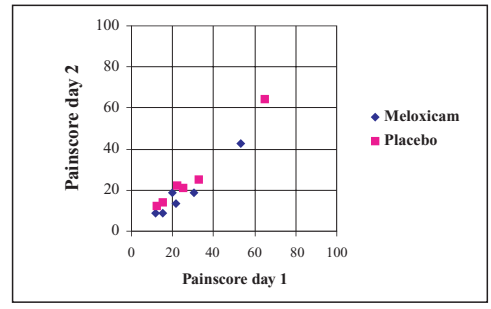

Figure 6. Painscore on VAS for all individuals, both groups. Day one is shown on x-axis and day 2 is shown on y-axis.

soft stimuli (using a cotton bud) and temperature change (using a spoon kept in a standard household freezer) of the previously infected and inflamed area.

Statistics

The change of painscore on the VAS from day one to day 2 equals the analgesic effect. Groups were compared using the Wilcoxon two-sample test using change in percent and absolute change.

Results

The results of pain assessments are shown in Figs. 1-6 and Table 1.

The painscores on VAS for all dogs ranged between 11.5 and 65 on day one before initiating treatment. On day 2 the scores had decreased by an average of 28.3 percent for group one and 8.3 percent for group 2 (Figs. 1-3).

Groups compared using the Wilcoxon two-sample test yielded $p = 0.064$ when comparing decrease of painscores on VAS in millimetres (Fig. 4).

When the groups' decrease of painscore on VAS was compared as a percentage, the Wilcoxon two-sample test yielded $p = 0026$ (Fig. 5).

The 5 dogs (cases 4, 7, 8, 9, 10) that clearly had not improved on day 2 were examined again on day 3. Four of these 5 dogs (cases 7, 8, 9, 10) were treated with antibiotics and placebo, belonging to group 2.

When the dog owners were interviewed after 3 weeks, all reported a complete recovery without relapses. The dermis of the 7 dogs accessible for re-examination after 3 weeks was diagnosed as having gone through a normal healing process. There was no abnormal reaction to soft touch, pinch or cold stimuli.

Discussion

Pain relief is an important aspect of treatment during inflammatory processes and for the well-being of the animal. The analgesic effect, according to the differences in scores on the VAS after only one day of treatment with meloxicam in the present study, indicates that meloxicam has an analgesic effect in the dermis of the canine species. After 3 weeks of treatment with antibiotics all dogs were fully recovered. Follow-up examinations and interviews revealed no signs of wind-up and there were no differences in healing between the 2 groups after termination of therapy.

An infection in the skin is sometimes a painful process due to the inflammatory processes initiated. The microorganisms will be reduced in numbers by the administration of antibiotics. This should eventually reduce the inflammatory process on the affected area. Therefore, a reduction of pain will be seen when the infection is treated with antibiotics.

NSAID inhibit cyclo-oxygenase 1 (COX-1) and 2 (COX-2). COX-1 inhibits platelet function via blockade of thromboxane A2 (TxA2) formation and COX-2 mediates inflammatory responses. Meloxicam has analgesic, anti-inflammatory, antipyretic and anti-exudative effects. After subcutaneous administration a maximum plasma concentration is reached after 2½ h. The half-life of meloxicam is 24 h. The main cause of meloxicam's effects is thought to be the inhibition of COX-2. Meloxicam also shows significant TxA2 inhibition, although less than traditional NSAID. The result is reduced synthesis of inflammatory mediators, prostaglandins, which play an important role in stimulating pain receptors (*Medical Products Agency* 2002, *Rinder et al.* 2002).

Pyotraumatic dermatitis is described as a superficial inflammatory process of undetermined cause and pathogenesis. Bacteria colonise the surface of the lesion but this is not a true skin infection. Preferred treatment is a corticosteroid, topical or oral. In addition, the area is

clipped, cleaned and treated with a drying solution and possibly antibiotic cream or ointment (*Scott et al.* 2000, *Reinke et al.* 1987, *Harvey, McKeever* 2000).

Pyotraumatic folliculitis is a superficial ulceration in the dermis, which also includes a deep suppurative and necrotizing folliculitis and occasional furunculosis. These types of lesions, true local pyodermas, have been described as thickened with surrounding papules and pustules. Treatment includes systemic antibiotics. The use of glucocorticoids is contraindicated due to possible immunosuppressive effect (*Scott et al.* 2000).

What appears to be a superficial process (i.e. pyotraumatic dermatitis, acute moist dermatitis) in clinical terms, could actually be a deep process (i.e. pyotraumatic folliculitis). Although the area is clipped and palpated, the 2 types are sometimes confused. In this study, the respective diagnoses for pyotraumatic dermatitis and pyotraumatic folliculitis were based on the clinical appearance of the skin lesions, and the 2 diagnoses were evenly distributed between the 2 groups. The diagnosis was not confirmed histologically as histological confirmation of the diagnosis was considered less important in these cases. The primary task was to assess the analgesic effect.

Regardless of whether a dermatitis is superficial or deep, the process can cause considerable pain and discomfort. In the present study, the dogs' reactions to palpation of the inflamed area were used to score pain. A study assessing postoperative pain in dogs showed that behavioural response (response to palpation, activity, mental status, posture and vocalisation) and physiological measurements can be used reliably to assess degree of pain and response to analgesics (*Firth & Haldane* 1999).

If meloxicam could be used as a complement to antibiotics in the treatment of pyotraumatic folliculitis, relief might be achieved in a shorter time compared to the use of antibiotics alone.

No signs of impaired healing were seen in this study. Reports have been published on the subject of NSAID and impaired healing of bone tissue in rats, humans and horses (*Bo et al.* 1976, *Giannoudis et al.* 2000, *Rohde et al.* 2000). The question of whether NSAID impair wound healing in skin is controversial and reports contradict each other. NSAID topically applied on dermal and epidermal wounds in pigs markedly reduced inflammation but did not influence the healing process (*Alvarez et al.* 1984). On the other hand, diclofenac and indomethacin have been shown to influence the healing of normal and ischaemic incisional wounds in rat skin. However, in certain doses the drugs improved the healing of normal wounds. The healing of ischaemic wounds, using a flap model, was unaffected after 10 days but decreased after 20 days (*Quirinia & Viidik* 1997).

Other studies considered the effects of meloxicam, previously named miloxicam, on cutaneous tissue in other species. The effects of meloxicam on acute inflammation in 6 ponies were assessed. Exudate leukocyte numbers were significantly reduced in drug-treated ponies, as were exudate concentrations of prostaglandin E and F (*Lees et al.* 1991).

The anti-exudative effect of meloxicam on subplantar induced oedema exceeded that of piroxicam, diclofenac, indomethacin and naproxen in a comparative study (*Engelhardt et al.* 1995). In addition, meloxicam showed greatest potency when comparing inhibition of granuloma formation induced by cotton pellets implanted into the subcutaneous space in rats.

This study shows that meloxicam seems to offer an analgesic effect during the processes involved in acute dermatitis in dogs. Further studies are needed on the use of meloxicam, as well as other NSAID, in treating dermatitis in the canine dermis.

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Sammendrag

Smärtstillande effekt av meloxicam vid akut dermatit, en pilotstudie.

En dubbelblindad studie genomfördes på 12 hundar med akut och smärtsam dermatit. Kliniskt representerades dessa av pyotraumatisk dermatit (hotspot) och pyotraumatisk follikulit (pyodermi). Sex hundar injicerades med meloxicam och sex gavs placebo. Grad av smärta registrerades på en visuell analog skala (VAS) innan administrering av substans. Detta upprepades under de följande 2-3 dagarna. Alla hundar gavs cefalexin oralt. De 6 hundar som gavs meloxicam och cefalexin hade en smärtlindring med ett medelvärde av 28,3% efter ett dygn. De hundar som gavs placebo och cefalexin hade en smärtlindring med ett medelvärde av 8,3%. Jämförelse av grupperna i Wilcoxon tvåprovtest (rangsummatest) av procenduell och absolut förändring gav $p = 0,026$ respektive $p = 0,064$. Resultaten tyder på att meloxicam har smärtstillande effekt vid akut dermatit hos hundar.

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