Relevance of NSAIDs for the treatment of metritis in cattle

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Metritis is an inflammation of the lining of the uterus. It mainly affects the endometrium (uterine lining) of cows that have recently freshened, but may sometimes extend to the myometrium (uterine wall) and the peritoneal (outer) layers of the uterus.

This inflammation is usually following an infection of the uterus by bacteria after calving (such as Fusobacterium necrophorum, Bacteroides spp, Escherichia coli).

However, the occurrence of metritis depends on three main parameters:

- The number and virulence of the bacteria present.
- The cow's natural defence mechanisms (impaired or not).
- The health status of the uterus.

An inflammatory condition

A rapid involution of the uterus after calving is key to naturally expelling fluid, placental membranes and bacteria from the reproductive tract.

Conditions such as dystocia, retained placenta, twins, stillbirth, prolapsed uterus, milk fever or abortion, or dirty calving equipment can quickly develop into metritis as an inflammatory condition.

Calving difficulty increases the risk of trauma to the uterine wall and may increase the susceptibility to disease by increasing the risk of harmful bacteria entering the reproductive tract.

Cows with assisted calving following dystocia are about 15.8 times more likely to develop severe metritis.

Clinically, the disease is expressed by discharge from the birth canal within 14 days post-calving. In the mild and moderate cases, only local signs can be seen: uterine discharge is mucoid, it may be thick and reddish in colour and has no unpleasant odour.

In the case of severe or systemic metritis, cows will exhibit one or more of the following clinical signs:

- Foul-smelling, purulent vaginal discharge.
- Elevated temperature.
- Decreased appetite.
- Dehydration.
- Depression, dullness, sickness.
- Diarrhoea.
- Reduced milk production.

An economic issue

In addition to longer term effects on fertility (cows with metritis have increased days between first service after calving and conception), in the short term metritis increases the susceptibility to ketosis, abomasal displacement and other infections such as mastitis.

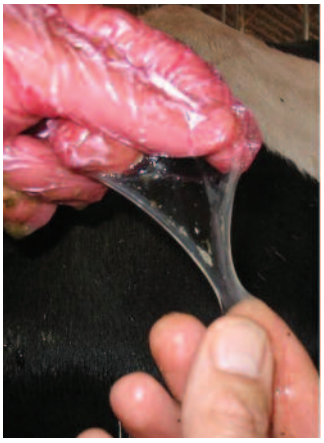
Its economic impact is significant when adding up the costs of treatment, discarded milk, reduced milk yield and reduced reproductive performance (lower fertility).

Metritis is thought to decrease daily milk production from 2 to 13kg during a period that can vary from 2-20 weeks after parturition. Some authors have reported a significant decrease in milk production of up to 2,647kg for the remaining lactation in multiparous cows with metritis, in comparison to unaffected cows.

A recent attempt to quantify the effect of postpartum uterine diseases (retained placenta and metritis) on milk production and culling showed that uterine disease was associated with reduced reproductive performance and reduced the chance of becoming pregnant.

Together with reduced milk production, this was identified as being a substantial risk factor for culling (Figs. 1 and 2).

Vaginal discharge score 0 (clear or no discharge) = healthy. (All four photographs courtesy of UBC Animal Welfare Program).



Vaginal discharge score 2 (less than 50% pus and bad smell with or without fever) = mild metritis.

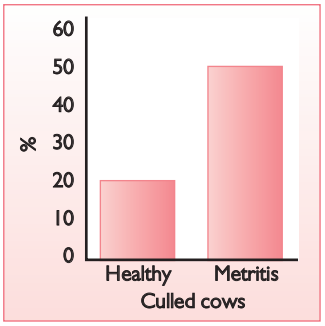


Fig. 1. Culling rate in cows with or without metritis (adapted from Wittrock et al. 2011).

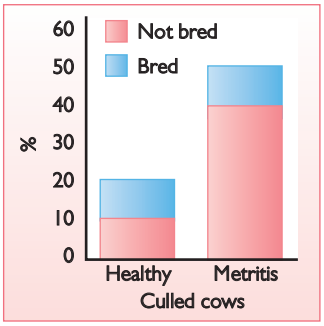


Fig. 2. Culling rate and pregnancy rate (adapted from Wittrock et al. 2011).

Recommended treatment

The treatment of metritis involves antibiotics which show a good distribution in the tissues such as tetracycline or beta-lactams. Treatments also often include uterine contractors such as prostaglandins or oxytocin.

Oxytocin, however, stimulates uterine contractions for no longer than 24-48 hours after calving.

Prostaglandins (PGF_{2a}) administration aims at inducing oestrus and leads to a stimulation of uterine contraction, which aids in expulsing purulent uterine fluid and debris.

Since prostaglandins are effective as of eight days after calving, they are typically used between 3-7 weeks postpartum. Administration of calcium may be helpful in those fresh cows which are frequently hypocalcaemic. Glucose precursors such as propylene glycol or propionate may improve appetite and prevent the risk of developing ketosis. Since metritis often comes with typical signs of inflammation such as fever, non-steroidal anti-inflammatory drugs (NSAIDs) naturally recommend themselves to control elevated temperature. NSAIDs are also indicated to counteract the effects of bacterial endotoxins.

Their analgesic properties may be helpful to alleviate pain and discomfort when they occur. From a theoretical standpoint, NSAIDs can therefore be considered useful drugs which may accelerate the recovery of the cows. Let's see what scientific evidence exists to support the theoretical justification.

Scarce scientific data

Surprisingly, only limited literature exists about the use of NSAIDs in combination with a standard antibi-

Continued on page 27

Continued from page 25
otic therapy for the treatment of puerperal metritis. Research done was based on the hypothesis that a treatment with NSAIDs could have positive effects on both the inflammatory process taking place in the uterine wall and on the uterine involution; this would improve cure rates, which could result in higher milk yield and improved reproductive performance.

While study results tend to support these assumptions, data also show that available molecules are not equally effective and do not deliver the same benefits.

Faster uterine involution

In a first study, the prostaglandin synthesis inhibitor flunixin was administered intravenously at a dosage of 2.2mg/kg of body weight on six occasions (twice daily on the first two days and once daily for the subsequent two) to cows with acute or subacute metritis, while a second group received a placebo.

Animals treated with flunixin had a faster uterine involution than controls and showed a postpartum oestrus earlier than controls.

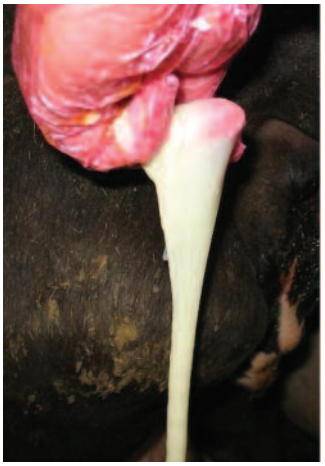
On the other hand, different treatments of induced post-partal endometritis with flunixin (2.2mg/kg orally twice daily on either days 3-6 or 11-14 post partum), either alone or combined with oxytetracycline did not influence recovery from infection or uterine involution.

A more recent study evaluated the effects of a single administration of 2.2mg/kg of flunixin in addition to a systemic antibiotic treatment in cows with acute puerperal metritis. Beneficial effects on clinical cure, milk yield or reproductive performance were not obvious.

The mixed results observed with flunixin are not clear and might be related to its short acting effects. Whether a repeated treatment (>4 days or multiple per day) would be more effective requires further investigation.

Another group of researchers conducted a randomised field trial in 10 commercial dairy herds to investigate the effects of the preferential COX-2 inhibitor meloxicam in cows with metritis. Animals were treated with either a single parenteral injection of 0.5mg meloxicam/kg body weight (treatment group, n=70) or left untreated (control group, n=57). Additionally, in both groups, animals received a standard therapy consisting of prostaglandin (125µg cloprostenol IM for three days), ergometrin+serotonin (13.8mg+ 3.3mg IM/day for three days) and an antibiotic (ceftiofur, 1mg/kg/day for three days). Ultrasographic examination was performed on days 7, 20 and 30 post partum and measures of uterine diameter were taken. Compared to the control group a significantly faster uterine involution was achieved on days 20 and 30 post partum in the meloxicam-treated cows (Fig. 3).

In addition to the demonstrated positive effect from using meloxicam on the diameter of uterus as the site of the inflammation, more research could be helpful to assess further effects on the clinical, but also on a potential mid term outcome of the treatment on reproductive performance.



Vaginal discharge score 3 (more than 50% pus and bad smell) = mild metritis.

Vaginal discharge score 4 (red/ brown watery discharge, rotting flesh, putrid smell and fever) = severe.

A painful condition?

In addition to being an inflammatory condition, it is worth considering that metritis is likely to also be associated with abdominal pain in cows, as it is the case in other species.

Although there is a widespread belief that cattle are stoic to pain, recent investigations have demonstrated that conditions such as mastitis or diarrhoea, or routine procedures such as disbudding are a significant cause of pain and discomfort in cattle which can be measured through feed intake, weight gain or behavioural modifications.

A survey carried out in 2003 in Finland to assess veterinarians' attitudes and practices to pain relief in animals revealed that acute metritis in cows scored 6.58 on a scale of one (lowest pain) to 10 (highest pain). The median score was seven (scores ranged from 2-10).

Another paper on the use of analgesics in the UK reported that cattle practitioners, when asked to estimate the severity of pain associated with acute metritis, gave a median score of 4, higher than that given to moderate mastitis (scored 3), using a 10-points scale on which 0 indicated no pain and 10 the worst pain imaginable.

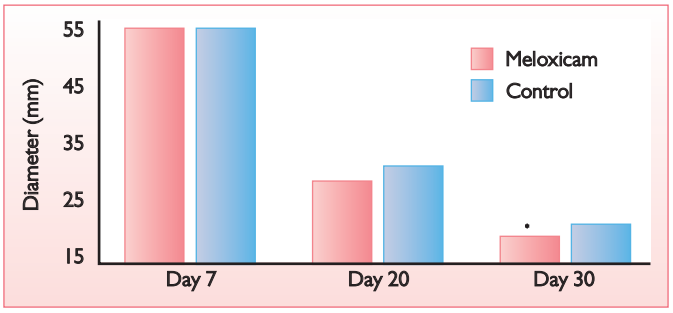
There was, however, a significant difference between the pain scores assigned by men and women, with women giving higher pain scores to acute metritis.

A recent survey performed in New Zealand with 166 dairy veterinarians revealed similar outcomes: the median score given to acute metritis was 5 on a 10-points scale.

This may indicate the readiness of the veterinary profession to address this issue and reconsider the cows' clinical disorders which were once thought to be painless.

Although it is still unclear at this point of time whether or not metritis is associated with either mild or acute pain, it does involve soft tissue inflammation and impacts the cow's well being. Similar to what is observed in cattle with respiratory diseases, diarrhoea or mastitis, NSAIDs can be expected to accelerate the resolution of the clinical signs and make the cow feel better and thus eat more. ■

Fig. 3. Mean of uterine diameter (mm) in 127 cows (*p<0.01).



References are available from the author on request