Toxic mastitis – treatment options

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SARA PEDERSEN explains the therapy methods available in targeting both the bacteria and endotoxin effects relating to this acute and critical condition in dairy cows.

TOXIC mastitis is a life-threatening condition for a dairy cow. Early identification and treatment are essential if mortality is to be avoided.

Unlike mild and moderate cases of mastitis, where treatment is mainly focused on targeting the bacteria involved, the treatment of toxic cases must also combat the effects of the resultant endotoxaemia.

Endotoxin is a component of the outer cell wall of Gram-negative bacteria and is released following cell death or during periods of rapid bacterial growth. The interaction between the cow’s immune response and the endotoxin triggers a complex cascade of events that often leads to severe pathophysiological consequences for the cow (Figure 1).

Therefore, treatment must be targeted not only at the bacteria involved in the mastitis, but also these systemic effects.

Fluids

Cows in endotoxic shock have a marked hypovolaemia and aggressive fluid therapy is an essential part of treatment. Eyeball recession and a prolonged skin tent time are good indicators of dehydration.
The most common route of administration of fluids in the toxic patient is intravenously, although oral fluids may be given in cases identified very early.

Due to the huge volumes involved, administering isotonic fluids to dehydrated adult cattle is usually time and cost prohibitive. Instead, hypertonic saline offers a more practical option in the field situation – 4ml/kg to 5ml/kg over four to five minutes can safely be administered, equivalent to approximately three litres in a 650kg cow.

Use of a 10G catheter and wide bore giving set allows faster administration.

Immediately after treatment, cattle should be provided with a supply of fresh water. While most will drink 20 to 40 litres within 10 minutes, those that don’t should be rumen pumped, since use of hypertonic saline relies on the uptake of water from the rumen to restore circulatory volume (Figure 2).

**NSAIDs**

NSAIDs possess anti-inflammatory, antipyretic, antiendotoxic and analgesic properties and therefore help combat many of the consequences of endotoxaemia.

The licensed NSAIDs available for use in cattle are flunixin meglumine, meloxicam, ketoprofen, carprofen and tolfenamic acid.

There are very few – if any – robust studies comparing the effectiveness of different NSAIDs in naturally occurring cases of toxic mastitis, with the majority of studies comparing an NSAID to a placebo in induced cases.

A large amount of data shows the use of NSAIDs in conjunction with antibiotics is beneficial, in comparison to antibiotics alone and, therefore, their use should be standard practice.

In the absence of robust trials, choice of NSAID usually comes down to clinician and/ or farmer preference based on route of administration, perceived effectiveness and frequency of administration. However, flunixin meglumine is widely recognised as having the most potent anti-endotoxic properties.

While all NSAIDs act via inhibition of cyclo-oxygenase (COX) in the arachidonic acid cascade, they do vary in their affinity for COX-2 versus COX-1.

Whereas COX-2 is upregulated in response to inflammatory stimuli (including endotoxin), COX-1 is required for “housekeeping” and protective inflammation, which maintains the intestinal mucosa, platelet aggregation and renal blood flow. Therefore, the ideal NSAID would target COX-2 only and not COX-1 - that is, prevent bad inflammation while protecting the good.
While no COX-specific NSAIDs are available, some are COX-2 selective and thus preferentially bind to COX-2 in comparison to COX-1. Both meloxicam and carprofen fall into this category, although the former is twice as selective.

Use of a COX-selective NSAID may aid in reducing the unwanted side effects of NSAID use, including gastrointestinal ulceration and compromised renal function.

**Antibiotics**

The use of antibiotics in cases of toxic mastitis remains controversial, as some may argue by the time clinical signs are seen, there are no longer any causal bacteria left.

However, the majority of cows with toxic mastitis will have a bacteraemia and, while Gram-negative organisms are the most commonly isolated bacteria, not all are *Escherichia coli* (Figure 3).

Therefore, when deciding on the most appropriate systemic antibiotic to use, it is important it is effective against Gram-negative organisms.

The frequency and duration of treatment is determined by the specific properties of the antibiotic being used, since some are concentration-dependent and thus only administered once, whereas others are time-dependent and require repeat administration.

While fluoroquinolones and cephalosporins are proven to be very effective in the treatment of toxic mastitis cases – due to concerns with resistance and overuse – it is recommended that they should be reserved for second-line treatments or for the most serious cases.

**Table 1** outlines the commonly used antibiotics, which are either specifically licensed for – or indicated in – the treatment of severe mastitis (including *E coli*).

**Additional therapies**

While fluids, NSAIDs and antibiotics are the main components of treatment, there are other therapies frequently used as part of a treatment plan.

Oxytocin can assist in milk let down in many mastitis cases and thereby aid the removal of mastitis related components.

However, it is unlikely to be of benefit in all cases of toxic mastitis, since those resulting in a severely swollen quarter are likely to have milk ducts blocked by inflammatory products and debris – mostly pus.

However, even if not aided by the use of oxytocin, frequent milking out of the affected quarter can
aid in removal of bacteria from the udder and has been shown to be beneficial in toxic cases.

Intravenous calcium supplementation can have multiple benefits in the toxic cow. Since many cases occur early in lactation it is expected the cow will at least be subclinically hypocalcaemic and calcium has also shown to aid in the excretion of toxins through the liver through binding.

**Summary**

Cows suffering from toxic mastitis require rapid and aggressive treatment to improve their chances of a successful outcome.

Due to the numerous effects of endotoxin release, recovery can often be prolonged and it is vital that throughout this time cows receive sufficient supportive therapy and nursing (TLC).

While early recognition and treatment of cases increases a cow’s chance of survival, prevention in the first instance is always preferable.

**References and further reading**

Figure 1. Pathophysiologic consequences of endotoxaemia in cattle (Smith, 2005).
Figure 2. Fluid therapy is an essential component when treating toxic mastitis.

Figure 3. The majority of toxic cases are caused by *Escherichia coli*, which can be acquired during the dry period.
<table>
<thead>
<tr>
<th>Group</th>
<th>Antibiotic</th>
<th>Commercial preparations</th>
<th>Dose</th>
<th>ROA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Penicillins</strong></td>
<td>Amoxicillin and clavulanic acid</td>
<td>CombiClav</td>
<td>1ml/20kg daily for 3-5 days</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Noroclav</td>
<td>1ml/20kg daily for 3-5 days</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Synulox RTU</td>
<td>1ml/20kg daily for 3-5 days</td>
<td>IM</td>
</tr>
<tr>
<td><strong>Sulphonamides</strong></td>
<td>Trimethoprim and sulfadiazine</td>
<td>Duphatrim IS</td>
<td>1ml/16kg daily up to 5 days</td>
<td>Slow IV/IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norodine 24</td>
<td>1ml/16kg daily up to 5 days</td>
<td>Slow IV/IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tribrissen 48%</td>
<td>1-1.5ml/32kg daily up to 5 days</td>
<td>IM</td>
</tr>
<tr>
<td><strong>Aminoglycoside</strong></td>
<td>Framycetin 15%</td>
<td>Framomycin</td>
<td>1ml/30kg twice daily for 3 days</td>
<td>IM</td>
</tr>
<tr>
<td><strong>Cephalosporins</strong></td>
<td>Cobactan 4.5%</td>
<td>Cobactan 4.5%</td>
<td>1ml/45kg daily for 2 days</td>
<td>IM</td>
</tr>
<tr>
<td>Only licensed for acute</td>
<td>Cobactan 2.5%</td>
<td>Cobactan 2.5%</td>
<td>2ml/50kg daily for 2 days</td>
<td>IM</td>
</tr>
<tr>
<td>mastitis caused by <em>E coli</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluoroquinolones</strong></td>
<td>Danofloxacin</td>
<td>Advocin 180</td>
<td>1ml/30kg once</td>
<td>SC/IV</td>
</tr>
<tr>
<td>Only licensed for acute</td>
<td>Baytril 10%</td>
<td>Baytril 10%</td>
<td>5ml/100kg daily for 2 days</td>
<td>Slow IV</td>
</tr>
<tr>
<td>mastitis caused by <em>E coli</em></td>
<td>Baytril Max</td>
<td>Baytril Max</td>
<td>5ml/100kg daily for 2 days</td>
<td>Slow IV</td>
</tr>
<tr>
<td></td>
<td>Powerflox 100mg/ml</td>
<td>Powerflox 100mg/ml</td>
<td>5ml/100kg daily for 2 days</td>
<td>Slow IV</td>
</tr>
<tr>
<td></td>
<td>Marboflox</td>
<td>Marboflox</td>
<td>1ml/50kg daily for 3 days</td>
<td>IV(1st only)/IM/SC</td>
</tr>
<tr>
<td></td>
<td>Marbocyl 10%</td>
<td>Marbocyl 10%</td>
<td>1ml/50kg daily for 3-5 days</td>
<td>SC/IV</td>
</tr>
<tr>
<td></td>
<td>Marbox</td>
<td>Marbox</td>
<td>1ml/50kg daily for 3 days</td>
<td>IV(1st only)/SC</td>
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<td></td>
<td>Marbonor 100mg/ml</td>
<td>Marbonor 100mg/ml</td>
<td>1ml/50kg for 3-5 days</td>
<td>IV/IM/SC</td>
</tr>
<tr>
<td></td>
<td>Ubiflox 100mg/ml</td>
<td>Ubiflox 100mg/ml</td>
<td>1ml/50kg daily for 3-5 days</td>
<td>IM/IV/SC</td>
</tr>
</tbody>
</table>
**Table 1.** Antibiotics either specifically licensed for – or indicated in – the treatment of acute mastitis cases (including *Escherichia coli*). Cephalosporins and fluoroquinolones should be used responsibly.