Enrofloxacin in dairy cattle with *Escherichia coli* mastitis

**Clinical scenario**
You have attended a clinical governance meeting at your practice about the use of antibiotics and the farm animal partners are keen to streamline the use of antibiotics in the dairy side of the business. Toxic mastitis was used as an example where the use of antibiotics could be standardised between vets; however, an argument broke out about whether you should use antibiotics at all in these cases. Most people seemed to agree that NSAIDs were beneficial, but questioned the use of antibiotics. You routinely use enrofloxacin in these cases (as that is what you were taught), along with an NSAID, but now you wonder if that is necessary.

**The question**
In [dairy cattle with *Escherichia coli* mastitis] does [the administration of enrofloxacin in combination with NSAIDs compared to NSAIDs alone] [improve clinical recovery]? 

**Search strategy**
The search strategy can be viewed at https://bestbetsforvets.org/bet168, it is also available as a supplement to this article on Veterinary Record’s website at http://veterinaryrecord.bmj.com/content/178/4/345

**Search outcome**
- Four papers found in Medline search
- One paper excluded as it is a review article/in vitro research/conference proceeding
- Three total relevant papers from Medline
- Eight papers found in CAB search
- One paper excluded as it did not meet the question
- Four papers excluded as they are review articles/in vitro research/conference proceedings
- Three total relevant papers from CAB
- Three relevant papers from both Medline and CAB Abstracts.

**Search last performed**
September 7, 2015.

**Comments**
Two of the three relevant papers contain data from the same study, so the most appropriate of the two is included. The paper that is not included is: Hirvonen, J, Eklund, K, Teppo, A M, Huszenicza, G, Kulcsar, M, Saloniemi, H & Pyörälä, S (1999) Acute phase response in dairy cows with experimentally induced *Escherichia coli* mastitis. *Acta Veterinaria Scandinavica* 40, 35-46

**Summary of evidence**

**Paper 1:** Efficacy of enrofloxacin in the treatment of naturally occurring, acute clinical *E.coli* mastitis (Suojala and others 2010)

**Patient group:** Lactating dairy cows (Finnish Ayrshire or Holstein Friesian breeds) with naturally occurring *E.coli* mastitis, n=132

**Study type:** Randomised controlled trial

**Outcomes:** Clinical cure (at two and 21 days) defined as no systemic signs, a normal udder and normal milk appearance. Bacteriological cure (at two and 21 days). Return to milk production of the affected quarter (at 21 days). Survival in the herd, assessed as remaining in the herd for three weeks after treatment and remaining in the herd six months later.

**Key results:** The clinical cure rate on day 2 was significantly lower in the enrofloxacin group (6.1 per cent, n=64) compared to the non-treated group (20 per cent, n=68), P=0.016. There was no significant difference in the clinical cure rate on day 21 between the two treatment groups (46.7 per cent compared with 57.1 per cent, respectively). Bacteriological cure rates were significantly higher in the enrofloxacin group on day 2 (odds ratio for cure was 3.32, P=0.002). Bacteriological cure rates on day 21 were similar in both treatment groups (90.5 per cent in the enrofloxacin group and 86.8 per cent in the non-treated group). Survival rates of cows at day 21 or survival in the herd at six months did not differ between the two treatment groups. Quarter milk production returned in 21.3 per cent of cows in the enrofloxacin group and 37.3 per cent of the untreated cows.

**Study weaknesses:** The randomisation method used (odd and even cow identification numbers) was predictable and therefore open to bias, and no blinding was used. There were differing supportive therapies available to each cow (eg, frequent milking, fluid therapy) and it was unclear whether the uptake of these therapies was significantly different between treatment groups. Some of the assessments made were subjective (eg, estimated quarter milk production). Administration of the second dose of enrofloxacin and some outcome measurements were reliant on owner compliance. No explanation was given for cases that were excluded from the study, and it was also unclear whether the exclusions were balanced across the treatment groups. Large amounts of data were missing and no sample size calculation was performed before data collection took place.


**Paper 2:** Efficacy and pharmacokinetics of enrofloxacin and flunixin meglumine for treatment of cows with experimentally induced *Escherichia coli* mastitis (Rantala and others 2002)

**Patient group:** Finnish Ayrshire cows with experimentally induced *E.coli* mastitis, n=6

**Study type:** Randomised controlled trial (cross over design)

**Outcomes:** Systemic and local clinical signs, daily milk yield and pharmacokinetic parameters (eg, serum and milk concentrations of enrofloxacin).

**Key results:** There were no significant differences in clinical signs between the two treatment groups and no statistically significant differences in the number of deaths between the two treatment groups, P=0.27. Cows that received enrofloxacin plus NSAID compared to NSAID alone produced 0.9 litres more milk per day during the study, P<0.05.

**Study weaknesses:** Mastitis was experimentally induced and cows varied in their severity of clinical signs; only three cows had moderate to severe clinical signs. The method of randomisation was not described and no blinding was used. A sample size calculation was not performed and the sample size was very small. There was an insufficient description of the clinical sign scoring systems used, as well as limited presentation of data and statistical analyses. No statistical significance level was stated.


**Comments**
The study by Suojala and others (2010) is a larger, field-based clinical trial which is more representative of the patients likely to be seen in clinical practice, whereas the study by Rantala and others (2002) was a smaller, experimentally induced *E.coli* mastitis trial. However, the methodological weaknesses of the Suojala and others study mean that interpretation and application of the results is difficult. The two studies used different NSAIDs, ketoprofen and flunixin, respectively. Further, high quality trials would be beneficial to address this question.

**Bottom line**
The evidence found does not support the use of enrofloxacin to improve clinical recovery in dairy cattle with *E.coli* mastitis.

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