EFFICACY OF ENROFLOXACIN IN THE TREATMENT OF BOVINE CLINICAL MASTITIS

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Introduction

Fluoroquinolones form a promising family of new bactericidal antimicrobials. Enrofloxacin is the first antimicrobial of this family available to veterinary medicine. Fluoroquinolones share a wide spectrum of acitivity but are most potent against gram-negative bacteria. They have a large volume of distribution and a low binding to plasma proteins, and are active at low concentrations. Compared with many other antimicrobials, they also have the advantage of being active against intracellular pathogens (8). Very few studies have been made of the pharmacokinetics of enrofloxacin in lactating cows. In one report, enrofloxacin was administered intravenously (IV) or intramuscularly (IM) to three cows (3). After both routes of administration, the concentration of enrofloxacin in milk rapidly exceeded that in plasma. At a dose of 2.5 mg/kg b.w., inhibitory levels against coliform bacteria and most staphylococci (> 0.25 µg/ml) were obtained in milk for approximately 24 hours. Using the same dose administered subcutaneously (SC), a concentration of 0.06 µg/ml or more was maintained in the serum and tissue of calves for 24 hours (6).

The bactericidal action of fluoroquinolones, their wide distribution in tissue and their activity against intracellular pathogens make them attractive for the treatment of staphylococcal mastitis. Enrofloxacin could solve the problem posed by the lack of a pharmacokinetically suitable antimicrobial for coliform mastitis. There are no published data on the efficacy of fluoroquinolones in the treatment of mastitis, except one preliminary report on norfloxacin in dry cow therapy (7).

Materials and methods

The present trial was carried out in the area of the Ambulatory Clinic of the College of Veterinary Medicine. Acute clinical cases of mastitis due to staphylococci or coliforms were treated with enrofloxacin (EN) or control treatment (penicillin G (PG) for staphylococci and supportive treatment only with no antibiotics (NA) for coliforms). Selection was based on bacteriological culturing and sensitivity testing before the start of therapy. In some cases, treatment had to be started before the sample results had been obtained and cases were included if they met the inclusion criteria. Clinical signs such as fever, inappetence, and soreness and edema in the affected quarter were of the same grade in both treatment groups. The inflammatory status of the quarters was evaluated by means of milk NAGase determination (4). About one third of cases in both staphylococcal groups were chronic (recurrent staphylococcal

infections).

Enrofloxacin (Baytril[R], Bayer) was administered SC at 2.5-5 mg/kg/day and penicillin G IM (Ethacilin[R], Intervet) at 25 mg/kg/day for 3-5 days. Supportive treatment included oxytocin (Partoxin[R], Ferrosan, 5-10 IU IV/IM) followed by frequent milking, and flunixin (Finadyne[R], Shering Plough) at 2.2 mg/kg/day IV/IM for 1-2 days. Oxytocin was administered and frequent milking advised in the antibiotic-treated groups as well. Twenty-five of the 42 mastitis cases treated with EN were caused by staphylococci (18 S.aureus and 7 CNS) and 17 by coliforms (12 E.Coli and 5 Klebsiella species). The control groups comprised 38 staphylococcal cases (22 S.aureus and 16 CNS) and 24 coliform cases (all E.coli). All the bacterial strains were in vitro sensitive to the drugs used. Follow-up samples were taken 3-4 weeks after treatment for bacteriological culturing, somatic cell count (SCC) and milk NAgase determination. In addition, the affected quarter was examined clinically and restitution of milk production recorded during the follow-up visit.

Results and discussion

Therapy responses in enrofloxacin-treatment and control groups in coliform and staphylococcal mastitis are shown in Table 1. Bacteriological cure rates in the coliform group were 59% with EN and 83% with NA (no antibiotics). Inflammatory reactions in the affected quarters as assessed by the milk NAGase level at the acute stage did not differ significantly between the groups (mean value of the EN group 216 units (U) and that of the NA group 240 U). Quarters infected by other than the original bacteria were classified as not recovered.

Table 1. Efficacy of enrofloxacin vs control treatment in clinical mastitis caused by coliform bacteria or staphylococci. Follow-up samples were taken 3-4 weeks after treatment and cure rates calculated based on bacteriological culturing and milk SCC and NAGase determination.

Bact.	Treat-ment[a]	N:o of quart.	Bacteriol. cure rate n	%	Complete[b] cure rate n	%	Same inf. n	%	Other inf. n	%
S.aureus	EN	18	3	17	3	17	13	72	2	11
- " -	PG	22	10	45	9	41	10	45	2	9
CNS	EN	7	2	29	2	29	2	29	3	43
- " -	PG	16	14	88	13	81	1	6	1	6
Staph.all	EN	25	5	20	5	20	15	60	5	20
- " -	PG	38	24	63	22	58	11	29	3	8
Coliforms	EN	17[c]	10	59	4	24	4	24	3	18
- "-	NA	24	20	83	13	54	1	4	3	13

[a]EN = enroflocacin, PG = penicillin G, NA = supportive treatment only
[b]No bacterial growth, SCC < 300 000/ml and NAGase inter-quarter ratio < 2.5 (value of diseased quarter divided by the lowest quarter value)
[c]Number of different species: Klebsiella 5, E.coli 12

The inflammatory reaction, as assessed using milk NAGase and SCC, disappeared slowly despite the fact that the infection had been eliminated. NAGase and SCC were at an acceptable level (the group with "complete cure", Table 1) 4 weeks after the treatment in 24% of the quarters in the EN group and in 54% of the quarters in the control group. Milk production had nearly ceased or was very low in many quarters with high SCC and NAGase values.

In staphylococcal mastitis, the bacteriological cure rate with EN was 20% and that with PG 63%. In both groups cure rates were higher in CNS than in S.aureus infections (29% vs 17% and 88% vs 45%). The inflammatory reaction at the acute stage was more severe in the S.aureus group treated with EN (mean NAGase value 336 U) than in the PG group (mean 274 U). Mastitis due to CNS produced a milder reaction (mean NAGase value 203 U). Rates of "complete cure" (Table 1) based on bacteriological examination, as well as milk SCC and NAGase levels in the affected quarter, were also calculated. In contrast to the coliform group, in mastitis due to staphylococci the inflammatory reaction in the quarter seemed to disappear within 4 weeks if the infection was eliminated, the bacteriological and complete cure rates being almost identical.

We conclude that the effect of systemic enrofloxacin treatment on clinical mastitis was not satisfactory. In this preliminary trial, the groups treated were too small to make any statistically reasonable calculations possible. In staphylococcal mastitis, systemic treatment with penicillin G gave much better results than EN. In general, our cure rates in mastitis due to S.aureus cannot be regarded as high. Nevertheless, they are in agreement with many other investigations showing that the therapy response in this form of mastitis is poor (1). Clinical signs disappear rapidly after treatment but the infections tend to persist in the quarter, particularly if they are chronic.

The poor cure rate with enrofloxacin is hard to explain. It is true that the agent is known to be more potent against gram-negative bacteria; moreover, staphylococcal infections are the most difficult to treat. The cases treated with EN also were more severe as indicated by the high initial NAGase values. Antimicrobial resistance or pharmacokinetic problems are excluded as possible reasons for the poor response. This question remains to be solved in further studies as we gain more experience about this agent in the treatment of animal infections.

In coliform mastitis, the cure rates with EN were inferior to those with supportive therapy only. Infections due to E.coli were thus eliminated spontaneously at a high rate, in agreement with the results of earlier studies. Recently, it has also been shown that administration of some antibiotics effective in vitro does not improve clinical recovery or elimination of bacteria in spontaneous and experimental E.coli mastitis (2,4,5). The fact that several Klebsiella cases, which are known to be therapy resistant, were included in the EN group could explain the lower cure rate in that group. Our results support previous findings suggesting that the value of antimicrobial therapy in coliform mastitis is questionable. The use of expensive antimicrobials such as enrofloxacin cannot be economically justified. A generally accepted definition of "cure" for clinical mastitis trials is still lacking. In view of the high elimination rate of bacteria in mastitis derived from E.coli, we suggest supplementation of the bacteriological criteria with others such as indicators of inflammation, when the efficacies of different treatments are compared in this form of mastitis.

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