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Comparative Efficacy of Local and Systemic Antibiotic Treatment in Lactating Cows with Clinical Mastitis

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ABSTRACT

The intramuscular administration of penethamate hydriodide over 3 consecutive days and the intramammary administration of an ampicillin/cloxacillin combination were compared in lactating cows suffering from infectious clinical mastitis in one quarter, through an open, randomized, controlled multicenter field trial. Clinical examinations were carried out on d 1 (immediately before treatment), 3, 8, 17, and 22. Milk samples were taken from affected quarters for bacteriological analysis on d 1, 17, and 22, and from all quarters for somatic cell count (SCC) determination on d 1, 8, 17, and 22. There was no significant difference in bacteriological and clinical cure rates between the 2 treatment groups. The systemic treatment with penethamate resulted more frequently in a reduction of the milk SCC below the threshold of 250,000 cells/mL. This also occurred in the adjacent quarters not affected by clinical mastitis but with an SCC above 250,000 cells/mL before treatment. These findings suggest that the parenteral treatment with penethamate provides collateral cure on the quarters of the cows affected by subclinical mastitis. The number of quarters per cow affected by clinical or subclinical mastitis should be considered when selecting an antibiotic treatment by the local or systemic route.
(**Key words:** antibiotic treatment, administration route, comparative efficacy, mastitis)

INTRODUCTION

Insufficient contact of the antibiotic with pathogenic bacteria at the site of infection is a major cause of mastitis treatment failure (Sandholm et al., 1990). The route of administration, intramammary or parenteral, of medicinal products to treat mastitis is an important issue (Ziv, 1980a). It determines the biological barriers encountered by the active compound and the routes by which it may make contact with the causal microorganism. Theoretically, the relative interest of each route depends mainly on the location of the bacteria in the udder and the physicochemical characteristics of the therapeutic molecule used. Highly lipophilic compounds able to pass through the epithelia, such as macrolides, fluoroquinolones and penethamate hydriodide, a prodrug of benzylpenicillin, are particularly suitable for the systemic treatment of bacterial infections in the udder (Ziv, 1980c).

However, the practical recommendations for the route of treatment are heterogeneous. In northern Europe, the parenteral route is widely used to treat all types of mastitis, whereas, in other countries, it depends more on how the disease is presented, e.g., the parenteral route is often reserved for the treatment of severe clinical mastitis or chronic infections caused by *Staphylococcus aureus* with bacteria located in the udder parenchyma.

Clinical studies comparing the efficacy of treatments given by either intramammary or parenteral routes are rare. At drying off, for example, the systemic treatment of subclinical infections with norfloxacin resulted in a higher bacteriological cure rate than that achieved by the intramammary administration of cephapirin (Soback et al., 1990). In cases of clinical mastitis during lactation caused by an experimental infection with *Streptococcus uberis*, no significant difference in bacteriological cure was reported between a regimen of systemic treatment with a combination of procaine penicillin and dihydrostreptomycin (3 daily injections of 5 g of penicillin and 6.25 g of dihydrostreptomycin) and an "aggressive" intramammary treatment regimen consisting of 6 administrations of a proprietary presentation containing penethamate, dihydrostreptomycin, and framycetin (Hillerton and Kliem, 2002). In a New Zealand field trial, where *Strep. uberis* was the predominant causative pathogen, systemic treatment with pen-

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ethamate (10 g followed 24 h later by 5 g) resulted in an overall bacteriological cure rate of clinical mastitis of 76.4%; intramammary administration of a combination of 1 g of procaine penicillin and 0.5 g of dihydrostreptomycin at 3 consecutive milkings achieved a cure rate of 84.9% (McDougall, 1998). This difference was explained by a significantly better efficacy of the intramammary treatment against the clinical infections caused by coagulase-negative staphylococci. On the other hand, the systemic treatment with penethamate allowed collateral cure of subclinical infections present in adjacent quarters.

The aim of this field study was to compare the efficacy of 2 antibiotic treatments differing in their active compounds (penethamate or an ampicillin/cloxacillin combination), and their route of administration (parenteral vs. local). Efficacy was assessed using bacteriological cure, clinical recovery, and milk SCC.

MATERIALS AND METHODS

Herds and Cows

The study was carried out in 171 farms in northeast France by 13 veterinarian investigators. Herd size varied from 19 to 148 dairy cows with herd average milk yields between 4300 and 10,600 kg/cow per year. Three hundred twelve lactating cows was recruited for the trial. They belonged to the French Holstein (76%) and the Montbeliarde (24%) breeds. The majority of the recruited cows were housed in loose barns (82%), rested on straw bedding (96%), milked twice a day (100%), and subjected to postmilking teat disinfection (91%). The geometric mean of milk SCC of the cows in the last month before their inclusion in the study was approximately 200,000 cells/mL.

Selection of Animals

To be included in the study, cows had to meet all of the following inclusion criteria: 1) clinical mastitis in only one quarter simultaneously exhibiting udder edema and macroscopically abnormal milk without or with systemic signs; 2) parity <4 lactations; 3) stage of lactation <6 mo; 4) no concurrent disease; 5) no teat lesions; 6) no clinical mastitis or anti-infectious or anti-inflammatory treatments within the last 14 d; and 7) no previous inclusion in the study.

To control the most significant confounding parameter, the study was stratified by parity by including the same number of cows (104) in their first, second, and third lactation.

After entry into the study, cows were withdrawn if there was deviation from the planned treatment regimens or they received additional treatment during the study period due to a concurrent disease arising or due to mastitis arising in another quarter in addition to that originally affected.

Treatment

Animals meeting the inclusion criteria were randomly allocated to a treatment, using a closed envelope method.

The systemic treatment consisted of daily intramuscular injections of penethamate hydriodide (Mamyzin/Stop M, Boehringer Ingelheim GmbH, Ingelheim, Germany) for 3 consecutive days at a dose of 15 mg/kg of BW on d 1, followed by 7.5 mg/kg on d 2 and 3 (1 μg of penethamate hydriodide provides 1 IU of penicillin G). The injections were made in the neck region, alternating the side of administration on each day of treatment.

The intramammary treatment consisted of the infusion (through the teat canal of the clinically affected quarter after disinfection of the teat end) of a proprietary combination containing 200 mg of cloxacillin and 75 mg of ampicillin (Ampiclox, Pfizer, Paris, France) once a day for 3 d, according to its licensed use in France.

Clinical Examinations

Cows included in the study underwent clinical examination at d 1, 3, 8, 17, and 22. The veterinarian investigator assessed general condition, rectal temperature, heart rate, udder edema, and appearance of milk; the farmer recorded decreases in feed intake and milk yield.

Rectal temperature and heart rate were measured directly, whereas other clinical parameters were scored on a numerical scale ranging from normal to slightly, moderately, or severely impaired.

Milk Sampling

Milk samples were aseptically collected (IDF, 1981) from the affected quarters on d 1 (immediately before treatment), 17, and 22 for bacteriological investigations. Samples were frozen at –20°C within 2 h of collection.

Further milk samples were collected from each quarter on d 1, 8, 17, and 22 into flasks containing potassium dichromate at a final concentration of approximately 0.1% for SCC determination.

Laboratory Procedures

The bacteriological investigations were carried out by the Public Veterinary Laboratory at Vesoul (France).

Bacteriological culture and identification were performed according to the National Mastitis Council stan-