The use of the dry cow therapy in the control of bovine mastitis

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ABSTRACT: After introducing the dry or nonlactating period of the cows the authors give a survey about the aims of the dry cow therapy. They show the main requirements of dry cow intramammary preparations and the possible use of systemic therapy. The adverse effects of dry cow therapy and the selective dry cow therapy are discussed. In the end some practical aspects of the dry cow therapy are highlighted.

Keywords: mastitis; dry cow; therapy

Contents

1. Drying off and the role of nonlactating period.

The nonlactating "dry" phase of the dairy cow is a specific period between two active lactating phases when the mammary gland changes dynamically both in structure and function. Benefits derived from a dry period involve more than improvements in the cow's nutritional status for the forthcoming lactation. Several studies (Akers and Nickerson, 1983; Nickerson and Akers, 1983; Sordillo *et al*., 1984a, b) have shown that adequate proliferation and differentiation of the mammary secretory epithelium during nonlactating period were essential for optimal synthetic and secretory functions in the ensuing lactation of cows. Coppock *et al*. (1974) found that dairy cows with 10- to 40-days nonlactating periods produced significantly less milk in the subsequent lactation than cows with a 40- to 60 days nonlactating period. Smith and Todhunter (1982) suggested three distinct stages during the nonlactating period: 1) period of active involution that begins with cessation of milking, 2) period of steady state involution that represents the time when mammary glands are fully involuted, 3) period of colostrum formation and the initiation of lactation. Based upon observed changes in bovine mammary tissue and secretion composition, the process of active involution is most likely completed within 21 days after drying off. This period is associated with an abrupt cessation of milk removal, engorgement of cisternal spaces, ducts, and alveoli with milk constituents, marked changes in mammary secretion composition, and regression of secretory tissue. The duration of steady state involution depends on the length of the nonlactating interval. Smith and Todhunter (1982) indicated that a minimal length of steady state involution may result in a decreased hormonally medicated lactogenic response which could be related to suboptimal production in the following lactation in cows with nonlactating periods of shorter than 40 days. Near parturition, mammary glands again undergo marked transition characterized by rapid differentiation of secretory tissue, intense growth, copious synthesis and secretion of proteins, fat and carbohydrates, and accumulation of colostrum (Oliver and Sordillo, 1988). The greatest increase in mammary DNA content of heifers occurred in the last trimester of pregnancy (Swanson and Poffenbarger, 1979). Morphogenesis of secretory capability in bovine mammary glands also became evident during the last few weeks of gestation (Sordillo and Nickerson, 1988).

A classic study by Neave *et al*. (1950) demonstrated that mammary glands were markedly susceptible to new intramammary infections (IMI) during the early dry period. After cessation of milking several important changes may affect susceptibility of mammary glands to new IMI: 1) the flushing effect of milking on bacteria colonizing the teat canal is terminated, 2) increased intramammary pressure that may cause leakage of milk and facilitate bacterial penetration of the streak canal, 3) the defence mechanisms of the mammary gland are at low level during early involution: low numbers of polymorphonuclear neutrophils, macrophages, and lymphocytes, and low concentration of lactoferrin and immunoglobulins (Oliver and Sordillo, 1989). New infections in the dry period are important for several reasons. During the 1st month of lactation, a quarter newly infected in the dry period will sustain a production loss equal to that of a quarter that retains an established infection throughout the dry period (Smith *et al*., 1968). If the infection persists throughout lactation, proportional production loss would be expected to continue. In addition, at least in herds with a low prevalence of (chronic) infection, most clinical mastitis cases in early lactation are the result of new dry period infections (Eberhart and Buckalew, 1977).

2. The aims of the Dry cow therapy

As it is general in the bovine medicine, the dry cow therapy is an intramammary treatment of udder with antibiotics administered at the end of lactation. Antibiotic treatment at drying off aims at both eliminating the existing IMI and preventing new infections (Neave *et al*., 1966). During the dry period, elimination of the infection with antibiotics is more likely than during lactation as the drug is not milked out, and a higher and more uniform concentration of antibiotics is maintained in the udder. In addition, there are no economic losses due to discarding of antibiotic containing milk (Sandholm and Pyörälä, 1995).

Experimental evidence suggests that dry cow therapy is effective in controlling IMI due to *Streptococcus agalactiae* and somewhat effective against *Staphylococcus aureus* (Natzke, 1971, 1981; Natzke *et al*., 1972; Eberhart and Buckalew, 1972; Sinkevich *et al*., 1974; Philpot, 1979; Ziv *et al*., 1981; Dodd, 1983; Bramley and Dodd, 1984). Exposure of mammary gland to these contagious pathogens during the dry period is most likely reduced in the absence of regular milking, so that therapy at drying off tends to control these pathogens effectively (Oliver and Sordillo, 1988). However, some studies showed that contagious pathogens, especially *Staph. aureus*, are likely to establish new infections after drying off in those herds where they are prevalent (Neave *et al*., 1950; Smith *et al*., 1966, 1967; Eberhart and Buckalew, 1972; Postle and Natzke, 1974; Ziv *et al*., 1981; Pankey *et al*., 1982;). Neave and Oliver (1962) reported that *Staph. aureus* could often be isolated from the teat skin after the last milking of lactation, but not from uninfected quarters 28 days later. This suggests that exposure to contagious pathogens is concentrated at the beginning of the dry period but becomes less intense as the dry period progresses. However, elimination of *Staph. aureus* by therapy is less successful than that of streptococci (Smith *et al*., 1967; Natzke, 1971; Ziv *et al*., 1981; Sandholm and Pyörälä, 1995).

Coliform bacteria and streptococci other than *Strep. agalactiae*, which includes primarily *Strep. dysgalactiae* and *Strep. uberis* (but sometimes also *Enterococcus faecalis* and other species of fecal streptococci) are ubiquitous in the cow's environment. Consequently, mammary glands are exposed continuously to environmental mastitis pathogens throughout the dry period, especially in herds in total confinement housing. Schukken *et al*. (1993) found that in low somatic cell count herd the administration of antibiotics at drying off resulted in lower clinical mastitis incidence in the dry period (10 cases for untreated vs. 1 case for treated quarters). The quarters that were infused with antibiotics had a reduction of minor mastitis pathogens at calving. Williamson *et al*. (1995) examined the prophylactic effect of a dry-cow antibiotic against *Strep. uberis*. The therapy reduced significantly the incidence of both dry period and post-calving infections. Hassan *et al*. (1999) noted a marked reduction in the number of infected quarters and clinical mastitis cases caused by *Strep. uberis* and *Strep. dysgalactiae* after dry cow treatment in 2 weeks after drying off. These studies suggest that dry cow therapy can play an important role in the prevention of new infections with these environmental organisms during the dry period.

3. Dry cow preparations

Because the udder is most susceptible to new infections during the first weeks (mostly caused by environmental pathogens e.g. *Strep. uberis*, and maybe contagious pathogens) and last weeks (mostly caused by environmental pathogens including coliform bacteria too) of the dry period (Smith *et al*., 1985; Oliver and Sordillo, 1988), optimally, the therapy should be extended over the whole dry period. The involuted udder is naturally resistant to gram-negative microorganisms because of the high concentration of lactoferrin, and the low citrate/lactoferrin molar ratio in secretions inhibits their establishment (Todhunter *et al*., 1982; Dutt, 1985), so their role in the dry period infections is minor in general. Dry cow antibiotic preparations, therefore, require good activity against *Staph. aureus* including β-lactamase producing strains, *Strep. uberis*, *Strep. dysgalactiae*, *Strep. agalactiae* and, if prophylaxis against summer mastitis is desired, they should also be effective against *Arcanobacterium pyogenes* (Ziv, 1994). Intramammary injectors containing narrow spectrum penicillins (penicillin, cloxacillin, oxacillin, and nafcillin), cephalosporins and spiramycin are therefore widely used.

The dry cow preparations are formulated (vehicles, solvents, pH) to cause minimal tissue irritation, to avoid damaging the secretory tissue and to prevent fibrosis. It is advantageous if the antibiotic is bound to the tissues for an extended period and does not immediately diffuse from the udder into blood. The antimicrobial effect must be long-lived, as the purpose is to form a deposit in the milk ducts of the udder from which the antibiotic is slowly released (Sandholm and Pyörälä, 1995).

The duration of the effect of the antibiotic can be regulated by pharmaceutical manipulation of the intramammary drugs, e.g. precipitating the antibiotic, dissolving it in a slowly absorbing oil or micro-encapsulation.

One significant limitation of antibiotic formulations used for dry cow therapy is the ineffectiveness in preventing new IMI during the periparturient period (Eberhart and Buckalew, 1977; Smith *et al*., 1985; Oliver, 1987). Boyd *et al*. (1987) and Oliver and Maki (1987) demonstrated that dry cow antibiotics persisted only for 14 to 28 days after infusion.

In contrast to widely used long-acting intramammaries, Osteras *et al*. (1991, 1999a) reported the use of short-acting, lactational preparations at drying off. They compared a long-acting and a short-acting injection containing penicillin and neomycin or streptomycin respectively. An injection of short-acting preparation was administered every second day before drying off had a significantly better effect in preventing new infection with *Staph. aureus* or *Strep. dysgalactiae* in untreated healthy quarters in cows with fewer than 3 infected quarters. This difference in preventive effect was greater in cows with one infected quarter during previous lactation (Osteras *et al*., 1994). This short-acting therapy resulted in better approach for eliminating major pathogens (*Staph. aureus* in particular) (Osteras *et al*., 1999a). However, their finding that the use of lactating formula increases the risk of resistance development decreases the value of these otherwise promising results according to the elimination of major pathogens (Osteras *et al*., 1999b).

4. Systemic dry cow therapy

Systemic dry cow therapy may have advantages: better distribution of a suitable drug in the udder tissue which may lead to better cure of IMI (Ziv, 1980) and avoidance of new infection which is a possible risk at administration of intramammaries (Boddie and Nickerson, 1986). In the last 10 years some reports were published dealing with systemic dry cow therapy. Bolourchi *et al*. (1996) found that systemic enrofloxacin or tylosin (a macrolide related to spiramycin) at drying off approached but did not exceed the efficacy of the local treatment with nafcillin, penicillin and dihydrostreptomycin. Norfloxacin-nicotinate was reported as an effective drug for systemic treatment of *Staph. aureus* IMI. In the same experiment oxytetracycline showed much lower activity (Soback *et al*., 1990). However, the promising results of this pilot study could not be confirmed in later experiments. Erskine *et al*. (1994) published similar findings concerning the oxytetracycline. In a study with 30 000 IU/kg spiramycin administered intramuscularly on 4 consecutive days at drying off, the bacteriological cure rate of cows with chronic subclinical *Staph. aureus* mastitis remained below 50% (Jánosi *et al*., 2001). Thus the suggested superiority of systemic administration at drying off, compared with conventional intramammary treatment, has not been proven in practice.

Despite these therapeutic failures, in general the systemic administration of antibiotics at drying off (penicillin; Johansson *et al*., 1995) or some weeks before parturition (tylosin; Zecconi *et al*., 1999) seems to be an effective, supplementary treatment for intramammary therapy of *Staph. aureus* IMI, which may be advisable for practice.

5. Possible adverse effects of dry cow therapy

It has been stated that the dry cow therapy may have the following adverse effects (Sandholm and Pyörälä, 1995):

1. Discarded meat and milk, if the cow is slaughtered within the withdrawal time or the cow calves prematurely.
2. A random antibiotic therapy kills the normal bacterial flora of the teat end and teat canal allowing pathogenic and antibiotic-resistant bacteria to colonize the area.
3. Large-scale use of antibacterials increases selection pressure to spreading of antibiotic-resistant bacterial strains.
4. Irritation of teat ends.
5. Unnecessary treatment of healthy quarters is expensive.

6. Selective dry cow therapy

To minimize the adverse effects of antibacterial treatment it has been suggested that only infected quarters or cows are treated at drying off. Poutrel and Rainard (1981) suggested that selective treatment of all cows with at least 1 California Mastitis Test (CMT)-positive quarter at 8 weeks before drying off is the simplest and most economic treatment for herds with a low mastitis infection rate.

According to the antimicrobial drug policy in Nordic countries (Forshell *et al*., 1996), the effects of selective dry cow therapy were studied. Although the selective dry cow therapy was reported as beneficial compared to no therapy (Osteras and Sandvik, 1996), the authors (Osteras *et al*., 1991) found that selective dry cow therapy on quarter basis determined from the results of single samples taken 1 to 6 weeks before drying off had given "inadequate" therapeutic response (i.e. new infection in non-treated quarters at drying off) in more than 50% of the cows. Its cause could be that the bacteriological findings from milk can vary from day to day because of intermittent shedding (Mattila, 1985), therefore at least two samples (e.g. 1 month and closely before drying off) could guarantee the adequate specificity. In another study (Osteras *et al*., 1999a) evaluating the real efficacy of methods used to identify the infected udders, the geometric mean of the cow composite somatic cell counts (SCC) of the last 5 to 6 months of lactation was the best predictor. However, the threshold value between quarters considered healthy or infected was 200 000/ml, e.g. much lower than generally supposed in practice. This finding is in good agreement with the earlier observations of Meek *et al*. (1980).

In addition to the difficulties in diagnosis, a weakness of selective therapy is that it ignores infections occurring during and after drying off. Selective quarter treatment (treat infected quarters only) results in a higher new infection rate in the dry period (Browning *et al*., 1990, 1994)

Selective cow treatment (treat all quarters of any cow infected in one or more quarters) is a preferred concession between selective quarter treatment and blanket therapy (treat all quarters of all cows) (Browning *et al*., 1994). This is in agreement with the opinion of Sandholm and Pyörälä (1995): decision as to whether to treat or not has to be made on the basis of the cow, not the quarter. If the cow has had acute or subclinical mastitis caused by contagious pathogens during lactation it is worth treating all the quarters of that cow with dry cow preparations. However, Natzke *et al*. (1975) calculated that in a 100-cow herd the production gain from prevention of only nine quarters (2.2% of quarters) would return the cost of antibiotic treatment of all cows. In addition, other studies have shown that in low prevalence herds in which selective therapy was used, infection rate was higher at calving than at drying off (Eberhart and Buckalew, 1977; Schultze, 1983). From these consideration it seems clear that selective therapy, as compared with complete one, cannot be justified economically in most herds (Eberhart, 1986).

7. Dry cow therapy in practice

Cows with clinical mastitis are treated according to normal practice before drying off. If mastitis caused by staphylococci early in lactation is a problem in the herd, dry cow therapy can be considered. Dry cow therapy is also recommended for the control of contagious mastitis caused by streptococci. Dry cow therapy is recommended for all cows that have had contagious mastitis during lactation (*Staph. aureus*, *Strep. agalactiae*, and *Strep. dysgalactiae*). Cows which have had a high milk cell count are also treated. Systematic dry cow therapy is recommended for herds with a high infection rate. Use of germicidal teat dipping during the dry period is also advised for these herds to reduce the exposure of pathogens on the teat end (Sandholm and Pyörälä, 1995).

On the other hand, it is important to mention that cows that have had at least one case of clinical mastitis and high geometric mean of SCC in the last 5 to 6 months before drying off should be considered for culling, because they retain a high risk of subsequently having a major pathogen (mainly *Staph. aureus* and *Strep. agalactiae*) (Osteras *et al*., 1999a).

Dry cow therapy is also suggested in herds with low somatic cell counts and low prevalence of contagious mastitis pathogens, to minimize the new dry period infections by environmental pathogens which can result in a high incidence of clinical mastitis in the early lactation (Eberhart, 1986; Oliver and Sordillo, 1988; Schukken *et al*., 1993).

Because continuing exposure to new bacteria during the dry period comes only from the cow's environment, it is reasonable to believe that minimizing exposure to bacterial loads in the environment will reduce a new infection rate (Neave and Oliver, 1962; Smith *et al*., 1985). Because of the susceptibility to infection in the prepartum period, special attention should be paid to the environment of calving cows (Rendos *et al*., 1975).

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