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Immunity and Mastitis: Is it possible to vaccinate?

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1. Introduction

Mastitis is an inflammation of the secretory tissues or milk ducts in the mammary gland in response to a bacterial infection. It affects the quantity and quality of milk production.

The causal agents of bovine mastitis are microorganisms that live in the udder of the cow and its enviroment. They can be divided into three groups according to their epidemiology: **1) contagious:** with bacteria such as *Staphylococcus aureus*, *Streptococcus agalactiae*, **2) those that are environmentally related:** such as *Streptococcus agalactiae* and Gram-negative bacteria such as *E. coli* and **3) opportunistic:** coagulase-negative *Staphylococci.*

Mastitis control is based on various measures that can include: 1) Proper and hygienic milking routine; 2) Proper use and maintenance of milking equipment; 3) Appropriate dry period therapy, 4) Treatment of clinical cases during lactation; 5) Treatment of skin problems of the udder and teats; 6) Culling of cows with chronic mastitis; 7) Examination of cows that will enter the farm as replacements, 8) Recording of data and 9) Maintaining a clean environment.

2. Is it possible to vaccinate?

Along with all the above-mentioned classic measures of control, we have added **another measure: vaccination.** Taking into account the difficulties we have when facing agents such as *S. aureus* or *E. coli* due to their poor response to antibiotic treatments, prevention through proper vaccination plus the above-mentioned measures would be of great importance.

In the case of mastitis caused by *Staphylococcus aureus*, dairy cows are the reservoirs of the bacteria. Results for antibiotic therapy are poor when the bacteria are found in the deepest udder tissue (Ma *et al*., 2004). Authors such as Blowey *et al* (1995), conducting a literature review of treatments with Cloxacillin, showed cure rates of mastitis caused by *S. aureus* of 24% of clinical cases and 40% for sub-clinical cases. The highest rate of therapy was during drying (60%), and that is why the treatment of choice for this bacterium is during drying. The low cure rate could be attributed to the ability of bacteria to survive the treatment when it is found intracellularly in epithelial cells or macrophages (Hensen *et al*., 2000; Herbet *et al* 2000).

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With regard to *E. coli*, according to the study by Sandholm *et al* (1995), antibiotic therapy would have little effect on improving symptoms caused by the bacterium. That is because these symptoms are, more than anything, caused by the bacterium's endotoxin. Vaccination aims to improve and enhance the immune system against a specific antigen.

In the case of vaccines against mastitis, what is sought is an adequate arrival of neutrophils to the place where the pathogenic agent is found and with the appropriate amount of immunoglobulins, opsonization and the subsequent phagocytosis occur. In addition, antibodies generated by vaccination, may also have an important role in neutralizing toxins, interfering with the adhesion mechanisms of bacteria and inducing the bacterial lysis. A review of the literature has shown benefits in the use of protective vaccines against *S. aureus* or *E. coli*. The effect of vaccination is seen in the next table:

Protective vaccines benefits against *S. aureus* or *E. coli*.
1) Reduction in the severity and duration of symptoms of coliform mastitis
2) Decrease in the rate of infections
3) Decrease in antibiotic use and its possible occurrence as residues in milk
4) Decrease in somatic cell counts and increases in daily production of milk

Nordaugh *et al*., (1994) used an inactivated vaccine of *S. aureus,* and showed its positive effect on the appearance of clinical cases in the vaccinated group of cows as opposed to 6% of cases in the non-vaccinated group. With regard to cases of subclinical mastitis caused by *S. aureus*, it was diagnosed in 8% of the vaccinated group and 14% of the unvaccinated group of cows.

In Israel, in a field trial, (Leitner *et al*., 2003) a vaccine composed of fragments of *S. aureus* obtained by sonication was used. It showed statistically significant beneficial effects with respect to milk production and somatic cell count in the group of vaccinated cows. The important thing to note in a vaccine against *S. aureus*, is to vaccinate as early in the life of the cow as possible. This immunization should be performed in pre-partum heifers, thereby avoiding potential infection that would compromise the productive life of the animal.

With regard to coliform mastitis, after performing a challenge with a virulent strain of *E. coli* in a group of cattle vaccinated with the *E. coli J5* bacterin and a non-vaccinated group, Hogan *et al*. (1995) showed that duration of intramammary infection, as well the intensity of the symptoms were lower in the vaccinated group. Deluyker *et al*. (2005) found in field tests that, although vaccination against *E. coli* does not help in reducing the number of cases in the vaccinated group compared with the non-vaccinated, there were significant differences in the number of cases of systemic toxic mastitis in favour of the vaccinated group.

In the case of *S. aureus,* various types of vaccines have been developed in the past with mixed results. These vaccines could be divided into the two major groups, 1) bacterin and 2) vaccines that include a component of the bacterium considered to be of antigenic importance.

The first group, with bacterins, are vaccines prepared with all of the components of the bacterial cell and they may be dead or alive; so, mastitis tests were developed with this type of vaccine by Pankey (1985) or Leitner *et al*. (2003).

The second group, are those vaccines that include elements of antigenic importance, these vaccines are developed from virulence factors such as:

a) Protein A, a component of the cell wall of the bacterium that binds to Immunoglobulins. (Pankey *et al*., 1985, Carter and Kerr, 2003)

b) Pseudocapsule, extracellular polysaccharide with antiphagocytic properties (Watson *et al*. 1992; Nordhaug *et al*., 1994)

c) Capsular antigens, such as expolysaccharide: also called Slime Associated Antigenic Complex (Yosida *et al*. 1987, Calzolari *et al*. 1997; Giraudo *et al*., 1997)

d) Alpha and Beta toxins (Herbelin *et al*., 1997)

e) Fibronectin binding protein, surface molecule that acts as a factor for bacterial adherence (Shkreta *et al*., 2004).

f) Clumping factor A, surface molecule that acts as a factor for bacterial adherence (Brouillette *et al*. 2002).

3. Vaccination trial against mastitis conducted in Spain

In a multicentre trial conducted on 6 dairy farms in Catalonia (Spain), 386 primiparous and multiparous dairy cows were divided in two groups. The first group consisted of 188 cows, and as control group was not vaccinated, while the second group of 198 cows was vaccinated. The vaccination schedule for this group consisted of a first dose of vaccine 45 days before the expected date of birth; the second dose was administered at ten days prior to delivery, and the third dose of vaccine was given at about 50 days postpartum.

The vaccine used contained antigens of the CP8 *S. aureus* strain, which is a high producer of the Slime Associated Antigenic Complex plus the *E. coli J5* strain. (Laboratorios Hipra, Amer, Girona, Spain).
Data collected were analyzed by logistic regression with an analysis of variance.

3.1. Somatic cell count, cure rate and additional pharmacological treatments during the assay

The somatic cell count was measured during the field trial. It is the most accepted parameter for monitoring udder health and milk quality (Laevens, 1997; Pyorala, 2003; Schukken *et al.*, 2003). The vaccinated group had a **cell count** of 324.1 x 103 compared to 581.4 x 103 in the control group. When compared in logarithmic form, **these differences were found to be statistically significant (p = 0.0182).**
The **cure rate** for vaccinated **multiparous cows** was 53.33% compared to 20.45% for the unvaccinated animals. This **difference was significant (p <0.05).** In primiparous animals, although the cure rate was favourable in the vaccinated group, the difference was not significant.
In the same trial, drug treatments were measured in both groups of cows, vaccinated and control. Twenty-four animals were treated for mastitis in the vaccinated group, 14 primiparous and 10 multiparous cows. Multiparous cows in this vaccinated group received 21 treatments, giving an average of 1.5, whereas primiparous animals received 13 treatments, and averaged 0.7. Moreover, in the control group, 40 animals received additional drug treatment, 28 of them were multiparous and 12 primiparous. The average for the non-vaccinated control group was 2.1 and 2.8 for multiparous and primiparous animals respectively. The statistical analysis of these results was that for the multiparous group this difference in necessary additional pharmacological treatments was significantly different (p = 0.003). As the number of treatments per cow was lower in the vaccinated group, the treatment time required is also less. These points are extremely interesting because they ultimately determine not only the **reduced use of drugs, but mean that less milk is discarded due to the use of antibiotics.**
The experiment conducted in Catalonia as well as the literature provides us with data showing positive effects of vaccines against mastitis. Whilst it is an element to be considered and recommended in the fight against mastitis, it should not be forgotten that it must be combined with traditional measures to control mastitis on a farm operation.

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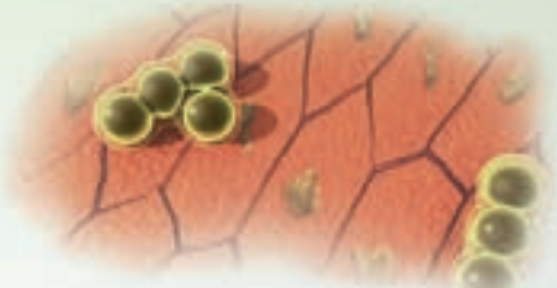

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