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Novel Therapeutic Approaches for the Management and Treatment of Bovine Mastitis

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Abstract

Bovine mastitis, or intramammary inflammation caused by infectious pathogens, is still regarded as a severe illness that has a negative impact on animal welfare as well as the dairy industry's bottom line through decreased output and higher culling rates. Mastitis affects dairy cattle on a rather regular basis. Based on clinical outcomes, bovine mastitis can be categorised as either clinical or subclinical. Due to milk rejection, deteriorated milk quality, early cow culling, medicine expenditures, veterinary charges, and higher labour costs for the farmer, both forms result in severe economic losses. Additionally, subclinical mastitis, which affects 20 to 50% of cows in a given herd, is the most common type of mastitis in contemporary dairy herds. Although it is very difficult to estimate the expense of subclinical mastitis, most experts concur that it can be up to 40 times more prevalent than clinical mastitis. Clinical and subclinical illness types are used in routine diagnosis. This emphasizes how important it is to identify and detect etiological agents at the farm level early and quickly, for which a number of diagnostic approaches have been developed. Mastitis in dairy cattle may develop as a result of a variety of predisposing factors, including physiological, genetic, pathological, or environmental causes. At the moment, antibiotics are utilized to treat mastitis. However, due to the indiscriminate use of antibiotics that has resulted in the emergence of numerous drug-resistant bacteria, the therapeutic success rate is low. These facts demonstrate the need for entirely innovative approaches to mastitis treatment and management that would assist protect the welfare of dairy animals.

Introduction

The term “Mastitis”, is commonly used for the major role in the first line of defense against invading inflammatory reactions in the mammary gland, although mastitis could technically be used to describe any udder injury that causes inflammation, this inflammatory response is caused by a microbial infection in the teat canal and mammary tissue. The bacteria that invade the mammary glands and teat canal grow and release toxins that harm the milk-secreting tissue and cause physical trauma, reducing the yield and negatively impacting the quality of milk and milk products. Based on epidemiology, the illness

is divided into two types: contagious and environmental mastitis (Garcia 2004). The former is caused by infectious bacteria like *Staphylococcus aureus (S. aureus), Streptococcus agalactiae (S. agalactiae), and Mycoplasma spp.*, which are transferred from an infected cow to a healthy cow most commonly during milking through the use of hands, towels, and/or the milking machine acting as bacterial reservoirs. The causal bacteria in environmental mastitis, on the other hand, come from the cow's surroundings, including bedding material, soil, dung, excrement, and stagnant water. They spread predominantly outside of the milking parlor (Garcia 2004).

Perspectives for new therapeutic approaches

Bacteriophage therapy for Mastitis

A class of viruses known as bacteriophages can infect and kill bacteria (Haq *et al.* 2012; Tiwari *et al*. 2014). Bacteriophage therapy, which uses pathogen-specific bacteriophages to treat a bacterial infection, is one of the alternate treatments for mastitis. They have the capacity to proliferate rapidly and the innate ability to target and eradicate certain bacteria, making them a promising candidate against harmful germs (Carson *et al*. 2010). According to certain research, phage therapy may be effective in treating mastitis caused by *E. coli* and *S. aureus*. However, more study is needed to examine the therapeutic potential of bacteriophages to treat bacterial infections linked to clinical and subclinical mastitis.

Bacteriophage endolysins

Endolysins, a different potential medication made from bacteriophages, are efficient against Gram-positive infections. They are the proteins that, during the phage lytic cycle, enable the phage to escape from the bacterial cell by destroying the peptidoglycan layer of the bacterial cell wall (Breyne *et al*. 2017).

Antimicrobial peptides

Antimicrobial peptides (AMPs), a new class of antibiotics, are important components of the innate immune system that kill invasive pathogens (Moravej *et al*.2018). They are effective against a variety of Gram-positive and Gram-negative bacteria, including some types that are drug-resistant. AMPs produce synergism when used along with conventional antibiotics (Chung and Khanum 2017). The "defensin" family of AMPs includes the beta-defensins. They serve as the first line of defense against IMIs that affect dairy cattle and are regarded as the most well-known genetically encoded antibiotics.

Nanotechnology

There have been numerous attempts to create a mastitis vaccination, but few have reported successful outcomes. It is evident that mastitis is caused by a variety of infections and their unique pathophysiology cannot be prevented by a single vaccine. The incidence, severity, and duration of infections in both lactating cows and heifers can be decreased by coliform vaccinations. *S. aureus*

vaccinations should be used in herds where this type of organism is a significant problem because they can decrease the frequency of new intra-mammary infection and raise the rate of spontaneous cure.

Cytokines

Another area that is currently being developed as a delivery method for antibacterial agents and other medications is nanoparticle technology (Gomes and Henriques 2016). Researchers are now able to create nano-sized particles (less than 100 nm) and use them for a variety of purposes, including medicine delivery. When opposed to conventional micron-sized particles, nanoparticles have larger surfaces and, as a result, interact with biological targets like bacteria more frequently. Since the phagocytes may take the nanoparticles up, they could be used as delivery methods in the treatment of cow mastitis. Additionally, according to the research, antibiotics can be added to the majority of nanoparticle delivery systems. According to reports, chitosan nanoparticles (Ch-NPs) have a significant therapeutic potential for treating cow mastitis (Orellano *et al*. 2019). Silver and copper nanoparticles, which are readily available metal nanoparticles, reduced the in vitro survival of *S. aureus* and *E. coli* without having a harmful effect on the mammary gland (Kalinska *et al*. 2019).

Stem cell therapy

During a bacterial infection, cytokine production and leukocyte populations are crucial to host defense and pathophysiological processes. Interleukin (IL)-1, -2, -6, and -8, as well as tumour necrosis factor-alpha, have all been identified as key players in the acute-phase reaction. They can increase the bactericidal activity of phagocytes and have chemotactic action that is responsible for leukocyte activation and recruitment. Numerous experimental investigations show that cytokine infusion, either with or without antibiotics, boosted the cure rate in mastitis caused by S. aureus. Finally, cytokines therapy appears to be a viable strategy, but additional research is needed to prove its potential as a treatment.

Native secretory factors

The health of the udder is significantly influenced by the stem cells of the cow mammary epithelial cells. These stem/progenitor cells can be used to correct structural/cytological abnormalities in the bovine udder caused by mastitis (Sharma and Jeong 2013). Additionally, mesenchymal stem cells have the capacity to control inflammatory responses, but the specific mechanism underlying this ability is still unknown.

Mastitis Vaccines

Natural whey protein from the mammary glands called lactoferrin (Lf) serves a variety of biological purposes. Limited anti-bacterial and anti-inflammatory actions stand out among other functions and can help treat mastitis. Lf's antibacterial properties result from its ability to bind iron, which is necessary for bacterial development in addition to being cationic in nature. When combined with various

antibiotics, such as penicillin G, its antibacterial properties can be strengthened (Petitclerc *et al*. 2007).

Conclusions

Mastitis continues to be a significant concern for the global dairy businesses, yet there is still no proven cure for it. The most popular approach to treating bovine mastitis at the moment is the use of antibiotics. However, this type of approach has several drawbacks because of the poor cure rate, rising rates of resistance, and antibiotic residues found in milk. For the diagnosis of mastitis, there are a number of reliable and affordable traditional diagnostic procedures, however, they lack sensitivity and specificity. Since they cannot deliver quick results, they cannot be widely used in the existing dairy production sector. Therefore, some researchers looked into alternatives to antibiotics in an effort to discover a successful method for treating bovine mastitis.

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