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Bovine Postpartum Metritis and its Therapeutics: A Review

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Abstract

Metritis is the inflammation of the uterus causing severe economic loss to the dairy farmers due to failure of conception at the appropriate time. Variety of microorganisms are responsible for causing metritis, among which *Arcanobacterium pyogenes,* coliforms and the Gram – negative anaerobes, *Fusobacterium* and *Bacteroides* species are frequently involved. Infections generally gain entry during calving and frequently associated with difficult birth (dystocia) and Retention of Fetal Membranes (RFM). Under normal condition the microorganisms are eliminated from the uterus during uterine involution by the normal Uterine Defense Mechanism (UDM). However, when the UDM is compromised due to various factors the clinical symptoms of metritis sets in and sometimes leading to the death of the animal. There is various therapeutics available to counteract metritis around the world with their own merits and demerits. This review presents an overall account of the postpartum metritis in dairy cows and its therapeutic measures.

Keywords: Cow, Metritis, Postpartum, Review, Therapeutics

1. Introduction

Metritis, endometritis, pyometra, RFM and some non specific infections of the uterus are the most important factors causing infertility in the dairy cattle. Many a times these postpartum reproductive disorders have common etiology and predispose to each other and share a common therapeutics regime. Most important causes of subfertility in diary cows are reported to be metritis and endometritis[1]. The bacterial infection of uterus may occur, during or immediately after parturition, coitus or while carrying out artificial insemination. The severity and persistence of infection in the uterus depends on the degree of contamination, uterine defence mechanism and presence of substrates for the growth of the microbes such as devitalized tissues. Inflammation of the uterus slows down the process of involution in the uterus and delays the onset of activities of the ovaries leading to economic loss due to systemic illness, loss of milk and meat production and marked drop in fertility.

2. Postpartum Metritis

Metritis is the inflammation of the uterus consisting of both the endometrial and the muscular layer[2,3]. Most of the cases occur during the first 10–14 days of delivery and sometimes it is referred as toxic puerperal metritis[2,3]. The uterus is filled with odourous, red – brown content mixed with necrotic and putrefied tissues[4]. Postpartum metritis usually follows an abnormal first or second stage of labor, especially where there has been severe dystocia. Metritis is also associated with uterine inertia, twin births, RFM, prolonged manipulations and injuries to the vulva and/or birth canal[5]. It has been found that up to 40 percent animals develop metritis within the first fourteen days of calving and in 10 to 15 per cent of these animals infection continues for at least another three weeks leading to a chronic uterine disease (endometritis)[4]. However, clinically the condition of metritis must be differentiated from endometritis. Endometritis refers to inflammation of the mucus membrane of the uterus, with mucoid,

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muco-purulent to purulent discharge from the vulva that appears three weeks after parturition or later[6].

3. Prevalence

The prevalence of metritis has been found to vary in different studies depending on the definition of the disease used. By applying the proposed standardized definition, metritis affects 10 to 20 per cent of dairy cows in Canada and US[7,8]. RFM is an important risk factor for development of metritis. Cows with 30 to 50 per cent of RFM will develop metritis[9]. In a study conducted on 9 high – yielding dairy herds located in Belgium grade 1 and grade 2 clinical metritis recorded was 20 and 15 per cent respectively[10]. Another study from India reported a higher prevalence rate of metritis as 28.90% in first calvers and 38.93% in all calvers in Karan fries cows[11].

4. Impact

Metritis is probably the most significant postpartum economic disease in dairy cattle, causing high losses because of longer days open and involuntary culling rates. It causes severe economic losses due to costs for treatment, milk withdrawal, reduced reproductive performance and premature culling. However, on milk production the impact of metritis is not clear as some studies reported negative impact and others not. The parity and the stage of lactation of the cow have an influence when there is a negative impact on milk production. The extent of this impact in pluriparous cows ranged between 2 and 13 kg of milk per day during a period which can vary from 2 to 20 weeks[7,12]. Overall, it may represent a production loss of 100 to 2,000 kg per lactation. The estimated milk loss (weighted average) attributable to metritis was $83/case of metritis[7].

5. Causative Organisms

The uterus becomes a good environment for growth of the bacteria immediately after parturition as it became warm; fluid filled and contains necrotic debris that facilitates the multiplication of the pathogens. Different bacteria isolated and cultured from postpartum uterus include: *Escherichia coli, Arcanobacterium pyogenes*, *Fusobacterium necrophorum, Bacteroides* species, *Staphylococcus* species, *Mannheimia haemolytica*, *Pasteurella* species, *Haemophilus somnus*, *Pseudomonas aeruginosa, Clostridium* species and *Streptococcus* species. Among these, *Arcanobacterium pyogenes,* coliforms and the Gram – negative anaerobes, *Fusobacterium* and *Bacteroides* species are commonly encountered[13]. Most of the other bacteria tend to be transient invaders that result in no or only minor inflammatory lesions that do not appear to affect subsequent fertility[3]. A combine infection of *Fusobacterium* and *Bacteroides* species together with *Arcanobacter pyogenes* are frequently encountered. They are probably the major causes of persistent metritis which are associated with impaired fertility. The coliforms are generally from gastrointestinal in origin and are very frequently isolated, but their real significance is not clear. They are likely incidental contaminants in the postpartum genital tract. Coliforms comprise 36% of bacterial isolates from normal postpartum cows and tend to be encountered more frequently in the early postpartum period. In cows exhibiting the signs of metritis, (e.g., depression and a fetid uterine discharge), coliforms were isolated in 29% of cases[3]. In some isolated cases, clostridia are present that rapidly manifest the disease which is serious and often fatal[5].

6. Symptoms

Animals suffering from metritis show both local and general symptoms[5]. Toxaemia, septicemia and pyrexia develop very commonly. The temperature of affected cows may be elevated to 40 – 41°C, but is more often subnormal. There is a rapid pulse rate (around 100/minute) and there may be elevated respiration. Animals are anorectic and dehydrated; they often have a toxemia – induced diarrhea and exhibit signs of shock. It is common for the infection to extend through the uterine wall into the peritoneum, causing a localized or general peritonitis. The uterus contains a large amount of toxic, fetid, reddish, serous exudates, containing pieces of degenerating fetal membranes. Exudate is frequently discharged from the vagina by straining efforts of the animal. Vaginal and uterine exploration of an affected case causes acute discomfort and is accompanied and followed by the most severe and persistent expulsive efforts. The cotyledons are swollen and the fetal membranes often remain firmly attached. The vaginal mucosa is inflamed and thickened, and the cervix is partially open. If untreated, the cow rapidly becomes recumbent, dehydrated and comatose. Death may ensure within few hours[14].

7. Pathophysiology

After calving, it is reported that around 90 % of cows have infected uterus with different kinds of bacteria[13,15]. Not all of the bacteria are harmful but when harmful bacteria are present, the uterus is most likely to get infected[16,17]. Bovine uterus after calving is contaminated with variety of organisms but it is not always associated with clinical symptoms. Metritis generally initiates with the establishment of the pathogenic organism to the uterine mucosa and their penetration through the epithelium and thereby releasing the toxins[15,17]. The immunity of the cow and the species and load of the bacteria involved in the infection is critical determinant for the establishment of the infection[17,18]. The bacterial load in the uterus disrupts the normal uterine defence mechanism leading to life-threatening infection[4]. The uterus after calving has a damaged epithelial surface with fluids and debris from the tissues that facilitates the growth of the bactreia[19]. Therefore, the establishment of postpartum uterine infection is dependent on load and virulent of the micro-organisms and also the condition and the natural uterine defense mechanism[20]. Normally, the basic contaminants are gradually eliminated from the uterus during first six weeks of calving[5]. This is achieved by rapid uterine involution and cervix, expelling out of uterine content, natural immune system that includes antibodies[5] and phagocytic cells[21]. Cows with difficult calving usually lost the ability to control the uterine infections naturally. Injuries during difficult calving and its manipulation[18] generally increase the risk to metritis. The normal phagocytosis by the uterine leukocytes is reported to be severely affected in conditions like difficult calving, retained fetal membranes and metritis[13]. When the postpartum uterus is compromised any of contaminating organisms gains the advantage and can lead to toxic puerperal metritis[2].

8. Therapeutics

Postpartum metritis is commonly treated with antibiotics or hormones, alone or in combination. Antibiotics may be administered systemically or are infused intrauterine. In more severe cases other symptomatic therapies like anti-inflammatory agents and intravenous fluid therapy are also advocated.

8.1 Intrauterine Infusions

For the treatment of metritis, different intrauterine therapies like antiseptics, antibiotics and immunomodulators are infused into the uterus to eliminate the bacterial infection, stimulate the normal uterine defense mechanism, or to increase the blood flow to the uterus. The most routinely used intrauterine therapy is the infusion of iodine solution in water or saline. However, now there are some studies which have reported harmful effects of iodine infusion on future reproductive performance of the cow. Single infusion of 50–100 mL of 2% polyvinylpyrrolidoneiodine (povidone-iodine) solution, as a routine therapy 30 days postpartum, has been reported as detrimental to fertility in cows with endometritis compared to non-treated animal[22]. Some advocated the infusion of 1 L of a 50 per cent dextrose solution into postpartum cows. The dextrose is responsible for causing tonicity in the uterine musculature, but no critical studies have been published. The increase in tonicity is likely due to the hyper tonicity of the dextrose solution, which might be accomplished with any hypertonic solution. It is not clear whether the infusion of an agent to increase uterine tone is useful for uterine involution or helpful for the treatment of metritis.

The most suitable treatment should eliminate harmful bacterial flora from the uterus, should not damage the uterus or disrupts its normal defense mechanisms. As a rule, intrauterine antibiotic infusion should be avoided as a treatment for postpartum metritis[3]. Many a times, infusion of intrauterine drugs has an uncertainty of its distribution throughout all layers of the uterus. Moreover, many drugs infused into the uterus may be absorbed systemically to some extent, therefore there are always concerns regarding appropriate meat and milk withdrawal periods. Many common drugs are not registered for intrauterine administration and are made ineffective in the uterus post delivery[3]. For example, aminoglycosides require an aerobic environment to be effective, not the anaerobic environment of the postpartum uterus. Presence of necrotic debris and purulent materials has a negative impact on the efficacy of sulfonamides and aminoglycosides. The performance of penicillin group of antibiotics and the cephalosporin are reported to decline when infused in the first 30-days postpartum due to presence of organisms producing inactivating (ß-lactamase) enzymes. Streptomycin and the tetracycline's are irritant to the bovine uterine mucosa and most of their formulations should not be used for intrauterine infusion. The intrauterine infusion of antibacterial has been found to have a detrimental effect on leukocyte function[3,13] and they increase the risks of contamination or further damage to the uterine tissue.

8.2 Systemic Antibiotics

Systemic antibiotic therapies are reported to have many advantages. The drug withdrawal times are generally well-established, better distribution inside the uterus, and they appears to have least harmful effect to the uterine environment. Penicillin is one of the most preferred antibiotics for postpartum metritis because it penetrates into all the layers of the uterus, is less expensive, and most of the bacteria penetrating the endometrium leading septicemia are responsive to penicillin[3,23]. Alternatively, ceftiofur sodium at the rate of 1 mg/kg IM or SQ may be used as systemic antibiotic therapy for 3 to 5 days with no withdrawal requirement. Ceftiofur sodium has been reported to concentrate in uterus at levels exceeding the mean inhibitory concentrations for *Arcanobacterium pyogenes*, *Fusobacterium necrophorum* and *Escherichia coli.* During a study involving cows affected with postpartum metritis, ceftiofur was administered at a dosage of 2.2 mg/kg daily for 5 days and was found as effective as procaine penicillin G or procaine penicillin G plus intrauterine infusion of oxytetracycline for the treatment[24]. Oxytetracycline probably is not a better option for systemic therapy as there is difficulty in reaching the MIC required for *A. pyogenes* in the lumen of the uterus[25].

8.3 Hormonal Therapy

Treatment with prostaglandins or its analogues are very effective in evacuating the uterus by uterine contraction when Corpus Luteum (CL) is present in one of the ovaries. But it is found that cows in early postpartum stage do not have a functional CL, so their uses have a limited application. Prostaglandins can be useful when the cows are around 30–45 days in milk. It will help to expel the unwanted uterine contents and bring the cows to first postpartum estrus. Another hormone that can be used is the oxytocin. Basically, it plays an important role in uterine contraction during calving. It causes uterine contraction for several days even after calving but whether, it improves the postpartum reproductive performances is questionable.

8.4 Ozone Therapy

Ozone disrupts the cell membrane of the micro-organisms and reported to diffuse through the protein coat of the nucleic acid of the viruses to kill them. In veterinary medicine ozone therapy is used as foam and pearls to treat uterine infections[26,27]. When ozone foam (Ringer spray G) is applied into the cows suffering from metritis and endometritis it has found to cure the conditions and can be an effective and alternative therapy with an overall better improvement on fertility in the cows[28].

8.5 Miscellaneous Drugs

Calcium is an essential trace-element that results smooth muscle contraction of the uterus. Immediately after calving most of the high yielding cows becomes deficiency in calcium leading to atonicity of the uterine musculature which ultimately causes retention of fetal membranes and metritis. Therefore, prescribing oral calcium during this period may be beneficial to prevent metritis. Sometimes after calving, cows loss their appetite and there may chances of developing ketosis in such animals which causes displaced abomasums or metritis. In such conditions supplementation with propylene glycol or propionate is beneficial.

9. Summary

Postpartum metritis is a global problem having higher prevalence worldwide mostly in high yielding dairy cows. Most of the currently used therapeutics includes antibiotics and hormones. Antibiotics have their own drawbacks like withdrawal period, residues in milk and meat, development of drug resistance and disruption of normal UDM etc. On the other, hand hormonal therapies are costly and not easily available. Therefore, the approach should be prevention of metritis from occurring in postpartum cows. This can be achieved by proper nutrition during pregnancy, hygienic conditions during calving, and using antioxidants in last month of gestation to prevent RFM and immediate veterinary care, if difficult birth is noticed.

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