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Postpartum Uterine Infections in Cows: Diagnosis and Treatment - An Overview

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Abstract

Postpartum uterine infections result from uterine contamination with pathogens during parturition. Most of the pathogens are environmental contaminants that are gradually eliminated during the first 6 weeks postpartum. Vaginoscopy is considered to be more accurate than rectal palpation for diagnostic purpose. Transrectal ultrasonography is helpful for the diagnosis of clinical endometrits and pyometra. Subclinical endometritis (SCE) can be detected after three weeks postpartum with the help of endometrial cytology. Administration of $PGF_2\alpha$ or intrauterine infusion of cephapirin is the treatment of choice for chronic endometritis but in case of SCE, results are inconsistent. Immunomodulators, ozone pearls or foam have also been used for treatment of postpartum uterine infections. Economic losses associated with uterine infections in dairy cattle are due to cost of diagnosis and treatment of the infection, associated milk reduction and reduced fertility.

Key Words: Uterine infection, Diagnosis, Treatment, Cows

Introduction

Most cows clear microorganisms contaminating the uterus by 6 weeks postpartum and those which fail to do so develop uterine infection and then fertility parameters are affected (Singh, 2000; Azawi, 2008). Postpartum uterine infections are treated with antibiotics, hormones or their combinations (Palmer, 2008). Limited research has been done to evaluate the use of immunomodulators as a treatment for cows having endometritis (Singh, 2000). Success of these therapeutic agents is aimed at the elimination of pathogens from the uterus, elimination of the adverse effects of inflammation products on fertility and number of times the drug is used and exposure of the entire endometrium to the drug (Sharma *et al.,* 2009).

Diagnosis of Uterine Infections

Clinical records of periparturient problems helps in identifying the animals at risk of uterine disease but does not provide specific diagnosis (McDougall, 2001). Systemic signs such as dehydration, anorexia and body temperature above 39.5°C in any cow occurring within 1-2 weeks of calving indicate puerperal metritis. Presence of a fetid, reddish brown, watery discharge along with systemic signs can be considered diagnostic for metritis (Palmer, 2015). Vaginal mucus can be used for

evaluating the presence and growth density of pathogenic bacteria contaminating postpartum uterine lumen (Peter *et al.,* 2011). Ultrasonography can be used to diagnose clinical endometritis on the basis of fluid in the lumen of the uterus and thickness of the endometrium (Barlund *et al.,* 2008). Other methods used for the diagnosis of postpartum uterine infection are endometrial cytology and biopsy sampling (Chapwanya *et al.,* 2010). Various methods used for diagnosing uterine infections after parturition are:

Uterine Palpation: Uterine palpation per-rectum is one of the most frequently used method to diagnose endometritis (Sheldon *et al.,* 2006). Diagnosis of clinical endometritis by per rectal palpation is difficult because uterine size and palpable quality of content may vary among individuals and depends on the stage of the postpartum period. Also, it lacks standardization so more prone to error (Foldi *et al.,* 2006).

Vaginoscopy: Visual inspection of the vaginal canal is done using a sterile metal or transparent barrel with a light source to inspect the presence of pus or abnormal discharge (Runciman *et al.,* 2008). Clear mucus is normal, whereas purulent and mucopurulent and foul smelling discharge is indicative of uterine infection (Dubuc *et al.,* 2010). Vaginoscopy lacks sensitivity when compared to endometrial cytobrush cytology for the diagnosis of both clinical and subclinical endometritis (Barlund *et al.,* 2008).

Ultrasonography: Ultrasonography is used extensively in diagnosis for endometritis but is dependent on the presence, volume and nature of uterine luminal fluid (Barlund *et al.,* 2008). Mateus *et al.* (2002) examined postpartum cows by transrectal ultrasonography (TRUSG) and found that volume of intrauterine fluid was significantly associated with impaired uterine involution and was positively correlated with bacterial growth.

TRUSG helps in diagnosis of subclinical endometritis (SCE) which include accumulation of fluid and increased endometrial thickness (Purohit *et al.,* 2013). Endometrial thickness with measurement of greater than 8 mm is less useful than endometrial cytobrush cytology using a polymorphonuclear cells (PMNs) threshold of greater than 8% to diagnose SCE between 28 and 41 days postpartum (Barlund *et al.,* 2008).

Endometrial Cytology: Endometrial cytology has been used as a diagnostic tool in horses but Kasimanickam *et al.* (2004) used a modified cytobrush to collect endometrial cytology samples in cows. This technique evaluates the relationship between polymorphonuclear cells (PMNs) and conception. Greater proportions of PMNs are indicative of uterine infection in early stages of the postpartum period. Cows with a high percentage of PMNs are slower to conceive than those with low PMNs (Barlund *et al*., 2008). Dubuc *et al.* (2010) reported that greater than 6% PMNs or a mucopurulent vaginal discharge is the most appropriate indicator of endometritis in cows at 35 days postpartum and greater than 4% PMNs is the most appropriate in cows at 56 days postpartum. Kasimanickam *et al.* (2004) defined SCE as the absence of visible purulent material in the vagina and a cytobrush cytology derived sample containing greater than 8% PMNs at 21-33 days postpartum or greater than 10% PMNs at 34-47 days postpartum.

Uterine Biopsy: Uterine biopsy and uterine bacteriological culture are the gold standard diagnostic methods for postpartum endometritis (Sheldon *et al*., 2006). Uterine endometrial biopsy requires expensive equipment and also the clinical utility of technique is limited due to the delay in acquiring results. Technique is time consuming, the procedure may negatively impact future fertility and it is difficult to perform (Sheldon *et al*., 2004).

Treatment of Uterine Infections

Postpartum uterine infections may be difficult to treat. Lochia that can provide an ideal breeding environment for bacteria should be eliminated from the uterus (Azawi, 2008). Endometritis can increase calving to conception interval, decrease the pregnancy rate and increase the culling rate.

So the purpose of treating endometritis is to improve reproductive efficiency (Sheldon and Noakes, 1998). Drugs used must be able to effectively target and eradicate the pathogens. Also, the entire endometrium must be targeted by the drug in order to ensure that the treatment is adequate (Azawi, 2008). Treatment efficiency is dependent on the severity of inflammation in the uterus, the time in which the treatment is given during the postpartum period and presence of corpus luteum (LeBlanc, 2008).

The current treatment regime for endometritis is mainly based upon two different protocols; antibiotics and administration of prostaglandin and its analogues. Other treatment regimes such as estrogen therapy are not as effective as prostaglandin injection or IU benzathinecephapirin therapy and may impair future reproductive performance in cows (Palmer, 2008).

A) Antibiotics

Antibiotics are administered either through intrauterine (I/U) or parentral routes for the treatment of uterine infections.

A1) Intrauterine therapy

Agents used for intrauterine infusion include Tetracycline (Shams-Esfanabadi *et al.*, 2004), diluted Lugol's iodine (Callahan and Horstman, 1987), Gentamicin, Sulphonamides, Iodine (Gilbert and Schwark, 1992), Ciprofloxacin (Singh *et al.*, 2004; Kumar *et al.,* 2014), Moxifloxacin (Purohit *et al.*, 2013), Ceftriaxone (Mahto *et al.*, 2012) and Cephapirin (Kumar *et al.*, 2013). Intrauterine infusion of Oxytetracycline can lead to high concentration in the caruncles and the endometrium but concentration is not sufficient in the myometrium and ovaries after 24 hours (Sheldon and Noakes, 1998).

Infusion of iodine solution in water or saline is most commonly used as an intrauterine therapy for treatment of metritis. Lugol's iodine helps in destroying phagocytic activity of the white blood cells within the uterus for several days (Azawi, 2008). Harmful effects of iodine infu-sion on future reproductive performance of the cow are also there (Deori and Phookan, 2015).

Cephapirin is a first generation cephalosporin effective against most gram-positive and gram-negative bacteria in the uterus. Cows having SCE that received cephapirin between 20 and 33 days postpartum had 89% conception rate compared to non-treated cows (Kasimanickam *et al.*, 2005). Cephapirin administration in cows between 27 and 33 days postpartum results in a 60% higher conception rate and 29% reduction in time to conceive compared to control (LeBlanc, 2008).

Presence of purulent material, organisms which produce β-lactamase enzymes has a negative impact on the efficacy of sulfonamides, aminoglycosides, penicillin group of antibiotics and cephalosporins upto 30 days postpartum (Paisely *et al.*, 1986). Also, drugs infused into the uterus may be absorbed systemically to some extent but there is always a concern regarding appropriate meat and milk with-drawal periods (Smith and Risco, 2002).

A2) Systemic antibiotic administration

Systemic antibiotic therapy has many advantages. The drug withdrawal times are generally well-established, better distribution inside the uterus and have least harmful effect to the uterine environment as compared to intrauterine infusion (Singh, 1998; Sharma *et al.*, 2009; Kumar *et al.,* 2014). Penicillin penetrates into all the layers of the uterus and is less expensive. So, it is one of the most preferred antibiotic for treatment of postpartum metritis (Smith and Risco, 2002). Alternatively, ceftiofur sodium at the rate of 1 mg/kg/bwt intramuscularly can be used as systemic antibiotic therapy for 3 to 5 days with no withdrawal requirement. Ceftiofur administration at a dosage of 2.2 mg/kg/bwt daily for 5 days is equally effective as procaine penicillin G or procaine penicillin G plus intrauterine infusion of oxytetracycline for the treatment (Smith *et al.*, 1998).

B) Prostaglandin

Major hormones involved in the process of uterine involution are prostaglandins, oxytocin and estradiol. These hormones act conjointly to promote uterine contractions, clearance of secundus and modulate local immune responses (Bondurant, 1999).

Prostaglandin therapy in the immediate postpartum period can result in increased uterine tone and expulsion of uterine fluid and bacteria rather than changing the hormonal influence through luteolysis. Two doses of $PGF_2\alpha$ intramuscularly 8 hours apart on day 8 postpartum in cows with acute puerperal metritis increased first-service conception rates by 17% in primiparous cows (Melendez *et al.*, 2004).

Time required for uterine involution was shorter in groups receiving synthetic $PGF_2\alpha$ (immediately after parturition) as well as $PGF_2\alpha$ plus GnRH (10-13 days after parturition) than the groups receiving only GnRH or no treatment (Sharawy *et al.*, 2015).

Kasimanickam *et al.* (2005) reported a 70% improvement in conception rate in cows with SCE which were treated with cloprostenol between 20 and 33 days postpartum compared to untreated cows. $PGF_2\alpha$ administration in cows with clinical endometritis (without a palpable CL) between 20 and 26 days postpartum decreased the pregnancy rate, whereas administration between 27 and 33 days postpartum resulted in an 18% improvement in pregnancy rate, irrespective of luteal status (LeBlanc *et al.*, 2002).

C) Other hormones

Estradiol stimulates myometrial contractions, phagocytosis and mucus production. Estradiol @ 5-10 mg per animal has been used for treatment of postpartum endometritis but the interval from treatment to conception was longer with estradiol treatment as compared to $PGF_2\alpha$ or intrauterine antibiotics (Sheldon and Noakes, 1998). Oxytocin is the other hormone which results in uterine contraction during calving and several days even after calving but its effect on the postpartum reproductive performances is questionable (Deori and Phookan, 2015).

D) Ozone therapy

Ozone disrupts the cell membrane of the micro-organisms and diffuse through the protein coat of the nucleic acid of the viruses to kill them (Duricic *et al.*, 2012[a]). When ozone foam (Ringer spray G) is applied into the cows suffering from metritis and endometritis, it cures the condition and can be an effective and alternative therapy which improves fertility in the cows (Duricic *et al.*, 2014). Intrauterine ozone treatment alone or combined with parentral antibiotics is more efficacious treatment for retained placenta in cows when compared to hormonal and parentral antibiotic treatment mo dalities (Duricic *et al.*, 2012[b]).

E) Immunomodulators and antioxidants

Stimulation of the uterine defense mechanism with the use of immunomodulators is useful to combat infection. Single intrauterine infusion of *E. coli* lipopolysaccharides (LPS) (100μg in 60 ml PBS), oyster glycogen (500 mg in 60 ml PBS) and autologous plasma (Sarma *et al.*, 2010) have been used. These infusions act as potent chemotractant with resultant increased influx of PMNs within the uterine lumen and significant decrease in uterine infection. Their routine use is difficult due to high costs and poor availability (Purohit *et al.*, 2015).

Use of antioxidants to treat uterine infections is very rare. Decreased clearance of free oxygen radicals in the uterine lumen can be resolved by the intrauterine infusion of 50 ml super oxidized water (Kaveh *et al.*, 2014), 50-100 ml of 3% hydrogen peroxide (Dolezel *et al.*, 2010), formosulfathiazole (Mari *et al.*, 2012), Vitamin A, E and selenium (Sengupta and Nandi, 2013). However, results after antioxidant administration are inconsistent (Purohit *et al.*, 2015).

Conclusion

Postpartum uterine infections have negative effect on subsequent reproductive performance of cows. Cytobrush technique is the most modern and accurate method for diagnosis. Treatment with hormones is expensive but antibiotics provide an inexpensive way to treat postpartum uterine infections. Timely diagnosis and treatment of uterine infections is necessary to prevent economic losses due to reduction in milk yield, increased interval to first estrus and subsequent infertility.

Conflict of Interest: All authors declare no conflict of interest.

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