Diagnosis and therapy of endometritis in dairy cows-A review

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Abstract
This scientific paper contains a synthesis of the literature on the main diagnostic and treatment procedures of endometritis in dairy cows, used up to now. The diagnosis of clinical endometritis is confirmed by the presence of purulent uterine discharge or cervical diameter >7.5 cm after 21 days of lactation, or mucopurulent discharge after 26 days of lactation without generalized symptoms. Miller et al. concluded that vaginoscopic examination is a more accurate method for detecting uterine infections than palpation per rectum. Uterine biopsy and cytology are the gold standard evaluation methods in the health of the endometrium, especially during the postpartum period. When clinical or subclinical endometritis is diagnosed, the clinician’s first choice is antibiotics, because of their low cost. Of all alternative therapies for the treatment of endometritis, the most potent and safe approach seems to be the use of prostaglandins (PG). The intrauterine infusion of immunomodulators and ozone therapy has also been used to treat postpartum endometritis. Signaling over the last decade of a large phenomenon of bacterial resistance to the medication has forced to the discovery of some effective ethnoveterinary products.

Keywords: dairy cow, endometritis, diagnosis, treatment

Introduction
Alteration of the reproductive function manifests itself through infertility and functional sterility, a pathological entity that in cattle, is a concern of specialists at the national and global level.

Postpartum uterine infections are associated with significant economic losses, due to unproductive expenses with feeding, high costs of diagnosis and treatment, associated with decreased milk production, losses by not realizing the number of calves and installing sterility. In cattle, bacterial contamination occurs in almost any uterus after birth (Griffin și colab., 1974, Huszenicză și colab., 1991, Sheldon și colab., 2002).

This bacterial load usually decreases in the first 3 weeks after calving but can last up to 14 weeks in some cows.

Endometritis defines infection located only at the endometrium and underlying glandular tissues. It is suggested that approximately 10-15% of cows develop endometritis after calving.

Recent studies classify endometritis into clinical and subclinical forms.

Clinical endometritis is characterized by the presence of a mucopurulent uterine secretion (approximately 50% pus, 50% mucus), or purulent (>50% pus) detected in the vagina 21 days after calving.

Subclinical endometritis is defined by the presence of >18% neutrophils in cytological samples collected on days 21-33 postpartum, or >10% neutrophils in samples from days 34-47 postpartum (Sheldon M.I., et al., 2004).

Direct-acting monitoring technology for tracking cattle behavior greatly facilitates farmer work. By analyzing the records, the specialist visualizes the behavior of animals step by step and direct the breeding activity in the sense of mounting (I.A.) or conducting a clinical examination.

Clinical examination
Clinical examination of cows begins with the inspection of the vulva, perineum, and tail to observe the character of vaginal secretions. The presence of purulent leaks and a cervical diameter >7.5 cm at 20 days postpartum, or mucopurulent discharge at 26 days are signs of clinical
endometritis (Le Blanc S., 2002). Transrectal examination by identifying the cervix, palpation of the uterus, ovaries and in pathological cases of salpinx is the most common diagnostic method in the case of clinical endometritis, even if it offers few indication (fluctuating uterine horn, thickened uterine wall, purulent secretions at the inferior vulvar commissure)(Purohit et al., 2010).

**Vaginoscopy**

Miller et al. (1980) concluded that vaginoscopic examination is a much more accurate method for diagnosing clinical endometritis than transrectal palpation. The vaginoscopic examination to assess the origin of the secretion can be done with a metal speculum with three Polanski type valves or one of plastic, previously disinfected. A simple, cheap and fast method is the manual examination of the content with the hand protected by the glove and its evaluation. It is a non-invasive method.

The presence or absence of uterine discharge at the time of vaginoscopy may be influenced by the severity of the infection, the uterine contractions, the rate of secretion removal, by the personnel performing the examination. Leaks in the closed cervix may not be detected, this does not automatically indicate the absence of endometritis (Kasimanickam R. et al.,2002).

An alternative approach for sampling vaginal contents is with the help of the Metricheck device, which consists of a 50 cm long stainless steel rod provided at one end with a 4 cm rubber hemisphere and at the other end with a metal handle.

The technique consists of introducing the Metricheck device through cleaned vulvar lips, advanced to the cranial extent of the vaginal fornix and then retracted back at an angle of 45 degrees. If no uterine discharges are observed in the hemisphere of the device, the device is re-introduced until purulent material may be visualized to the convex surface.

The character of the vaginal mucus can be scored as well as odor(Fig. 1). The smell reflects the presence of certain bacteria in the uterus. Clear mucus denotes a small number of bacteria in the uterus, and purulent discharge with score 3 for a fetid odor was associated with the presence of infection in the uterus.

![Endometritis scoring scheme](image)

Figure 1. Endometritis scoring scheme: score 0= clear or translucent mucus; score 1= mucus containing flecks of white or off-white pus; score 2=discharge containing ≤ 50% white or off-white mucopurulent material; score 3= discharge containing ≥ 50% purulent material, white or yellow, occasionally sanguineous (I.M. Sheldon et. Al./ Theriogenology 65 (2006) 1516-1530).
**Uterine pH**

The pH of the uterine lumen is different in the stages of the oestrus cycle, with the lowest value occurring 2 days prior to ovulation, and at oestrus, the value is 7.30 (Mather E.C., 1975).

In normal breeding cows, the pH of the vaginal mucus is 7.2 ± 1.10 compared to 8.23 to 8.80 in cows with endometritis, metritis (Boitor I. Et al., 1980).

An impediment in the determination of uterine pH is the lack of the development of special sensing probes that can be introduced directly into the bovine uterus.

**Uterine microbiology**

A wide variety of microbes invade the uterus during the pre- and the postpartum period and when their number is high they can produce endometritis/metritis, and measurable effects of endometritis are manifests through impacts on reproductive performance.

Bacterial infection may cause the inflammation of the endometrium at many cows, associated with denudation of the uterine mucosa and alteration of the secretion with early embryonic death.

Following examination of the uterine secretions, the most common pathogens involved in uterine infections are Streptococcus spp., Staphylococcus spp. and Bacillus spp. isolated from healthy cows during the first 10 days of lactation, while Arcanobacterium pyogenes, Fusobacterium necrophorum, Escherichia coli, Prevotella melaninogenicus have been isolated from cows with clinical signs of endometritis (Bonnet et al. 1991, Bondurant 1999, Huszeniczta et al. 1999, Gilbert et al. 2007).

Endometrial infection with E.coli precedes infection with A. pyogenes and possibly bovine herpesvirus 4 and this is associated with clinical disease severity and impact on fertility (Dohmen et al. 2000, Williams et al. 2007, Donofrio et al. 2008). Bovine herpesvirus (BoHV-4) is the only virus commonly associated with uterine infections that develop in the uterus after gestation, being widespread in the EU (Castrucci et al. 1986, Ackermann 2006, Monge et al. 2006).

In 1990, Pateria A.K. and Rawal CVS describe the "white side test" which uses the cervical mucus of suspected cows which is heated with sodium hydroxide solution up to a boiling point. The reaction is considered positive when the color turns yellow. This test has the greatest advantage of establishing the degrees of infection in just a few minutes. The bases of this test are the correlation between the number of leucocytes present in the mucus and the intensity of the yellow color (Pateria A.K. et al., 1990).

The safest way to get cells from the uterus is through the use of cytobrush or uterine lavage (Barlund C.S., 2007).

Pascottini et al. (2015) modified this technique, under the name of cytotape, by using a paper tape attached to the cytobrush.

**Uterine lavage**

A sterile pipette was introduced into the uterus and 20 ml of sterile saline was infused and transrectal massage of the uterus was performed for 5-10 s before aspiration of a least 2 ml of the fluid(Barlund C.S., 2007).

The collected liquid was transferred to a sterile plastic tube and centrifuged for 15 minutes. After the centrifugation, the supernatant is removed, and from the sediment, slides were executed in a similar manner to those from the cytobrush (Barlund C.S., 2007).

The cytological evaluation was performed by counting at least 100 cells (endometrial cells, PMNs, squamous cells) to provide a quantitative assessment of endometrial inflammation.
In 2013, Madoz et al. have established that the general limit for the percentage of PMN is 5% between days 21 and 62 postpartum. In the case of nulliparous, the limit of 1% was established, the limit identified at the time of artificial sowing.

Chapwanya et al. (2010) describe the biopsy of the uterus as a cornerstone in the evaluation of the health status of the endometrium, especially in the post-operative period.

The uterine biopsy can be performed using the Haupner device, a tool most commonly used in cattle, which is guided in the cervix by transrectal manipulation (Chapwanya A. et al., 2009). Endometrial biopsy facilitates the development of an individual profile of the animal in terms of cellular and molecular changes in the puerperal period.

**Ultrasonographic evaluation of the volume of uterine fluid**

Ultrasonographic evaluation can be a quick and useful technique for identifying fluid in the uterus as an indicator of an inflammatory process.

Detection of ≥ 2 mm of fluid in the uterine lumen after ultrasonographic visualization leads to sample collection using the cytobrush technique and microscopic assessments to determine the percentage of polymorphonuclear cells (Jaureguiberry M. et al., 2017).

For establishing the diagnosis of subclinical endometritis, the reference point is the 5% value of polymorphonuclear cells (Madoz et al., 2013).

**Therapeutic approaches**

Dhaliwal GS et al. (2002) state that "the uterus appears to have a considerable capacity for spontaneous recovery in a large proportion of animals, probably does not require any therapy, especially as some therapies are ineffective and may even cause more harm than good."

Once the diagnosis is established, the clinician’s first choice at the start of treatment is antibiotics, due to the low cost.

The first route of administration of antibiotics in endometritis should be intrauterine, as it leads to increased drug concentration in the uterine cavity and endometrium, and absorption into the systemic circulation is relatively small (Masera J. et al., 1980).

Lugol solution infusion is the most widely used intrauterine therapy for the treatment of endometritis. This helps to stop the phagocytic activity of the white cells in the uterus for several days (Azawi, 2008).

The administration of systemic antibiotics is chosen in the treatment of clinical endometritis in chronic forms.

The most traditional antibiotic chosen is Oxytetracycline, but due to the local irritating nature and the high doses (2-4g / day, for 3-5 days) opt for better alternatives. The efficacy of two other traditional antibiotics, Amoxicillin, and Aminoglycosides is questionable.

The efficacy of penicillin administered intrauterine is also questionable (Thurmond MC et al., 1998).

The use of fluoroquinolones has demonstrated clinical efficacy (Purohit GN et al., 2007). Recently, new generations of Cephalosporins (third and fourth) have been shown to be effective against most pathogens, and the first generation of Cephalosporins (Cefapirine) is recommended for intrauterine administration (LeBlanc S.J. et al., 2002).

In the case of chronic endometritis, after much antimicrobial therapy, it is recommended to combine an antibiotic with an imidazole derivative (Metronidazole, Tinidazole) (Sirohi N.S., et al., 2000).

Of all the alternative therapies for the treatment of endometritis, the most powerful and safe approach seems to be the use of prostaglandins (PG).
The treatment with PGF2α in the immediate postpartum period may increase uterine tone and expel uterine fluid and bacteria, rather than luteolysis hormone change (Melendez et al., 2004).

Estradiol stimulates myometrial contractions, phagocytosis and mucus production. Estradiol at a dose of 5 mg per animal is used for the treatment of postpartum endometritis, but the rate of conception is longer compared to administration of PGF2α or intrauterine antibiotics (Sheldon and Noakes, 1998).

The use of oxytocin has favorable results during calving and several days after, but not for enhancing postpartum reproductive performance (Deori and Phookan, 2015).

Intrauterine infusion of immunomodulators, such as E. coli lipopolysaccharides (endotoxin), infusion with serum, plasma or hyperimmune serum or leukotriene B4 has been widely reported.

E. coli lipopolysaccharides have a curative effect for all types of endometritis, except for the chronic type with cystic dilatation of the endometrial glands. The use of this type of treatment most often has a positive prognosis, the endometritis being usually cured and the cows can be inseminated to the next estrus.

Antioxidants, such as vitamins C and E, are known to be modulators of oxidative stress and to reduce endometrial damage at both the biochemical and histological levels (Guneys M. et al., 2007).

Ozone destroys the cell membrane of microorganisms and diffuses through the protein layer of the nucleic acid of viruses to kill them (Duricic et al., 2012).

The application of foam-shaped ozone to the uterus with endometritis or metritis combined with parenterally administered antibiotics is more effective than the parenteral administration of antibiotics and hormones.

Regulation of the European Council (Nos. 834/2007 and 889/2008) and the Swiss on organic farming imposes a preference for complementary veterinary medicine, such as the use of herbal products for treating animal diseases.

In the treatment of infertility and diseases of the female genital tract, the most commonly used plants are from the Lamiaceae family, commonly known as aromatic plants (basil, mint, rosemary, sage, thyme, oregano, lavender), Malvaceae (hibiscus, cotton, cocoa), Rubiaceae (Coffea Arabica), Amaryllidaceae (Allium sativum), Thuja occidentalis. The mode of administration of the remedies in the case of diseases of the genital tract can be external (washes, friction) or internally (oral, intravaginal, intrauterine) (Schmid Kathrin et al., 2012).

Homeopathic remedies consist of either commercial preparations (granules, tinctures, oils, ointments, aqueous extracts, linings, powders, macerations) or decoctions, infusions as well as fresh or dried herbs.

Bibliografie


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