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Review Paper

AN UPDATE ON UTERINE INFECTIONS IN DAIRY CATTLE

Marc Drillich

Address of author: Clinic for Reproduction, Faculty of Veterinary Medicine, Free University of Berlin, Germany

E-mail: drillich@bestandsbetruung.de

Summary: Inflammation of the uterus, described as acute metritis or chronic endometritis is one of the most common disorders in the postpartum period of dairy cattle. Acute metritis is characterised by reddish-brown and fetid discharge, a body temperature ≥ 39.5°C, often associated with a depressed general attitude, reduced feed intake and decreased milk yield. Bacteria cultured from the uterus are mainly *Escherichia coli*, *Arcanobacterium pyogenes*, and obligate anaerobic species *Fusobacterium necrophorum* and *Prevotella spp*. The recommended therapy of acute metritis is based on a systemic antibiotic treatment without any intrauterine manipulations. Chronic endometritis is defined by the occurrence of purulent or mucopurulent vulvar discharge more than three weeks postpartum. In contrast to acute metritis, chronic endometritis is not associated with an elevated body temperature. For the diagnosis, vaginal inspection via speculum has been demonstrated to be more accurate than rectal palpation. Reproductive performance of affected cows is impaired in the course of lactation. For chronic endometritis, the administration of $PGF_{2\alpha}$ or the intrauterine infusion of Cephapirin is recommended as treatment of choice. In the last years, some new aspects on subclinical endometritis, detected more than three weeks postpartum have been elucidated. In the absence of clinical signs of endometritis, the percentages of polymorphonuclear leukocytes in cytological smears taken from the endometrium or small amounts of fluids in the uterine cavity detected by ultrasound indicate a mild inflammation of the uterus. There is consensus that subclinical endometritis has a significant negative impact on reproductive performance. The treatment of subclinical endometritis, however, is still under discussion. Prostaglandin $F_{2\alpha}$ as well as the intrauterine infusion of Cephapirin or proteolytic enzymes have been tested, but results are not consistent.

Keywords: cattle diseases; endometritis – diagnosis; drug therapy; cattle

Introduction

Inflammation of the uterus, described as acute metritis or chronic endometritis is one of the most common disorders in the postpartum period of dairy cattle. Acute metritis is characterised by reddish-brown, fetid discharge and pyrexia. Chronic endometritis is defined by the occurrence of purulent or mucopurulent vulvar discharge more than three weeks postpartum. The therapy of acute metritis is based on a systemic antibiotic treatment. For chronic endometritis, the administration of $PGF_{2\alpha}$ or intrauterine antibiotics is recommended. In the last years, some new aspects on subclinical endometritis, detected by cytological examinations and the use of ultrasound have been elucidated. There is consensus that subclinical endometritis has a significant negative impact on reproductive performance.

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Acute metritis

Acute metritis is also referred to as postpartum metritis, toxic puerperal metritis or septic metritis and occurs within the first 10 days after parturition. It is characterised by fetid, watery, and reddish-brown to purulent vulvar discharge and an elevated body temperature ≥39.5°C (1). Referees on which body temperature can be regarded as fever range from 39.2°C (2) to 39.7°C (3). The palpation of the uterus per rectum reveals an enlarged and flaccid uterus. Acute metritis is often associated with a depressed general attitude, reduced feed intake and decreased milk yield.

Risk factors for acute metritis were categorised by Sheldon and Dobson (4) into uterine damages (stillbirth, dystocia, twins, cesarean section, retained placenta, delayed uterine involution), metabolic conditions (milk fever, ketosis, left displaced abomasum) and the balance between pathogenicity and immunity (disruption of neutrophil function, type of bacterial flora, proges-

terone and glucocorticoide administration, early formation of a corpus luteum, level of hygiene).

Infection of the postpartum uterus and uterine defense mechanisms

The infection and to some extent the inflammation of the uterine wall during and after parturition must be accepted as a physiological process (5). Pathogenic species for metritis isolated from the uterine cavity are *Escherichia (E.) coli*, *Arcanobacterium (A.) pyogenes*, and obligate anaerobic species *Fusobacterium (F.) necrophorum* and *Prevotella spp.* (5, 6). Beside the quantity and quality of bacteria in the uterus, the efficiency of uterine defense mechanisms determines the severity of metritis. The uterine defense mechanisms consist of anatomical and physical barriers, i.e. the vulvar and cervical closure as well as the cell-mediated and humoral immune systems. The initial cellular response to an infection of the uterine wall is an influx of polymorphonuclear leukocytes (PMN) and macrophages. Immunoglobulins and opsonins are released from the endometrium (7, 8).

Antibiotic treatment of acute metritis

An ideal treatment of metritis should eliminate bacteria from the uterine cavity and the subendometrial layers without inhibiting uterine defense mechanisms. It should provide optimal reproductive performance in the current lactation, and not cause economic losses by milk withdrawl. In the last years, strategies for the therapy of acute metritis were focused on a systemic antibiotic treatment. The efficacy of a systemic administration of penicillin, oxytetracycline, or ceftiofur in cows with acute metritis or retained fetal membranes, often associated with acute metritis, has been demonstrated in several studies with regard to clinical cure rates and reproductive performance (2, 3, 9, 10, 11). Ceftiofur concentrations exceeded the minimum inhibitory concentration (MIC_{90}) for *A. pyogenes*, *E. coli*, *F. necrophorum* in blood and endometrial tissue within two hours after administration (12).

The efficacy of a local antibiotic treatment (solutions or uterine pills) is a controversial issue in the literature (2, 5, 9, 11). A recent multi-located field trial on cows with retained fetal membranes has shown that the additional use of antibiotic pills had no benefits compared with the sole systemic antibiotic use of ceftiofur (11). Negative interactions between antibiotic drugs and the uterine environment, the inhibition of the uterine defense mechanism by irritating drugs, solutions and antibiotics, and a questionable therapeutically efficacy of antibiotics within the inflamed uterine wall and the oviducts are some reasons to reject a local treatment (5). The application of higher dosages of antibiotic drugs to reach a MIC_{90} in the uterine wall increases the risk for antibiotic residues in milk and is not in accordance to legal drug regulations and the guidelines for a prudent use of antibiotic drugs.

Additional treatment

Clinical trials on the application of non-steriodal antiinflammatory drugs in the early postpartum period did not show beneficial effects on clinical cure rates (13). The use of estradiol to stimulate uterine motility and immunity is not approved for uterine disorders in the European Union. In addition, recent studies demonstrated no positive effects on the prevention or treatment of acute metritis (3, 10). In severe cases of acute metritis, a rehydration therapy applied systemically and/or by drenching seems to be helpful to wash out toxins.

Chronic endometritis

Chronic endometritis is also referred to as clinical endometritis and is characterised by the presence of mucopurulent or purulent exudate in the vagina three weeks or more after parturition (1). In contrast to acute metritis, chronic endometritis is not associated with elevated temperature and depressed general attitude. Several methods for diagnosing endometritis have been established, including adspection of the vulva, perineum and the tail, combined with manual palpation of uterus and cervix per rectum, and/or vaginal inspection. Clinical findings by *rectal palpation* of the uterus are asymmetric uterine horns, thickened uterine wall, palpable presence of fluid (5), and a cervical diameter of more than 7.5 cm (14). V*aginal inspection* via speculum, however, is more accurate than rectal palpation (5, 14). Rectal palpation as well as vaginoscopy are indirect diagnostic methods and can not verify the inflammation of the uterus itself. *Uterine swabs* for microbiology as a routine diagnostic tool for chronic endometritis is not practical and associated with high costs (5). Common bacteria isolated from cows with chronic endometritis are *A. pyogenes*, *E. coli,* as well as *F. necrophorum* and *Prevotalla spp* (1, 5). Infections with *Chlamydophila spp* can also result in chronic endometritis (15). Positive

findings, however, provide only evidence for an infection but not for endometritis. *Biopsy* of the uterine endometrium provides informations about local histological alterations. The manipulation itself, however, can impair subsequent fertility of the tested cows (16).

Numerous attempts were made to categorize chronic endometritis. An endometritis scoring by Williams et al. (17) is online available at

http://www.rvc.ac.uk/AboutUS/Staff/sheldon/ResearchInterests/Gallery/index.cfm. Cloudy discharge and clear mucus with flakes of pus in the absence of an enlarged uterus can be regarded as signs for mild endometritis. An enlarged, fluid-filled uterus accompanied with an enlarged cervix and purulent discharge indicates a severe endometritis (17). Pyometra is defined as an enlarged fluid-filled uterus without any visible discharge and the presence of a corpus luteum (1, 5).

The best time for diagnosis is controversial. Some studies have shown a tendency to self-recovery from endometritis within the postpartum period. Therefore it seems rational that the diagnosis should be performed about three to four weeks after calving (14, 18).

The impact of chronic endometritis on reproductive performance is characterised by decreased service and conception rates, and consequently by prolonged days to first service and days open. The number of cows pregnant is decreased while the risk for culling is increased (5, 19, 20, 21).

Treatment of chronic endometritis

In general, the treatment of chronic endometritis is based on two different strategies, i.e. an intrauterine treatment with antibiotics or a systemic treatment with prostaglandin $F_{2\alpha}$ (4, 19, 22). It has been discussed whether cases of mild endometritis have to be treated at all (18, 19). Studies on subclinical endometritis, however, indicate to treat all cows with any signs of endometritis (23, 24, 25). The central mechanism of a treatment with $PGF_{2\alpha}$ and its analogues is the luteolytic activity of $PGF_{2\alpha}$, followed by onset of estrus (5). The myometrium contracts and uterine fluids such as pus can pass through an open cervix. The influx of PMN into the mucosa increases and mucus containing immunoglobulins is produced (8).

Some studies described an intrauterine antibiotic treatment with cephapirin as equally efficacious or superior to the application of $PGF_{2\alpha}$ (20, 21, 26). With regard to a prudent use of antibiotic drugs in food producing animals and to minimize the risk of provoking antibiotic resistance, the application of antibiotics should be limited to cases that can not be controlled by $PGF_{2\alpha}$.

The uterine infusion of antiseptics has been routinely used in veterinary practice in several countries for many years. Intrauterine infusions, however, failed to show positive effects on subsequent reproductive performance (19, 22, 27), but have been described as detrimental on uterine defense mechanisms and the epithelium of the oviducts (27). Studies on intrauterine applications of herbal extracts (22) or proteolytic enzymes (28) provided some promising approaches, but failed to give convincing results compared to the application of $PGF_{2\alpha}$.

Subclinical endometritis

In the absence of clinical signs of chronic endometritis, alterations in the uterine lumen or uterine wall can be defined as subclinical endometritis. Some recent studies described the diagnosis and treatment of subclinical endometritis. *Ultrasonography* as a non-invasive method visualizes small amounts of fluid in the uterine lumen (24, 29). False positive findings might result from clear mucus in the uterus appearing during estrus. Therefore, the ovaries should be scanned as well to define the stage of the estrus cycle. *Endometrial cytology* can be performed by flushing the uterus to obtain endometrial cells or taking samples with a cytobrush from the endometrium. The percentage of PMN in the cytological preparation provides information on the presence of subclinical endometritis. The threshold value for PMN varies between authors from 5 to 18% (23, 24, 30). It has been demonstrated that cows with subclinical endometritis have a depressed reproductive performance in the current lactation (23, 24). For the treatment of subclinical endometritis, intrauterine infusions with cephapirin as well as the administration of $PGF_{2\alpha}$ have been recommended (25). Other studies, however, did not confirm the efficiency of this treatment (30, 31).

The challenge for veterinarians is an accurate diagnosis and efficacious treatment of cows with acute, chronic and subclinical endometritis. The efficacy of a treatment must be evaluated with regard to cure rate and subsequent reproductive performance. The objective of herd health management must be the prevention of metritis by adequate feeding, hygienic calving conditions and careful obstetrical assistance.

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NOVOSTI S PODROČJA MATERNIČNIH OKUŽB PRI KRAVAH MOLZNICAH

M. Drillich

Povzetek: Vnetja maternice, ki jih opisujemo kot akutni metritis ali kronični endometritis, so ena izmed najpogostejših motenj v poporodnem obdobju pri kravah molznicah. Za akutni metritis so značilni rdečerjav smrdljiv izloček, telesna temperatura ≥ 39.5 °C, ki jo pogosto spremlja splošna potrtost živali, zmanjšana ješčnost in zmanjšana proizvodnja mleka. Iz materničnega brisa izoliramo predvsem bakterije vrste *Escherichia coli*, *Arcanobacterium pyogenes* ter obligatne anaerobe *Fusobacterium necrophorum* in *Prevotella spp.* Priporočeno zdravljenje akutnega metritisa temelji na sistemskem zdravljenju z antibiotiki brez kakršnih koli posegov v maternico. Kronični endometritis definiramo ob pojavu gnojnega ali sluzasto-gnojnega izcedka, ki se pojavi po tretjem tednu po porodu. V nasprotju z akutnim metritisom kroničnega ne spremlja povišana temperatura. Vaginalni pregled s spekulumom se je izkazal za boljše diagnostično sredstvo kot pa rektalni. Med laktacijo se reprodukcijska sposobnost prizadetih krav zmanjša. Pri kroničnem endometritisu se priporoča aplikacija prostoglandina $F_{2\alpha}$ ($PGF_{2\alpha}$) ali intrauterina infuzija cefapirina. Zadnja leta so prinesla tudi nekaj novih pogledov na subklinični endometritis, ki ga zaznamo po treh tednih po porodu. Kliničnih znakov endometritisa ni, vendar v citoloških brisih endometrija ali v majhni količini tekočine v maternični svetlini (ki jo zaznamo z ultrazvokom) lahko ugotovimo odstotek polimorfonuklearnih levkocitov, ki kažejo na blago vnetje maternice. Sprejeto je splošno mnenje, da subklinični endometritis izrazito negativno vpliva na reprodukcijsko sposobnost, o načinih zdravljenja pa se še razpravlja. V poskusih so uporabili aplikacijo $PGF_{2\alpha}$ in intrauterino infuzijo cefaprina ali proteolitičnih encimov, vendar se rezultati teh testov ne ujemajo.

Ključne besede: govedo, bolezni; endometritis – diagnostika; zdravila, zdravljenje; govedo