Scientific Works. Series C. Veterinary Medicine. Vol. LXIV (1), 2018
ISSN 2065-1295; ISSN 2343-9394 (CD-ROM); ISSN 2067-3663 (Online); ISSN-L 2065-1295

# THE EFFECT OF INTRA-UTERINE TREATMENT WITH DILUTED N-ACETYLCYSTEINE ON BOVINE ENDOMETRITIS

**Nicolae Tiberiu CONSTANTIN, Alexandru ȘONEA**

University of Agronomic Science and Veterinary Medicine, Faculty of Veterinary Medicine Bucharest, 105, Splaiul Independenței Str., 050097, Bucharest, Romania,

Correspondig author email: constantin.ntiberiu@yahoo.com

***Abstract***

*After the voluntary waiting period, a chronic uterine infection or a persistent inflammation in the cow may be associated with disruption of the architecture of the endometrial layer and glandular hypersecretion. The aim of our work, the first of this kind in Romania, was to evaluate the efficacy of 3% N-acetylcysteine (NAC) against the clinical endometritis. The mucolytic effect of NAC can be use to break up mucus produced by an glandular irritated layer. Besides this, NAC has a antioxidant, cytoprotection and antiinflamatory role, and at a 8% concentration it can be bactericidal. This study was carried out between 2016-2017 on 43 cows with clinical signs of endometritis after 50-60 days postpartum from a dairy farm situated in Ploiești county. The clinical endometritis was diagnosed by evalution of uterine discharge detected in the vulva. Cows were randomly splited to NAC treatment (NAC) and non-NAC treatment (nNAC) groups. All of these were clinically evaluated, and a cervical swab for microbiology laboratory was collected. The NAC group (n=21) received an intrauterine treatment of enrofloxacin+oxitetraciclin+iodoform (2.5g+5g+5g/100ml) in 20 ml dosages. After 12 hours, an infusion of 3% NAC was intrauterine administred for 3 days. The nNAC group received 20 ml of saline, for 3 days instead of 3% NAC and the same quantity of enrofloxacin+oxitetraciclin+iodoform solution. The clinical heal rate was definited as the percentage of females with no signs of clinical endometritis (clear mucus at the vaginoscopy), at the examination in first estrus following treatment. Cows were artificially inseminated following the hormonal therapy. As a main conclusion, the group of cows treated with NAC presented a pregnancy rate of 66.7% in contrast with non NAC group, where the pregnancy rate was 54.6%.*

***Key words:*** *N-acetylcysteine, cows, chronical endometritis, pregnancy rate.*

## INTRODUCTION

The health condition of high-yielding dairy cows is particularly at risk in the transition period, which includes the 3 weeks before and 3 weeks after parturition, broadly correspondding to periparturient period (LeBlanc et al., 2011; Trevisi et al., 2012; Islam et al., 2014).

In this season, animals undergo pronounced physiological changes that might cause suppression of the host defence mechanisms including both the cellular and humoral response of the immune system and an increase in susceptibility to uterine and mammary gland infection (Mulligan et al., 2008; Tan et al., 2012).

Bacteria, like *Escherichia coli*, *Arcanobacterium pyogenes*, *Pseudomonas aeruginosa*, *Pasteurella multocida*, *Staphylococcus aureus*, *Streptococcus uberis*, *Clostridium* spp., *Prevotella* spp. and *Fusobacterium* spp., compromises animal welfare, as well as causing subfertility and infertility because of uterine inflammation and/or infection represented by metritis, clinical and subclinical endometritis (Singh et al., 2008; Kaçar and Kaya, 2014; Zobel et al., 2014).

Clinical endometritis is basically referring to a local inflammation of the endometrium, characterized by the presence of purulent or mucopurulent (> 50% pus) material in the vagina ≥ 21 days postpartum originating from the uterus, not accompanied by systemic illness.

It affects around 20 % of dairy cows between 21 to 40 days postpartum (LeBlanc et al., 2002; Pascottini, 2016).

These diseases may prolong the days open until first service, days open until pregnancy, the intercalving period, the conception rate and the risk of cows being culled due to infertility (Đuričić et al., 2015).

Current therapies of cows suffering from endometritis aim to eliminate intrauterine (i.u.) fluid and mucus by uterine lavage and/or administration of antibiotics or other types of drugs. Recently, i.u. administration of N-

acetylcysteine (NAC) has been shown to support antibiotic therapy in cows and mares (Tras et. al., 2012; Witte et al., 2012) with endometritis. N-acetylcysteine disrupts disulfide bonds between mucin polymers and thus exhibits mucolytic properties (Matsuyama et al., 2006). Furthermore, it possesses antioxidant properties, can protect the equine colon mucosa after reperfusion injury and has protease-inhibiting capacities (Rötting et al., 2003).

## MATERIALS AND METHODES

### *Animals*

The study population consisted of 43 Holstein cows, divided into two groups (NAC treatment (NAC) *n*=21, and non-NAC treatment (nNAC) *n*=22) based on the uterine findings, from two industrial dairy farms in south of Romania. Cows were housed in ties stalls and individually fed a total mixed ration (TMR) twice daily and water ad libitum. A close-up diet was fed beginning 3 weeks prior to expected calving date, a fresh cow diet was fed beginning the day of calving through 3 weeks postpartum, and a lactation diet was fed from 3 weeks postparturition. The animals from the two groups had a physiological puerperium but the exclusion criteria included birth assistance, receiving systemic antibiotic therapy within 50-60 days prior to calving, abnormal internal genitalia (including adhesions), BCS < 2,5, systemic diseases, retention of foetal membranes, any kind of dystocia, including caesarean section, lameness, puerperal mastitis. Only cows following the second to the fourth partus were involved in the study.

### *Experimental protocol and clinical evaluations*

All the cows were examined by rectal palpation and vaginoscopicaly examinated 50-60 days postpartum. Transrectal palpation served to assess uterine size and symmetry of the uterine horns as well as uterine fluctuation, and purulent or mucopurulent vaginal discharge. The NAC group (*n*=21) received an intrauterine treatment of enrofloxacin + oxitetraciclin + iodoform (2.5g+5g+5g/100ml) in 20 ml dosages. After 12 hours, an infusion of 3% NAC was intrauterine administred for 3 days. The nNAC group (*n*=22) received 20 ml of saline, for 3 days instead of 3% NAC and the same quantity of enrofloxacin + oxitetraciclin + iodoform solution. The clinical heal rate was definited as the percentage of females with no signs of clinical endometritis (clear mucus at the vaginoscopy), at the examination in first estrus following treatment. Healthy cows were artificially inseminated following the hormonal therapy.

### *Bacterial culture*

A uterine and/or cervical culture is an essential tool to determine the etiology of uterine infection. Briefly, the vulva was cleaned thoroughly with a dry paper towel. A cervical swab for microbiology laboratory was collected., transferred into sterile tubes and carefully transported at 4°C to the Faculty of Veterinary Medicine, Bucharest for further bacteriology testing.

### *Statistical analysis*

Reproductive parameters such as pregnancy rate (PR), calving to pregnancy interval (CPI), calving interval CI) and cure rate (CR) were take in consideration and calculated in Microsoft Excel 2010.

## RESULTS AND DISCUSSIONS

The clinical cure rate in NAC group (77.2%) was significantly higher than nNAC group (43.4%). The group of cows treated with NAC presented a pregnancy rate of 66.7% in contrast with nNAC group, where the pregnancy rate was 54.6%. In a simmilar study, Tras and col., (2014) obtained a CR (83.3%) and PR (66.7%) significantly higher for NAC group than (55.5% and 27.8% respectively) for nNAC group. Regarding to CPI and CI reproductive parameters NAC group shows a shorter intervals in contrast to nNAC group, as we can see in tabel number 1. In the cervical swab samples of cows, *Corynebacterium* ssp., *S. aureus*, and *E. coli* were isolated.

| Study parameters | NAC | nNAC |
|---|---|---|
| **PR** | 66.7% | 54.6% |
| **CPI** | 93 days | 107 days |
| **CI** | 389 days | 401 days |
| **CR** | 77.2% | 43.4% |

## CONCLUSION

The results suggested that NAC may be beneficial for treating genital tract infections presenting purulent discharge such as clinical endometritis due to the clinical features of NAC for cost saving, and has got no illegal residues in edible tissues of farm animals. Although it is first article in Romania of this kind, further studies are needed to clarify the efficiency of NAC intrauterine treatment in cows.

## REFERENCES


Đuričić D., Valpotić H., Samardžija M., 2015. Prophylaxis and therapeutic potential of ozone in buiatrics: Current knowledge. Animal Reproduction Science, 159:1-7.

Islam R., Kumar H., Krishnan B.B., 2014. Investigation on leukocyte profile of periparturient cows with or without postpartum reproductive disease. Asian Pacific Journal of Reproduction 3(1): 57-63.

Kaçar C., Kaya S., 2014. Uterine infections in cows and effect of reproductive performance. Kafkas Univ Vet Fak Derg 20(6):975-982.

LeBlanc S.J., Duffield T.F., Leslie K.E., Bateman K.G., Keefe G.P., Walton J.S., Johnson W.H., 2002 – Defining and diagnosing postpartum clinical endometritis and its impact on reproductive performance in dairy cows. Journal of dairy sicence, 85:2223-2236

LeBlanc St.J., Osawa T., Dubuc J., 2011. Reproductive tract defense and disease in postpartum dairy cows. Theriogenology 76, 1610–1618.

Matsuyama T., Morita T., Horikiri Y., Yamahara H., Yoshino H., 2006 - Improved nasal absorption of salmon calcitonin by powdery formulation with *N*-acetyl-L-cysteine as a mucolytic agent. Journal of Control Release, 115:183– 8.

Mulligan F.J., Doherty M.L., 2008. Production diseases of the transition cow. The Veterinary Journal 176, 3–9.

Pascottini O.B., 2016 – Subclinical endometritis in dairy cattle: a practical approach. PhD these, Gent University, Belgia.

Rötting A.K., Freeman D.E., Eurell J.A., Constable P.D., Wallig M., 2003 - Effects of acetylcysteine and migration of resident eosinophils in an in vitro model of mucosal injury and restitution in equine right dorsal colon. Ainmal journal of veterinary reseach, 64:1205–12.

Singh J., Murray R.D., Mshelia G., Woldehiwet Z., 2008. The immune status of the bovine uterus during the peripartum period. The Veterinary Journal 175(3):301-309.

Tan X., Li W-W., Guo J., Zhou J-Y., 2012. Down-regulation of NOD1 in neutrophils of periparturient dairy cows. Veterinary Immunology and Immunopathology 150, 133– 139.

Tras B., Dinc D.A., Uney K., - 2014. The effect of N-aceltylcysteine on the treatment of clinical endometritis and pregnancy rate in dairy cows. Eurasia journal of veterinary science, 30(3):133-137.

Trevisi E., Amadori M.,, Cogrossi S., Razzuoli E., Bertoni G., 2012. Metabolic stress and inflammatory response in high-yielding, periparturient dairy cows. Research in Veterinary Science 93, 695–704.

Witte T.S., Melkus E., Walter I., Senge B., Schwab S., Aurich C., Heuwieser W., - 2012. Effects of oral treatment with N-acetylcysteine on the viscosity of intrauterine mucus and endometrial function in estrous mares. Theriogenology, 78(6):1199-208

Zobel R., Martinec R., Ivanović D., Rošić N., Stančić Z., Žerjavić I., Flajsig B., Plavec H., Smolec O., 2014. Intrauterine ozone administration for imporving fertility rate in Simmental cattle. Veterinarski arhiv, 84(1):1-8.