



Treatment of the retained placenta in dairy cows: Comparison of a systematic antibiosis with an oral administered herbal powder based on traditional Chinese veterinary medicine



Dongan Cui^{a,b}, Shengyi Wang^{a,b}, Lei Wang^{a,b}, Hui Wang^{a,b}, Jianxi Li^{a,b}, Xin Tuo^{a,b}, Xueli Huang^{a,c}, Yongming Liu^{a,b,*}

^a Lanzhou Institute of Husbandry and Pharmaceutical Sciences of Chinese Academy of Agricultural Sciences, Lanzhou 730050, PR China

^b Engineering & Technology Research Center of Traditional Chinese Veterinary Medicine of Gansu Province, Lanzhou 730050, PR China

^c College of Veterinary Medicine, Northwest A&F University, Yangling, Shaanxi 712100, PR China

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ABSTRACT

Cows affected with retained placenta are at a higher risk of developing puerperal metritis. Herbal remedies bear a high potential to treat postpartum uterine diseases in cows. The aim of this randomized clinical trial was to compare an herbal powder and ceftiofur hydrochloride in the treatment of cows affected with retained placenta and for puerperal metritis prevention. The herbal powder was prepared from a combination of *Leonurus artemisia* (Laur.) S.Y. Hu F, *Angelica sinensis* (OLIV.) DIELS (radix), *Ligusticum chuanxiong* HORT (radix), *Sparganiumstoloniferum* (Graebn.) Buch.-Ham.exJuz (radix), *Curcuma zedoaria* (Christm.) ROSC (radix), *Cyperu srotundus* Linn. (radix), and *Glycyrrhiza uralensis* FISCH (radix). A total of 157 cows diagnosed with retained placenta were randomly divided into 2 treatment groups. Cows in the herbal group ($n=85$) were treated with an oral dose of 0.5 g crude herb/kg bw once daily for 1–3 day(s), and cows in the control group ($n=72$) were treated with ceftiofur hydrochloride (2.2 mg/kg bw, i.m.) twice daily for 3 consecutive days. Seventy-three cows had total expulsion of the placenta within 72 h following initial herbal treatment, yet no cows in the control group expelled the placenta during the same time period, and 50 out of 73 cows achieved total expulsion of the placenta following only one herbal treatment. The median time of retained placenta shedding (20.0 vs. 101.5 h; $P < 0.01$) was shorter in the herbal group than in the control group. The logistic regression analysis indicated that the oral administration of the herbal powder tended to have superior clinical efficacy in metritis prevention compared to the systemic administration of ceftiofur hydrochloride in cows affected with retained placenta (8.2% vs. 11.1%, $P=0.057$, OR 5.771) within 21 days after parturition. Additionally, fewer cows in the herbal group required additional therapeutic antibiotics compared to the controls (8.2% vs. 26.4%, $P=0.003$). Evidence from this randomized controlled clinical trial suggested that the herbal powder is a clinically effective treatment for retained placenta and the prevention of puerperal metritis and, thus, might have great potential for the medical management of retained placenta in dairy cows.

1. Background

Retained placenta is a frequently diagnosed uterine disease in early-postpartum cattle (Beagley et al., 2010). Cows with retained placenta are at a higher risk of developing puerperal metritis (Han and Kim, 2005; Sandals et al., 1979). Puerperal metritis has been identified as one of the main reasons for reduced fertility in cows with retained placenta. Consequences of cases of retained placenta on farm profitability are partly dependent on when metritis occurs (Laven and Peters, 1996). Thus, an ideal medical therapy for retained placenta should

prevent puerperal metritis in cows.

Generally, the dominant approach to retained placenta in cattle in the field is to locally or systemically administer antibiotics. Goshen and Shpigel (2006) demonstrated that intrauterine antibiotic treatment is beneficial for metritis prevention in cows affected with retained placenta. As a third generation cephalosporin, ceftiofur does not result in antibiotic residues in the milk when used according to the label directions, and it has been widely applied to treat cows affected with retained placenta and metritis prevention in clinical practice (Liu et al., 2011; Risco and Hernandez, 2003). However, current reports indicate

* Corresponding author at: Lanzhou Institute of Husbandry and Pharmaceutical Sciences of Chinese Academy of Agricultural Sciences, Lanzhou 730050, PR China.
E-mail address: Yongmliu@126.com (Y. Liu).

that antibiotic therapy, including intrauterine antibiotics and systemic antibiotics, generally has low efficacy in hastening the separation and expulsion of the retained placenta (Drillich et al., 2006, 2007; Haimerl and Heuwieser, 2014; Risco and Hernandez, 2003; Stevens et al., 1995). Therefore, the challenge is to develop alternative strategies to manage these two conditions in cows. Ethnoveterinary medicines play a pivotal role in animal health care worldwide (Ayrle et al., 2016; Lans et al., 2007; McGaw and Eloff, 2008; Mayer et al., 2014; Pieroni et al., 2006; Van der Merwe et al., 2001), and medicinal plants are often used to treatment livestock affected with retained placenta (Cui et al., 2014b; Fall and Emanuelson, 2009; Mohan and Bhagwat, 2007; Moreki et al., 2012). Traditional Chinese veterinary medicine (TCVM) has always focused more on the body's response to pathogenetic factors than on pathological mechanisms (Editorial Committee of Encyclopedia of China's Agriculture, 1991) and, thus, offers new options for the treatment of postpartum uterine diseases in cows (Song, 1988; Yang et al., 2006).

In TCVM theory, blood stasis is an important underlying pathology of certain postpartum diseases (Bensky and Gamble, 1993; Luo, 1986; Yang et al., 2006), and retained placenta and/or puerperal metritis both fall within the blood stasis syndrome category (Editorial Committee of Encyclopedia of China's Agriculture, 1991). Evidence from clinical trials suggests that there are beneficial effects of herbal remedies for postpartum uterine diseases in dairy cows (Cui et al., 2014a; Cui et al., 2014b; Cui et al., 2015; Mohan and Bhagwat, 2007). The herbal powder used in the present study was designed according to the therapeutic principle of "promoting blood circulation and removing blood stasis, regulating qi flow and relieving pain" for the treatment of postpartum uterine diseases, including retained placenta and puerperal metritis in cattle, and consists of *Leonurus artemisia* (Laur.) S.Y. Hu F, *Angelica sinensis* (OLIV.) DIELS (radix), *Ligusticum chuanxiong* HORT (radix), *Sparganiumstoloniferum* (Graebn.) Buch.-Ham.exJuz (radix), *Curcuma zedoaria* (Christm.) ROSC (radix), *Cyperu srotundus* Linn. (radix), and *Glycyrrhiza uralensis* FISCH (radix) (Appendix Table A1). According to traditional Chinese veterinary medicine theory, these herbs, mixed as presented, could resolve the blood stasis syndrome caused by retained placenta and, thus, can be used for the treatment of retained placenta and to lower puerperal metritis risks in postpartum cows.

The hypothesis of the present study is that cows with retained placentas treated with an oral administered herbal powder will experience shorter time to recovery, a reduced incidence of metritis subsequent to retained placenta, and will require fewer antibiotics compared to cows treated with ceftiofur hydrochloride. The aim of this randomized trial was to compare an oral administered herbal powder and ceftiofur hydrochloride in the treatment of cows with retained placenta and for the prevention of puerperal metritis under field conditions.

2. Materials and methods

2.1. Herbal powder preparation

The herbal powder used in the present study was composed of seven dried herbs (Appendix Table A1) that were obtained from Hui Ren Tang Chinese Medicine Co., Ltd. (Lanzhou, China), and the herb quality criteria were congruent with Chinese pharmacopoeia (The Pharmacopoeia Commission of PRC, 2010). After pre-processing by washing and drying, all herbs were ground to a homogenous powder and mixed to obtain the herbal powder with 80–100 mesh particle size (150–180 µm).

2.2. Animals and herds

The present study was approved by the Institutional Animal Care

and Use Committee of Lanzhou Institute of Husbandry and Pharmaceutical Sciences of the Chinese Academy of Agricultural Sciences (SCXK20008-0003). This trial was conducted in two large commercial dairy farms with similar management practices in Lanzhou city, China. The animals were housed in free-stall facilities with cubicles, rubber mats and slotted floors and moved into loose housing systems in large, completely covered open sheds with straw bedding at least 1 week before the expected calving. The cows were fed hay *ad libitum* and a total mixed ration (TMR) consisting of corn silage, corn meal, barley and mineral supplements. Cows were milked three times daily in computer controlled milking parlors, and the herd-average milk yield varied between 7200 and 9100 kg per lactation in both herds. All cows were identified by ear tags and freeze marking.

2.3. Enrollment criteria

The treatment groups included cows with retained placenta after calving between August 2014 and December 2015. In this trial, retained placenta was diagnosed as retention of fetal membranes at 12–24 h after delivery of the calf, and the clinical diagnosis was established by Doctor Li or Tuo in the two farms respectively, who also diagnosed, treated and recorded all periparturient disease conditions. The enrolled cows were 3–7 years old (2–5 lactations) and had a BCS (Body Condition Score) between 2.5 and 3.5 during the periparturient stage (Edmonson et al., 1989). In addition, all cows involved in this trial were studied for only 1 lactation session and all newborns were delivered in good condition.

2.4. Exclusion criteria

Any cows suffering from conditions such as caesarean section during a previous or current calving, displaced abomasum, laminitis, postpartum acute diarrhea or ketosis were excluded from the study due to the possible influence of these conditions on the results. Additionally, cows with incomplete treatments or other deviations from the treatment protocol were retrospectively removed from the trial.

2.5. Study design and clinical examination schedules

During the study periods, a total of 2125 cows calved and retention of the fetal membranes occurred in 221 cows. After completing the baseline evaluation, 141 cows having spontaneous delivery, 9 cows having twins, and 22 cows given with dystocia were enrolled in this trial. The 141 cows allocated to one of two groups based on their ear-tag numbers (the odd-numbered cows in the herbal group, and even-numbered cows in the control group), and the 9 cows and 22 cows were randomly assigned to 1 of the two groups by using random-number tables with a block size of 4 (SPSS software, version 17.0), 91 cows in herbal group, 81 cows in the control group. After treatment, fifteen cows were withdrawn from the final analyses. In herbal group, two cows were excluded for displaced abomasum, three cow for acute mastitis and one cows for serious lameness. In the control group, three cows were excluded for acute mastitis, four cow for displaced abomasum and two cows with interrupted treatment for application problems. Finally, two groups of animals (herbal group, $n=85$; control group, $n=72$) were created for further statistical analysis. The Fig. 1 shows the disposition of the enrolled cows.

The day of the retained placenta diagnosis was considered day 1 and was also the first day of treatment. Animals treated with herbal powder or ceftiofur hydrochloride were submitted for veterinary examination on the next routine 2-h interval visit. Obstetrical examinations were performed 72 h after initial treatment by palpation of the uterus per the rectum and/or vaginoscopy to evaluate uterine discharge and uterus status after thoroughly cleaning and disinfecting the

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