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# Denaverine hydrochloride and carbetocin increased welfare during and after parturition and enhanced subsequent fertility in cattle

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#### **ABSTRACT**

The objectives of the current study were to investigate the influence of denaverine hydrochloride and carbetocin on softening and dilatation of the birth canal, the need for assistance during parturition, calf mortality, retention of fetal membranes, endometritis, and subsequent fertility. Altogether 200 animals (100 cows and 100 heifers) of the Simmental breed were divided into 2 groups: treatment (n = 100) and control (n = 100). Animals in the treatment group received denaverine hydrochloride and carbetocin (a maximum of twice for each, depending on the progression of labor) during delivery over a maximum of 4 waiting periods (30 min each), whereas control animals experienced the same waiting periods but received no treatment. The treatment protocol had a positive influence on the ease of calving and postpartum reproductive health. The treatment increased the number of animals with the birth canal dilated by more than 25 cm, and halved the need for any assistance at parturition. In addition, treatment decreased the occurrence of difficult calving, the need for episiotomy, the appearance of birth canal lesions, and clinical endometritis. The treatment protocol had an effect throughout the entire puerperal period, as treated animals conceived with fewer artificial inseminations (1.3 vs. 1.6 artificial inseminations/pregnancy) and sooner (67 vs. 78 d open) compared with control animals. Denaverine hydrochloride and carbetocin administered in combination during parturition affected the progression and ease of calving, and thus the welfare of cows in labor and subsequently. However, further studies are needed to confirm the findings and to establish best practices.

**Key words:** cattle, denaverine hydrochloride, parturition, welfare

#### INTRODUCTION

All pain compromises animal welfare, and dystocia was ranked as one of the most painful conditions in cattle by cattle practitioners in the United Kingdom (Huxley and Whay, 2006). Other veterinary practitioners ranked pain due to dystocia as 7 on a 10-point scale, where 10 represented the maximum pain (Whay et al., 2008). Some Scandinavian countries have proscribed the use of double-muscled cattle breeds and restricted the use of mechanical calf pullers to veterinarians to reduce suffering and pain during delivery (Mee, 2008).

Obstetrical assistance less than 1 h after the appearance of the fetal hooves increases the risk of prolonged assistance, dystocia, use of a calf puller, downer cow syndrome, and reduced perinatal vigor. The delay of assistance for more than 2 h increases the duration of calving and induces hyperlactatemia in the neonate without conferring any additional benefits (Egan et al., 2001; Mee, 2004). Duration of second-stage labor of 2 h can be tolerated by heifers and cows providing normal position and posture of the fetus can be maintained (Gundelach et al., 2009). The occurrence of dystocia, however, increases culling and mortality rates (McClintock, 2004), stillbirth (Mee, 2004), and the risk of respiratory and digestive disorders in both the cow and calf, as well as retained placenta, uterine diseases, mastitis, and hypocalcaemia (Oltenacu et al., 1988; Lombard et al., 2003, 2007). Cows that experience dystocia are more likely to experience it again during subsequent calving (Mee et al., 2008). The total cost of dystocia was assessed to be 4 times greater than the treatment costs alone when the costs of the consequences of dystocia listed previously were included (Oltenacu et al., 1988).

Denaverine hydrochloride (**DH**) is a neurotropic-musculotropic spasmolytic agent with additional analgesic activity (Hüller, 1970; Scharein and Bromm, 1998). It is used in the treatment of smooth muscle spasms of the gastrointestinal and urogenital tract (Hüller, 1970), as well as in the treatment of postoperative abdominal pain and in the field of obstetrics. According to the instructions, DH softens the birth canal soft tissue, has

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an anesthetic effect on its surface, and increases the influence of carbetocin (CT; Staab et al., 2003); however, very little has been published on DH effects.

It is commonly known that oxytocin increases the frequency of uterine contractions and strengthens them during parturition (al-Eknah and Homeida, 1991), and contractions can be fortified with exogenous administration of oxytocin. Oxytocin stimulates contractions at least by increasing prostaglandin release (with which it has a synergistic effect) and by increasing Ca<sup>2+</sup> concentration (MacKenzie and Burns, 1997). The administration of oxytocin during parturition, or within 2 h after, can prevent placental retention (Squire, 1980; Miller and Lodge, 1984; Roberts, 1986; Fields and Fields, 1996; Mollo et al., 1997; Drillich et al., 2007), although contradictory views on the effects were reported (Arthur, 1979; Hickey et al., 1984). It has been estimated that the total pregnancy rate in cows with retained placenta is reduced by approximately 15% compared with that for unaffected cows (Fourithon et al., 2000).

A prolonged uterotonic effect can be achieved by using agonistic analogs of oxytocin with longer biological activity, such as CT (Cort et al., 1979; Eulenberger et al., 1986; Bernhard et al., 1993; Sobiraj et al., 1998). The uterotonic effect of a single intramuscular administration of either oxytocin (50 IU) or its long-acting agonist CT (0.35 mg) were compared in a field study on early postpartum dairy cows after normal parturition (LeBlanc, 2008). It transpired that both drugs significantly increased the frequency and strength of uterine contractions, mainly during the first post-treatment hour. However, the uterotonic effects were almost equal, and a prolonged effect of CT could not be demonstrated.

The principal aim of the current study was to explore means to decrease pain and injury during parturition to improve cattle welfare. The detailed objectives were to study the influence of DH on softening and dilatation of the birth canal (primary cervix and vulva), and to study the effects of DH followed by administration of CT on the need for assistance during parturition and on calf mortality. In addition, consequences of these treatments were studied on retention of fetal membranes and endometritis rates, as well as on subsequent fertility.

## **MATERIALS AND METHODS**

### Animals

The study was performed on 11 commercial dairy farms in the central region of Croatia (Sisačko-Moslavačka County), each with 30 to 100 Simmental cows. The management was similar on all farms and

the average annual milk yield ranged between 5,168 and 6,689 kg. Lactating cows, dry cows, and heifers were housed separately in freestalls, in groups of 30 to 90 animals, with the possibility to graze during the day from March until November. During the cold period, animals also had the possibility to go out voluntarily. Animals were fed hay ad libitum. Twice a day a concentrate consisting of barley, oats, corn, soybean, and minerals mixed with straw and silage made of corn and grass was provided. Propylene glycol was added to the ration of high-yielding animals (cows tended to produce more than 6,000 kg/lactation).

Before the experiment began, all pregnant animals were scored for body condition according to Edmonson et al. (1989) from 2 to 5 mo of pregnancy. Only those animals with a BCS between 2.5 and 3.5 were included; the rest were excluded due to the possible influence of obesity or poor condition on the results. In addition, animals suffering from diseases such as polyarthritis, recurrent mastitis (animals having mastitis more than once during previous or current lactation), increased SCC (>200,000 cells/mL of milk) for more than 3 mo during previous or current lactation, or laminitis, as well as animals having extremely defective construction of hind limbs or previous caesarean section and animals given birth by the time of arrival or having had twins, were excluded for the same reason. Animals were divided randomly into 2 groups, treatment (T) and control (C), with cows and heifers separated. Animals were included in the experiment to assemble 100 cow- and heifer-calving cases. The parity of cows varied between 1 and 7 at the beginning of the experiment, being on average 4.3 and 4.4 in groups T and C, respectively. The experiment was conducted from May 2008 until June 2009.

#### Experimental Protocol

The cattle owners were directed to call for 1 of the 3 veterinarians involved in the study to be present immediately after detection of any signs of incipient parturition. The inclusion criteria explained previously were checked once again, and animals not fulfilling criteria were excluded. After thorough obstetric examination, the diagnosis of parturition was established based on cervix opened more than 10 cm with several signs of obvious distress in the cow (excessive restlessness, repeatedly lying down and standing up, lateral recumbency, vocalization, repeated abdominal muscle contractions, repeatedly raising the tail). To measure dilatation of the vulva and cervix, fingers (side by side) of 1 or 2 hands were inserted and, if not sufficient, a fist of 1 or both hands were inserted first into the vulva horizontally, stretching the canal to its maximum

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