Anim. Reprod., v.10, n.3, p.252-257, Jul./Sept. 2013

Managing gestation in cattle

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Abstract

Once a cow becomes pregnant, the effect of pregnancy loss on its reproductive cycle is a topic of great interest for dairy herds. This paper reviews the factors of a non-infectious nature that affect the pregnancy maintenance during the late embryonic/early fetal period. Some clinical suggestions on bovine neosporosis and coxiellosis are also highlighted.

Keywords: coxiellosis, early fetal period, late embryonic period, neosporosis, pregnancy loss.

Introduction

Factors of non-infectious nature related to late embryonic/early fetal loss

Dairy herds are under ever-increasing pressure to improve their efficiency and primary attention is usually directed towards postpartum reproductive disorders. However, it is also of great interest to understand the effects of pregnancy loss on the reproductive cycle once a cow is pregnant. Following a positive pregnancy diagnosis, late embryonic/early fetal loss is becoming the most common complication of gestation in high producing dairy herds. In the cow, the embryonic period of gestation extends from conception until the end of the differentiation stage (about 45 days), and the fetal period spans from day 45 of gestation to parturition (Committee on Bovine Reproductive Nomenclature, 1972). Placentation finishes before day 60 of gestation, the period in which pregnancy is considered to be firmly established and the chances of loss are reduced (Ball, 1997). In dairy cattle, the risk of early fetal loss seems to increase under conditions of intensive management (Santos *et al*., 2004; López-Gatius *et al*., 2009). An early fetal loss of 10-12% is a commonly accepted figure. Losses, however, are further aggravated in specific populations such as: lactating parous cows, which show a 3.6-times more of pregnancy loss than pregnant heifers (Labèrnia *et al*., 1996; López-Gatius *et al*., 2004b); cows with previous postpartum disorders such as placenta retention or pyometra, with a pregnancy loss of 1.8 and 2.6 times higher respectively, than cows not suffering the disorder (López-Gatius *et al*., 1996); cows inseminated by a particular bull, which show 2 to 22 times higher risk of pregnancy loss (López-Gatius *et al*., 2002, 2004c, 2007); cows bearing twins, with a pregnancy loss of 3 to 7 times higher for twin pregnancies than single pregnancies (López-Gatius *et al*., 2002, 2006; García-Ispierto *et al*., 2006; Silva-del-Rio *et al*., 2009). Moreover, in warm countries such as Spain, summer heat stress is a major factor associated dramatically not only with conception (Labèrnia *et al*., 1998; López-Gatius, 2003; García-Ispierto *et al*., 2007) but also with fetal loss (López-Gatius *et al*., 2004c, d; García-Ispierto *et al*., 2006). Suboptimal concentrations of progesterone in blood related to high milk production (Bech-Sàbat *et al*., 2008; Rhinehart *et al*., 2009) could also explain some of these losses during the late embryonic/early fetal period (Ayad *et al*., 2007; Gábor *et al*., 2008) and why rates can exceed 20% in high production systems (Cartmill *et al*., 2001; Grimard *et al*., 2006). The fact that intravaginal progesterone supplementation may reduce the incidence of pregnancy loss during the early fetal period supports this idea (López-Gatius *et al*., 2004d; Alnimer and Lubbadeh, 2008). In fact, early fetal loss, peaking between days 40 and 50 of gestation (López-Gatius *et al*., 2004c; Santos *et al*., 2004), is becoming the most common complication of gestation in high producing dairy cows in our geographical area, where more than 90% of pregnancy losses following pregnancy diagnosis occur usually before day 90 (López-Gatius and Garcia-Ispierto, 2010; López-Gatius, 2012).

Factors of infectious nature related to pregnancy loss

Neosporacaninum is a protozoan parasite with a wide host range but with a preference for cattle and dogs. Since the description of *N. caninum* as a new genus and species in 1988, bovine neosporosis has become a disease of international concern as it is among the main causes of abortion in cattle (Dubey and Lindsay, 1996; Dubey and Schares, 2011). At present there is no effective treatment or vaccine. *Neosporacaninum* is one of the most efficiently transplacentally transmitted organisms in cattle. Up to 95% of calves are born infected (Dubey *et al*., 2007). The majority of calves born from infected mothers are clinically normal, but they are infected for life and *N. caninum* infection can be maintained over several generations by vertical transmission (Pabón *et al*., 2007). Abortion is the main clinical manifestation of bovine neosporosis with most abortions occurring at 5-7 months

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Received: May 5, 2013
Accepted: June 30, 2013

of gestation (Dubey *et al*., 2007). For example, in our geographical area of study, based on the odds ratio, the risk of abortion was found to be 12-19 times higher in *Neospora*-seropositive dairy cows than in seronegative cows, ranging from 30 to 44% in seropositive animals (López-Gatius *et al*., 2004a, b), and maintaining a similar risk of abortion over several years (Pabón *et al*., 2007). In fact, in commercial dairy herds routinely examined by us in a reproductive management program, 0% is a common figure for the abortion rate during the second and third terms of gestation for *Neospora*-seronegative animals (Almería and López-Gatius, 2013). However, chronic *N. caninum* infection prior to pregnancy seems to be not responsible for abortion before day 90 of gestation (López-Gatius *et al*., 2004b).

Coxiellaburnetii is an intracellular bacterium spread worldwide that causes Q fever in animals and also in humans. Domestic ruminants such as cattle, goats and sheep are considered to be the primary reservoir species for exposure of humans (Arricau-Bouvery and Rodolakis, 2005). Bacteria have been found in placenta or aborted fetuses (Parisi *et al*., 2006), and the main clinical manifestations are late abortion (Woldehiwet, 2004), infertility (To *et al*., 1998) and metritis and placenta retention (López-Gatius *et al*., 2012). Interactions throughout gestation between *Neospora*- and *Coxiella*-infection have been furthermore described in cattle. Both the *N. caninum* and *C. burnetii* infection or the presence of both modifies endocrine patterns throughout gestation. Cows seropositive to both *Neospora* and *Coxiella* had higher plasma progesterone levels (Garcia-Ispierto *et al.*, 2010), and stable *Coxiella*-seropositivity (Garcia-Ispierto *et al.*, 2011).

This presentation, based mainly on our results in northeast Spain, expresses our views on factors affecting early fetal loss in high producing dairy herds and therapeutic approaches to the disorder. Some clinical suggestions on bovine neosporosis and coxiellosis are also highlighted.

Parity status and pregnancy losses

Grouping data derived from two studies reported that (Labèrnia *et al*., 1996; López-Gatius *et al*., 2004b) 2.6% of pregnant heifers suffered fetal loss, whereas 9% losses were registered for 5124 lactating pregnant cows. Our values are comparable to those obtained between 1949 and 1955: 2.5% of losses for heifers and 13% for multiparous Holstein-Friesian cows (Mares *et al*., 1961), and to those compiled from the literature by Santos *et al*. (2004): pregnancy loss was 10.7% for lactating cows and 4.2% for dairy heifers. These findings suggest that genetic selection for high milk production did not affect the incidence of losses during the last decades. Parturition and metabolic stress associated with lactation seems to compromise fetal survival.

The problem of twin pregnancies

Using cows carrying singletons as reference and compiling five studies (López-Gatius *et al*., 2002, 2004c, 2006; López-Gatius and Hunter, 2005; García-Ispierto *et al*., 2006), the minimum odds ratio registered for pregnancy losses for twin pregnancies was 3.1 compared with cows bearing singletons. In the warm period, up to 54% of losses were registered in twin pregnancies (López-Gatius *et al*., 2004c).

Since genetics appears to be a major regulatory factor for twinning rates last decades (Johanson *et al*., 2001), it is reasonable to suggest that increased twinning is a consequence of selection for milk yield, but aside from genetic progress, improvements in nutrition and management practices have led also to a continuous increase in the milk yield. Probably, the improved management at the farm level has diminished the risk of embryo loss in twin pregnancies and thus raised the twinning rate. It is therefore foreseeable that over the years to come, the twinning rate will continue to increase along with milk production.

Twin reduction

Twin pregnancies are undesirable in dairy cattle since they increase not only the risk of early pregnancy loss, but also have many negative effects such as increased abortion, dystocia, retained placenta, calf mortality, occurrence of freemartins, postpartum therapy, and longer rebreeding intervals (Nielen *et al*., 1989; Andreu-Vázquez *et al*., 2012a). Such negative effects of twinning might be diminished by reducing the embryo number in dairy cows.

We evaluated embryo reduction methods by manual rupture of the amniotic vesicle of a twin embryo (López-Gatius, 2005; Andreu-Vázquez *et al*., 2011) or bytrans vaginal ultrasound-guided embryo aspiration (Andreu-Vázquez *et al*., 2012b). Although these techniques should be further investigated, both can provide in the future a satisfactory way for twin reduction in dairy cattle.

It should be noted here the fact that lactation number (López-Gatius *et al*., 2005a), previous twining, as well as environmental factors, such as photoperiod and season and management related to synchronization protocols affect significantly the incidence of twin pregnancies (Andreu-Vázquez *et al*., 2012c).

Spontaneous twin reduction has also been described in cows that remain pregnant. Interestingly, most embryonic mortality (one of the two embryos) occurs at around days 35-40 of gestation so that the fate of twin pregnancies progressing normally until day 60 is either the delivery of both twins or abortion. No fetal death appears to occur after this time point (López-Gatius and Hunter, 2005; López-Gatius *et al*., 2010). Thus, the detection of live twins on day 60 of gestation has enormous implications for the management policy

of a herd. For example, since twins are delivered up to seven days earlier than singletons, the dry-off period can be advanced several days for non-aborting cows carrying twins. Additional care at parturition can further reduce the risk of calf mortality in a twin pregnancy.

Additional corpus luteum, a factor associated with reduced fetal loss

Additional corpus luteum has demonstrated to be a very strong factor reducing fetal loss in pregnancies with a greater number of corpora lutea than the number of embryos. On a total of 363 pregnant cows with an additional corpus luteum derived from five studies (López-Gatius *et al*., 2002, 2004c, 2006; García-Ispierto *et al*., 2006; Bech-Sàbat *et al*., 2008), 1.7% suffered fetal loss, whereas 9.9% losses were registered for 3643 pregnant animals with no additional corpus luteum. However, spontaneous reduction of the additional corpus luteum in multiple ovulating cows that remain pregnant can occur under certain forms of stress (López-Gatius *et al*., 2010).

Therapeutic approaches to early fetal loss

Progesterone is required for supporting gestation; it influences secretor functions of trophoblast and pituitary during the first trimester of gestation (Ayad *et al*., 2007). However, one of the consequences of high milk production is an increased metabolic rate linked to a greater dry matter intake. This process reduces plasma concentrations of steroid hormones such as progesterone (Sangsritavong *et al*., 2002). In fact, milk production can affect negatively plasma progesterone concentrations at the onset of the fetal period (Bech-Sàbat *et al*., 2008; Rhinehart *et al*., 2009). Therefore, it seems reasonable to suppose that one of the causes of early fetal loss in high producing dairy cows could be the suboptimal concentrations of progesterone. Thus, strategies that induce the formation of an additional corpus luteum may help to increase progesterone levels in high producers. However, although treatment with GnRH at AI (López-Gatius *et al*., 2006) and with GnRH or hCG at pregnancy diagnosis (Bartolomé *et al*., 2006; Stevenson *et al*., 2008) clearly increased the number of additional corpora lutea, treatment did not reduce fetal loss in any of the studies.

In order to test the hypothesis that suboptimal progesterone concentrations may compromise conceptus development, we treated pregnant cows with progesterone at pregnancy diagnosis during four weeks (López-Gatius *et al*., 2004d). The risk of pregnancy loss was 2.4 times higher in non-treated cows (n = 549) than in treated ones (n = 549). Under these conditions, intravaginal progesterone supplementation has the potential to reduce the incidence of pregnancy loss during the early fetal period. We could speculate that progesterone supplementation at pregnancy diagnosis could favor placentation, fetal development, or both.

In a more recent study in two herds with high incidence of fetal loss (Bech-Sàbat *et al*., 2009), in cows with one single corpus luteum, the probability of pregnancy loss decreased by a factor of 0.51 in cows treated with progesterone, compared to the GnRH treatment. However, in cows with two or more corpora lutea, progesterone treatment increased the likelihood of pregnancy loss by a factor of 3, compared to GnRH treatment. These results suggest that at pregnancy diagnosis (i.e.: days 28-34), it is so important to register the number of corpora lutea as the number of embryos.

The practical implications of these findings are that in herds with a high incidence of early fetal loss of a non-infectious nature, treatment at the time of pregnancy diagnosis with progesterone in cows with one single corpus luteum and with GnRH in cows carrying twins should offer considerable benefits (Bech-Sàbat *et al*., 2010).

Crossbred pregnancies reduce the abortion risk in *Neosporacaninum*-infected dairy cows

An important finding of our studies addressing the control and prevention of cattle neosporosis in dairy cattle is that the use of beef bull semen reduces the risk of *N. caninum*-associated abortion (López-Gatius *et al*., 2005b). Our retrospective analysis of the effects of different cross-breed pregnancies on the abortion risk in *Neospora*-infected dairy cows returned abortion rates from 32% of 482 cows inseminated with Holstein-Friesian semen, to 22% of 49 cows inseminated with Charolais semen, 20% of 191 cows inseminated with Belgium Blue semen, 19% of 89 cows inseminated with Piedmontese semen, and 10% of 304 cows inseminated with Limousin semen (Almería *et al*., 2009).

Questions regarding bovine coxiellosis

Reproductive disorders related to coxiellosis are frequently described in cattle, but the results are often inconsistent. For example, based on serology, *Coxiella*-seropositivity was linked to placenta retention, to changes in the interval from parturition to conception (with the lowest interval parturition-conception for cows with low level of seropositivity), early pregnancy (cows becoming pregnant before day 90 postpartum), and maintenance of gestation during the early fetal period, while it failed to affect rates of abortion after day 90 of gestation or stillbirth (López-Gatius *et al*., 2012). Extensive studies are needed to understand better the effect of *Coxiella*-infection in the dairy herds.

Concluding remarks

Once a cow has been diagnosed pregnant, early fetal loss is becoming the most common complication of pregnancy in high producing dairy herds. Factors

strongly affecting early fetal loss are parity (cows versus heifers), semen-providing bull, warm season, and twin pregnancies, whereas the presence of an additional corpus luteum has been identified as a strong positive factor favoring pregnancy maintenance. Progesterone and GnRH treatment have the potential to reduce the incidence of pregnancy loss in cows with one or two or more corpora lutea, respectively, in herds with a high incidence of early fetal loss of a non-infectious nature. From a practical point of view, assessment of normal development of gestation on day 60 after insemination is suggested.

Different crossbreed pregnancies carry different abortion risks in *Neospora*-infected dairy cows. The use of beef bull semen (especially Limousin) dramatically reduces the risk of abortion.

Acknowledgments

This work was partly supported by the Spanish CICYT grants AGL2012-39830-C02-01/GAN and AGL2012-39830-C02-02/GAN.

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