Relationship of Maternal Plasma Progesterone and Estrone Sulfate to Dystocia in Holstein-Friesian Heifers and Cows

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ABSTRACT. Thirteen primiparous and 41 multiparous Holstein-Friesian cattle were used to study the relationship between maternal plasma progesterone (P_4) and estrone sulfate (E_1S) concentrations and the prevalence of dystocia. The calvings in 4 heifers and 30 cows were normal (eutocia), while the calvings in 9 heifers and 11 cows were difficult (dystocia). Neither the concentrations of P_4 nor E_1S were different between the groups with eutocia and dystocia from days 90 to 270 of pregnancy. However, a few days prior to parturition, eutocial cows and heifers showed a sharp decline of plasma P_4, while dystocial cattle did not show such a remarkable decline of P_4 concentration. Plasma P_4 levels in dystocial cows a few days antepartum were significantly higher than in eutocial animals ($P<0.05$ or $P<0.01$). Prepartum E_1S concentrations were significantly lower ($P<0.05$) in dystocial than eutocial cattle during the prepartum period from days 6 to 1 in heifers and from days 3 to 1 in cows. These results suggest that insufficient production of E_1S and delayed regression of the corpora lutea are possible causes of dystocia in cattle.—KEY WORDS: bovine, dystocia, estrone sulfate, progesterone.

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Dystocia has been a long-standing problem in bovine reproduction, particularly in primiparous heifers. Cattle that experience dystocia are more likely to be culled from the breeding herd due to late conception or failure to rebreed [5, 12, 37], and calves from a difficult birth are more likely to die or experience neonatal diseases [8, 11, 25]. Moreover, problems during parturition result in reduced milk production [6, 25] and increased costs of management and veterinary services [27].

The causes of difficult calving have been extensively studied and many causal factors associated with fetal [23, 26, 27, 36], maternal [27, 34], combination of fetal and maternal [27, 36], genetical [7–9, 33–35], and environmental [2] factors have been implicated.

Maternal causes of dystocia include uterine inertia, cervical spasm and incomplete dilation, fetopelvic disproportion and uterine torsion [22]. Ripening of the cervix and dilation of the cervix are hormone dependent and are influenced by elevation of plasma estrogens, decline of progesterone (P_4) and increased secretion of $PGF_{2\alpha}$ [21]. It is, therefore, hypothesized that insufficient production of estrogens and delayed decline of P_4 could adversely affect the progress of parturition, leading to dystocia.

O'Brien and Stott [28] previously reported that low serum estradiol-17β ($E_2\beta$) and high P_4 levels were found in dystocial heifer groups 23–12 days prepartum compared to heifers with normal calvings. A possible association between low urinary estrogen excretion, from day 260 of gestation to parturition, and a high incidence of dystocia has also been suggested [31, 32]. Likewise, Erb *et al.* [15] indicated that lower than normal levels of plasma $E_2\beta$ and delayed decline of P_4 before parturition were associated with physiological dystocia. To the contrary, it has been reported that increases of plasma P_4 concentration on the day before calving and of estrone sulfate (E_1S) concentration on the day after calving decreased the odds of difficult calving [30]. Moreover, Graaf *et al.* [17] reported insignificant differences in corrected plasma hormone (P_4, E_1, E_1S, $E_2\beta$ and E_2S) concentrations from 29 to 9 days prepartum between heifers with and without dystocia. Thus, earlier studies have shown no consistent endocrinological feature associated with dystocia.

The objective of the present experiment was to determine if prevalence of dystocia could be influenced by prepartum maternal plasma E_1S and P_4 concentrations in dairy cattle.

MATERIALS AND METHODS

A total of 54 Holstein-Friesian cattle (13 heifers and 41 cows) which were tied in stalls at Rakuno Gakuen University Dairy Farm and calved between July 1996 and July 1997, were used in this experiment. Parities of the cows varied from one to six. The cows were milked twice daily and outdoor exercise in a paddock was allowed for 3 to 4 hr after morning milking. All the animals were inseminated artificially using frozen-thawed semen from 7 Holstein bulls, and were fed according to Japanese Feeding Standards for Dairy Cattle [1]. All animals were healthy and well nourished during the study.

Blood samples (10–20 m*l*) were extracted from the tail vein using 21 gauge needles into heparinized vacuum test tubes once every month from days 90 to 180 of gestation; every 2 weeks from days 181 to 270 of gestation and every day from day 271 of gestation to parturition. The blood was immediately centrifuged (1700 × g, for 15 min), and plasma obtained was stored at −20°C in plastic tubes until

hormone analysis.

Plasma concentrations of P_4 [39] and E_1S [29] were quantified by a radioimmunoassay. The sensitivity of the assays were 1.0 *pg*/tube and 29.7 *pg*/tube, respectively. The intra- and inter-assay coefficients of variation were 9.0% and 11.5% for P_4, and 11.4% and 12.7% for E_1S, respectively.

The calves were weighed before colostrum was given and the dams weighed within 24 hr postpartum. The ratio of calf birth weight to dam post-calving weight was calculated for each individual by calf birth weight × 100/ dam weight. Calving was considered as 'eutocia' if it needed either no assistance or assistance by one person with or without calving ropes for a few minutes, or 'dystocia' if it needed either two or more persons equipped with a mechanical puller or veterinary assistance to perform caesarean section [30]. Other variables included calf sex and gestation length.

Effects of dystocia on hormone concentrations were evaluated by analyses of variance by individual gestation stages and across gestation stages within classifications of dystocia. Incidence of dystocia between groups were compared by the Chi-square test. Differences among means were tested using Least Significant Difference. Variations in the data are given as standard error (SE).

RESULTS

All the calves delivered from the 54 cattle had normal presentation, and were singletons.

Incidence of dystocia was higher for heifers (9/13; 69.2%) than cows (11/41; 26.8%) ($P<0.01$). All 4 heifers with male calves and 5 of 9 heifers with female calves experienced dystocia ($P>0.05$), while 10 of 27 cows with male calves and 1 of 14 cows with female calves experienced dystocia ($P<0.05$).

In the heifers and cows, calf birth weights averaged 43.0 ± 1.5 and 49.0 ± 0.6 kg, dam weights 683.5 ± 10.6 and 761.4 ± 11.2 kg, ratios of calf birth weight to dam post-calving weight 6.3 ± 0.3 and 6.5 ± 0.1, and gestation lengths 282.3 ± 1.2 and 283.7 ± 0.5 days, respectively. Significant differences were not found in these items between eutocial and dystocial heifers or cows. The incidence of dystocia was not influenced by sire, and was not different between parities in cows. Moreover, there were no significant differences in maternal hormonal concentrations between dams which had male or female calves.

Changes of maternal plasma P_4 concentrations during pregnancy in eutocial and dystocial heifers are shown in Fig. 1 (a). The changes of P_4 in both eutocial and dystocial heifers throughout the sampling period appeared to have a downward, but not significant, trend as gestation progressed. The difference in P_4 between days 2 and 1 prepartum was significant in eutocial heifers ($P<0.05$). There was a significant ($P<0.05$) difference in plasma P_4 concentrations between eutocial and dystocial heifers at day 1 prepartum. At this day, eutocial heifers exhibited lower plasma P_4 concentrations compared with the dystocial heifers.

Changes of maternal plasma P_4 concentrations in normal and dystocial cows during pregnancy are presented in Fig. 1 (b). The changes of P_4 in both eutocial and dystocial cows throughout the entire sampling period resembled that of the eutocial and dystocial heifers, but decreased significantly as gestation progressed ($P<0.0001$), P_4 concentrations were particularly decreased ($P<0.01$) during the last 3 days prepartum only in eutocial cows. Moreover, the concentrations of P_4 on days 2 and 1 prepartum were lower in eutocial cows than in dystocial cows ($P<0.05$).

Changes of maternal plasma E_1S concentrations during pregnancy in normal and dystocial heifers are shown in Fig. 2 (a). Plasma concentrations of E_1S tended to increase along with the progress of gestation between days 90 and 270 of gestation both in eutocial and dystocial heifers. E_1S concentrations increased significantly as gestation

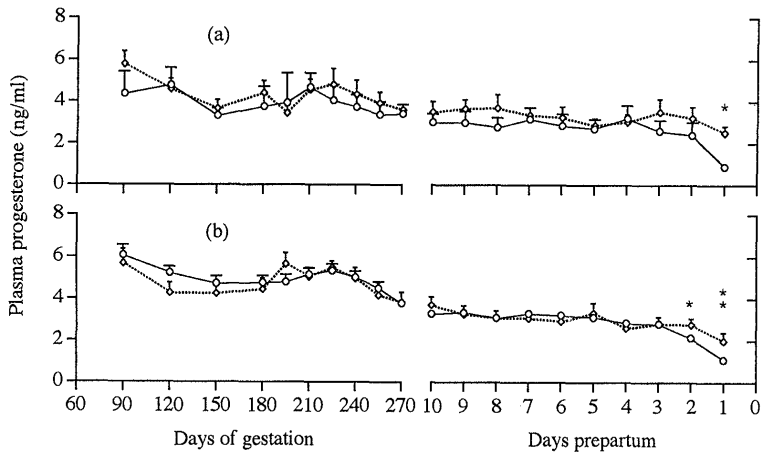

Fig. 1. Comparison of concentration profiles of plasma progesterone between eutocial (—○—) and dystocial (···◇···) heifers (a) or cows (b). * and ** indicate significant differences from eutocial cattle (*P<0.05, **P<0.01).

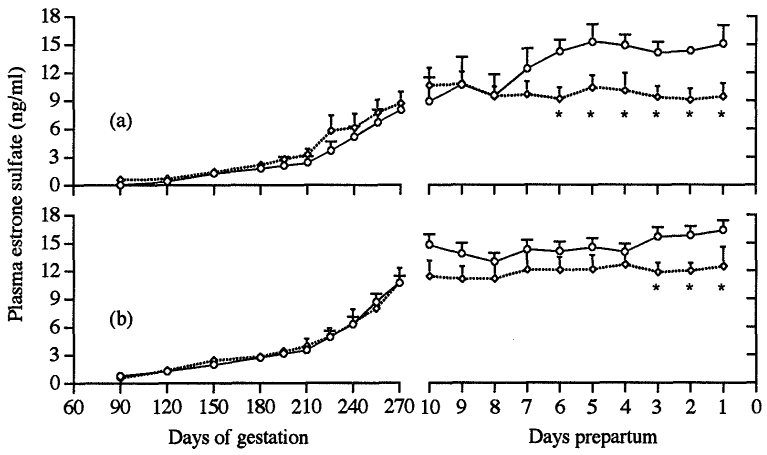

Fig. 2. Comparison of concentration profiles of plasma estrone sulfate between eutocial (-○-) and dystocial (···◇···) heifers (a) or cows (b). * indicates significant differences from eutocial cattle (*P<0.05).

progressed (P<0.0001), while E_1S concentrations between eutocial and dystocial heifers were not different. From days 10 to 1 prepartum, E_1S concentrations in dystocial heifers appeared to reach a plateau, while those in eutocial heifers continued to increase even though the difference among days were not significant. Consequently, E_1S concentrations were higher (P<0.05) in eutocial heifers than in dystocial heifers from days 6 to 1 prepartum.

Changes of maternal plasma E_1S concentrations during pregnancy in normal and dystocial cows are presented in Fig. 2 (b). The changes of E_1S with gestation in both eutocial and dystocial cows throughout the entire sampling period simulated that of the eutocial and dystocial heifers. However, higher (P<0.05) concentrations of E_1S in eutocial cows compared to dystocial cows were observed only between days 3 and 1 prepartum.

There were no significant differences in the mean (in animals with eutocia and/or dystocia) concentrations of P_4 and E_1S between cows and heifers. However, cows with dystocia showed significant differences in P_4 concentrations from 2 days prepartum while dystocial heifers showed significant differences at 1 day prepartum compared to eutocial cows and heifers, respectively. Plasma E_1S concentrations in dystocial heifers, on the other hand, were significantly lower at a much earlier period (from days 6 prepartum), but at a much later period (from days 3 prepartum) in dystocial cows compared to eutocial heifers and cows, respectively.

DISCUSSION

In the present study, no significant difference in P_4 or E_1S concentrations were found between eutocial and dystocial primipara or multipara until the last 1–6 days before parturition. These results might imply that the primary hormonal effects on calving apparently do not occur until the last 1–6 days of gestation, and that P_4 and E_1S may contribute to gestational maintenance and fetal well-being. Moreover, some investigators [28, 30, 31] have provided evidence that the effects of P_4 and estrogens on dystocia occur within 23 days prepartum, similar to the findings in the present study.

In the current study, dystocial cattle, especially multipara exhibited a delay in the P_4 concentration decreases which precede parturition, and the changes were less pronounced than in eutocial heifers or cows. The results demonstrate that not only the magnitude of the prepartum decreases in P_4 but also their timing are important for normal parturition. This implies that earlier and significant decreases in P_4 prepartum might play a positive role in the normal delivery of the calf. With regard to the mechanism, it may be speculated that earlier and significant decreases in P_4 prepartum may play a role in removing the antagonism of P_4 on the myometrial activity, cervical dilatation and the estrogens action. Jöchle *et al.* [24] found increased dystocia rates in cows treated with 100 mg progesterone daily in combination with 10 mg flumethasone to induce parturition.

The conclusion is inescapable that the level of E_1S before parturition may also be one of the major hormonal factors affecting dystocia, and high E_1S concentrations seem to prepare the dam better for parturition, as observed in the present study; E_1S concentrations 3 to 6 days prepartum were higher in eutocial cattle than in dystocial cattle. Olujohunghe *et al.* [30] also reported that increases of E_1S concentration on the day after calving, but not before parturition, decrease the odds of difficult calving. The present study showed for the first time a significant decrease in E_1S concentrations 3 to 6 days prepartum in cows and heifers with dystocia, respectively. Estrogen stimulates $PGF_{2\alpha}$ synthesis from the placental membranes and myometrium which in turn causes regression of the corpora lutea. Elevation of $PGF_{2\alpha}$ lowers the threshold to oxytocin, and oxytocin and/or $PGF_{2\alpha}$ leads to myometrial contractility [20]. Estrogen also correlated positively with relaxation of the pelvic ligaments prepartum [4]. Therefore, these results suggest that a decrease in secretion rate of E_1S from the

fetal placenta before calf delivery, together with the existing rate of metabolic clearance, may result in the concentration of maternal plasma E_1S falling below the level necessary for normal estrogen control of parturition, e.g. of myometrial activity, cervical dilatation, fetal behaviour, righting reflexes and late correctional movements, resulting in difficult calving [16, 30]. Induced parturition is found to be more successful in animals with high endogenous estrogen levels than in animals with low levels [10, 19].

Some previous studies differ from results of the present study in the following respects: (1) increases of plasma P_4 concentration on the day before calving decrease the odds of difficult calving [30]; (2) differences in plasma P_4 or E_1S concentrations between heifers with and without dystocia were not significant [17]. These differences may be attributed to differences in breed and environment as these factors are known to influence progesterone production [3, 40]. While Hereford × Friesian heifers were used in the study of Olujohungbe *et al.* [30] in the UK, Holstein-Friesian heifers were used in the present study. Although no significant differences were observed in plasma P_4 or E_1S between heifers with and without dystocia in samples collected 29 to 9 days prepartum similar to the results of Graaf *et al.* [17], significant differences were noted within the last week prepartum in the current study.

Dystocia is more common in primiparous heifers than in multiparous cows [14, 25]. The present study likewise observed increased incidence of dystocia in primipara than in multipara. More research is needed to determine whether the variances in the timing of significant differences observed in P_4 and E_1S concentrations between animals with eutocia and dystocia makes a contribution to differences in the incidence of dystocia between heifers and cows.

In the present study, all calves were singletons. In dams with twins, dystocia often occurs [18], and P4 and E_1S concentrations differ from dams with singletons [13, 38]. To date, no study has compared the concentrations of P_4 and E_1S in cows or heifers with twins which had dystocia or eutocia. Future studies should focus along this direction.

In conclusion, these results suggest that the insufficient production of E_1S and delayed regression of the corpora lutea might be possible causes of dystocia in cattle.

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