Maternal serum progesterone concentration during pregnancy and lamb birth weight at parturition in Javanese Thin-Tail ewes with different litter sizes

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Abstract

Pregnant ewes, (N=38), with similar body weight and age (19, 13 and 6 carrying 1, 2 and 3 fetuses, respectively) were used to study the relationship between maternal serum progesterone concentration during pregnancy and lamb birth weight at parturition. Average maternal serum progesterone concentration in the ewes carrying 1, 2, and 3 fetuses was: 5.3±0.3, 6.2±0.7 and 6.6±0.5 ng/ml, during weeks 0 to 7 of gestation; 16.9±1.4, 25.3±1.5, and 26.8±2.5 ng/ml, during weeks 8 to 20; and 13.2±1.0, 18.7±1.0, and 19.8±1.7 ng/ml, during the entire gestation period respectively. Total lamb birth weight in ewes carrying 1, 2, and 3 fetuses was 1.9±0.1, 3.2±0.2, and 4.2±0.4 kg, respectively. In the respective litter sizes, ewes with higher mean serum progesterone concentration during the whole pregnancy gave birth to lambs with higher birth weight (r^2=0.76, 0.42 and 0.46, for ewes carrying 1, 2 and 3 fetuses, respectively). The results of the study indicated that prenatal growth could probably be improved by increasing endogenous secretion of maternal progesterone during pregnancy.

Author Keywords: Progesterone; Birth weight; Pregnancy; Sheep

Article Outline

1. Introduction

In sheep, the greater the litter size, the lower the lamb birth weight (Rattray et al., 1974; Bradford et al., 1986). The lower birth weight with the increased litter size could be due to a lower prenatal growth and conditions (Dziuk, 1992). Lower birth weight at parturition and milk production during lactation are the major factors affecting the high mortality rate of the lambs during the preweaning period in Javanese thin-tail sheep (Obst et al., 1980; Sutama et al., 1988; Sutama, 1992; Tiesnamurti, 1992).

Progesterone, along with other hormones directly related to pregnancy, is known for its role in the maintenance of pregnancy through its effects on uterine stromal cell differentiation (Bell, 1984) and secretion of uterine milk protein and stimulation of placental growth and hormone secretion (Bell, 1984; Wheeler et al., 1987; Mulholland et al., 1994). During the placental phase of pregnancy (8 to 20 weeks of gestation), progesterone and placental lactogen are reported to influence nutrient flow to the placenta through its effect on the maternal tissue metabolism (Shirling et al., 1981; Sutter-Dub et al., 1981; Fowden, 1995).

Previous observations suggest lower peripheral progesterone in overfed animals as a reason for the lower embryonal survival and birth weight (Hard and Anderson, 1979; Parr et al., 1987; Ashworth, 1991). Supplementation of progesterone in the overfed animals during early pregnancy has been demonstrated to restore fetal growth and birth weight similar to those in the control animals (Kendall and Hays, 1960; Parr et al., 1987; Ashworth, 1991). These results indicated that progesterone, and probably other hormones and factors secreted by the ovary, corpus luteum, placenta and uterus, could have a significant role in improving prenatal growth.

The dramatic changes in progesterone secretion with increased litter size and the advance of pregnancy in ewes (Manalu et al., 1995; Manalu and Sumaryadi, 1998) and goats (Manalu et al., 1996) could have physiological effects on prenatal growth. However, there are limited experiments to explore the possible correlation of the endogenous secretion of progesterone during pregnancy with prenatal growth in polytocous animals. This present study was designed to correlate mean maternal serum progesterone concentration during pregnancy with lamb birth weight in different fetal numbers in Javanese thin-tail pregnant ewes.

2. Materials and methods

2.1. Experimental design and protocol

Thirty-eight pregnant Javanese Thin-Tail sheep, (19, 13 and 6 ewes carrying 1, 2, and 3 fetuses, respectively) with similar body weight (20–22 kg) and age (2–3 years) at the time of breeding were used in the trial. The experimental ewes were injected (i.m) twice with 1 ml of $PGF_{2\alpha}$ (Prosolvin, Intervet, North Holland, The Netherlands) with an 11-day interval. Three days after the last prostaglandin injection, the ewes were mated naturally by group mating. Blood samples were drawn one day after the last prostaglandin injection (week 0 of pregnancy), and then 10 days after the last prostaglandin injection (7 days after the predicted ovulation, as the end of week 1 of pregnancy). Blood samples were drawn weekly (at the same time of a day) until parturition (weeks 2 to 20 of pregnancy). Birth weight was determined by weighing lambs (individually) at parturition. All ewes gave birth after week 20 of pregnancy, but the day of parturition varied within the 21st week of pregnancy. Weeks of pregnancy were calculated from the predicted day of ovulation (3 days after the last prostaglandin injection).

2.2. Blood sampling and processing

Blood samples in aliquot of 10 ml were drawn with plain vacutainer or sterile syringes from the jugular vein from around 900 to 1000 h weekly. The sampling time was executed consistently prior to feeding. The day of weekly bleeding was chosen based on the 7-day interval from the predicted day of ovulation (assigned as day 3 after the last prostaglandin injection). The blood samples were allowed to clot in a cool ice box and transported to the laboratory for further separation of serum by centrifugation. The serum samples were then kept frozen (−20°C) for later progesterone analyses.

2.3. Progesterone analyses

Serum progesterone concentration was measured in duplicate by the solid-phase technique radioimmunoassay (Diagnostic Products Corporation, Los Angeles, CA), with slight modification for ovine progesterone concentration ranges (Manalu et al., 1996). The radioactivity of progesterone-bound tubes were counted in an automatic gamma counter. The concentrations of standard progesterone samples were used to construct a standard curve ranging from 0.1 to 20 ng/ml. A sample volume of 100 μl serum was used in the assay for samples with serum progesterone concentrations ranging from 0.1 to 20 ng/ml. For samples with progesterone concentrations lower than 0.1 ng/ml, the sample volume was increased to 200 μl to bring the progesterone concentrations in range with the standards used. All serum progesterone concentrations were within the range of the standard progesterone used to construct the standard curve. Inter- and intra-assay variation coefficients were 9.0 and 4.0%, respectively.

2.4. Statistical analyses

Progesterone concentrations were the mean during two phases of pregnancy: the embryonic (weeks 0 to 7), and fetal (weeks 8 to 20) phases of pregnancy. The main effects of litter size and phases of pregnancy with their respective interaction on maternal serum progesterone concentration were tested by an ANOVA, using (animal×phase) as an error term, in a randomized design with factorial arrangement (unequal *n*). Variations in the mean serum progesterone during the total gestation period and lamb birth weight were tested by an ANOVA in a randomized design. The mean maternal serum progesterone concentrations during the whole pregnancy in the respective litter size were correlated with lamb birth weight by using regression and correlation analysis (Snedecor and Cochran, 1982).

3. Results

There was no effect of fetal number on serum progesterone concentration during the embryonic phase (weeks 0 to 7) of pregnancy. Mean maternal serum progesterone concentration during weeks 0 to 7 of pregnancy in the ewes carrying 1, 2, or 3 fetuses was 5.3±0.3, 6.2±0.7, and 6.6±0.5 ng/ml, respectively. During weeks 8 to 20 of gestation, ewes carrying multiple fetuses had a higher progesterone concentration (P<0.01) than those carrying a single fetus. There was no significant difference in serum progesterone concentration between ewes carrying twin and triplet fetuses. The mean maternal serum progesterone concentration during weeks 8 to 20 of pregnancy in the ewes carrying 1, 2, or 3 fetuses was 16.9±1.4, 25.3±1.5 and 26.8±2.5 ng/ml, respectively. Ewes carrying multiple fetuses had a higher mean serum progesterone concentration (increased to 42.1 and 50.3% for twins and triplets, respectively), when compared to those carrying a single fetus (P<0.05). There was, however, no difference in the mean serum progesterone concentration during pregnancy between ewes carrying 2 and 3 fetuses. The mean maternal serum progesterone concentration during the whole period of pregnancy in the ewes carrying 1, 2, or 3 fetuses was 13.2±1.0, 18.7±1.0, and 19.8±1.7 ng/ml, respectively (Table 1).

Table 1. Mean (±SE) maternal serum progesterone (ng/ml) during weeks 0 to 7 ($W_{0–7}$), weeks 8 to 20 ($W_{8–20}$, and during the whole pregnancy period ($W_{0–20}$), and mean lamb birth weight [a]

	Progesterone (ng/ml)			Lamb birth weight (Kg)
LS [b]	$W_{0–7}$	$W_{8–20}$	$W_{0–20}$	
1	5.3±0.3 [c]	16.9±1.4 [c]	13.2±1.0 [c]	1.9±0.1 [c]
2	6.2±0.7 [c]	25.3±1.5 [c]	18.7±1.0 [c]	1.6±0.1 [c]
3	6.6±0.5 [c]	26.8±2.5 [c]	19.8±1.7 [c]	1.4±0.1 [c]

[a] Means and SE of 19, 13, and 6 ewes carrying 1, 2, and 3 fetuses, respectively.

[b] LS, litter size, number of fetuses carried, 1, 2, or 3.

[c] Refers to significant difference (P< 0.05).

As normally observed in prolific sheep, the increased litter size increased the total lamb birth weight curvilinearly, with a resultant decrease in average lamb birth weight (P<0.01). Total lamb birth weights in the ewes carrying 1, 2, or 3 fetuses were 1.9±0.1, 3.2±0.2, and 4.2±0.4 kg, respectively. Total lamb birth weight in the ewes carrying triplets increased by 114 and 28% when compared to those carrying a single or twin fetuses, respectively. The ewes carrying twin fetuses had a total lamb birth weight increase by 67% when compared to those carrying a single fetus. The mean lamb birth weight in the ewes carrying triplet fetuses decreased by 28 and 17% when compared to those in carrying a single or twin fetuses, respectively. In the ewes carrying twin fetuses the average lamb birth weight decreased by 17% when compared to those carrying a single fetus (P<0.05) (Table 1).

Ewes carrying a single fetus, had higher mean maternal serum progesterone concentrations during weeks 0 to 7, 8 to 20, and during the entire pregnancy, and higher lamb birth weight at parturition (P<0.05) (r^2=0.57, 0.75, and 0.76, respectively). The distribution of total lamb birth weight at various maternal serum progesterone concentrations in the ewes carrying a single fetus are setout in Fig. 1. In the ewes carrying twins, ewes with higher mean maternal serum progesterone concentration during weeks 8 to 20, and during the entire gestation had a higher lamb birth weight at parturition (*P*<0.05) (r^2=0.48 and 0.42, respectively). There was a negative correlation between the mean maternal serum progesterone concentration during weeks 0 to 7 with the total lamb birth weight at parturition in this litter size. Distribution of total lamb birth weight at various maternal serum progesterone concentrations in ewes carrying twin fetuses is presented in Fig. 2. In the ewes carrying three fetuses, ewes with higher mean maternal serum progesterone concentration during weeks 0 to 7, 8 to 20, and during the entire pregnancy had a higher lamb birth weight at parturition (*P*<0.05) (r^2=0.54, 0.52, and 0.46, respectively). Distribution of total lamb birth weight at various maternal serum progesterone concentrations in the ewes carrying triplet fetuses are setout in Fig. 3.

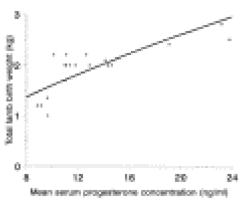
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Fig. 1. Total lamb birth weight at parturition within various ranges of serum progesterone concentrations during the entire gestation period in Javanese thin-tail sheep carrying a single fetus.

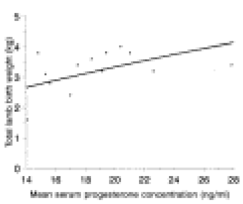
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Fig. 2. Total lamb birth weight at parturition within various ranges of serum progesterone concentrations during the entire gestation period in Javanese thin-tail sheep carrying twin fetuses.

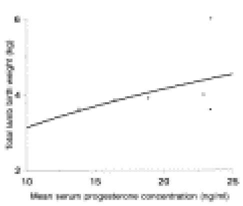
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Fig. 3. Total lamb birth weight at parturition within various ranges of serum progesterone concentrations during the entire gestation period in Javanese thin-tail sheep carrying triplet fetuses.

4. Discussion

The reason for higher maternal serum progesterone with increased litter size and advance of pregnancy in Javanese thin-tail ewes was setout by Manalu et al. (1995) and Manalu et al. (1996) and Manalu and Sumaryadi (1998). Ewes with a higher litter size had higher ovulation rates (Piper and Bindon, 1984; Bradford, 1985; Bradford et al., 1986) that resulted in higher number of corpora lutea as sources of progesterone during the embryonic phase (weeks 0 to 7) of pregnancy and, probably, throughout the pregnancy period. However, the increased maternal serum progesterone concentration was not linearly correlated with the increased number of corpora lutea in goats (Amstrong et al., 1982; Amstrong et al., 1983a and Amstrong et al., 1983b) and in sheep (Quirke et al., 1979; Sumaryadi and Manalu, 1995), as there are greater variation in size and activities with the increased number of corpora lutea and the placenta. The dramatic increase in maternal serum progesterone concentration during the fetal phase (weeks 8 to 20) of pregnancy is due to the role of the placenta as a source of progesterone (Ricketts and Flint, 1980; Sheldrick et al., 1981). Ewes with a higher litter size had heavier placental tissue (Rattray et al., 1974; Manalu et al., 1998), however, the higher the litter size the lower the weight of the individual placenta (Bell, 1984). Variations in the number and activities of the corpora lutea and the decreased individual weight of the placenta with the increased litter size could affect the greater variations in maternal serum progesterone concentration in the ewes carrying multiple fetuses.

The effect of progesterone on the increased lamb birth weight could have been mediated through its role in directing gene expression in uterine stromal cells (Mulholland et al., 1994) that resulted in stimulation of the uterine and placental growth. Better developed uterine environment could increase nutrients and growth factor secretions and exchanges required to support the developing embryo (Findlay et al., 1981; Bell, 1984; Ashworth and Bazer, 1989a and Ashworth and Bazer, 1989b; Ashworth et al., 1989; Ashworth, 1991 and Ashworth, 1992). Current results indicated that superovulated ewes with higher serum progesterone concentration had heavier uterine tissue and fetal weight at the end of the embryonic phases of pregnancy (week 7 of pregnancy) (Manalu et al., 1998).

Better developed placentas could contribute more to the growth of the fetus (Robinson et al., 1995), as nutrients supply in the placenta was not a limiting factor. The effect of progesterone concentration during placental phase of pregnancy on lamb birth weight is probably, in part, mediated by the reported effects of progesterone on body energy reserves partitioning to the placenta. Some reports indicated that higher progesterone levels could mobilize more fatty acid and glucose from body reserves to the maternal circulation (Shirling et al., 1981; Sutter-Dub et al., 1981; Fowden, 1995) that, in turn, could be used by the fetus through the placenta and increased fetal growth (Robinson et al., 1995; Fowden, 1995). A better developed placenta produced more placental lactogen and other hormones and factors (Robinson et al., 1995) that could eventually influence fetal growth through their effects on maternal body energy reserves mobilization (Annison et al., 1984; Bell, 1984; Fowden, 1995) and fetal glycogen synthesis (Hill, 1989; Breier et al., 1994).

In the ewes carrying twins, serum progesterone concentration was negatively correlated to the lamb birth weight at parturition, while in the ewes carrying singletons and triplets the correlation was positive. When weekly-individual data were observed closely, there was an indication that ewes with a continuing higher serum progesterone concentration throughout and during the placental phase of pregnancy had heavier lambs at parturition. In the ewes carrying twins, some ewes having higher serum progesterone levels during the luteal phase of pregnancy did not maintain higher concentrations during the placental phase of pregnancy. Some ewes with lower progesterone levels during the luteal phase of pregnancy had a higher progesterone concentrations during the placental phase of pregnancy and vice versa.

The greatest increase in serum progesterone concentration observed in this study occurred at the same period of fastest growth rate of the fetus, i.e. during placental phase of pregnancy (Rattray et al., 1974). The increased lamb birth weight with the increased maternal serum progesterone concentration in the ewes carrying a single fetus was greater than in those carrying multiple fetuses. This observation seems to be associated with the ratio between the mean progesterone level and fetal numbers, which decreased with an increased fetal number.

These data also indicated that there are some factors other than serum progesterone concentration that also contributes to the prenatal growth. Placental weight was also reported to be positively correlated with the fetal insulin secretion (Bell, 1984). Litter size was also reported to be positively correlated with the placental lactogen secretion (Hayden et al., 1979 and Hayden et al., 1980; Butler et al., 1981), and placental lactogen was reported to have lipolytic and diabetogenic activities (Annison et al., 1984; Bell, 1984; Fowden, 1995), and to increase fetal glycogen synthesis (Hill, 1989; Breier et al., 1994). The increased lipolytic and diabetogenic activities of placental lactogen and secretion of fetal insulin would increase nutrient availability in the maternal circulation and facilitate organic matter deposition in fetal tissue, resulting in a higher fetal growth.

There is still ample room for progesterone and other hormones and factors, secreted by the ovary, corpus luteum and placenta, to exert an effect on improving prenatal growth, especially in the ewes carrying a bigger litter size. Increasing maternal serum progesterone beyond normal concentrations, by superovulation, had been shown to increase fetal weight at week 15 of pregnancy (Manalu et al., 1998). The overall effects of increasing endogenous secretion of progesterone by superovulation on lamb birth weight are being studied.

5. Conclusion

The increased maternal serum progesterone concentration during pregnancy had a significant effect on the lamb birth weight at various litter sizes in Javanese Thin-Tail sheep. The effects were greater in the ewes carrying a single fetus.

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