THE EFFECT OF SUPEROVULATION PRIOR TO MATING ON FETAL GROWTH IN LAMBS FROM JAVANESE THIN-TAIL EWES

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ABSTRAK

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Duapuluh sembilan fetus (11 ekor dari 9 induk yang tidak disuperovulasi dan 18 ekor dari 8 induk yang disuperovulasi) telah diamati untuk mempelajari pengaruh superovulasi sebelum perkawinan pada bobot fetus, panjang fetus, panjang badan dan tungkai, lingkar dada, bobot badan, kepala, Ieher, tungkai dan organ jeroan. Induk yang disuperovulasi, meskipm dengan jumIah anak seperindukan yang lebih tinggi, mempunyai pertumbuhan fetus yang lebih besar seperti ditunjukkan oleh bobot dan panjang fetus, panjang dan bobot badan dan tungkai yang lebih tinggi pada umur 49 hari kebuntingan. Pada umur kebuntingan 105 hari, domba superovulasi dengan anak kembar (≥3) mempunyai pertumbuhan fetus yang sarna dengan anak tunggal dan kembar dari induk yang tidak disuperovulasi. Akan tetapi, domba superovulasi dengan anak tunggal mempunyai pertumbuhan fetus yang lebih pesat seperti ditunjukkan oleh robot dan panjang fetus, pajang badan dan tungkai, lingkar dada, dan bobot badan dan tungkai, dan organ jeroan dibandingkan dengan anak tunggal dan kembar dari induk yang tidak disuperovulasi. Hasil percobaan ini menunjukkan bahwa superovulasi sebelum perkawinan dapat digunakan untuk memperbaiki pertumbuhan prenatal selama kebuntingan.

Kata kunci: Superovulasi, pertumbuhan fetus, kebuntingan, domba

ABSTRACT

MANALU, W. 1999. The effect of superovulation prior to mating on fetal growth in Iambs from Javanese thin-tail ewes. *Jurnal Ilmu Ternak dan Veteriner 4* (4): 243-250.

Twenty-nine fetuses (11 fetuses *from* 9 non-superovulated ewes and 18 fetuses from 8 superovulated ewes) were used to study the effect of superovulation of ewes prior to mating on fetal weight, fetal length, the length of the body and limbs, chest circumference, weights of the body, head, neck, limb, and viscera. Superovulated ewes, though with a higher litter size, had a greater fetal growth as was indicated by the greater fetal weight and length, the length and weight of the body and limb on day 49 of pregnancy. On day 105 of pregnancy, superovulated ewes with multiple fetuses (≥3) had similar fetal growth than non-superovulated ewes with single and twin fetuses. However, superovulated ewes with a single fetus had greater fetal growth as was shown by the greater fetal weight and length, the length of the body and limbs, chest circumference, and weight of the body, limb, and viscera when compared to those non-superovulated ewes with a single or twin fetuses. The results of the experiment suggested that superovulation of ewes prior to mating could be used to improve fetal prenatal growth during pregnancy.

Key words: Superovulation, fetal growth, pregnancy, sheep

INTRODUCTION

Birth weight and postnatal life of rhany domestic animals are profoundly affected by prenatal growth conditions (DZIUK, 1992). Growth and development of the embryo during the embryonic stage of pregnancy are influenced by uterine factors (DENKER, 1994). The growth of the uterine tissues with the overall biochemical changes before implantation are stimulated by estradiol in combination with progesterone (MULHOLLAND *et al.,* 1994). Fetal growth during the fetal stage of pregnancy are influenced by placental growth and development (ROBINSON *et al.,* 1995).

Ewes with higher mean serum progesterone during pregnancy give birth to heavier lambs at parturition (MANALU and SUMARYADI, 1998). Superovulation increases maternal serum progesterone concentration, uterine and fetal weight during pregnancy (MANALU *et al.,* 1998), and maternal serum progesterone, fetal weight and uterine weight are positively correlate (MANALU, 1999). Superovulation improves birth weight especially in the multiple litter size (MANALU *et al.,* 1999c). This paper reports the effects of superovulation prior to mating on fetal weight and length, the length and weight of the body parts and viscera in sheep.

MATERIALS AND METHODS

Experimental design and protocol

Forty of Javanese thin-tail ewes lambs, ranging from 14 to 16 kg and 1 to 1,5 years of age at the beginning of experiment, were maintained in individual pens with a two-month adaptation to the experimental conditions prior to treatment..

The experimental ewes were injected twice with 7.5 mg of PGF2a (i.m) at.an II-day interval. Twenty of the experimental ewes were injected with 700 IV of PMSG (Folligon, Intervet, North Holland) at the time of the last prostaglandin injection (around the end of diestrus), to stimulate superovulation and to increase circulating maternal progesterone concentrations, and the others (20 ewes) with saline as a control. Two days after the last prostaglandin injection, at the onset of estrous cycle, the experimental ewes were individually mated. During pregnancy, the ewes were fed ad libitum with a high quality of ration (15% CP and 75% TDN). At the beginning of the experiment, 20 ewes were allocated to be sacrificed at week 7 of pregnancy, and the others (20 ewes) at week 15 of pregnancy. Of the 20 ewes slaughtered at week 7 of pregnancy, only nine ewes (6 non-superovulated ewes [with a mean CL number of 3.0 ± 0; and single fetus] and 3 superovulated ewes 9 with a mean CL number of 7.0 ± 0.6; and only twin and three triplets) were actually pregnant. Of the 20 ewes slaughtered at week 15 of pregnancy, only eight ewes (3 non-superovulated ewes [with a mean CL number of 2.7± 0.7; and one single and three twins] and 5 superovulated ewes [with a mean CL number of 8.2 ± 1.1; five singles, one triplet and one quadruplet) were actually pregnant (Tables 1 and 3). The other ewes were nonpregnant, and were excluded from the data analysis. The number of observed fetuses in the non superovulated ewes was 11 (6 and 5 fetuses at weeks 7 and 15 of pregnancy, respectively), and in the superovulated ewes was 18 (8 and 10 at weeks 7 and 15 of pregnancy). The number and weight of fetuses were, determined for each ewe and tIle fetal body parts (the head, neck, body, fore and hind legs) and viscera (the liver, heart, kidney, and lungs) weights were measured. The length of the fetus, the body parts (the body and legs) was recorded to the nearest 1 mm. At 7 weeks of age, the viscera could not be separated from the fetus and therefore weights were not recorded.

Statistical analyses

Since the number of observations was limited, and uneven distribution of fetal number within the same treatment in each age of pregnancy, the differences between means of parameters measured for non-superovulated and superovulated ewes were analyzed by using Student Test (SNEDECOR and COCHRAN, 1982). Observations on week seven and week 15 of pregnancy were also analyzed separately.

RESULTS

Week 7 of pregnancy

All non-superovulated ewes had a single litter size, and superovulated ewes had multiple fetuses (2 and 3), and therefore total fetal weight was greater ($P < 0.05$) in the superovulated ewes (with means 9.5 ± 0.3 and 34.5 ± 2.6 g, in the non-superovulated and superovulated ewes, respectively). Given the higher litter size in the superovulated ewes, average fetal weight in the superovulated ewes was consistently higher than in non-superovulated ewes (with means 9.5 ± 0.3 and 12.9 ± 0.7 g, in the non-superovulated and superovulated ewes, respectively) (Table 1). In spite of the higher litter size, the fetus of superovulated ewes had greater skeletal growth with a longer linear size and chest circumference ($P < 0.05$). Average fetal length, the length of the body and legs, and tile chest circumference are presented in Table 1. The weights of the head, body, hind leg of tile fetus of superovulated ewes were greater than those of non-superovulated ewes. However, the weights of the neck and fore leg were similar ($P > 0.05$) in the fetuses of superovulated and superovulated ewes (Table 2).

Table 1. Number of corpora lutea, fetuses, fetal weight, feta11ength, chest circumference, fore and hind limbs lengths of the non-superovulated and superovulated ewes slaughtered at week 7 of pregnancy

Treatment	Ewes	Number of		Fetal weight (g)		Fetal length (cm)		Chest Circum ference (cm)	Leg length (cm)	
	ID	CL	Fetus	Total	Individual	Body	Fetus		Fore	Hind
Non-superovulation	I (80)	3	1	8.5	8.5	2.9	10.3	4.6	2.7	2.6
	2 (79)	3	1	9.6	9.6	3.3	10.5	4.4	2.5	2.3
	3 (86)	3	1	10.6	10.6	3.2	9.8	4.5	2.6	2.1
	4 (19)	3	1	8.5	8.5	2.9	10.3	4.6	2.7	2.6
	5 (10)	3	1	10.0	10.0	3.2	10.5	4.5	2.8	2.6
	6 (06)	3	1	9.5	9.5	3.2	9.9	4.6	2.8	2.4
	Mean	3.0b	I.0b	9.5b	9.5b	3.1 b	10.2b	4.5b	2.7b	2.4b
	SE	0.0	0.0	0.3	0.3	0.07	0.1	0.03	0.05	0.08
Superovulation	7 (35)	7	3	40.6	14.5	3.6	10.7	5.4	3.6	3.2
					14.3	3.4	10.8	5.1	3.5	3.0
					11.8	3.0	10.6	4.9	3.0	2.8
	8 (34)	6	3	32.9	10.2	3.3	10.7	4.4	3.1	3.0
					11.1	3.4	10.8	4.7	2.8	2.9
					11.6	3.4	10.6	4.7	2.9	2.8
	9 (038)	8	2	30.0	15.0	3.5	11.5	5.5	3.4	3.3
					15.0	3.8	11.5	5.3	3.3	3.1
	Mean				12.9b	3.4 b	10.9b	5.0b	3.2 b	3.0a
	SE				0.7	0.08	0.13	0.14	0.1	0.06

a.b Different superscript in the same column refers to significant differences between non-superovulated and superovulated fetus

Table 2. The weights of the fetal head, neck, body, fore and hind legs of the non-superovulated and superovulated ewes slaughtered at week 7 of pregnancy

Treatment	Ewes ID	Weight (g)								
		Head	Neck	Body	Fore leg	Hind leg	Liver	Heart	Kidney	Lung
Non-superovulation	I (80-1)	2.8	0.7	3.9	1.2	0.8	nd	nd	nd	nd
	2 (79-1)	2.5	0.3	4.3	0.5	0.4	nd	nd	nd	nd
	3 (86-1)	2.5	0.6	4.3	0.6	0.4	nd	nd	nd	nd
	4 (19-1)	2.8	0.7	3.9	1.2	0.8	nd	nd	nd	nd
	5 (10-1)	2.8	0.6	4.2	0.7	0.6	nd	nd	nd	nd
	6 (06-1)	2.9	0.9	4.1	0.8	0.5	nd	nd	nd	nd
	Mean	2.72b	0.6a	4.12b	0.8a	0.58b				
	SE	0.07	0.08	0.07	0.12	0.07				
Superovulation	7 (353)	3.8	0.9	7.0	1.1	0.8	nd	nd	nd	nd
		4.0	0.9	6.6	1.2	1.1	nd	nd	nd	nd
		3.3	0.6	5.4	1.0	0.8	nd	nd	nd	nd
	8 (34-3)	2.8	0.4	4.3	0.8	0.4	nd	nd	nd	nd
		2.8	0.3	5.1	0.7	0.5	nd	nd	nd	nd
		2.8	0.4	5.5	0.8	0.6	nd	nd	nd	nd
	9 (38-2)	4.3	0.7	7.4	1.0	0.8	nd	nd	nd	nd
		4.5	0.5	7.0	1.1	0.9	nd	nd	nd	nd
	Mean	3.6a	0.59a	6.04a	0.96	0.74				
	SE	0.24	0.08	0.39	0.06	0.08				

1Numbers in parenthesis are ewes number and litter size

a.b Different superscript in the same column refers to significant differences between non-superovulated and superovulated fetus

Week 15 of pregnancy

Litter size of the non-superovulated and superovulated ewes was not significantly different. However, superovulated ewes had three singletons, one triplet and quadruplet. fetuses, respectively, while non-superovulated ewes had one singleton and two twins, respectively. Total mean fetal weight in the superovulated (1137.9 ± 257.3 g) was higher than non-superovulated ewes (885.2 ± 207.3 g), with average fetal weight in the non-superovulated and super-ovulated ewes was being 530.0 ± 36.1 and 569.0 ± 48.3 g, respectively) (Table 3). When individual data observed closely, average fetal weight of superovulated ewes with a single fetus was in the order of 760 g or greater, while that of non-superovulated ewes was lower than 615 g. The lengths of the fetus, body, hind leg and chest circumference were similar in the superovulated and non-superovulated ewes (Table 3). However, the length of the fore leg of superovulated fetus was longer than that of non-superovulated fetus ($P < 0.05$). The weights of the body parts and viscera were similar, except liver weight was higher in the fetus of superovulated ewes than that of non-superovulated ewes (Table 4). When individual data observed closely, averages of all fetal variables measured in the superovulated ewes with a single fetus were higher than those of non-superovulated ewes. Given that 70% of the fetuses in the superovulated group were multiple (≥ 3), the nonsignificant difference in linear size and weight of the body parts and viscera indicated that superovulation improved fetal growth.

Table 3. Number of corpora lutea, fetuses, fetal weight, fetal length, chest circumference, fore and hind limbs lengths of the non-superovulated and superovulated ewes slaughtered at week 15 of pregnancy

Treatment	Ewes ID	Number of		Fetal wight (g)		Fetal length (cm)		Chest circumfrence	Limb length (cm)	
		CL	Fetus	Total	Individual	body	Fetus		Fore	Hind
Non-superowlation	1 (90)	4	2	951.6	535.0	13.9	38.1	18.2	15.1	16.5
					411.0	13.5	35.2	16.5	16.8	16.7
	2 (97)	2	2	1206.4	596.4	16.0	37.5	19.9	17.3	18.4
					610.0	14.8	39.5	18.3	17.2	18.0
	3 (89)	2	1	497.6	497.6	15.0	36.2	18.7	15.5	17.5
	Mean	2.1b	1.7a	885.2b	530.0a	14.6a	37.3a	18.3a	16.4b	17.4a
	SE	0.7	0.3	207.3	36.1	0.4	0.8	0.5	0.5	0.4
Superovulation	4 (03)	6	4	2079.5	492.9	14.9	40.4	19.5	17.8	18.7
					404.8	13.4	35.2	16.6	16.4	16.8
					615.0	14.4	37.9	18.4	18.6	19.1
					566.8	15.8	39.8	18.3	18.5	18.3
	5 (73)	7	3	1305.1	432.7	13.5	36.0	16.4	17.1	16.9
					409.0	13.4	35.5	15.7	17.3	15.8
					463.4	14.1	37.1	16.1	17.6	16.6
	6 (45)	9	1	775.1	775.1	15.8	41.8	21.5	17.8	17.7
	7 (68)	12	1	770.0	770.0	16.7	41.4	19.5	20.2	20.7
	8 (50)	7	1	760.0	760.0	16.5	39.6	19.9	23.1	21.0
	Mean	8.2a	2.0a	1137.9a	569.0a	14.9a	38.5a	18.2a	18.4a	18.2a
	SE	1.1	0.6	257.3	48.3	0.4	0.8	0.6	0.6	0.6

[a,b] Different superscript in the same column refers to significant differences between non-superovulated and superovulated fetus

Table 4. The weights of the fetal head, neck, body, fore and hind legs and the viscera (the liver, kidney, heart and lung) of the non-superovulated and superovulated ewes slaughtered at week 15 of p regnancy

Treatment	Ewes ID 1	Weight (g)								
		Head	Neck	Body	Fore leg	Hind leg	Liver	Heart	Kidney	Lung
Non-superovulation	I (90-2)	105.1	30.1	241.0	69.8	77.2	27.9	5.0	6.4	19.8
		87.5	30.0	167.0	51.8	57.0	20.0	3.7	5.0	16.1
	2 (97-2)	1I1.0	39.9	262.0	81.0	84.5	28.8	4.5	7.4	21.5
		106.3	39.5	266.0	83.4	87.1	28.4	5.5	7.3	18.9
	3 (89-1)	93.8	29.2	224.0	65.8	66.0	32.0	4.4	6.4	22.5
	Mean	100.74a	33.74a	232.00a	70.36a	74.36a	27.42b	4.62a	6.50a	19.76a
	SE	4.35	2.44	17.92	5.70	5.68	1.99	0.30	0.43	1.11
Superovulation	4 (03-4)	1I1.6	43.4	281.7	84.5	86.0	36.8	5.3	7.4	25.6
		78.5	22.0	164.8	49.6	51.1	16.1	3.8	5.9	14.3
		90.7	71.3	222.0	65.8	69.4	90.3	3.9	5.6	22.0
		106.2	32.2	269.5	74.5	71.8	32.1	3.4	6.8	26.9
	5 (73-3)	87.1	24.6	179.9	62.5	60.0	25.0	3.9	5.8	18.1
		91.3	29.8	187.0	59.5	64.6	25.8	4.2	5.6	18.8
		81.8	28.2	144.7	55.8	55.5	22.0	3.1	5.2	16.4
	6 (45-1)	124.6	44.8	384.0	93.4	89.9	63.8	7.7	10.0	33.5
	7 (68-1)	1I5.5	49.0	314.0	98.8	93.1	51.4	5.9	10.1	24.2
	8 (50-1)	122.8	47.5	316.0	100.3	100.1	47.9	6.1	10.3	23.0
	Mean	101.01a	39.28a	246.36a	74.47a	74.15a	41.12a	4.73a	7.27a	22.28a
	SE	5.43	4.73	24.87	5.90	5.40	7.20	0.46	0.66	1.80

'Numbers in parenthesis are ewes number and litter size

[a.b] Different superscript in the same column refers to significant differences between non-superovulated and superovulated fetus

DISCUSSION

The results of the present observation strongly confirmed that superovulation prior to mating improved fetal growth. In the ewes slaughtered at week 7 of pregnancy, superovulation increased fetal linear size and weight, though litter size was larger. Given the larger litter size in the superovulated group in this age of pregnancy, similar fetal variables in the non-superovulated and superovulated groups would mean an improvement in fetal growth. since larger litter size decreases average or individual fetal weight and its linear size (RATTRAY *et al.,* 1974). However, in the superovulated group, with larger litter size, fetal weight, fetal length, chest circumference, limbs length, the weight of the head, body, and hind leg were dramatically higher than in the non-superovulated group, with a nonsignificant but still numerically higher neck and fore leg weights. It meant that superovulation not only improved fetal size of multiple fetus similar to that of a single fetus, but even exceeded the variables to a greater extent.

In the group of ewes slaughtered at week 15 of pregnancy, superovulation did not significantly, but numerically, increase all variables measured, except the length of fore leg and liver weight were greater in the superovulated fetuses. Again, since 70% of the fetuses in the superovulated group were multiple fetuses, the similarity in the fetal size meant a greater improvement in fetal growth of the multiple fetuses. Singleton fetus in tllis group (Tables 3 and 4) had distinctly greater size than multiple fetuses in the same group, and in the non-superovulated group. The deficiency of this study, however, was the unequal distribution of litter size in the treatment group so the effect of superovulation in different litter size could not be tested statistically. Nevertheless, this preliminary work could stimulate further experiment in exploring the use of superovulation in improving animal production. The effects of superovulation on fetal growth were greater during the embryonal stage of pregnancy than during the fetal stage of pregnancy. This could be due to the lower magnitude of progesterone concentrations in the superovulated ewes slaughtered at week 15 than those slaughtered at week 15 of pregnancy (MANALU *et ai.,* 1998), since during this period of observation maternal nutritional status does not influence fetal growth (RATTRAY *et ai.,* 1974), and the ewes were fed ad libitum with a high quality ration.

How did superovulation improve prenatal growth? Superovulation of animals increases preovulatory estrogen and progesterone concentration after ovulation (KANEKO *et al.,* 1990; SCHALLENBERGER *et al.,* 1990; MEHMOOD *et al.,* 1991; SAVIO *et ai.,* 1991; WUBISHET *et al.,* 1991; KANEKO *et al.,* 1992; MANALU *et al.,* 1998). In sheep, the increased maternal serum progesterone concentration is maintained during pregnancy and associates with the increased fetal and uterine weights (MANALU *et al.,* 1998). The level of maternal progesterone concentrations during pregnancy highly correlates with uterine, placental, and fetal growths (MANALU, 1999). The increased serum progesterone concentrations could have a dramatic effect on the stimulation of uterine growth, since progesterone is found to direct gene expression in uterine stromal cells (MULHOLLAND *et ai.,* 1994). Some other hormones and growth factors secreted by the corpora lutea (i.e., estradiol, relaxin and growth factors) might have been increased and have additive effects on uterine growth (MURRAY, 1992; HUANG *et al.,* 1997). Insulin-like growth factor system is one of a number of regulatory system mediating steroid hormone actions in the uterus, and its secretion increases during early pregnancy in the superovulated rat (KATAGIRI *et al.,* 1996).

Greater uterine growth could increase uterine secretions (SUMARYADI *et al.,* 1994), and could have improved the synchrony between uterus and embryo and fetus (ASHWORTH, 1992; GANDOLFI *et al.,* 1992; GEISERT *et al.,* 1992) leading to a greater fetal growth. The effect of superovulation on uterine and fetal growth could be partly associated with the increased secretory activities of the uterine gland, and the size of the placenta as a result of the increased hormonal stimulation produced by the corpus luteum, and estrogen in combination with progesterone are reported to change secretory activity of the uterine glandular epithelium (MURRAY, 1992). A better developed uterine environment could increase nutrients and growth factor secretions and exchanges required to support the developing embryo (FINDLAY *et li.,* 1981; BELL, 1984; ASHWORTH and BAZER, 1989a,b; ASHWORTH *et al.,* 1989; ASHWORTH, 1992).

Increase in placentall size and placental lactogen production could in part contribute to the fetal growth. Placental weight positively correlates with placental lactogen concentration and fetal weight (SCHOKNECHT *et al.,* 1991), estrogen and progesterone concentrations (RASBY *et al.,* 1990). Other study reports that placental lactogen and insulin-like growth factor have positive correlations with fetal size in the end of pregnancy in sheep (GLUCKMAN and BARRY, 1988). Insulin-like growth factor also associates with the enhancement of bone maturation in the fetus (ROBINSON *et al.,* 1995). This could explain why the lambs of superovulated ewes had longer linear size.

Previous observation shows that ewes with higher progesterone concentrations during pregnancy have heavier lambs at parturition in a single and multiple litter sizes (MANALU and SUMARYADI, 1998; MANALU and SUMARYADI, 1999).Administration of progesterone in the early pregnancy in sheep and cattle improves fetal weight (GARRETT *et al.,* 1988; KLEEMANN *et al.,* 1994). Superovulated ewes have heavier lambs at parturition, especially with multiple litter size (MANALU *et al.,* 1999c). The implication of the results obtained in this study is that prenatal growth of the mammalian fetus could be improved by increasing endogenous hormonal secretion during pregnancy by superovulation. The number of follicles in the ovaries of female mammalians is abundant and only a small part of them are ovulated during the life time of the animal. Since the hormones and growth factors secreted should be comparable to the number and size of corpora lutea formed, the increase in hormones of pregnancy should be in proportion, and should be no harm to the conceptus. However, study in rats showed that superovulation increases embryonic loss (KATAGIRI *et al.,* 1996) due to changes in electrolyte composition of uterine luminal fluid caused by the increased secretion of insulin-like growth factor I (KATAGIRI *et al.,* 1997) in response to hyperestrogenaemia. Study in sheep shows that estrogen concentrations in the superovulated ewes during early and mid pregnancy does not different from those in non-superovulated ewes (4.83 ± 0.40 and 5.56 ±0.37 pg/ml in the non-superovulated and superovulated ewes, respectively, at week 7 of pregnancy, and 11.04 ± 0.74 and 11.57±0.42 pg/ml in the non-superovulated and superovulated ewes, respectively, at week 15 of pregnancy) (MANALU *et al.,* 1999, unpublished observation).

Regardless of the tendency of higher embryonic loss in the superovulated rats, superovulation in sheep has been succeeded in maintaining pregnancy until parturition, and the lambs of superovulated ewes could survive with a better performance at least until weaning (MANALU *et al.,* 1999c). In addition, superovulation of ewes prior to mating increases milk production during lactation (MANALU *et al.,* 1999a,b; FRIMAWATY and MANALU, 1999), which have positive effects on lambs preweaning growth (MANALU *et al.,* 1999c) in meat-producing animals or in increasing milk production in dairy animals. In conclusion, superovulation of ewes prior to mating improved fetal growth (linear growth and weight) at least until day 105 of pregnancy. The effect of superovulation on fetal growth was greater during the embryonal stage than during fetal stage of pregnancy. The effects of superovulation on fetal growth, lamb growth and milk production merits further study using a greater experimental unit with different litter size as well as different mammalian species.

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