MAK HILL Publications Journal of Animal and Veterinary Advances

Research Article
doi: 10.36478/makjava.2024.3.1.4

OPEN ACCESS

Key Words
Progranulin, morkaraman sheep, pregnancy

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Received: 10 June 2024
Accepted: 30 July 2024
Published: 15 August 2024

Citation: Banu Atalay, 2024. Article Comparison of Serum Progranulin Levels in Early and Late Pregnancy Periods in Morkaraman Sheep. J. Anim. Vet. Adv., 23: 1-4, doi: 10.36478/makjava.2024.3.1.4

Comparison of Serum Progranulin Levels in Early and Late Pregnancy Periods in Morkaraman Sheep

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ABSTRACT
Progranulin is a recently discovered pleiotropic growth factor-like protein produced from various tissues that is involved in various pathological and physiological processes. The aim of the present study was to determine serum progranulin levels in Morkaraman sheep, a common sheep breed in the Southeastern Anatolia Region, during early and late pregnancy. For this purpose, 32 healthy, pregnant Morkaraman sheep were selected and blood samples were taken between October and March 2023-2024. Early and late pregnancy periods were determined as sampling times. Serum progranulin levels (ng/ml) were measured from the blood samples taken and the relationship between pregnancy periods was determined. Accordingly, it was observed that serum progranulin levels were higher in early pregnancy compared to late period. As a result, it was suggested that this decrease in serum progranulin levels in late pregnancy may be related to decreased ovarian and follicular activity. In addition, a contribution was made to the literature on early and late pregnancy periods in Morkaraman sheep.

INTRODUCTION

Progranulin (PRGN), is a pleiotropic growth factor-like protein produced in various tissues and plays a role in various pathological and physiological processes such as embryogenesis, wound healing, host defense, tumor formation and cartilage degeneration ([1-2]). PGRN was previously known to be expressed by many cell types including skeletal muscle, chondrocytes, hematopoietic cells, epithelial and endothelial cells, neurons and macrophages and in recent years it has been reported to be one of the new adipokines secreted from adipose tissue[3]. As a different function, PRGN is also reported to sometimes act as a growth factor, anti-inflammatory agent or adipokine, depending on the target tissue[3-5]. PRGN is critical for the attachment of the developing embryo to the endometrium layer of the uterus and the protection of cervical tissue during fetal growth due to its anti-inflammatory effect. In addition, high levels of PRGN have been reported in the placenta during angiogenesis[6]. In case of PRGN release and dysfunction, remodeling of the cervical tissue may occur, which may lead to the risk of miscarriage[7].Despite these features being known, the number of publications showing the relationship between PRGN levels and pregnancy periods on most animal species and breeds is low and has not been examined for some breeds so far. For this reason, in this study, we aimed to determine the serum PRGN levels in the early and late pregnancy periods of Morkaraman sheep, which are widely raised in our region, to show the relationship between them and to contribute to the literature.

Morkaraman sheep, which can be defined as a breed resistant to diseases and hunger and can be raised in the arid climate regions of Turkey where there are poor, sparsely grassed pastures and fallow grain farming is carried out, i.e. in inadequate environmental conditions, make significant contributions to the country and the breeder economy[8]. In this study, 32 pregnant Morkaraman sheep from Batman Province (Turkey), Southeastern Anatolia Region, known as one of the general distribution regions of the Morkaraman breed, were used.

The present study was conducted to fill the gap in literature regarding the recently identified PRGN peptide in various species and breeds of animals, in Morkaraman sheep, which is a local species suitable for the climate of Turkey, in terms of productivity and living conditions and a breed specific to the Anatolian geography and to determine the serum PRGN levels at various pregnancy periods and to add them to the literature. Thus, it is expected that the data obtained will enable the evaluation of pregnancy-related problems in the future and comparisons with normal pregnancy PGRN values.

MATERIALS AND METHODS

Before starting the study, local ethics committee permissions for the design and implementation of the study were obtained from Dicle University and the current study was carried out in accordance with these principles. The animal material used in the study consisted of Morkaraman breed female sheep raised in the vicinity of Balpinar village within the borders of Batman province and registered with ear tags in the sheep-goat information system of the Ministry of Agriculture and Forestry. The period between October and March, when the mating and pregnancy processes of sheep generally occur in 2023-2024, was selected as the sampling time. The animals were first subjected to a general health check. Ultrasonic pregnancy examination was performed on sheep suspected to be pregnant by random sampling method and the first 32 of those determined to be pregnant were included. The sheep selected for the study were recorded according to their ear numbers to be sampled again in the future. The sheep were subject to the same feeding and care conditions. The early pregnancy period was determined as approximately the first 100 days of pregnancy and the late pregnancy was determined as approximately the last 100 days.

During the mentioned periods, 10 ml blood samples were taken from the registered sheep by intravenous puncture into commercial blood collection tubes (Greiner Bio-One VACUETTE™ Z Serum Blood Collection Tubes) without anticoagulant from the vena jugularis. Blood samples were centrifuged at 3000 rpm in a Hettich UNIVERSAL 320 R model refrigerated centrifuge to separate the serum. Serum samples obtained at the end of centrifugation were divided into sterile eppendorf tubes and stored in a deep freezer at -80°C until measurement.

After thawing plasma samples at the time of measurement, serum PGRN levels (ng/ml) were measured using the Ewe Progranulin (PGRN) species-specific ELISA Kit (Product code: SG–70706, CHINA) kit on a BIOBASE-EL10A BIOBASE model ELISA device. The measurement was carried out according to the manufacturer's instructions.

Data obtained from samples of sheep in early and late pregnancy periods (also called dry period) were statistically analyzed using General Linear Model Univariate and IBM SPSS v25 statistical program. Differences between groups were determined by Duncan Multiple Comparison Test (Steel and Torrie 1980).

RESULTS AND DISCUSSIONS

For the study, serum progranulin levels in Akkaraman sheep during early pregnancy and dry periods were examined and presented in Table 1.

When Table 1 is examined, it is seen that PRGN levels are generally lower in the late periods of pregnancy in 28 animals compared to the early periods (P<0,05). While no difference was observed between the two sampling times in 2 animals, a very slight increase was observed in the late period compared to the early period in 2 animals.

In our previous study examining the relationships between PRGN hormonal response and biochemical parameters in Akkaraman sheep, we found that serum PRGN levels were higher in the early period of pregnancy compared to the late period and we interpreted this as resulting from PRGN secreted from the endometrial tissue[9]. These data confirmed the finding in the current study that serum PRGN levels were higher in the early period than in the late period in Morkaraman sheep and this situation can again be attributed to the same explanation.

Table 1: Plasma PRGN levels determined in early and late pregnancy periods in Morkaraman sheep (n=32)

	Pregnancy Period		Differences	
Sheep number	Early Pregnancy (First 100 days) (ng/ml)	Late Pregnancy (Last 100 days) (ng/ml)	Numerical differences (ng/ml)	% differences
1	1.57	1.28	0.29	18.47
2	1.61	1.41	0.2	12.42
3	1.66	1.38	0.28	16.87
4	1.69	1.26	0.43	25.44
5	1.67	1.43	0.24	14.37
6	1.73	1.18	0.55	31.79
7	1.82	1.71	0.11	6.04
8	1.78	1.13	0.65	36.51
9	1.89	1.67	0.22	11.64
10	1.91	1.66	0.25	13.08
11	1.87	1.21	0.66	35.29
12	1.93	1.26	0.67	34.71
13	1.79	1.33	0.46	25.69
14	1.86	1.12	0.74	39.78
15	1.91	1.23	0.68	35.60
16	1.69	1.47	0.22	13.02
17	1.77	1.01	0.76	42.94
18	1.84	1.13	0.71	38.59
19	1.87	1.21	0.66	35.29
20	1.76	1.61	0.15	8.52
21	1.83	1.59	0.24	13.11
22	1.88	1.66	0.22	11.70
23	1.73	1.68	0.05	2.89
24	1.71	1.71	0	0
25	1.66	1.66	0	0
26	1.64	1.62	0.02	1.22
27	1.69	1.55	0.14	8.28
28	1.72	1.63	0.09	5.23
29	1.67	1.69	-0.02	-1.19
30	1.55	1.67	-0.12	-7.74
31	1.93	1.26	0.67	34.71
32	1.67	1.43	0.24	14.37
Mean ±SD	**1.76±0.11a**	**1.44±0.22b**	**0.32±0.27**	**17.65±14.66%**

a, b : The difference between the data in the same row is significant (P<0.05).

In addition, low PRGN levels measured in late pregnancy may be related to decreased follicular activity as pregnancy progresses. As evidence of this, a study showing that FSH, a physiological activator of ovarian functions, promotes progranulin expression in ovarian carcinoma cells in vitro can be given[10]. Since FSH levels and follicular development naturally decrease or even stop during pregnancy, low PRGN levels in late pregnancy are expected.

In a study conducted by Ersoy[11], low progranulin levels in human blood were associated with ovarian failure. In obese women, polycystic ovary syndrome was associated with increased progranulin levels in the ovary[12].

In an in vitro study on cat ovaries, it was reported that PRGN increased the accumulation of proliferation markers such as PCNA and cyclin 1 and decreased the expression of cytoplasmic apoptosis markers bax and caspase 3. It is known that the increase in PCNA and cyclin 1 production by granulosa cells results in ovarian cell proliferation and ultimately follicular development. The growth and development of ovarian follicles are characterized by increased proliferation and decreased apoptosis of follicular cells[12]. Low PRGN levels in the early follicularly stationary phase of pregnancy should be considered as a desired situation for the continuation of pregnancy. Therefore, the current observations can again be associated with the low progranulin, which is considered to be the physiological stimulator of ovarian folliculogenesis, in late pregnancy[13].

CONCLUSION

Based on the findings obtained as a result of this study, Progranulin levels in Morkaraman sheep, which is considered a breed specific to Anatolia, are presented. The results of the study provide literature information on serum PRGN levels in healthy Morkaraman sheep. In addition, these data will be guiding in future examinations of pregnancy data based on breeds on sheep, in the diagnosis of pregnancy-related diseases, and even in some cases when PRGN levels will be evaluated in the treatment or when PRGN will be used for therapeutic or preventive purposes.

Note: The Authors declare that there is no conflict of interest.

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