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EFFECTS OF DEXAMETHASONE ON MATERNAL BODY WEIGHTS AND SOME PHYSIOLOGICAL PARAMETERS IN PREGNANT YANKASA SHEEP AND SAHEL GOATS IN MAIDUGURI, NIGERIA

Dauda Yahi[1]*, Nicholas A. Ojo[1], Gideon D. Mshelia[2], Victoria A. Maina[2] and Mohammed B. Mahre[2]

[1]Department of Veterinary Physiology, Pharmacology and Biochemistry and [2]Department of Veterinary Surgery and Theriogenology, Faculty of Veterinary Medicine, University of Maiduguri, Nigeria.

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ABSTRACT

Effects of dexamethasone on maternal body weights and some physiological parameters were investigated in pregnant Yankasa sheep and Sahel goats. Despite its clinical use in both humans and animals, dexamethasone has been associated with several side effects such as intra uterine growth restriction (IUGR) and altered weight gain and homeostasis in both humans and animal models. Eleven adult Sahel goats comprising 10 does and 1 buck and 11 yankasa sheep comprising of 10 ewes and 1 ram were used for this study. Pregnancy was achieved by natural mating after oestrus synchronization. After successful synchronization and fertile mating, the animals were randomly separated into 4 groups of 5 animals each. Accordingly, the groups were as follows: Dexamethasone treated sheep, non-dexamethasone treated / control sheep, Dexamethasone treated goat, and non-dexamethasone treated / control goat. Dexamethasone injection was given at 0.25 mg/kg body weight. Body weights, rectal temperatures, respiratory and pulse rates were measured on weekly basis in each animal at resting state using standard methods. There was no significant ($p>0.05$) difference in body weights between the untreated / control and dexamethasone treated groups in either of the species during the study. Rectal temperature, respiratory and pulse rates increased significantly ($p<0.05$) in dexamethasone treated groups in both species compared to their respective untreated / control groups. It was concluded that the responses of pregnant Yankasa sheep and Sahel goats to dexamethasone treatment with respect to these parameters were similar.

Keywords: Dexamethasone, pregnancy, body weight, physiological parameters, goats, sheep

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INTRODUCTION

The work of Liggins [1] showed that synthetic glucocorticoids accelerate foetal lung development in sheep. Subsequent clinical trial in humans demonstrated significant decreases in morbidity and mortality in premature babies whose mothers received synthetic glucocorticoids (dexamethasone) during threatened

***Correspondence: E-mail: yahidauda@gmail.com; Tel: +2348037811882**
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preterm delivery [2]. It has now become routine clinical practice to treat women with threaten preterm delivery with dexamethasone to improve outcomes in premature babies [3]. In animals dexamethasone use is primarily as a therapeutic agent. It is commonly used to effectively treat disease conditions such as inflammation, acetonaemia/ketosis, non-specific skin disease, shock, fatty liver syndrome and stress [4, 5, 6, 7].

Despite its clinical use in both humans and animals, dexamethasone has been associated with several side effects such as intra uterine growth restriction (IUGR) and altered weight gain in both humans and animal models [8, 9]. There were reports on marked reduction in maternal weight gain in guinea pig and women following repeated doses of synthetic glucocorticoids [10, 11, 12]. John *et al.* [13] reported increase in body weight in mouse while significantly increases in temperatures, pulse and respiratory rates in broiler chickens following dexamethasone treatment [14, 15].

During pregnancy, maternal weight gain affects foetal growth [16]. Small neonate size at birth is attributable to poor growth and shortened gestation. Low rate of pregnancy weight gain is associated with increased risk of preterm birth [17], or spontaneous preterm delivery risk [18] . Maternal physiology and metabolism influence gestational weight gain. Maternal homeostasis changes can alter placental structure and function, influencing foetal growth [19]. In addition, during the transition from foetal to neonatal life, some foetal vital organs remains inactive at certain stage of development and most of the foetal physiological functions are regulated by maternal physiology [20].

There are conflicting reports on the effects of dexamethasone on body weights of different non-pregnant animal species and humans [10, 11, 12, 13]. This suggests interspecies variation. However, the physiology of pregnancy presents well-defined challenges to the maternal organism that are unparalleled in the physiology of the non-pregnant. As there is paucity of information on the effects of dexamethasone on body weights and physiological parameters in pregnant Yankasa sheep and Sahel goats, the purpose of this study was to evaluate and compare the effects of dexamethasone on body weights and some physiological parameters in pregnant Yankasa sheep and Sahel goats.

MATERIALS AND METHODS

Eleven apparently healthy adult Sahel goats comprising 10 does and 1 buck and 11 Yankasa sheep comprising of 10 ewes and 1 ram were used for this study. The animals were purchased from Maiduguri livestock market and private farms in Maiduguri Metropolis. The ages of the does and the ewes ranged between 2 to 2½ years, while that of the ram and the buck were 3 and 3½ years respectively, based on dentition and breeding history [21]. The weights of does ranged between 20 to 25 kg; that of ewes ranged between 28 and 35 kg, while that of the buck and the ram were 30 kg and 39 kg respectively. Body Condition Score (BCS) of between 3.0 and 3.5 was maintained throughout the period of the experiment in all the animals. Breeding history, abdominal palpation and ballottement, nature of mammary secretions, conditions of udder were used in selecting non- pregnant animals [22]. The animals were managed intensively in the University of Maiduguri livestock research farm and were acclimatized for six weeks before the commencement of the experiment. The feed rations consisted of wheat offal, beans husks and hay from groundnut leaves. Mineral salt licks and water were provided *ad libitu*m. During the stabilization period, the animals were treated with oxytetracycline LA (Introxin-200®, Interchiemie, Venray, Holland) at 20 mg/kg body weight and ivermectin (paramectin®, Pharma Swede, Egypt) at 200 µg/kg body weight. The males and the females were initially kept in different pens until the time of service.

Estrus Synchronization

All animals were synchronized at the end of the acclimatization period using 250 µg cloprostenol (Estrumate®, Schering Trough Animal, Germany) given intramuscularly at 11 days interval, as reported previously [23]. The females were teased with aproned males daily and all the females that came into

estrus after the second treatment were allowed to be served naturally by the male. Days of estrus were recorded and considered as day 0 of the gestation. After successful synchronization and fertile mating, the animals were randomly separated into 4 groups of 5 animals each. Accordingly, the groups were as follows: Dexamethasone treated sheep (DTS), Non-dexamethasone treated sheep / control (NDS), Dexamethasone treated goat (DTG), and Non dexamethasone treated / control goat (NDG).

Dexamethasone treatment

All animals in the dexamethasone treated group were administered dexamethasone (Dexaphan®, Pharma Pharmaceuticals, Swede-Egypt) intramuscularly at 0.25 mg/kg body weight on days 1, 3 and 5 during first trimester; days 51, 53 and 55 during second trimester, and days 101, 103 and 105 during the third trimester of gestation. The animals were keenly observed for possible clinical changes throughout the period of the study. The pregnancies were later confirmed by failure to return to estrus and by ultrasonograhic examination using Draminski Ultrasound Pregnancy Detector (UPD-PD032013EX-1.2, Draminsky Agricultural Engineering Co. Inc., Owocowa-Olsztyn, Poland).

Measurements of Vital Parameters

The initial body weights, rectal temperatures, pulse rates and respiratory rates were measured and recorded. This was continued on weekly basis for sixteen weeks. The weights of the pregnant animals were measured using a weighing scale (Hana, TB-Boss-1, China; Capacity: 0-120 kg). The weight of the Field Assistant was taken first and then on holding each animal, the combined weights were taken. The weight of each animal was obtained by subtracting the weight of the Field Assistant from the combined weights.

Rectal temperatures were measured using a standard clinical centigrade thermometer (Cocet, China) inserted gently into the rectum and held for one minute. Pulse rate was determined by holding the tail and feeling for the coccygeal artery with the thumb and index finger. The pulsation was counted for one minute. Respiratory rate was determined by counting the abdominal movements per minute.

Statistical Analysis

Data collected were pooled on biweekly basis and expressed as Means ± Standard Deviation (S.D). The Significant differences between the dexamethasone treated and non-dexamethasone treated groups were compared using Paired Student's t – test. Significant differences were considered at $p < 0.05$. The statistical software package, GraphPad InStat® version 3.0 [24] was used for the analysis.

RESULTS

The results of the effect of dexamethasone treatment on body weights and rectal temperature of pregnant sheep and goats are presented in Table 1. The maternal body weights of both sheep and goats in the dexamethasone treated and untreated / control groups showed steady increase with increasing stage of pregnancy throughout the period under study. However, there was no significant difference in body weights between the two groups in either of the species at any point in time as there was no significant $(p>0.05)$ difference in percentage weight increase between the dexamethasone treated and untreated / control groups with advancing stage of pregnancy. On the other hand, body temperature increased significantly $(p<0.05)$ in dexamethasone treated groups in both species compared to their respective untreated / control groups from day 42 to day 112 of gestation.

There was significant $(p<0.05)$ increase in pulse and respiratory rates between the dexamethasone - treated groups in both species compared to their respective untreated /control groups from day 42 to day 112 of gestation (Table 2).

Table 1: Effects of dexamethasone on maternal body weights and rectal temperatures in pregnant Yankasa sheep and Sahel goats

Parameters	Group*	Sheep								
		Periods of observation (days)								
		0	14	28	42	56	70	84	98	112
Body weight (kg)	DTS	32.50±3.00	34.90±0.50	35.29±0.27	35.40±0.32	35.8±0.77	36.6±0.38	37.21±0.45	38.22±0.60	38.50±0.33
			(6.88)	(1.27)	(0.31)	(1.12)	(2.20)	(1.63)	(2.64)	(0.73)
	NDS	32.40±2.80	34.80±0.80	35.28±0.20	35.38±0.24	35.80±0.50	36.68±0.25	37.25±0.30	38.30±0.50	38.50±0.28
			(6.89)	(1.36)	(0.28)	(1.17)	(2.20)	(1.60)	(2.74)	(0.70)
Temperature (^{o}C)	DTS	38.40±0.33	38.40±0.35	38.42±0.26	38.90±0.48[a]	38.81±0.50[a]	38.95±0.24[a]	39.51±0.38[a]	39.12±0.38[a]	39.40±0.40[a]
	NDS	38.40±0.30	38.38±0.28	38.40±0.22	38.39±0.21	38.28±0.30	38.40±0.31	38.30±0.23	38.25±0.28	38.32±0.37
Parameters	Group*	Goat								
		Periods of observation (days)								
		0	14	28	42	56	70	84	98	112
Body weight (kg)	DTG	22.50±2.60	25.50±0.44	25.80±0.48	26.90±20	27.30±0.36	28.50±0.50	28.80±0.60	28.90±0.90	29.00±0.20
			(11.76)	(1.16)	(4.08)	(1.45)	(4.21)	(1.05)	(0.35)	(0.35)
	NDG	22.50±2.50	25.50±0.50	25.80±0.28	26.00±0.27	27.31±0.30	28.40±0.50	28.70±0.30	28.80±0.05	28.90±0.22
			(11.76)	(1.16)	(3.73)	(1.86)	(3.84)	(1.04)	(0.35)	(0.35)
Temperature (^{o}C)	DTG	38.50±0.20	38.50±0.28	38.60±0.24	38.92±0.26[a]	38.95±0.33[a]	40.00±0.21[a]	40.10±0.25[a]	39.94±0.29[a]	40.00±0.30[a]
	NDG	38.40±0.25	38.40±0.28	38.40±0.30	38.39±0.23	38.40±0.41	38.50±0.27	38.39±0.40	38.37±0.35	38.38±0.25

DTS = Dexamethasone treated sheep; NDS = Non dexamethasone treated sheep (control); DTG = dexamethasone treated goats; NDG = Non dexamethasone treated goats (control) [a] = significant (P<0.05) increase compared to respective control group *N = 5 for each group

Figures in parenthesis represent percentage increase from preceding gestational age

Table 2: Effects of dexamethasone on maternal respiratory and pulse rates in pregnant Yankasa sheep and Sahel goats

Parameters	Group*	Sheep								
		Periods of observation (days)								
		0	14	28	42	56	70	84	98	112
Respiratory rate (per min)	DTS	30.50±0.34	30.60±0.25	30.50±0.22	33.30±0.42[a]	33.30±0.50[a]	34.80±0.29[a]	34.50±0.35[a]	33.23±0.38[a]	34.28±0.40[a]
	NDS	30.40±0.32	30.50±0.40	30.50±0.25	30.39±0.27	30.40±0.36	30.20±0.50	30.40±0.28	30.40±0.27	30.39±0.31
Pulse rate (per min)	DTS	72.50±0.50	72.50±0.40	73.00±0.38	73.50±0.40[a]	75.50±0.30[a]	74.70±0.40[a]	74.30±0.26[a]	75.50±0.32[a]	75.60±0.38[a]
	NDS	72.40±0.20	72.50±0.30	72.50±0.21	72.40±0.50	72.50±0.28	72.41±0.25	72.49±0.15	72.38±0.36	72.20±0.50
Parameters	Group*	Goat								
		Periods of observation (days)								
		0	14	28	42	56	70	84	98	112
Respiratory rate (per min)	DTG	30.40±0.50	30.24±0.20	30.47±0.28	30.50±0.30[a]	31.50±0.45[a]	32.66±0.50[a]	34.59±0.24[a]	33.49±0.58[a]	34.60±0.25[a]
	NDG	30.50±0.50	30.25±0.24	30.30±0.23	30.40±0.32	30.38±0.30	30.29±0.40	30.40±0.31	30.31±0.29	30.30±0.36
Pulse rate (per min)	DTG	72.30±0.24	72.40±0.50	72.50±0.60	73.80±0.43[a]	73.60±0.28[q]	75.30±0.29[a]	74.44±0.50[a]	75.35±0.22[a]	74.40±0.27[a]
	NDG	72.20±0.22	72.50±0.20	72.50±0.50	72.60±0.27	72.50±0.39	72.39±0.24	72.36±0.31	72.29±0.41	72.30±0.45

DTS = Dexamethasone treated sheep; NDS = Non dexamethasone treated sheep (control); DTG = dexamethasone treated goats; NDG = Non dexamethasone treated goats (control)

[a] = significant ($P<0.05$) increase compared to respective control group

*N = 5 for each group

DISCUSSION

It is expected that body weight increases with advancing pregnancy in proportion to the accumulation of maternal tissue, growth of the foetus and the placenta as well as the increase in the amount of foetal fluids.

However, what is novel is the rate of increase. Although there was steady increase in maternal body weights in both dexamethasone - treated and untreated / control groups with advancing stage of pregnancy, the lack of effect of dexamethasone on rate of maternal weight increase in both species suggests that dexamethasone has little or no effect on maternal and/or foetal growth during pregnancy in these species. Prenatal exposure to dexamethasone has been reported to decrease foetal weight in both humans and animals [9, 25].

The steady increase in maternal body weights of sheep and goats in both the control and dexamethasone treated groups could be attributed to better care and adequate nutrition. Adequate nutrition is regarded as the ultimate regulator of growth and reproduction [26].
Although dexamethasone is known to increase feed intake, appetite and visceral adiposity [21], it did not increase body weights in the pregnant sheep and goats in this study probably due to counter balance by increased muscle or fat catabolism and lipolysis during pregnancy in order to sustain energy balance [27]. Due to increased energy requirements caused by pregnancy, pregnant subjects are at risk of developing hypoglycemia and ketosis. Hypoglycaemia usually induces compensatory lipolysis in adipose tissues and enhances fat mobilization as a compensatory mechanism [28, 29].

The lack of effect of dexamethasone on rate of maternal weight gain observed in this study contrasts with other studies on humans and some animal models [10, 11, 12, 21, 30]. There were reports of marked reductions in maternal weight gain in mice and guinea pig following repeated administration of synthetic glucocorticoids [10, 11]. Amar *et al*. [12] reported significant decrease in body weight of Wistar rats treated with low doses of dexamethasone compared with the untreated / control group and attributed this to a reduction in abdominal fat accumulation. The differences from the present study may be due to species difference and physiological status in response to dexamethasone or methodology involved as the subjects of their experiments were non-pregnant.

The increase in body temperature, pulse and respiratory rate in dexamethasone - treated groups compared to untreated /control in both species may be due to elevated level of serum thyroid hormones (T_3) level and the stimulation of heat production or cardiovascular function by dexamethasone. The thyroid hormones control the process of metabolism and energy production which also causes heat generation. Therefore, there is a direct relationship between body temperature and thyroid function. Sabeur *et al.* [31] explained that dexamethasone increases plasma T_3 levels and metabolism of protein in muscle as well as some vital physiological parameters in chickens. The results of this study are similar to the earlier reports obtained in broiler chickens [14, 15].

CONCLUSIONS AND RECOMMENDATION

Prenatal dexamethasone treatment increased maternal body temperatures, respiratory and pulse rates but did not influence body weight gain during pregnancy in pregnant Yankasa sheep and Sahel goats. The responses of both species to dexamethasone treatment with respect to these parameters were similar. Therefore, it may be of clinical relevance to monitor these variables when pregnant animals of these species are to be treated with dexamethasone.

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