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RESEARCH ARTICLE

Effect of single dose dexamethasone (0.1 mg/kg) on white blood cell counts and serum glucose levels in healthy ewes

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Koyunlara tek doz deksametazon (0.1 mg/kg) uygulamasının akyuvar sayısı ve serum glikoz düzeylerine etkisi

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Öz

Amaç: Araştırmanın öncelikli amacı sağlıklı koyunlara tek doz deksametazon (0.1 mg/kg, SC) uygulamasının akyuvar sayısı ve serum glikoz düzeyine etkisini belirlemektedir. Ayrıca deksametazonun diğer bazı hemogram ve serum biyokimyasal parametrelere etkisi de değerlendirilmiştir.

Gereç ve Yöntem: Araştırmada 8 adet sağlıklı Akkaraman koyuna 0.1 mg/kg (SC, tek doz) dozunda deksametazon uygulandı. Uygulamadan önce (0. saat, kontrol) ve sonraki 4, 8, 12, 24, 36, 48 ve 72. saatlerde kan örnekleri alındı. Akyuvar sayısı, alyuvar sayısı, platelet sayısı, hemogram ve hematokrit değerleri kan hücresi sayım cihazında ölçülürken, serum glikoz, laktat dehidrogenaz, alkalin fosfataz, total bilirubin, alanin aminotransferaz, aspartat aminotransferaz, gamma glutamiltransferaz, total protein, albümin, kan üre nitrojen, kreatinin, kolesterol, trigliserit, yüksek yoğunluklu lipoprotein ve düşük yoğunluklu lipoprotein düzeyleri otoanalizörde ölçüldü.

Bulgular: Kontrol (0. saat) zamanla karşılaştırıldığında, deksametazonun akyuvar sayısı ve serum glikoz düzeyini yükselttiği ($P<0.05$) belirlendi ve bu yüksek düzeylerin 48 saat süresince devam ettiği gözlendi. Ayrıca total bilirubin, trigliserit ve kan üre nitrojen düzeylerinde istatistiki değişimler gözlendi, ancak bu değişimlerin referans aralıklar içinde olduğu tespit edildi.

Öneri: Koyunlara deksametazon uygulamasının akyuvar sayısı ve serum glikoz düzeyini yükseltebileceği ve bu yüksek değerlerin 2-3 gün süresince belirlenebileceği ifade edilebilir.

Anahtar kelimeler: Deksametazon, hemogram parametreler, biyokimyasal parametreler, koyun

Abstract

Aim: Aim of this research was to determine that effect of single dose dexamethasone (0.1 mg/kg, SC) on the white blood cell counts and serum glucose levels in healthy ewes. In addition, effects of dexamethasone on the other hemogram and serum biochemical values were evaluated.

Materials and Methods: Totally healthy 8 Akkaraman sheep were received with 0.1 mg/kg (SC, single dose) dexamethasone. Blood samples were taken before (0. hour, control) and after treatments at 4, 8, 12, 24, 36, 48 and 72 hours. White blood cell, red blood cell, platelet, hematocrit and hemoglobin levels were measured by hemocell counter, whereas serum glucose, lactate dehydrogenase, alkaline phosphatase, total bilirubin, alanine aminotransferase, aspartate aminotransferase, gamma glutamyltransferase, total protein, albumin, blood urea nitrogen, creatinine, cholesterol, triglyceride, high density lipoprotein and low density lipoprotein levels were determined by auto-analyzer.

Results: Dexamethasone increased ($P<0.05$) white blood cell and glucose levels when compared to Control (0 hour), and higher levels of these values were monitored during 48 hours. In addition, statistically significance changes were determined in the total bilirubin, triglyceride and blood urea nitrogen concentrations, but these results were within reference range.

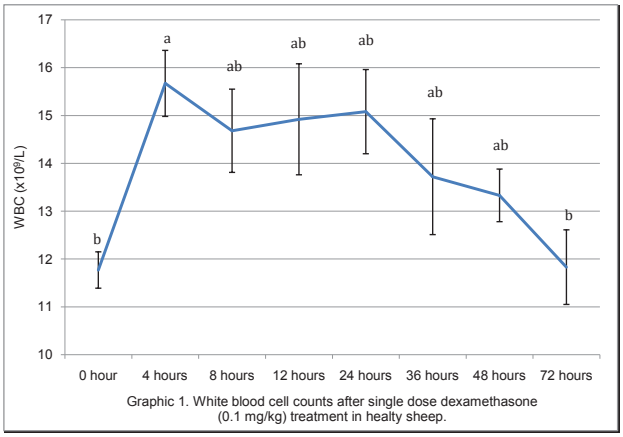
Conclusion: It may be stated that dexamethasone increases white blood cell count and glucose levels in sheep and its effect may be determined during 2-3 days after treatments.

Keywords: Dexamethasone, hemogram values, biochemical values, sheep

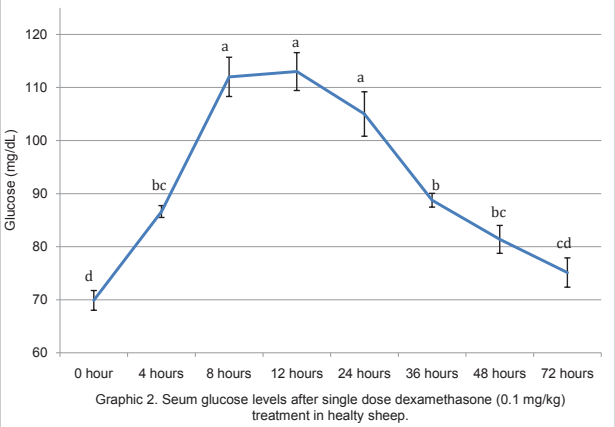
Introduction

Glucocorticoids (Cortisol, corticosterone) are secreted from adrenal cortex in the body. They have many different effects on the system and organs and play essential role in the hemostasis. Glucocorticoids play role in the response to stress, blood pressure regulation, fluid-electrolyte balance, immune functions and cellular energy metabolism. In addition, they affect protein, lipid and carbohydrate metabolism. Proteins and lipids are converted to glucose by glucocorticoids during the stress-induced activation. Glucocorticoids induce glucose production and diminish peripheral glucose uptake (Buckingham 2006, Gross and Cidlowski 2008, Macfarlane et al 2008). Glucocorticoids depress T and B cells and phagocytes activities and acquired immune functions (Gensler 2013), while they increase white blood cell counts in the circulatory system (Kaya 2002).

Dexamethasone, a synthetic glucocorticoid drug, has long half-lives. It has anti-inflammatory, anti-allergic and immune depressive effects, hence; dexamethasone may be preferred in the treatments of shock types, allergic reactions (systemic or local), autoimmune disease, etc. It is especially used in the pregnancy toxemia and termination of pregnancy in ewes. Many detailed information (Dosage, laboratorial-clinical effects, side effects, etc.) exist when glucocorticoids are used in the small animal practice, whereas there is no sufficient data when dexamethasone is used in sheep (Bastan and Salar 2013, Er and Dik 2013). Effect of dexamethasone on the many metabolism (protein, lipid, energy, etc.) and system (Kaya 2002) is considered; it has been hypothesized that dexamethasone may show similar effect and this effect may be determined by measuring some hemogram and biochemical values in sheep, as well.



Graphic 1. White blood cell counts after single dose dexamethasone (0.1 mg/kg) treatment in healty sheep.



Graphic 2. Seum glucose levels after single dose dexamethasone (0.1 mg/kg) treatment in healty sheep.

The first aim of this research was to determine that effect of dexamethasone on the serum glucose level and white blood cell (WBC) counts. In addition, effect of dexamethasone on the other hemogram [Red blood cell (RBC), platelet, hemogram, hematocrit] and serum biochemical [Lactate dehydrogenase (LDH), alkaline phosphatase (ALP), total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamytransferase (GGT), total protein, albumin, blood urea nitrogen (BUN), creatinine, cholesterol, triglyceride, high density lipoprotein (HDL), low density lipoprotein (LDL)] values was also determined.

Materials and Methods

Totally 8 Akkaraman (58±6 kg, >3 years) sheep were administered with 0.1 mg/kg (SC, single dose) dexamethasone (Dekort® amp, Deva Ilac, Istanbul, Turkey). Study protocol was approved by Ethic Committee of Veterinary Faculty, Selcuk University (No: 2016/08). Blood samples were taken before (0. hour, control) and after treatments at 4, 8, 12, 24, 36, 48 and 72 hours. WBC, RBC, platelet, hematocrit, hemoglobin levels were measured by hemocell counter (BC-2800 Auto Hematology Analyzer, Mindray Bio-Medical Electronics, Shenzen, China), whereas serum glucose, LDH, ALP, total bilirubin, ALT, AST, GGT, total protein, albumin, BUN, creatinine, cholesterol, triglyceride, HDL and LDL levels were determined by auto-analyzer (ILab-300 plus, Instrumentation Laboratory, Milano, Italy).

Data were presented as mean±SE. Study results were evaluated by ANOVA and Tukey test. $P<0.05$ level was accepted statistically significant.

Results

WBC and glucose levels are shown in Graphic 1 and 2, respectively, whereas other hemogram and serum biochemical values are presented in Table 1 and 2, respectively. After dexamethasone treatment, higher WBC level was determined ($P<0.05$) at 4th hour when compared to sampling times (Graphic 1). Peak glucose concentration was determined at 12th hour after dexamethasone administration (Graphic 2). In addition, higher glucose levels obtained from 8, 12 and 24th hours were statistically significant ($P<0.05$) from other sampling times. Dexamethasone caused statistically significance ($P<0.05$) fluctuations in the total bilirubin, BUN and

Table 1. Hemogram values of sheep after dexamethasone (0.1 mg/kg, single dose, SC) treatments (mean±SE).

	0 hour	4 hours	8 hours	12 hours	24 hours	36 hours	48 hours	72 hours
RBC (x10^{12}/L)	9.26±0.34	9.46±0.37	9.28±0.35	8.80±0.35	8.89±0.27	9.10±0.17	9.18±0.31	8.61±1.26
PLT (x10^{9}/L)	422±32.4	411±28.3	446±28.5	388±37.8	376±42.5	398±20.7	364±18.4	369±39.0
HGB (g/dL)	9.43±0.32	9.36±0.45	8.08±1.20	8.82±0.37	8.80±0.27	9.26±0.21	9.16±0.34	10.0±0.32
HTC (%)	36.6±1.03	37.5±1.58	36.7±1.28	34.5±1.32	34.2±0.87	35.4±0.86	35.4±1.04	37.7±0.71

RBC: Red blood cell, PLT: platelet, HGB: Hemoglobin, HTC: Hematocrit.

Table 2. Serum biochemical values of sheep after dexamethasone (0.1 mg/kg, single dose, SC) treatments (mean±SE).

	0 hour	4 hours	8 hours	12 hours	24 hours	36 hours	48 hours	72 hours
LDH (U/L)	448±48.2	499±35.5	543±42.7	520±41.4	473±28.7	479±31.6	464±31.3	494±32.0
ALP (U/L)	82.8±7.62	76.6±5.28	79.9±7.10	83.6±6.34	94.4±9.47	89.8±7.74	88.8±9.58	87.0±8.66
Tbil (mg/dL)	0.24±0.01^{a}	0.18±0.03^{ab}	0.22±0.04^{ab}	0.20±0.03^{ab}	0.13±0.02^{ab}	0.11±0.01^{b}	0.17±0.02^{ab}	0.19±0.02^{ab}
ALT (U/L)	12.4±1.16	12.9±1.20	12.6±1.25	12.5±1.13	11.4±1.03	12.0±1.14	12.1±1.10	10.5±0.94
AST (U/L)	86.3±7.27	87.8±8.07	90.6±8.47	86.5±8.04	79.0±5.77	78.0±6.50	78.8±6.22	77.0±5.83
GGT (U/L)	34.8±2.08	36.1±2.06	37.1±2.11	37.0±1.62	36.3±2.05	39.8±2.53	41.6±2.85	44.3±3.29
Tprot (g/dL)	5.99±0.13	6.16±0.17	6.25±0.30	6.39±0.20	6.32±0.14	6.50±0.14	6.36±0.23	6.44±0.21
Alb (g/dL)	2.90±0.05	3.01±0.04	3.07±0.12	3.18±0.12	3.18±0.07	3.25±0.06	3.18±0.04	3.17±0.02
BUN (mg/dL)	8.90±0.51^{b}	10.1±0.53^{ab}	11.4±0.60^{ab}	11.4±0.70^{ab}	9.08±0.58^{b}	9.36±0.72^{b}	11.8±0.83^{ab}	12.7±0.84^{a}
CR (mg/dL)	0.78±0.04	0.74±0.04	0.74±0.05	0.67±0.05	0.72±0.03	0.73±0.04	0.75±0.03	0.84±0.03
CHL (mg/dL)	61.6±2.98	61.8±2.82	65.4±4.14	65.9±3.60	65.3±3.25	69.6±3.64	68.1±4.24	67.0±4.42
TRG (mg/dL)	10.3±0.75b^{cde}	7.00±0.46^{de}	7.75±1.22^{cde}	5.87±0.85^{e}	16.5±1.59^{a}	12.8±0.75^{ab}	11.5±0.65^{bc}	10.8±1.11^{bcd}
HDL (mg/dL)	37.6±1.86	38.8±2.13	40.6±2.87	40.5±1.79	39.5±1.85	43.1±2.43	42.9±2.83	41.9±3.10
LDL (mg/dL)	34.8±3.01	34.5±2.62	36.8±3.28	38.3±3.47	35.6±2.91	39.1±3.22	38.1±3.47	35.9±3.63

LDH: Lactate dehydrogenase, ALP: Alkaline phosphatase, Tbil: Total bilirubin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma glutamyltransferase, Tprot: Total protein, Alb: Albumin, BUN: Blood urea nitrogen, CR: Creatinine, CHL: Cholesterol, TRG: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein, $^{a, b, c, d,e}$: Different letters in the same line are statistically significant (P<0.05).

triglyceride levels. There was no statistically significance determined (P>0.05) in the other hemogram (RBC, platelet, hematocrit, hemoglobin) and biochemical (LDH, ALP, ALT, AST, GGT, total protein, albumin, creatinine, cholesterol, HDL, LDL) values.

Discussion

Dexamethasone is a synthetic glucocorticoid drug and recommended parenterally at the dose of 0.04-1 mg/kg in the treatment of pregnancy toxicity, shock, termination of pregnancy in sheep (Bastan and Salar 2013, Er and Dik 2013). In the current research, dexamethasone increased (P<0.05) WBC levels at 4th hours after treatment, and this higher levels were observed (P>0.05) during 48 hours (Graphic 1). Peak WBC level was higher (15.67 x10^{9}/L) 33 percent when compared to control time (11.77 x10^{9}/L, 0. hour), and this increase of WBC count was out of reference range (2.5-12 x10^{9}/L), as well (Bulbul 2013). Dexamethasone did not affect RBC, platelet, hemogram and hematocrit levels (Table 1). Glucocorticoids may increase circulatory WBC counts (Kaya 2002). It has been reported that dexamethasone increased WBC counts and did no effect hemoglobin and hematocrit levels in ewes (Sekin et al 1994, Er et al 2016). In fact, effect of dexamethasone on the WBC counts may depend on dose or animal kinds. Increased WBC counts were reported in female turkeys after dexamethasone treatment, but similar effect of dexamethasone was not observed in males (Huff et al 2015), and increased WBC counts were determined in cows (Thanasak et al 2004). These results may indicate dexamethasone directly affect WBC level in sheep and has no effect other hemogram values.

Dexamethasone increased (P<0.05) the glucose concentration at 8th hours, and higher glucose levels were monitored during 48 hours (Graphic 2). Peak glucose level (113 mg/dL) was higher 63 percent when compared to control time (69.87 mg/dL, 0. hour), and this peak level of glucose was

higher from reference range (40-80 mg/dL), as well (Bulbul 2013). Increased glucose levels within first day have been reported in sheep after dexamethasone treatment (Er et al 2016). It is well known that glucocorticoids increase serum glucose levels via impairing peripheral glucose uptake (Macfarlane et al 2008), decreasing glucose utilization, and increasing hepatic production (Moghadam-Kia and Werth 2010); hence, hyperglycemia is occurs. This result may indicate that 0.1 mg/kg dose of dexamethasone dramatically increases serum glucose level and this increased level of glucose may be observed during 2 days in sheep. Decreased total bilirubin and increased BUN levels were determined ($P<0.05$) at 36th and 72nd hours, respectively, when compared to control time (0. hour). In addition, statistically significant fluctuations were determined in the triglyceride levels (Table 2). Although these changes are below the reference range of ewes (Bulbul 2013), serum lipids may increase during glucocorticoids therapy. However, mechanism of hyperlipidemia of glucocorticoids is not fully understood (Moghadam-Kia and Werth 2010).

Conclusion

It may be stated that dexamethasone, a synthetic glucocorticoid, directly affects white blood cell counts and glucose metabolism during 2-3 days in sheep, and these effects of dexamethasone are considered in the evaluation of laboratory values in sheep when dexamethasone is administered.

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