



RESEARCH ARTICLE

Importance of fasting serum glucose, haemoglobin A1c and fructosamine in the diagnosis of diabetes

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Özet

Ersan B, Ok M. Diyabetin teşhisinde serum açlık glikoz, hemogloblin A1c ve fruktozaminin önemi. *Eurasian J Vet Sci*, 2011, 27, 1, 13-18

Amaç: Tavşanlarda iki farklı doz (100 ve 175 mg/kg) alloxan ile oluşturulan deneysel diabetes mellitus'un teşhisinde, klinik, hematolojik ve biyokimyasal parametrelerdeki değişimlerin değerlendirilmesidir. İkinci amacı ise hastalığın teşhisinde glikoz, glikozile hemogloblin ve fruktozaminin önemini ortaya koymaktır.

Gereç ve Yöntem: Tavşanlar rastlantısal olarak 2 gruba ayrıldı. Birinci grupta 12, ikinci grupta 13 tavşan vardı. Birinci gruptaki tavşanlara 100 mg/kg dozunda, 2. gruptaki tavşanlara 175 mg/kg dozunda alloxan intravenöz yolla verildi. Eritrosit, lökosit, hemotokrit, hemogloblin, trombosit, ortalama hücre volümü ve ortalama hücre hemogloblin konsantrasyonları belirlendi. Serum açlık glikoz, fruktozamin, insülin, hemogloblin HbA1c, kolesterol, trigliserid, üre, aspartat aminotransferaz ve alanin aminotransferaz düzeyleri ölçüldü.

Bulgular: İstatistiksel olarak, her iki grupta serum açlık glikoz, fruktozamin, HbA1c, total kolesterol ve trigliserid düzeylerinde önemli artış, insülin, eritrosit, hemotokrit ve hemogloblin düzeylerinde ise azalma ($p<0.05$) belirlendi.

Öneri: Diabetes mellitusun teşhisinde serum açlık glikoz, fruktozamin ve hemogloblin A1c önemli diagnostik indikatör olabilir.

Abstract

Ersan B, Ok M. Importance of fasting serum glucose, haemoglobin A1c and fructosamine in the diagnosis of diabetes. *Eurasian J Vet Sci*, 2011, 27, 1, 13-18

Aim: The primary aim of this study was to evaluate the changes in hematological and certain biochemical parameters in the diagnosis of rabbits with experimental diabetes mellitus induced with two different doses of alloxan monohydrate (100 and 175 mg/kg). The secondary aim of this study was to determine the importance of glucose, haemoglobin A1c and fructosamine in the diagnosis of the disease.

Materials and Methods: Rabbits were randomly allocated to two groups. The first group included 12 rabbits and the second group included 13 rabbits. Hundred and 175 mg/kg dose of the alloxan solutions were given intravenously to the first group and second group, respectively. White blood cell, red blood cell, haemoglobin, platelet counts, paced cell volume, mean corpuscular haemoglobin concentration and mean corpuscular volume values were determined. Fasting serum glucose, fructosamine, insulin, haemoglobin HbA1c, total cholesterol, triglyceride, urea, aspartate amino transferase and alanin amino transferase levels were measured.

Results: Statistically significantly increases of serum fasting glucose, fructosamine, haemoglobin A1c, total cholesterol and triglyceride concentrations and decreases of serum insulin levels and red blood cell, paced cell volume and haemoglobin values were determined ($p<0.05$) in both groups.

Conclusion: Fasting serum glucose, fructosamine and haemoglobin A1c could be more important indicators for the diagnosis of diabetes mellitus.

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► Introduction

Diabetes mellitus (DM) is a complex disorder caused by a multitude of factors; it is characterized by insulin deficiency or dysfunction, resulting in hyperglycemia, glycosuria, and abnormal lipid and protein metabolism (Remillard 1999, Başoğlu and Sevinç 2000, Kim et al 2006, Bakirel et al 2008). The disease occurs in two forms based on the ability of pancreatic beta cells to continue to produce and secrete insulin: (I) insulin-dependent diabetes mellitus (IDDM), in which the loss or destruction of beta cells leads to complete lack of insulin and (II) non-insulin-dependent diabetes mellitus (NIDDM), in which beta cells retain some functional ability (Garcia and Bruyette 1998, Burski et al 2004). Worldwide projections suggest that more than 300 million people will have diabetes by the year 2025 and the global cost of treating diabetes and its complications could annually reach up to trillion US\$ (Somani et al 2006).

DM is well documented in dogs, cats, rats and mice and probably occurs in most mammals (Kimmel et al 2002). The cause of DM is probably multifactorial. Factors such as genetics, obesity, diet, inflammatory/infectious conditions, exposure to toxic chemicals or drugs causing insulin resistance, immune-mediated disease destruction of islet cells, and destruction of islet cells secondary to pancreatitis may play a role (Feldman and Nelson 2004, Parsons et al 2007). There have been changes in the human diabetic population in last decade especially; an increase in the incidence of type 1 diabetes has been noted world wide (Onkama et al 1999). Spontaneous DM is reported in most dog breeds (Feldman and Nelson 2004). Female dogs had an increased risk of DM when compared to males (Guptill et al 2003). DM is characterized by glycosuria, osmotic polyuria, polyphagia and polydipsia (Tiftik et al 1992, Feldman and Nelson 2004, Kim et al 2006). It is reported that serum alanine amino transferase (Smith et al 2002), glucose (Kimmel 2000), fructosamine (Davison et al 2005, Chansaisakorn et al 2009), haemoglobin A1c (HbA1c) (Lost and Marca 2001, Chansaisakorn et al 2009), triglyceride (Goldberg 2001), and total cholesterol (Nelson 2000) concentrations increase in DM. Endogenous insulin level usually decreases in DM (Khan 2005, Martin et al 2006). Parsons et al (2007) also reported that endogenous insulin level in diabetic dogs with ketoacidosis significantly decreased.

The primary aims of this study were to evaluate the changes in hematological and biochemical parameters in the diagnosis of rabbits with experimental induced diabetes mellitus by injection of two different doses of alloxan monohydrate (100 and 175 mg/kg) and to determine the importance of glucose, HbA1c and fructosamine in the diagnosis of the disease.

► Materials and Methods

• Animal material

The study involved 25 healthy white male rabbits (7-9 months, 2.5-3.7 kg). Rabbits were kept in a cage for 20 days for adaptation and standardization at 21 °C in a well ventilated air-conditioned room during the study. Rabbits were fed commercially prepared pellet feed (CP® 5701), containing 12% water, 18% crude protein, 12% crude cellulose, 8% crude ash, 1-2% Ca, 0.5% P, 0.1-0.2% Na, 0.6% NaCl, vitamins and some micro elements. The rabbits were given free access to sufficient tap water. This experimental study was conducted in accordance with Veterinary Faculty Ethic Committee of Selcuk University.

• Induction of the diabetes

Rabbits were randomly allocated to two groups. The first group included 12 rabbits and the second group included 13 rabbits. The rabbits were fasted for 24 h prior to the induction of diabetes mellitus. Blood samples were collected from the Arteria auricularis of all the rabbits, before alloxan monohydrate administration for induction diabetes mellitus. Fresh solution of alloxan monohydrate (Sigma, Aldirch, 6125, Switzerland) was prepared by dissolving it in normal saline at a concentration of 100 mg/mL just prior to injection. This solution was given via auricular vena at a dose of 100 mg/kg in the first group (Kim et al 2006), and given via at a dose of 175 mg/kg in the second group (Waters 1950) immediately after preparation. Following the injection, 100 mL glucose solution (5% dextrose) was added to the water of the rabbits for three days in order to prevent hypoglycemic shock. Diabetes was confirmed on the 4th day of the experiment after the alloxan injection by the presence of fasting hyperglycemia (fasting blood glucose level >300 mg/dL).

• Collection of blood samples

Blood samples were obtained at 0 minute (just before alloxan injection) and 4, 8, 12 and 16 days after the alloxan injection. Blood samples were taken from the Arteria auricularis of all the rabbits. The rabbits were fasted for 16 h prior to blood sampling. Blood samples were taken at 09.00 a.m. each time, an aliquot of blood was placed into EDTA-containing a plastic tube for haematocytometry. Blood samples for serum biochemical analyses were collected into plain tubes, allowed to clot at room temperature, and centrifuged and the serum was harvested and stored at -20 °C until analyzed.

• Blood and serum biochemical parameters

A complete blood count (CBC) was performed by Medonic CA 530 Thor within two hours of collection. The serum fasting glucose, total cholesterol (TCh), triglyceride (TG), urea (BUN), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were measured by using an autoanalyser (Vitros-350, Johnson & Johnson Firm). Blood HbA1c level was measured with HPLC method in three hours of collection

by using the autoanalyser (Drew D5-5) (Davidson et al 2005). Serum insulin level was detected using chemiluminescence method on an autoanalyser (Boehringer-Mainheim Elecsyse 1010, Roche diagnostic), Serum fructosamine was determined by colorimetric method on an autoanalyser (Cobas integra 400, Roche diagnostic).

• Statistical analysis

Statistical analyses were performed using package programme (SPSS 12.0), as reported by Akgül (2003). One way analysis of variance (ANOVA) and Duncan test were used for comparing the data ($p < 0.05$).

► Results

• Clinical findings

Rabbits were clinically observed throughout the experiment. The rabbits exhibited polyuria, polydipsia, polyphagia and weight loss. These clinical signs observed in the rabbits were more severe in the second group when compared to the first group. Five rabbits in the first group and 7 rabbits in the second group died within three days of alloxan injection.

• Biochemical findings

Biochemical parameters are presented in Table 1. Fasting serum glucose, HbA1c, fructosamine, and triglyceride concentrations of the rabbits in the first and the second group significantly increased ($p < 0.001$) throughout the experiment. Changes in serum cholesterol levels of rabbits in the first group were not significant while it significantly increased in the second group ($p < 0.001$) during the experiment. Serum insulin concentration determined in both of groups significantly decreased ($p < 0.001$) during the experiment. Alterations in serum BUN, ALT and AST concentrations were insignificant in both groups.

Table 1. Some serum biochemical parameters of the first and second groups (mean±SE).

	First group (days)					Second group (days)				
	0 (n:12)	4 (n:7)	8 (n:7)	12 (n:7)	16 (n:7)	0 (n:13)	4 (n:6)	8 (n:6)	12 (n:6)	16 (n:6)
Glucose mg/dL	99.0±8.0 ^b	340±54 ^a	383±43 ^a	370±45 ^a	382±21 ^a	90.1±5.0 ^b	417±15 ^a	441±23 ^a	503±50 ^a	445±39 ^a
Fruc mmol/L	288±8.6 ^b	375±14 ^a	361±32 ^a	360±18 ^a	355±38 ^a	272±7.8 ^c	325±22 ^b	532±42 ^a	499±47 ^a	409±56 ^{ab}
HbA1c %	2.41±0.6 ^c	2.56±0.7 ^c	3.29±0.4 ^b	3.74±0.4 ^b	4.56±0.9 ^a	2.76±0.5 ^d	3.11±0.5 ^c	3.73±0.3 ^c	4.15±0.4 ^b	5.23±0.6 ^a
Insulin μ IU/mL	20.1±0.2 ^a	14.1±0.3 ^b	13.1±0.2 ^b	14.1±0.3 ^b	10.1±0.1 ^c	20.3±0.6 ^a	13.1±0.4 ^b	11.1±0.1 ^c	9.04±0.1 ^d	8.12±0.8 ^d
TCh mg/dL	48.7±3.7 ^a	51.1±4.6 ^a	47.5±2.1 ^a	45.0±0.1 ^a	45.0±0.1 ^a	62.3±8.6 ^b	52.6±5.0 ^b	376±35 ^a	431±37 ^a	365±47 ^a
TG mg/dL	57.1±9.1 ^c	241±26 ^a	196±15 ^b	223±27 ^a	214±60 ^a	139±30 ^c	213±48 ^b	558±15 ^a	575±0.5 ^a	573±0.8 ^a
BUN mg/dL	43.7±4.1 ^a	36.5±2.0 ^a	37.6±2.1 ^a	45.0±3.1 ^a	43.3±3.8 ^a	43.8±3.3 ^a	42.1±4.5 ^a	58.7±5.3 ^a	58.3±3.8 ^a	49.6±8.2 ^a
AST IU/L	46.8±5.5 ^a	44.2±5.8 ^a	40.5±4.6 ^a	45.5±4.7 ^a	48.8±4.4 ^a	34.3±2.0 ^a	37.1±2.0 ^a	35.8±8.7 ^a	34.1±0.2 ^a	38.0±6.7 ^a
ALT IU/L	59.2±8.7 ^a	60.4±9.6 ^a	62.0±7.1 ^a	61.2±10 ^a	63.1±7.2 ^a	51.5±3.2 ^a	54.8±10 ^a	52.8±9.3 ^a	48.1±3.3 ^a	56.6±8.0 ^a

Fruc; fructosamine, HbA1c; hamoglobin A1c, TCh; total cholesterol, TG; triglyceride. ^{a, b, c, d}, different letters in the same line are statistically significant ($p < 0.05$).

• Hematologic findings

Hematologic results are presented in Table 2. Blood RBC, PCV and Hb concentrations significantly de-

creased in both groups throughout the experiment. Blood WBC counts on the 4th day ($p < 0.05$) and thrombocyte counts throughout the study ($p < 0.001$) increased in both groups. MCV concentrations also slightly increased ($p < 0.05$) in both groups during the experiment. MCHC levels did not significantly change between the groups throughout the experiment.

► Discussion

Alloxan monohydrate induces diabetes mellitus through causing permanent damage to the beta cells of the pancreas (Arai et al 2002, Burski et al 2004). DM is characterized by glycosuria, osmotic polyuria, polyphagia and polydipsia (Tiftik et al 1992, Kim et al 2006). Kim et al (2006) reported that diabetes mellitus was induced in dogs by injection of alloxan monohydrate at the dose of 100 mg/kg, While Zalesk and Bryla (1978) reported induction of diabetes mellitus in rabbits by injecting alloxan monohydrate at the dose of 200 mg/kg through the Auricular vein. Waters (1950) also reported alloxan monohydrate injection via auricular vein at the dose of 175 mg/kg induced diabetes mellitus in rabbits. The results of this investigation demonstrated that the administration of a single dose of alloxan to rabbits produced a reproducible model of diabetes mellitus. Three days after alloxan injection, rabbits exhibited polyuria, polyphagia and polydipsia. The clinical and laboratory findings were more severe in rabbits in the second group when compared to the rabbits in the first group. Severe polydipsia was observed in many of the rabbits. Moreover, 5 rabbits in the first group and 7 rabbits in the second group died within three days of alloxan injection. The cause of high mortality among rabbits might have been related to hypoglycemia or renal toxicity induced by alloxan (Kim et al 2006).

Fasting blood glucose levels in healthy cats and dogs were reported to be 75-120 mg/dL (Nelson 1985, Başoğlu ve Sevinç 2004, Fracassi et al 2007), while

Table 2. Hematologic parameters of the first and second groups (mean±SE).

	First group (days)					Second group (days)				
	0 (n:12)	4 (n:7)	8 (n:7)	12 (n:7)	16 (n:7)	0 (n:13)	4 (n:6)	8 (n:6)	12 (n:6)	16 (n:6)
RBC x10 ⁶ /mm ³	6.50±0.2 ^a	5.47±0.1 ^b	5.54±0.2 ^b	5.57±0.2 ^b	5.97±0.1 ^{ab}	6.10±0.1 ^a	3.32±0.5 ^c	3.52±0.4 ^c	3.93±0.5 ^c	4.41±0.2 ^b
PCV %	36.6±0.9 ^a	32.2±1.2 ^a	32.4±1.4 ^a	33.1±1.8 ^a	35.6±1.6 ^a	33.4±0.6 ^a	20.9±2.2 ^b	22.4±1.8 ^b	24.9±2.9 ^b	25.8±1.6 ^b
Hb g/dL	11.7±0.4 ^a	10.2±0.4 ^b	9.78±0.3 ^c	10.3±0.2 ^b	10.6±0.3 ^a	10.9±0.2 ^a	7.00±0.5 ^b	7.45±0.4 ^b	8.11±0.7 ^b	8.11±0.6 ^b
WBC x10 ³ /mm ³	7.52±0.5 ^b	9.30±0.3 ^a	7.82±0.6 ^b	7.84±1.1 ^b	6.57±0.4 ^b	9.48±1.5 ^{ab}	13.8±2.2 ^a	10.3±0.7 ^{ab}	7.50±1.3 ^b	5.40±0.8 ^b
PLT x10 ³ /mm ³	273±27 ^b	391±33 ^{ab}	434±58 ^a	369±33 ^{ab}	364±39 ^{ab}	334±72 ^b	479±95 ^b	603±60 ^a	413±51 ^b	481±56 ^{ab}
MCV fl	56.6±1.4 ^b	59.2±1.8 ^a	58.7±1.8 ^a	59.4±2.0 ^a	59.8±1.6 ^a	54.9±1.6 ^b	65.4±3.4 ^a	64.7±4.9 ^a	64.1±3.5 ^a	58.9±3.1 ^{ab}
MCHC g/dL	32.1±0.4 ^a	31.6±0.4 ^a	30.2±0.5 ^a	31.8±1.4 ^a	29.9±0.6 ^a	32.8±0.2 ^a	34.1±1.9 ^a	33.9±1.2 ^a	33.2±1.6 ^a	31.6±2.2 ^a

^{a, b, c, d}; different letters in the same line are statistically significant (p<0.05).

fasting blood glucose levels in healthy rabbits were 75-155 mg/dL (Friend ve ark 1981). The most significant laboratory findings in the diagnosis of diabetes mellitus are persistent fasting hyperglycemia (>200 mg/dL) and glycosuria (Nelson 1985, Turgut 2000, Kimmel 2002, McGuire et al 2002, Khan 2005). It was reported that fasting plasma glucose concentrations significantly increased in alloxane-induced diabetic dogs (Tiftik et al 1992, Arai et al 2002, Kim et al 2006). Similarly, Friend et al (1981) and Burski et al (2004) reported that a significant increase in fasting plasma glucose level in alloxane-induced diabetic rabbits. In the present study, it was found that the fasting serum glucose concentrations of the rabbits in the first and the second groups significantly increased (p<0.001) throughout the experiment. However, the increase observed in the serum fasting glucose concentrations of rabbits in the second group was higher than that of rabbits in the first group. The cause of high serum glucose levels observed in this group may be related to the administration of high-dose (175 mg/kg) of alloxan, as administration of high-dose (175 mg/kg) alloxan causes marked damage to pancreatic beta cells, reducing insulin secretion from pancreatic beta cells, and thus resulting in hyperglycemia. These finding are consistent with the results obtained by many other researchers (Friend et al 1981, Arai et al 2002, Burski et al 2004, Kim et al 2006, Fracassi et al 2007).

Serum fructosamine measurements should be performed in the diagnosis and monitoring of diabetes mellitus (Jensen 1993, Loste and Marca 2001, Davison et al 2005). Fructosamines are stable ketamine compounds formed when glucose in the open chain form reacts non-enzymatically with amino groups of proteins. Serum fructosamine increases with prolonged hyperglycemia or prolonged hyperproteinemia (Jensen 1995). Kimmel et al (2000) and Davison et al (2005) reported that median serum fructosamine concentrations in diabetic dogs were high and Martin et al (2006) also reported that serum fructosamine concentrations (>340 µmol/L) significantly increased in obese dogs. High serum fructosamine concentrations were also determined in hypothyroid dogs (Reusch et al 2002). Lost and Marca (2001) reported that

the determination of blood glycosylated hemoglobin and fructosamine levels was a significant and reliable criterion in the diagnosis of diabetes. In this study, serum fructosamine concentrations of the rabbits in the first and the second groups significantly increased (p<0.001) during the experiment. However, serum fructosamine concentrations of the rabbits in the second group were higher than that of the rabbits in the first group. It was reported that fructosamine could be used as the indicator of hyperglycemia, either due to stress or diabetes mellitus in some animals, especially in cats (Crenshaw 1996, Loste and Marca 2001). The results of this study indicated that fructosamine could also possibly be used in the diagnosis of diabetes mellitus in rabbits. These results were consistent with the results reported by Kimmel et al (2000), Lost and Marca (2001) and Davison et al (2005).

Blood glycosylated hemoglobin measurement may be useful in the diagnosis and monitoring of diabetes mellitus in human as it reflect the plasma glucose concentration for the previous months (Cerami et al 1978). In normal human beings, HbA1c constitutes approximately 3% of the total hemoglobin concentration, while in human diabetics, HbA1c values range from 6% to 10% of the total hemoglobin concentration (Trivelli et al 1971, Wong et al 2006). Wood and Smith (1980) found that HbA1c concentration in healthy dogs was 3% of the total hemoglobin concentration and it was between 3% and 7% in diabetic dogs. The period of hyperglycemia required to elevate HbA1c in dogs is unknown, but it would be expected to be approximately the same as that of human beings, because dogs have a similar RBC life span (approx 120 days). If times are similar, measured HbA1c would reflect plasma glucose status for preceding 3 to 4 weeks, which would be more useful to monitor insulin therapy (Wood and smith 1980). On the other hand, Lost and Marca (2001) reported that the determination of glycosylated hemoglobin and fruktosamin levels could provide useful information in the diagnosis and control of diabetes. Glycosylated hemoglobin is an indicator of the blood glucose concentration over the preceding two to three months (Nelson 2000). In this study, it was observed that blood HbA1c concentra-

tions of the rabbits in the first and the second group progressively increased ($p < 0.001$) during the experiment. However, in our study, the cause of the 2-3 fold increase observed in the HbA1c levels may be related to the short time of the experimental period. Serum fasting glucose, fructosamine and HbA1c parameters in rabbits with diabetes mellitus may be used as diagnostic indicators. These findings are consistent with the results of Wood and Smith (1980) and Nelson (2000).

Type-I or insulin-dependent DM is caused by the lack of insulin and results from the progressive destruction of the insulin-producing beta cells in the pancreas. A decrease is observed in the blood endogenous insulin level while an increase in blood glucose level in DM are observed (Nelson 2000, Khan 2005, Kim et al 2006, Martin et al 2006, Parsons et al 2007). Alloxan is the selective agent that destroys the beta cells of pancreas and causes type-1 diabetes mellitus (Powers 2001, Arai et al 2002, Burski et al 2004, Feldman and Nelson 2004). Kirk et al (1993) determined that the insulin levels in cats with type-1 diabetes mellitus were significantly lower when compared to the insulin levels in cats with type-2 diabetes mellitus. Parsons et al (2007) reported that endogenous insulin levels in dogs with diabetic ketoacidosis had a significant decrease. In this study, it was determined that the serum insulin concentrations of the rabbits in the first and the second groups significantly decreased during the experiment and decrease was more marked in the second group. These results were consistent with the results of Arai et al (2002) and Burski et al (2004).

One of the most important problems in patients with diabetes is dyslipidemia. Dyslipidemia is defined as the increase of triglyceride and cholesterol levels in the blood. Insulin regulates the biosynthesis and metabolism of triglycerides and the turnover of triglycerides cholesterol in lipoproteins at several major points in both the metabolic pathway and at the cellular receptor and absorption pathway (Goldberg 2001); in addition, it is a major regulator of adipose tissues lipid metabolism. Insulin resistance develops in patients with diabetes mellitus. Therefore, blood triglyceride and cholesterol levels increase in diabetes mellitus (Khan and Flier 2000). In diabetic patients, high-density lipoprotein (HDL) levels decrease, but low-density lipoprotein (LDL) and triglyceride levels increase (Kreisberg 1998, Nelson et al 2000). Hypercholesterolemia and hypertriglyceridemia usually occur in dogs with hypothyroidism and diabetes mellitus (Ford et al 1993). Nelson et al (2000) reported that serum cholesterol levels significantly increased in a cat with diabetes mellitus. In this study, serum triglyceride concentration of the rabbits in the first and the second group significantly increased and unlike first group, serum total cholesterol levels of rabbits in the first group during the experiment, serum

total cholesterol concentrations of the rabbits in the second group significantly increased during the experiment.

It is reported that normocytic normochromic anemia can rarely be observed in the diabetics (Ford et al 1993). Normal values in healthy rabbits are; WBC: 5-12.5 $\times 10^3$ μL , RBC: 5-8 $\times 10^6$ μL , Hb: 10-17 g/dL, PCV: 35-50, thrombocyte 250-650 $\times 10^3$ μL , MCV: 58-67 fl and MCHC: 29-37 g/dL (Khan 2005). In the present study, RBC, PCV and Hb concentrations of the rabbits in the second group were much below the reference values but these were within normal reference limits in first group (Khan 2005), MCV concentrations of the rabbits in the both group slightly increased but MCHC level did not change so it could be stated that mild normocytic normochromic anemia developed in rabbits in the second group. There may be a close relationship between the formation of anemia and the alloxan dose. Nelson (1985) has reported that leucocytosis may occur in diabetic patients. In this study, blood WBC counts of the rabbits in the both groups increased on the 4th day of the experiment. The increase in leucocytes count might be related to the inflammation caused by the drug (Turgut 2000). Blood thrombocyte counts of the rabbits in the both groups significantly increase during the experiment, but these values were within normal reference limits reported for rabbits (Khan 2005).

► Conclusion

Diabetes mellitus in the rabbits was successfully induced by a single dose of alloxan monohydrate via intra-venouse route. The clinical and laboratory findings of the rabbits in the second group were more severe. Serum fasting glucose, fructosamine, HbA1c and triglyceride concentrations increased and insulin level decreased in all rabbits with diabetes mellitus. Moreover, normocytic normochromic anemia occurred in rabbits in the second group. Serum fasting glucose, fructosamine and HbA1c may be reliable indicators for diagnosing DM.

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