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Protective effect of *Vaccinium myrtillus* on Paraoxonase Activity, Some Biochemical Parameters and Pancreatic Functions in Diabetic Rats

Diyabetik Sıçanlarda *Vaccinium myrtillus*'un Paraoksonaz Aktivitesi, Bazı Biyokimyasal Parametreler ve Pankreas Fonksiyonları Üzerindeki Koruyucu Etkisi

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ÖZET

Amaç: Diyabet, dünyada halk sağlığı alanında en büyük sorunlardan biridir. Şifalı bitkiler arasında yer alan *Vaccinium myrtillus L.* özütü, güçlü antioksidan aktiviteye sahiptir. Bu amaçla, deneysel diyabetik sıçanlarda *Vaccinium myrtillus* ekstraktının serum paraoksonaz (PON1), pankreas enzim düzeyleri ve lipid düzeyleri üzerine olası etkileri araştırıldı.

Materyal ve Metot: Bu çalışmada toplam 32 erkek sıçan (Wistar albino) kullanıldı ve dört gruba ayrıldı. Kontrol(C), diyabetik (D), *Vaccinium myrtillus* (VM), diyabet artı *Vaccinium myrtillus* (DVM) grupları. D ve DVM gruplarında, tek doz intraperitoneal 45 mg/kg streptozotosin kullanılarak deneysel diyabet oluşturuldu. *Vaccinium myrtillus* özütü, VM ve DVM gruplarına oral gavaj yoluyla 1.2 mg/kg/21 gün olarak uygulandı. Çalışmanın sonunda; serum HbA1c, lipid parametreleri, amilaz, lipaz ve paraoksonaz (PON1) enzimleri analiz edildi.

Bulgular: VM (VM ve DVM) ile tedavi edilen diyabetik gruplarda HbA1c önemli ölçüde azaldı. Diyabetik deneklere VM uygulandıktan sonra kolesterol, LDL-C ve VLDL-C seviyeleri önemli ölçüde azalırken, diğer lipidlerin önemsiz bir şekilde azaldığı bulundu. *Vaccinium myrtillus* ekstresi DVM grubunda D grubuna göre pankreas enzimlerinde hafif bir düşüşe ve paraoksonaz enziminde istatistiksel olarak anlamlı bir artışa neden oldu.

Sonuç: Elde edilen veriler, *Vaccinium myrtillus* ekstresinin diyabetle ilişkili komplikasyonların önlenmesinde potansiyel koruyucu bir rol oynayabileceğini desteklemektedir.

Anahtar Kelimeler: *Vaccinium myrtillus*, diyabet, Paraoksonaz, Pankreas Fonksiyonu, Lipidler.

ABSTRACT

Objective: Diabetes is one of the biggest problems in the field of public health in the world. *Vaccinium myrtillus* L. extract, among the medicinal plants, has powerful antioxidant activity. For this aim, the possible effects of *Vacillus myrt*illus extract on serum paraoxonase (PON1), pancreatic enzyme levels, and lipid levels in experimental diabetic rats were investigated.

Material and Method: A total of 32 male rats (Wistar albino) were used in this study and divided into four groups. Control (C), diabetic (D), *Vaccinium myrtillus* (VM), diabetes plus *Vaccinium myrtillus* (DVM) groups. In D and DVM groups, experimental diabetes was induced using a single dose of intraperitoneal 45 mg/kg streptozotocin. *Vaccinium myrtillus* extract was administered as 1.2 mg/kg/21 days by oral gavage in VM and DVM groups. At the end of the study; serum HbA1c, lipid parameters, amylase, lipase, and paraoxonase (PON1) enzymes were analyzed.

Results: HbA1c was significantly reduced in diabetic groups treated with VM (VM and DVM). Cholesterol, LDL-C, and VLDL-C levels were significantly reduced after VM was administered to diabetic subjects, while other lipids were found to decrease insignificantly. *Vaccinium myrtillus* extract caused a slight decrease in pancreatic enzymes and a statistically significant increase in paraoxonase enzyme in the DVM group compared to group D.

Conclusion: The obtained data support that *Vaccinium myrtillus* extract may play a potential protective role in preventing diabetes-associated complications.

Keywords: *Vaccinium myrtillus*, Diabetes, Paraoxonase, Pancreas Function, Lipids.

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INTRODUCTION

Diabetes mellitus (DM) is a rapid growing metabolic disease and one of the global health the problem is expected to increase to 360 million affected people by 2030 (Ryden et al., 2013). Chronic hyperglycemia and disturbances in the metabolism of carbohydrates, proteins, and lipids, are the main

characteristic of this disease. The incidence of diabetes stems from insulin resistance and insulin insufficiency (Alberti and Zimmet, 1998).

Wide ranges of approaches have been adopted for diabetes treatment ranging from environmental properties' alteration to therapeutic drugs usage. Chemicals have various mechanisms of action, eventually resulting in the reduction of hyperglycemia (Krentz and Bailey 2005). These drugs are known to have many adverse health effects making researchers seek for alternative agents from natural sources (Kos et al., 2012; Stein et al., 2013). Potent candidates are plants and their contents; several plants have been used in the treatment of diabetes in traditional medicine (Li and Perera, 2012) since they contain many bioactive compounds that exhibit anti-diabetic activities via various pathways (Wang et al., 2013).

Vaccinium myrtillus L. (bilberry) is a medical plant that has been used for the treatment of many diseases, including DM in traditional medicine (Helmstädter and Schuster, 2010). Phytochemicals in this plant, especially anthocyanin, a phenolic compound, are responsible for ant-diabetic activity via antioxidant and anti-inflammatory actions (Chu et al., 2011).

Anthocyanins exhibit their anti-diabetic activity by improving insulin resistance, protecting pancreatic beta cells from oxidative damage and increasing insulin secretion (Sancho and Pastore, 2012). *Vaccinium myrtillus L.* and its pigments also have roles in attenuation in contributing factors to diabetes, including obesity and impaired lipid metabolism (Asgary et al., 2015).

Paraoxonase1 (PON1) is calcium-dependent glycoproteins enzyme associated with high-density lipoproteins (HDLs) and possesses detoxifying activity via organophosphate hydrolysis. Clinical importance of this enzyme is associated with anti-oxidant activity and anti-atherogenic property by protecting low-density lipoproteins LDL from oxidative modification. This enzyme protects LDL from oxidation through hydrolyzing lipid peroxides and retarding macrophage-mediated LDL oxidation (Mackness and Mackness, 2015).

The aim of this study is to examine the effect of the administration of *Vaccinium myrtillus* L. fruits' extract on both paraoxonase activities and lipoproteins levels in experimental diabetic rats.

MATERIAL and METHOD

Animal

Thirty-two (32) rats weighing 250-300 grams were supplied from the experimental Animal Unit of Van Yuzuncu Yil University. Subjects were divided equally into four groups (n=8): control (C), diabetes (D), *Vaccinium myrtillus* extract (VM), diabetes plus *Vaccinium myrtillus* extract (DVM). During three weeks of the study, rats were exposed to 12 hours light/dark system in 18-22 C°. The rats were left for 21 days for acclimatization before the experiment. This method was accepted by Experimental Animal Ethical Committee belonging to Van Yuzuncu Yil University (Order Number: 2016/04 Date: 05.05.2016).

Experimental procedure

Diabetes was induced in D and DVM groups by injecting 45mg/kg single dose streptozotocin (Sigma-Germany) dissolved in cold citrate buffer pH:4.5 intraperitoneally (İP) (Vardi et al. 2005).

1. Control group (C): This group has been fed standard rat diets and they were given distilled water using intragastric gavage.

2. Diabetes group (D): Diabetes group was induced using 45 mg/kg STZ injection and a standard normal diet was given. After 72 hours, blood glucose of blood from the tail puncture has been measured and the rat's more than 270 mg/kg blood glucose was accepted as diabetes.

3- Group of *Vaccinium myrtillus L.* (VM): Along with the normal diet, a dose of 1.2 mg/kg of *Vaccinium myrtillus* L. extract (Bilberry, GNC, USA)

dissolved in distilled water was given to every rat using intragastric gavage (Grace et al., 2009).

4- Group of Diabetes and *Vaccinium myrtillus L*. (DVM). Diabetes was induced in this group by injecting a single dose of 45 mg/kg streptozotocin intraperitoneally given. After 72 hours, blood glucose of blood from tail puncture has been measured and the rats more than 270 mg/kg blood glucose was accepted as diabetes. a dose of 1.2 mg/kg of *Vaccinium myrtillus* L. extract (Bilberry, GNC, USA) dissolved in distilled water was given to every rat using intragastric gavage (Grace et al., 2009).

Sample collection

Blood glucose taken from tail puncture during the experimental period was determined using glucometer equipment and strips from eBsensor (Taiwan) company. All samples more than 270 mg/dl blood glucose was accepted as diabetes. After 21 days of the experimental periods, under anesthetic conditions, blood was taken from heart puncture into both jell tubes and EDTA tubes. Blood glucose analysis and HbA1c level were measured on the same day. The sera were preserved at -20 C^o until the day of analysis of paraoxonase enzyme, pancreatic functions, and lipoprotein levels.

Biochemical parameters and analyses

Serum paraoxonase (PON) activities were analyzed using the spectrophotometric kit supplied by Rel assay (Turkey) using the automated colorimetric method. The levels of glucose, HbA1c, lipoproteins and pancreatic enzymes were determined using kits and biochemical auto analyzers by (Cobas C311, Roche- Germany).

Statistical analysis

Comparisons among groups and among tissues were done using the nonparametric Kruskal-Wallis test and then the Mann-Whitney U-test as the post hoc test correction was used. Data were given as median (minimum-maximum) and P-values <0.001 and <0.049 were considered to be statistically significant, respectively. For statistical analysis, the SPSS 13.0 for Windows statistic package program was used (SPSS Inc., Illionis, USA)..

RESULTS

Biochemical parameters, pancreatic enzyme activity, and paraoxonase enzyme levels of the groups are presented in Table 1. Serum glucose level was increased significantly ($p<0.05$) in the diabetes group (D) in comparison with control group (C). No significant difference ($p<0.05$) in glucose level between the control group (C) and *Vaccinium myrtillus* group (VM) can be seen. Treatment with *Vaccinium myrtillus* was associated with significant decrease ($p<0.05$) in glucose levels in DVM group if they compared to diabetes group (D).

HbA1c level was significantly increased ($p<0.05$) in the diabetes group (D) in comparison with control group (C). HbA1c levels showed no significant difference ($p<0.05$) in *Vaccinium myrtillus* group (VM) compared to control group (C). Treatment of diabetes with *Vaccinium myrtillus* extract showed a significant decrease ($p<0.05$) in HbA1c level in DVM group compared with diabetes (D) group.

Cholesterol was significantly decreased ($p<0.05$) in *Vaccinium myrtillus* group (VM) in comparison to control group (C). Administration of *Vaccinium myrtillus* extract caused significant decrease ($p<0.05$) in DVM group in comparison with their corresponding model diabetes D group.

Diabetic rats in group D showed a non-significant increase ($p>0.05$) in triglycerides in comparison with the control (C) group. Giving *Vaccinium myrtillus* extract to *Vaccinium myrtillus* group (VM) caused significant decrease ($p<0.05$) in TG level in comparison to control group (C). Treatment with *Vaccinium myrtillus* extract showed decrease in triglycerides in DVM group (84.83±15.59 mg/dl) in comparison to Diabetes D group while the change was not statistically significant ($p>0.05$).

In this study, diabetes caused a significant increase ($p<0.05$) in HDL levels in diabetic group (D) compared to the control group (C). There was a significant decrease ($p < 0.05$) in *Vaccinium myrtillus* group

(VM) if compared to the control group (C). Feeding *Vaccinium myrtillus* extract was related with significant decrease (p<0.05) in HDL level in DVM group in comparison with diabetic group (D).

The development of diabetes was associated with a non-statistically significant, Increase (p>0.05) in LDL levels in diabetes (D) group in comparison to the control group (C). The results showed no significant difference (p>0.05) in LDL level between *Vaccinium myrtillus* (VM) and control (C) group. Treatment with *Vaccinium myrtillus* extract caused a significant decrease (p<0.05) in LDL level in DVM group in comparison with D group.

Amylase level was decreased significantly (p<0.05) in the diabetes group (D) compared to the control group (C). No significant change (p>0.05) was obtained from the results between *Vaccinium myrtillus* (VM) and control (C) group. After treatment with *Vaccinium myrtillus* extract, there was a statistically non-significant decrease (p>0.05) in amylase in DVM group compared to the diabetes group (D).

Development of diabetes by streptozotocin was associated with a significant increase (p<0.05) in lipase activity in the diabetes (D) group compared to the control (C) group. No significant change (p>0.05) can be seen between *Vaccinium myrtillus* group (VM) and the control group (C) for lipase. The treatment by *Vaccinium myrtillus* extract showed a slight but not statistically significant (p>0.05) decrease in lipase activity in DVM group in comparison to diabetes (D) group.

Paraoxonase activity was decreased significantly (p<0.05) in diabetes (D) group compared to the control group (C). Giving *Vaccinium myrtillus* extract caused significant increase (p<0.05) in *Vaccinium myrtillus* group (VM) in comparison to control group (C). Treatment with *Vaccinium myrtillus* extract caused statistically a significant increase (p<0.05) in DVM group in comparison to the diabetes (D) group.

Table 1. Serum glucose, hemoglobin A1c, total cholesterol, total triglyceride, lipoprotein, lipase, amylase and paraoxonase levels of rats in groups.

	Control (C) X±SD	**Diabetes (D)** X±SD	***V. myrtillus* (VM)** X±SD	**Diabetes+ *V. myrtillus* (DVM)** X±SD	**p**
Glucose (mg/dL)	158±42 a	636±84 c	230±55 a	464±220b	0.001
HbA1c (%)	3,8±0,1 c	8,0±0,8 a	3,8±0,2 c	6,7±1,8 b	0.001
TC (mg/dL)	56±9 b	77±11 c	44±4 a	52±10 ab	0.001
TG (mg/dL)	94±13 b	101±32 b	54±13 a	84±16 b	0.001
HDL-C (mg/dL)	51±9 b	61±7 c	41±3 a	46±5 ab	0.001
LDL-C (mg/dL)	20±7 ab	25±4 b	14±4 a	17±10 a	0.016
VLDL-C (mg/dL)	18±3 bc	22±6 b	11±3 a	17±3 c	0.001
Amylase U/L	1073±75 b	681±238 a	1008±59 b	575±183 a	0.001
Lipase (U/L)	7,8±1.2 a	21,3±5,8 b	6,8±1,3 a	19,3±7,8 b	0.001
Paraoxonase (U/L)	34,0±29,3 ab	3,6±5,3 a	51,9±42,2 b	17,5±27,4 ab	0.049

Differences between mean values with different letters are significant (P<0.001-0,049).

HbA1c, Hemoglobin A1c; TG, triglyceride; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low- density lipoprotein cholesterol.

Data were expressed as mean±SD.

DISCUSSION

In this study, the effect of *Vaccinium myrtillus* L. extract on paraoxonase enzyme activity, lipoproteins and pancreatic enzyme levels were studied. Despite anti-diabetic activity of *Vaccinium myrtillus* L. extract, the possible protective activity of this plant against diabetic cardiovascular complications via enhancing paraoxonase activity was also examined.

The extract of this plant contains many bioactive compounds that exhibit this anti-diabetic activity including anthocyanins and flavonoids such as quercetin and catechin (Chu et al., 2011). The role of anthocyanins emphasizes many mechanisms including improvement of insulin resistance and increasing insulin level, reduction in carbohydrates catabolism and, protection of pancreatic beta cells from oxidative damage (Sancho and Pastore, 2012). The overall consequence of these actions is a reduction in blood glucose as concluded in this study and agreed to the previous studies (Asgary et al., 2015).

Antioxidant activity of both anthocyanins and phenolic compounds in *Vaccinium myrtillus* is one protective mechanism against oxidative damage of pancreatic beta cells by caused by oxidative stress. It is known that hyperglycemia in diabetes leads to the generation of reactive oxygen species (ROS), and this causes beta cellular apoptosis and eventually leads to damage of the beta cells (Ahren, 2005).

The significance of the determination of HbA1c is the clarification of the anti-diabetic activity of *Vaccinium myrtillus* extract in chronic terms since; this parameter is applicable for the detection of chronic rather than acute hyperglycemia. Moreover, most of the other previous works have focused on glucose only (Asgary et al., 2015).

The results of the present study showed about 28% and 17% decrease in the levels of glucose and HbA1c respectively by using 300 mg/kg of anthocyanins. Because of the importance of the dose used in alternative medicine, and because it was approved that greater hypoglycemic activity was obtained from the greater dose of anthocyanins, it's important to study further different doses of anthocyanins (Grace, 2009).

The results obtained from the current study indicate that inducing diabetes with streptozotocin was associated with a significant increase in total cholesterol, triglycerides, LDL, and VLDL. These findings are in agreement with the results obtained from previous studies (Adiels et al., 2006; Yadav, 2013).

Diabetic dyslipidemia is implicated with increased risks of cardiovascular complications. A key point of the pathophysiology in dyslipidemia is an elevation in triglycerides-rich VLDL levels by the liver (Farbstein and, Levy, 2012). It was known that the overproduction of large particles of VLDL is one of the most important mechanisms of triglycerides elevation in type 2 diabetes (Adiels et al., 2006).

Insulin hormone has its roles since it inhibits the secretion of chylomicrons which are molecules of lipoproteins that transfer triglycerides and cholesterols from enterocytes to the circulation through the lymphatic system. Thus, insulin level decreases in diabetes, causing excessive secretion of chylomicrons, thereby inducing hyperlipidemia (Xiao and Lewis, 2012).

Elevation in LDL levels in diabetes is induced mainly by the increased the levels of triglycerides and insulin resistance (Nakajima et al., 2011). The mechanism of production of LDL includes the transfer of triglycerides from VLDL via the action of cholesterol ester transfer (CETP). Thus, the presence of VLDL which contains a large amount of triglyceride is required for the production of LDL and this may explain hypertriglyceridemia- related increase in LDL level in diabetes (Taskinen and Borén, 2015).

In general, cholesterol elevation in diabetes may result from increased glycation of cholesterol- rich

lipoproteins, insulin deficiency and, insulin resistance. It was known that the synthesis of cholesterol is up-regulated in insulin resistance and type 2 diabetes. Moreover, this increase was related to insulin resistance independently to obesity (Gylling et al., 2010).

Results from the present study showed that giving *Vaccinium myrtillus* extract to diabetic rats caused a reduction in cholesterol, triglycerides, LDL, and VLDL. The same results were obtained from other previous studies (Asgary et al., 2015, Kruger et al., 2014). These findings indicate that the extract of *Vaccinium myrtillus* is positively associated with the improvement of diabetic dyslipidemia and may alleviate most of the abnormalities in diabetes (Asgary et al., 2015). Anthocyanins and other bioactive compounds may account for the improvement of diabetic dyslipidemia via the regulation of enzymes involved in lipoprotein metabolism (Tsuda et al., 2003).

General mechanisms by which anthocyanins ameliorate abnormalities in lipid metabolism include antioxidant activity, anti-inflammatory activity and, anti-ischemic effect and cardioprotective effects of this substance (Kruger et al., 2014). By these actions, anthocyanins are able to reduce insulin resistance and incidence of diabetes and these are confirmed by some studies (Tsuda et al., 2003).

A decrease in cholesterol level after *Vaccinium myrtillus* feeding in this study may result from the effect of anthocyanins content via increasing fecal cholesterol content. A study showed that anthocyanin from certain plants caused a decrease in plasma levels of cholesterol via increasing acidic and neutral sterols in the faces (Liang et al., 2013).

Results of HDL levels from this study disagreed with the previous studies and also contraindicated with our hypothesis. It was known that HDL level has decreased in diabetes, and this reduction is associated with the pathophysiology of diabetes and the development of a diabetic complication, especially cardiovascular complication. However, the conflicts of our result in HDL level may arise from technical issues either in the experimental animal management, preparation of plant extract solution method and/or HDL level assay procedure (Farbstein and Levy, 2012; Kostapanos, 2014).

According to the results obtained from the current, study, inducing diabetes by streptozotocin caused a significant decrease in amylase levels in rats. And also giving *Vaccinium myrtillus* extract in diabetic rats led to a further decrease in amylase activity. Diabetic reduction of amylase was also found in previous studies (Nakajima et al., 2011; Yadav et al., 2013; Mahmood and Kahraman, 2019;).

Many mechanisms have been suggested to interpret exocrine pancreatic deficiency in diabetes. As long as diabetes disease affects the pancreas organ, this effect comprises also the modification in the exocrine portion. The first important explanatory mechanism is related to the insulin hormone. Insulin is known to have trophic activity on amylase hormone via acting on acinar cells. So in diabetes, one consequence of insulin deficiency is a decrease in amylase. In contrast to insulin, glucagon prossesses an inhibitory effect on amylase activity. Thus, elevation of the glucagon level may the associate with amylase reduction (Singh et al., 1998). Histological modifications due to diabetes as pancreatic fibrosis, atrophy and fatty infiltration result in loss of acinar cells (Matsuda et al., 2014).

Results of amylase sometimes show conflict results. In some studies increase the activity of this enzyme has been observed in type 1 diabetes and diabetic ketoacidosis. The difference in pathological picture and mechanism of development of this type of diabetes may stand behind amylase elevation (Yadav et al., 2013).

The study supported that administration of *Vaccinium myrtillus* extract to the diabetic rats was associated with a 15.5% reduction in amylase activity. Inhibitory effects on amylase level can be regarded as one mechanism of hypoglycemic activity of this plant since many other plants extracts have targeted amylase in their anti-diabetic activities. By reducing amylase, these plants have restricted carbohydrate

sources because the function of amylase is catabolism of intestinal carbohydrate (Cheng et al., 2013).

The sudden increase in blood glucose level in type 2 diabetes is mediated by hydrolysis of starch by the action of amylase. Therefore, the finding of amylase inhibition by *Vaccinium myrtillus* extract is significant for illustrating of one mechanism of hypoglycemic activity exhibited by this plant (Gray, 1995).

In the present study, the development of diabetes caused a significant increase in lipase activity. And the treatment of diabetic rats with *Vaccinium myrtillus* extracts was associated with a slight decrease in lipase. The degree of this reduction was not statistically significant; however, it was about 10%. The diabetic increase in lipase has also been observed in other studies (Steinberg et al., 2014; Mahmood and Kahraman 2019).

A slight reduction in lipase activity (10 %) after treatment with *Vaccinium myrtillus* has been observed in this study. Anti-lipase activities of bioactive compounds from many plants other than *Vaccinium myrtillus* were approved in previous studies (Jeong et al., 2014; Dechakhamphu and Wongchum, 2015).

Lipase enzyme exhibits main role in lipid absorption in the small intestine via hydrolysis of triglycerides from dietary fats to fatty acids. So, by inhibiting lipase, *Vaccinium myrtillus* extract is able to decrease fatty acid absorption and thus participate in the alleviation of dyslipidemia and obesity (Hegele et al., 2001). Anti-lipase activities of bioactive compounds in *Vaccinium myrtillus* plant may account for lipase reduction. It was concluded that extracted phenolic compounds especially quercetin showed strong inhibitory effects against lipase enzyme (You et al., 2012). Similarly, some types of anthocyanins have decreased lipase activity (Guo et al., 2012).

In the present study, paraoxonase (PON) activities have declined in diabetes, and treatment of diabetic rats with *Vaccinium myrtillus* extract caused an increase in the activity of this enzyme. Reduction in PON in diabetic subjects has been observed in many previous works (Abbott et al., 1995, Ying, 2010).

PON is associated with HDL and its' clinical role is the prevention of LDL from peroxidation. However, the decrease in this enzyme in diabetes may result from the disruption in association of the enzyme molecule to HDL. Normally, PON is associated to HDLs that contain Apo A-1 proteins and clusterin. It was known that there is a loss or weakness in the correlation between the enzyme protein, Apo A-1, and HDL molecules. In addition, a larger portion of the enzyme protein may be inactive in diabetes due to the existence of endogenous circulating inhibitors and/or due to increased glycosylation of paraoxonase (Abbott et al., 1995).

The current study showed that *Vaccinium myrtillus* extract caused an increase in PON in diabetic subjects. Increase in PON level by effects of various plants fond by other researchers (Takaeidi et al., 2014; Mahmood and Kahraman 2019).

Bioactive compounds in our plant possibly drive the elevation of PON activity, and this can be regarded as one mechanism of antioxidant activity of this plant. Anthocyanins were known to have a critical role in improving PON activity, and this caused enhancement in cholesterol efflux capacity in hypercholesterolemic rats. This finding has the linked lipid-lowering ability of anthocyanin to PON increasing the ability of this substance (Zhou et al., 2014). Increase in PON activity contributes to the improvement of HDL function and aortic cholesterol reduction (Farrell et al., 2015).

The significance of stimulatory effects of *Vaccinium myrtillus* on PON activity which is concluded in the present study can be clarified by important positive roles in health and those multiple physiological roles that exhibited by this enzyme. PON is able to prevent LDL from oxidation and inhibits cell membrane oxidation, thus, this enzyme is regarded as an atheroprotective enzyme since LDL concentration is directly related to the incidence of atherosclerosis. PON1 participates in the antioxidant activities of HDL. Deficiency in PON activity is common in

many diseases related to inflammatory basics and this is deficiency is believed to result in dysfunction of HDL and consequently promote inflammation and atherosclerosis. Because of all of these positive roles of PON in health especially related to coronary heart disease (CHD), *Vaccinium myrtillus* extract may exhibit preventive roles in the progression of these diseases via increasing PON activity and improving dyslipidemia. However, despite these conclusions, further confirmatory studies may be required.

Conclusions

Vaccinium myrtillus L. extract presented antidiabetic activity against experimental diabetes. Our studies have shown that *Vaccinium myrtillus* L. extract can be helpful in improving hypoglycemia and alleviating dyslipidemia in diabetes. Feeding *Vaccinium myrtillus* L. extract to diabetic rats caused a significant decrease in blood glucose level and glycated hemoglobin (HbA1c) and reduced the levels of total cholesterol, triglycerides, LDL, and VLDL. *Vaccinium myrtillus* L. extract administration to diabetic rats was associated with a slight decrease in the pancreatic exocrine function via decreasing both amylase and lipase enzymes. This study suggests that *Vaccinium myrtillus* L. may play an important role in the prevention of diabetes and its complications.

Conflict of interest

The authors declare that there is no conflict of interest.

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Evaluation of The Behavior Changes in Mothers Caused by Covid-19 Positivity

Annelerde Covid-19 Pozitifliğinin Neden Olduğu Davranış Değişikliklerinin Değerlendirilmesi

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ÖZET

Amaç: Bu çalışmada Covid-19 pozitif annelerin rol ve ebeveyn davranışlarında meydana gelen değişikliklerin incelenmesi amaçlanmıştır.

Materyal ve Metot: Veri toplamak için sosyo demografik soru formu ile Anlamsal Farklılık Ölçeği-Anne Olarak Kendim (SDÖ) ve Annenin Ebeveyn Davranışı Ölçeği - Ebeveyn Forumları (MPBS) kullanılmıştır. Araştırma Gaziantep ilinde ve Eylül-2020 ayında yapılmıştır. Web tabanlı bir anket tasarlandı. Çalışmada elde edilen verilerin analizinde SPSS 24.0 istatistik paket programı kullanıldı**.**

Bulgular: Katılımcıların %66,7'si 18-32 yaşları arasında, %66,7'sinin eğitim düzeyi lise ve üzeri, %97,4'ü 1 ve 2 çocuk sahibi ve % 53,8'i ev hanımıdır. Katılımcıların% 84,8'inin kronik bir hastalığı olmadığı, %86,4'ünün evinde yaşlı bir bireyin olmadığı belirlenmiştir. Katılımcıların% 82,9'unun Covid-19 sürecini evde geçirdiği, % 36,4'ünün Ağustos ayında Covid-19 pozitif olduğu, % 62,1'inin ise birden fazla semptomu olduğu bulunmuştur. Ayrıca, katılımcıların %15,2'sinin semptomlarının bir haftada azaldığı, % 47,7'si Covid-19'dan korunmak için hijyen kurallarına uyduğu görülmüştür. Katılımcıların % 93,2'si sosyal çevresi ile ilişkilerinin Covid-19 sürecinden olumsuz etkilendiği ve % 80,3'ünün aile içi ilişkilerinin Covid-19 sürecinden olumsuz etkilendiği belirlenmiştir. Katılımcıların Anlamsal Farklılık Ölçeği-Anne Olarak Kendim toplam puanı 38.63 ± 8.10 idi. 18-32 arası yaştaki annelerin Anlamsal Farklılık Ölçeği-Anne Olarak Kendim ortalama puanı diğer annelere göre daha düşüktü ve iki anne grubu arasında (18-32 yaş ve 33 yaş üstü) istatistiksel olarak anlamlıydı. Katılımcıların MPBS toplam puanı 49.03 ± 6.30 idi. Katılımcıların demografik verileri arasında Annenin Ebeveyn Davranışı Ölçeği - Ebeveyn Forumları puanı açısından anlamlılık bulundu. Ancak, her iki grubunda MPBS toplam puan ortalamasının düşük olduğu görülmüştür.

Sonuç: Covid-19 pozitif annelerin annelik rolü ve ebeveynlik davranışları ölçeklerinden düşük puan aldıkları saptanmıştır.

Anahtar Kelimeler: Annelik rolü, Covid-19, Ebeyevn davranışları.

ABSTRACT

Objective: In this study, it was aimed to examine the changes in the role and parental behaviors of Covid-19 positive mothers**.**

Material and Method: The questionnaire form and Semantic Differential Scale-Myself As Mother (SDS) and Mothers Parental BehaviorScale -Parental Form (MPBS) were used to collect the data. The research was carried out in Gaziantep, in September, 2020. A web-based survey has been designed. SPSS 24.0 statistical package program was used in the analysis of the data obtained in the study.

Results: of the participants are 66.7% between the ages of 18-32, 66.7% of them have high school or higher education level, 97.4% have 1 or 2 children and 53.8% are housewives. It was determined that 84.8% of the participants did not have a chronic disease, and 86.4% did not have an elderly individual at home. It was found that 82.9% of the participants spent the Covid-19 process at home, 36.4% were positive for Covid-19 in August, and 62.1% had more than one symptom. Also, of participants' 15.2% symptoms decreased in a week, 47.7% of the participants used hygiene rules foractions to protect from Covid-19. 93.2% of the participants' social relations were affected negatively by the Covid-19 process. 80.3% of the participants' family relations were affected negatively by the Covid-19 process. Semantic Differential Scale-Myself as Mother meanscore total score of theparticipantswas 38.63±8.10. Semantic Differential Scale-Myself as Mother meanscore of mothers aged between 18-32 was less thanothe rmothers, and there is statistical significance between the two mother groups (18-32 age and 33 andaboveage). MPBS total score of the participants was 49.03±6.30. Value was found a mong the participants' demographic data in terms of MPBS score. However, the mean Mothers Parental Behaviours Scale - Parental Form total score was found to be low in both groups.

Conclusion: As a result of this research, it is determined Covid-19 Positive Mothers of Maternity and Parental Behaviors have owers cores.

Keywords: Mothers role; Covid-19; Parental behaviors.

INTRODUCTION

Acting as a mother and a parent is a very complex, multi-stage process. The theory and model of being a mother help facilitate the complex parenting process. Mercer has identified four factors that are effective in gaining a motherhood role and emphasised the importance of these factors. These factors are; nursing, individual, health and environment. The transition to the role of motherhood is the process of learning the woman's maternity behaviour. In this process; shaping the identity of the mother, gaining the role of motherhood, which is, becoming a mother is realized (Tomey and Alligood, 1998; Mercer, 2004; Mercer, 2006; Özkan and Polat, 2011; Feenstra et al., 2019).

Maternity role acquisition is a combination of social roles and developmental behaviors and attitudes that begin in the prenatal period, continue in the postnatal period and are completed with the formation of maternal identity development (Tomey and Alligood, 1998; Mercer, 2004; Mercer, 2006; Meighan and Mercer, 2014). The role function area is related to the individual's roles in society and expresses social integrity. The responsibilities that the individual takes throughout her life and all the roles she fulfils are evaluated in this field. The area of mutual commitment includes all interactions of the individual with the environment and the other people (Özkaraman et al., 2012; Taşkın, 2015).

Insufficiency in parenthood is where one or more caregivers show a current or potential inadequacy in providing a constructive environment that supports/nourishes the child's growth and development. This can happen from parents, child, maturational and situational (personal, environmental) reasons. Factors originating from the parent include single parenting, adolescent parenting, abuse, swearing, emotional disorder, alcoholism, drug addiction, terminal disease, acute illness, and accident victims. Factors originating from the child are: Being born with an unwanted pregnancy, having unwanted sex (especially in our culture, a boy is much more desired), having unwanted characteristics (having an anomaly, looking like someone whose parents do not like), being physically or mentally disabled, having hyperactivity, having a terminal illness. Maturational factors; adolescent parents are situations such as the parents' conflict or abuse with their own parents, parent's surreal expectations from the child, and the child's psycho-social expectations cannot be met. Situational (personal, environmental) factors could be disease, imprisonment / conviction, moving, disruption of the nuclear family, inconsistency of caregiver or care-giving techniques, ignorance, lack of role model, relationship problems, marital conflict, divorce, separation, step parent, a new sibling, care of an elderly, economic problems (Ursavaş et al., 2014; Heydarpour et al., 2017). Many reasons such as illnesses, personal problems and psychological problems can negatively affect maternal roles (Ursavaş et al., 2014). Today, Covid-19 has caused changes in maternal roles (Spinelli et al., 2020). Coronavirus (Covid-19) belongs to the same category of viruses which cause SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome) (Huang et al., 2020; Novel, 2020). The virus gives rise to seriously acute respiratory infections and is asymptomatic or mild or acute symptomatic (Huang et al., 2020).

The effects of the interactional behaviours of parents (especially mothers) as primary caregivers, who are among the close environment of children and with whom they interact most in childhood, on children's development have been demonstrated both theoretically and practically (Çalışır, 2003; Mahoney and Mac Donald, 2004). Therefore, this research was planned considering the importance of mothers in child development, and it is aims to examining changes in the maternal role of mothers and parental behavior due to the Covid-19 outbreak.

MATERIAL and METHOD

The Population of the Research

While the population of the research was composed of all mothers who use social media, the sample consisted of mothers who were positive for Covid and had children aged 4-9.

Collection of Data

The questionnaire form and Semantic Differencial Scale-Myself As Mother (SDS), and Mothers's Parental Behaviour Scale-Parental Form (MPBS) were used to collect the data.

Socio-demographic questionnaire: There are various questions about Covid-19 and motherhood in the socio-demographic questionnaire [age, educational status, residence and region, marital status, occupation, number of children, whether there is a child with chronic disease at home, whether there is a 65-year-old person at home, the date and symptoms of Covid19 disease, reduction in the role of mother whether there is the disease, the place where the disease is (home or hospital ...), the duration of the disease, whether to donate plasma or not, whether to have a Covid-19 vaccine, advice to those who do not have the disease, whether there are those who have the disease around, who is infected by the disease, family and social questions about how it affects their relationships, what measures they take and whether they comply with the measures].

Semantic Differential Scale-Myself as Mother

This measures the evaluation dimensions of "myself as mother" concept. Scoring was obtained by using 11 items of a 22-item scale. These 11 items were distributed among the 22-item opposite adjective pairs (e.g., in the event that the fast-slow adjective pair was taken into consideration for scoring, the moving-moving adjective pair was eliminated). Eleven items constitute 11 opposite adjective pairs with a 7-point. To prevent the participants from giving biased answers, three items were assessed by reverse scoring. The third, seventh and eighth items were evaluated over "one" point instead of "seven" points. The validity and reliability study of the Turkish version of the scale defined by Walker et al. (1986), based on the factor analysis of responses given by 104 mothers, was conducted by Çalışır (2003). Higher total scores obtained from the scale indicate a positive self-assessment of motherhood. The lowest and highest points obtained from the "Myself as Mother" scale were 11 and 77, respectively. The Cronbach's alpha of this scale was found to be. 81 − .85 by Walker et al., and. 73–.74 by Çalışır (2003). In this study, Cronbach's alpha of this scale was .69 (Walker et al., 1986).

Mothers Parental Behaviours Scale - Parental Form

Parental Behavior Questionnaire-Parent Form was also developed by Sessa et al., (2001) and adapted into Turkish by Vargün (2019). Also, this scale was developed for mothers with preschool children to evaluate their parental behaviour. This scale examined mothers' parental behaviours in three dimensions: sensitivity, hostility, and structure. The participants answered the relevant items on a 4-point Likert-type scale (1 = strongly agree, 4 = strongly disagree) (Sessa et al., 2001; Vargün, 2019)

Application of the Research

The research was conducted in descriptive and cross-sectional type in Gaziantep-Turkey at September. A web-based survey has been designed (A face-to-face study could not be conducted due to the Covid-19 epidemic). The answers to the questionnaire were obtained by responding online by the participants with the help of their desktop, tablet or laptop computer and mobile devices (Whatsapp, mail, Instagram, etc.) No reward was given to the participants in return for filling out the questionnaire and data were collected through the volunteering of the participants.

Data Analysis

SPSS 24.0 (Statistical Package of Social Sciences for Windows) statistical package program was used to analyze the data obtained in the study. Independent t-test, frequencies analysis were used for statistical calculations. Statistical significance level was taken as $p < 0.05$.

Ethical Dimension of the Research

Ethical permission of the study was taken from A University Ethics Committee Commission on 14.09.2020 (Number of meetings 2020/25). Volunteers of the participants were taken as basis. Interviews were made with the participants who agreed to participate at a time available.

RESULTS

66.7% of the participants are between the ages of 18-32. 66.7% of the participants have high school and above education. 97.4% of the participants have 1 and 2 child. 53.8% of the participants are housewife. 84.8% of the participants haven't chronic ill. 86.4% of the participants don't live with an old person. 82.9% of the participants don't need hospitalization. 36.4% of the participants were Covid-19 positive at August. 62.1% the participants have more than one symptom.

Also, most of the participants have weakness (15.2%). 47.7% of the participants used hygiene rules for actions to protect from Covid-19. 93.2% of the participants' social relative affected negative from Covid-19 process. 80.3% of the participant's family relative affected negative from Covid-19 process (Table 1).

Table 1. Demographic analysis of research.

Data		n=132	%
Age	18-32 age	88	66.7
	33 and above age	44	33.3
Education	Secondary education and down education	44	33.3
	High school and above education	88	66.7
Child number	1 and 2 child	89	97.4
	3 and above child	43	32.6
Job	Housewife	71	53.8
	Working	61	46.2
Chronic ill	Yes	20	15.2
	No	112	84.8
Living with an old person	Yes	18	13.6
	No	144	86.4
Hospitalization	Yes	23	17.4
	No	109	82.9
Want to be vaccinated	Yes	72	54.5
	No	60	45.5
The month Covid is 19	March	1	0.8
	April	3	2.3
	May	4	3.0
	June	9	6.8
	July	26	19.7
	August	48	36.4

	September	41	31.1
Symptoms	More than one symptoms	82	62.1
	Weakness	20	15.2
	Headache	8	6.1
	Cough	6	4.5
	Fever	5	3.8
	Throat ache	3	2.3
	Shorthess of breath	2	1.5
	Nousea vomiting	2	1.5
	Diarrhea	2	1.5
	Loss of smell and taste	1	0.8
	No symptoms	1	0.8
Actions to protect from Covid-19	I care about my nutrition	25	18.9
	Alternative medicine application	28	21.2
	Vitamin supplements	15	11.4
	Hygiene rules	63	47.7
	Nothing	1	0.8
Impact on social relative	Positive	9	6.8
	Negative	123	93.2
Impact on family relative	Positive	26	19.7
	Negative	106	80.3

SDS total score of the participants were 38.63±8.10. SDS mean score of 18-32 between age mothers was down than other mothers and there is statistical significance between the two mother groups (18-32 age and 33 and above age) (Table 2).

Table 2. Comparison of SDS in terms of demographic data

Data	Group	n=132	X± S.D.	t	p
Mother age	18-32 age	88	37.60±7.44		
	33 and above age	44	40.70±9.02	2.10	**0.03**
Education status	Secondary education and down education	44	48.20±6.36		0.29
	High school and above education	88	49.44±6.27	1.05	
Job	Housewife	71	38.36±8.78		
	Working	61	38.95±7.28	0.41	0.67
Child number	1 and 2 child	89	37.84±7.98		
	3 and above child	43	40.27±8.20	1.61	0.10
*SDS total score			38.63±8.10		
		min: 15.00	**max:** 68.00		

MPBS total score of the participants were 49.03±6.30. Significance was found among the demographic data of the participants in terms of MPBS score. But, every group have down MPBS total score mean (Table 3).

Table 3. Comparison of MPBS in terms of demographic data

Data	Group	n=132	X± S.D.	t	p
Mother age	18-32 age	88	37.60±7.44		
	33 and above age	44	40.70±9.02	2.10	0.29
Education status	Secondary education and down education	44	39.15±7.85		0.59
	High school and above education	88	38.37±8.26	0.52	
Job	Housewife	71	48.71±6.65		
	Working	61	49.40±5.92	0.63	0.53
Child number	1 and 2 child	89	49.49±5.73		
	3 and above child	43	48.04±7.38	1.10	0.27
MPBS total score	**min:** 34.00 **max:** 63.00		49.03±6.30		

DISCUSSION

The findings of this research determined that Covid 19 positivity negatively affected mothers' maternal roles and parental behaviors. We determined that SDS total score of the participants were 38.63±8.10 and MPBS total score of the participants were 49.03±6.30 (Table 2-3). Parents experience burnout due to being at home with their 7-24 children during the Covid-19 epidemic (Chung, 2020; Griffith, 2020). Experts caution that the Covid-19 pandemic is an instance of traumatic stress and will likely worsen existing mental health difficulties and lead to the development of new disorders in others for an extended period of time (Galea et al., 2020; Griffith, 2020). Pines et al. (2020) found that the mental health of parents worsened during the Covid process (Pines et al., 2020). Also, reports from families during the peak of Covid-19 in the U.S. indicate Covid-19-related stressors are heightened for those caring for children (Park et al., 2020; Russel et al., 2020).

It is stated that maternal role is affected from age, personality traits, educational status, health status, self-concept, health perception, social support, mood and income level of the baby, emotional structure of the mother, environmental and social factors (Heydarpour et al., 2017). But in the research, it was found significant only age factor. SDS mean score of 18-32 between age mothers was down than other mothers and there is statistical significance between the two mother groups (18-32 age and 33 and above age) (Table 2).

82.9% of the participants don't need hospitalization. 36.4% of the participants were Covid-19 positive at August (Table 1). It is thought that the religious sacrifice holiday on these dates and the increase in the intimacy in interpersonal relations during this holiday, the increase in the travels between the provinces (family visits are made) contribute to the increase in the Covid case rates. In addition, the removal of Covid-19 pandemic restrictions in the country as of June also contributed to this situation. The increase in the number of cases in the country on these dates, it is also monitored in the T.R. Ministry of Health Covid-19 Information Page (T.R, 2020).

62.1% the participants have more than one symptoms (Table 1). The most common symptoms at onset of Covid-19 illness are fever, cough, and fatigue, while other symptoms include sputum production, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia (Çelik, 2020; Ho et al., 2020; Huang, 2020; WHO, 2020). Due to the Covid-19 pandemic, the World Health Organization and other major authorities recommend frequent hand washing and applying proper hand hygiene procedures as one of the cheapest, easiest, and most important ways to prevent the spread of a virus (WHO, 2020). We determined that; 47.7% of the participants used hygiene rules for actions to protect from Covid-19 (Table 1). Also, to prevent virus transmission, the Centers for Disease Control and Prevention recommends frequent hand washing with soap and water (Crain and Thompson, 1986),

It was determined that; 93.2% of the participants' social relative affected negatively from Covid-19 process. 80.3% of the participants' family relatives affected negative from the Covid-19 process (Table 1). In the studies conducted, it has been reported that the family and social lives of individuals are negatively affected during the Covid process (Marchetti et al., 2020; WHO, 2020). Higher total scores obtained from the scale indicate positive self-assessment of motherhood. The lowest and highest points to be obtained from "Myself as Mother" scale are 11 and 77, respectively (Crain and Thompson, 1986; Çalışır, 2003). SDS total score of the participants were 38.63±8.10 (Table 2). This score was down for mothers. Also, SDS mean score of 18-32 between age mothers was down than other mothers and there is statistical significance between the two mother groups (18-32 age and 33 and above age) (Table 2). The higher scale scores in older mothers can be attributed to the mothers of older ages being more experienced and knowing more about motherhood. MPBS total score of the participants were 49.03±6.30. Significance was found among the demographic data of the participants in terms of MPBS score. But, every group have down MPBS total score mean (Table 3). In a study conducted during the Covid pandemic process, it was determined that parents were exhausted and needed psychological support (CDC, 2019). Covid-19 lockdown could partially explain parents' feelings of being emotionally drained and insufficiently prepared to meet parental demands. In another study, it was reported that the Covid-19 process had negative consequences on the parental role, the roles of the parents were disrupted due to the stress experienced during this period, and this situation poses a risk to the health of the child (Spinelli et al., 2020). This situation is clearly seen in this study. The role of motherhood was adversely affected during this period. The results obtained in the two scales (SDS and MPBS) evaluating maternal roles in the study were similarly low. According to this result, we can say that the Covid-19 epidemic negatively affected the roles of mothers with Covid-19.

CONCLUSIONS

As a result of this research; it is determined Covid-19 Positive Mothers of Maternal Roles and Parental Behaviors have down scores. SDS total score of the participants were 38.63±8.10. SDS mean score of 18-32 between age mothers was lower than other mothers and there is statistical significance between the two mother groups (18-32 age and 33 and above age). MPBS total score of the participants were 49.03±6.30. Significance was found among the demographic data of the participants in terms of MPBS score. But,

every group have lower MPBS total score mean. According to this result, considering that Covid-19 negatively affects the roles of mothers, thus negativities in parental behaviors will reflect on their children, it can be said that child health is at risk.

Also, 84.8% of the participants haven't chronic ill. 86.4% of the participants don't live with an old person. 82.9% of the participants don't need hospitalization. 36.4% of the participants were Covid-19 positive at August. 62.1% the participants have more than one symptom. Also, most of participants have weakness (15.2%). 47.7% of the participants used hygiene rules for actions to protect from Covid-19. 93.2% of the participants' social relative affected negative from Covid-19 process. 80.3% of the participants' family relative affected negative from Covid-19 process. In all these results, it showed us that the Covid epidemic still showed its effect and negatively affected people socially, psychologically and physically.

Conflicts of Interest

The authors report no actual or potential conflicts of interest.

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There are no funders for this study.

The Patient Consent

Patient consent was obtained from the participants in this study.

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Are There Any Changes in Serum Renal Parameters in Patients Undergoing ESWL Therapy?

ESWL tedavisi gören hastalarda serum böbrek fonksiyon değerlerinde herhangi bir değişiklik olur mu?

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ÖZET
Amaç: Bu çalışmanın amacı, ESWL(Extracorporeal Shock Wave Lithotripsy) tedavisinin böbrek fonksiyon değerleri üzerine olan etkilerini incelemektir.
Materyal ve Metot: Kasım 2019 ve Ekim 2020 tarihleri arasında, böbrek taşı nedeniyle ESWL tedavisi yapılan ve çalışma kriterlerine uyan 50 erişkin hasta ile gerçekleştirildi. Ürogenital anomalisi olan ve soliter böbrekli hastalar çalışmaya alınmamıştır. Hastaların ortalama yaşı 37,2(26-67) idi. Hastaların 31'i(%62) erkek, 19'u(%38) kadındı. Hastalara 3 seans ESWL yapıldı ve seanslar arası süre 7 gün olarak belirlendi. İlk ESWL seansından bir gün önce rutin serum değerleri (Rutin I) alındı, ilk ESWL seansından bir gün sonra (Rutin II) ve 3. ESWLseansından bir gün sonra (Rutin III) tekrarlandı**.**
Bulgular: Kan serumu elektrolit değerleri, serum kreatinin değeri, glomerül filtrasyon hızı (GFR) ve bikarbonat değerlerinin rutinler arasında istatistiksel olarak farklı olmadığı görüldü.
Sonuç: Çalışmamızda elde ettiğimiz bulgulara göre, ESWL'nin üst üriner sistem taşlarının tedavisinde kullanımının hastalarda böbrek tübüllerinde disfonksiyona yol açmadığı, böbrek fonksiyon değerlerinin takibine gerek olmadığını göstermektedir.

Anahtar Kelimeler: Extracorporeal Shock Wave Lithotripsy, Böbrek taşı, Renal fonksiyon ve glomerüler filtrasyon hızı.

ABSTRACT
Objective: The goal of this research was to explain the effects of ESWL on renal function (Extracorporeal Shock Wave Lithotripsy)..
Material and Method: This study was carried out retrospectively between November 2019 and October 2020, with 50 adult patients scheduled to perform an ESWL treatment because of a diagnosis of kidney stone and to completed the study protocol. In all of these patients, there was no urogenital abnormality, and none had a solitary kidney. Patients' mean age was 37.2 (between 26 and 67 years of age). Of patients, 31 (62%) were male and 19 (38%) were female. Three ESWL sessions were carried out in the patients and the time between sessions was set at 7 days. The routines collected one day before the ESWL (Routine I) protocol were repeated one day after the first session (Routine II) and one day after the end of all ESWL (Routine III) sessions.
Results: There wasn't any statistically significant difference among routines in terms of the ratio of serum electrolytes, serum creatinine, GFR and spot urine/protein.
Conclusion: The findings indicate that the renal function tests do not need to assess whether ESWL leads to a tubular functional dysfunction in patients when treating upper urinary system stone disease.

Keywords: Extracorporeal Shock Wave Lithotripsy (ESWL), Renal stone, Renal function and glomerular filtration rate (GFR).

INTRODUCTION

Urolithiasis is one of the most common urinary diseases and its incidence tends to increase with age (Akinci et al., 1991). Although ESWL treatment has been an effective treatment since 1980, great progress has been made in the treatment of urinary tract stones. It is accepted as an important treatment option in upper, lower and middle calyx, renal pelvis and upper ureteral stones. Also, it is known that the success of ESWL is high, especially in small stones. Pregnancy, uncorrected coagulopathy and active urinary tract infection are considered absolute contraindications. The experience of the urologist and patient preference are also very important in the selection of treatment. The high success rate of ESWL in upper ureteral stones and

the potential undesirable side effects of other alternative treatments make ESWL the primary treatment modality in this group. This method of urolithiasis treatment is accepted because it offers non-operative treatment (Turna et al., 2005).

With this study, we aimed to estimate the possible side effects of ESWL on the group of patients with nephrolithiasis. Between November 2019 and October 2020 in our clinic, 50 adult patients who were diagnosed with a kidney stone and were underwent an ESWL treatment was enrolled into this study. We retrospectively investigated the effect of ESWL on kidney stones and discussed the subject by comparing it with the previous studies in the literature.

MATERIAL and METHOD

In our study, the data of 82 patients who were diagnosed with kidney stones and were scheduled for ESWL procedures who applied to our outpatient clinic between November 2019 and October 2020 were analyzed. Thirty-two of the patients were excluded from the study because they didn't comply with the study protocol.

Patients' mean age was 37.2 (between 26 and 67 years of age). Of patients, 31 (62%) were male and 19 (38%) were female. None of these patients suffered from a urogenital abnormality or had a solitary kidney. We examined patients with nephrolithiasis in our study. Patients with ureterolithiasis, cystolithiasis and urethrolithiasis were excluded from the study. Four of the patients, two male and two female (8%) was determined in an upper calyx stone, a mid calyx stone in 8, five male and three female (16%), a lower calyx stone in 9, six male and three female (18%) and a pelvis stone in 29, eighteen male and eleven female (58%).

The device employed in this procedure was an ELMED brand fluoroscopy focusing lithotripter. A maximum of 3000 shock-wave, accompanied with a 7-18 kv power was applied at each session. Three ESWL sessions were carried out in the patients and the time between sessions was set at 7 days. All patients who met the study criteria were included in a single group. The remaining 32 patients failed to complete the study protocol due to various reasons such as pain, non-compliance with the treatment, and inability to start the treatment because of acute infection. The routines collected one day before the ESWL (Routine I) protocol were repeated one day after the first session (Routine II) and one day after the end of all ESWL (Routine III) sessions. Fifty patients were able to complete this study protocol.

Before initiating the ESWL procedure, total blood count, serum BUN and creatinine levels, prothrombin time and partial thromboplastin time, total urine analysis and urine culture of all patients were evaluated. Antibiotic treatment was applied for patients who have bacterial reproduction in their urine culture, ESWL procedure was initiated to patients without reproduction in their urine culture. Creatinine (Cr), Na, K, Cl, Ca, P, Mg and venous blood gases of in blood serums were studied one day before the patients underwent a ESWL procedure. A total urine analysis was conducted. Protein and creatinine levels were studied in spot urine, plus a 12-hours urine was collected to calculate GFRs. This was the completion of Routine I. The next day patients underwent a first session of ESWL.15 days later the second session of ESWL and 30 days later the third session of ESWL were performed. Routine II was completed one day after the first session of ESWL while Routine III was completed one day after the end of the sessions of ESWL. GFRs of patients were calculated by the aid of the creatinine clearance formula [Clearance = U/PXV; U: Content of creatinine in urine (mg/dl); p: Plasma creatinine (mg/dl), and V: Amount of urine (ml)]. The biochemical tests of patient serums, venous blood gases and the protein/creatinine content in spot urine were measured by repeated measured variance analysis and the level of significance was considered 5% ($p<0.005$).

IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, US) were used for the statistical analysis. Descriptive statistics were provided as mean for continuous

variables, and as percentage for categorical variables. Differences between more than two dependent groups were examined by Repeated measures analysis of variance. A p value of <0.05 was considered statistically significant.

RESULTS

No major complications were observed in any of the patients during the ESWL procedure. However, a stone path (strain strasse) developed in three patients and endoscopic ureteral stone-removing procedure was applied. Additionally, fever was noticed in two patients (mean 38 C degree) and this finding improved after appropriate antibiotic therapy. One patient was hospitalized for a single day due to severe pain. To understand whether ESWL affected renal functions, we measured the glomerular filtration rate (GFR), blood creatinine level and the bicarbonate level in venous blood gas. Calculated GFR values were found 86.06 ± 16.45 ml/min in Routine I, 88.42 ± 17.80 ml/min in Routine II and 90.16 ± 17.62 ml/min in Routine III. Alterations in GFR were within physiological limits and there was no any significant difference (p>0.05). The blood creatinine level was 1.06 ± 0.15 mg/dl at Routine I, 1.03 ± 0.13 mg/dl at Routine II and 1.03 ± 0.10 mg/dl at Routine III. Similarly, there was no any significant difference in blood creatinine level (p>0,05). Blood bicarbonate levels in blood samples collected from venous blood vessels without using a tourniquet was determined as 26.10 ± 1.27 mmol/L for Routine I, 25.21 ± 1.59 mmol/L for Routine II and 24.64 ± 1.47 mmol/L for Routine III. Also there was no any significant difference between bicarbonate levels in groups (p>0.05). The relationship between parameters related with renal functions and repeated routines are summarized in Table 1.

Table 1. Before and after ESWL, changes of GFR, bicarbonate and serum electrolytes

	I. Routine	II. Routine	III. Routine	p*
GFR (ml/min)	86.06 ± 16.45	88.42 ± 17.80	90.16 ± 17.62	0.400
Creatinine (Blood) (mg/dl)	1.06 ± 0.15	1.03 ± 0.13	1.03 ± 0.10	0.108
Bicarbonate (Blood gas) (mmol/l)	26.10 ± 1.27	25.21 ± 1.59	24.64± 1.47	0.302
Phosphorus (mg/dl)	3.15 ± 0.30	3.12 ± 0.27	3.14 ± 0.33	0.613
Calcium(mg/dl)	9.52 ± 0.31	9.55 ± 0.27	9.57 ± 0.25	0.788
Chlorine (mmol/l)	102.59± 1.81	102.91 ± 1.70	102.25 ± 1.41	0.732
Magnesium (mmol/l)	2.06± 0.15	2.07 ± 0.14	2.08 ± 0.16	0.658
Sodium (mmol/l)	138.98 ± 1.99	140.19 ± 2.40	139.45 ± 1.45	0.636
Potassium (mmol/l)	4.03 ± 0.29	3.97 ± 0.24	3.96 ± 0.25	0.561

* Repeated measures analysis of variance.

(I) : Routines obtained one day before ESWL

(II) : Routines obtained one day after the first ESWL session

(III) : Routines obtained one day after the end of all ESWL sessions.

DISCUSSION

ESWL is a less invasive method in the treatment of urinary system stone disease when compared to alternative operative methods. The procedure is also considered as one of the first in the treatment options of urinary system stone disease because it is easy to apply and in general, does not require hospitalization of the patient and plus has lower morbidity ratios. After it's wide spread use in urinary

system stone disease, miscellaneous studies related with the impact of ESWL on renal functions and different results were obtained in the acute and chronic term.

In animal model studies, a positive correlation has proven to be between histological renal tubular damage and urinary enzyme excretion generated by the shock wave energy (Weichert-Jacobsen et al., 1997; Weichert-Jacobsen et al., 1998). In different studies which were carried out, after the ESWL treatment, it has been shown that acute histological damage took place in structures including renal parenchyma, renal vessels and renal tissues and also led renal morphological changes such as subcapsular hematoma and focal parenchymal damage (Gunasekaran et al., 1989; Evan et al., 1991; Preminger, 1993). However, it was displayed that even though these damages in the renal units which were exposed to ESWL complied with the area to where shock wave energy spreads (Gunasekaran et al., 1989; Karlsen et al., 1991). Also they were closely associated with ESWL treatment parameters such as the number of shock waves, shock wave energy and host factors like renal immaturity, the presence of pyelonephritis and intact renal nerve (Evan et al., 1998; Evan et al., 1999; Connors et al., 2000; Connors et al., 2003; Willis et al., 2005). Especially in animal studies had shown that ESWL treatment did not have any effect on the renal development or animal growth. In addition, when the impacts of ESWL on renal function parameters were studied, in the treated renal unit it was demonstrated that reduction in renal plasma flow (RPF) and glomerular filtration rate (GFR) were acute and temporary. Also, this decline returned to baseline level within 24 hours (Connors et al., 2000, Evan et al., 1998, Willis et al., 1996). In a study conducted in the pediatric population, it was found that the long-term follow-up after ESWL for treatment of renal stones no effect on renal growth and no development of chronic diseases (El-Nahas et al., 2013). Of course, we also do not consider that at the microscopic level, ESWL is harmless or innocent in morphological, histological and physiological damage caused by its mechanical power and energy in stone fragmentation and comminution. However, we believe that in a way which supports our study this damage is transient and has no long-term effects on patients, who were selected according and treated with the appropriate protocol to the literature.

Literature data about the effects of ESWL treatment is more limited in human kidney. In physiological studies related to urinary enzymes and other markers indicating urinary injury, temporary increase related to those markers has been shown to return to normal levels within a few days or weeks after the treatment ESWL (Assimos et al., 1989; Recker et al., 1992; Rutz-Danielczak et al., 1992). Some researchers have evaluated urinary enzyme excretion and renal function parameters before and after ESWL treatment. In studies carried out by Karlsen et al., 1991; Rutz-Danielczak et al., 1992; Gupta et al., 1995; Goel et al., 1996; Ilgın et al., 1998 and which were related with GFR, it was reported that GFR values returned to baseline after the sudden temporary reduction or remained stabil after ESWL. In studies conducted by Pienkny et al., 1999 and Perry et al., 2000, in patients undergoing simultaneous bilateral ESWL treatment, even after their long follow-up period (mean, 3,5 years and 21 months) not any deterioration or impairment in renal function was shown. In our study, we found no any significant difference between GFR values which were calculated before the treatment was started, one day after the end of the first and third session. Findings obtained from our study, demonstrate a parallelism with the findings of investigators mentioned above. However, in a study carried out by Sheir et al., 2003, in the literature, showed a significant increase in GFR values after ESWL, but in a study carried out by Saxby, 1997, a significant decrease was observed and finally, in a study carried out by Cass, 1994, some patients displayed a decrease while some displayed an increase. When compared, findings obtained in our study demonstrate some differences with the findings of the investigators mentioned

above. We suggest that ESWL does not have an effect on GFR. Patients who were included in the study had bilateral kidneys and their biochemical parameters were within normal limits. Routines were not calculated separately, and total GFR was estimated. Therefore, even though GFR was altered in a kidney which was subjected to ESWL, we think that this variation was compensated by the aid of the other kidney.

Commonly, in the literature, serum creatinine is assessed together with GFR. In a study carried out by Greenstein et al., 1990; Karlsen et al., 1991; Gupta et al., 1995 and El-Assmy et al., 2008, the investigators presumed that ESWL was not capable to change serum creatinine values. The findings we have obtained from our study is compatible with the findings as mentioned in the literature above, regarding serum creatinine levels. No any significant difference was determined in serum creatinine levels before and after ESWL therapy. In a study conducted by Saxby, 1997, serum creatinine levels appeared to increase after a ESWL procedure. However, the result obtained from this study does not show parallelism with our study and other studies. We assume that ESWL does not alter serum creatinine levels.

In a study carried out by Saxby, 1997, it was shown that ESWL procedure caused an increase in serum calcium levels when compared with serum calcium levels prior the procedure. In our study, findings obtained with serum calcium levels does not show a parallelism with the findings obtained from the above study of the investigator. Accordingly, we assume that ESWL does not affect serum calcium levels. We also assume that, the reason that serum calcium levels were not altered, could rely on the fact that ESWL does not have an effect on tubular reabsorption. In a study carried out by Villany et al., 2001, it was determined that ESWL caused no any difference in serum sodium and serum potassium levels. In our study, we also found that there was no any significant difference between serum sodium and serum potassium levels, before and after ESWL. This data shows a similarity when compared with the data obtained from Villany.

No any studies were found in the literature related with serum phosphor and magnesium. In our study there is no any significant difference in serum phosphor and magnesium levels and the results obtained are within normal physiological limits.

Consequently, ESWL serum electrolytes, does not generate a significant difference on serum GFR and creatinine and serum bicarbonate studied in venous blood gas. ESWL treatment did not affect GFR, proteinuria and serum electrolytes in kidneys. The number of cases is extremely few in this study.

According to our opinion, ESWL which is used in the treatment of renal stones did not have a negative effect on GFR, proteinuria and electrolyte balance, when used in a short-term period, as the procedure is considered to be a safe method, but principally advanced studies related with the renal tubular function must be conducted.

Conflicts of Interest

The authors report no actual or potential conflicts of interest.

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Orjinal Araştırma Makalesi/ Original Paper

Investigation of the Effect of Vitamin C In The Prevention of Transport-Induced Stress in Ring-Necked Pheasant (*Phasianus colchicus*)

Halka Boyunlu Sülünlerde (*Phasianus colchicus*) Nakil Kaynaklı Stresin Önlenmesinde C Vitamininin Etkinliğinin Araştırılması

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ÖZET
Amaç: Bu çalışmada, halka boyunlu sülünlerde (*Phasianus colchicus*) nakil kaynaklı stresin önlenmesi veya azaltılmasında C vitamininin etkinliği araştırıldı.
Materyal ve Metot: Çalışmada, 8-12 aylık yaşta, canlı ağırlıkları 1140-1525 g aralığında değişen toplamda 30 sülünden (15 erkek ve 15 dişi) oluşan bir kontrol ve iki deneme grubu oluşturuldu (n=10/grup). Deneme gruplarına sırasıyla 200 (AA1) ve 400 (AA2) mg/kg dozunda C vitamini günlük olarak içme suları içerisinde verildi. Bir haftalık uygulama sonrasında sülünler iki saat boyunca nakil stresine maruz bırakıldı. Plazma kortikosteron (CS) düzeyleri ile heterofil/lenfosit (H/L) oranları taşıma öncesi ve sonrası belirlendi.
Bulgular: Nakil öncesi ve sonrası elde edilen değerler karşılaştırtıldığında, kontrol grubunda CS değerlerinde ve H/L oranlarında nakil sonrası anlamlı artış belirlenirken (P<0,001), AA1 ve AA2 gruplarında sadece plazma CS düzeyinde anlamlı artış saptandı (Sırasıyla, P<0,05 ve P<0,001). Her üç grupta ölçülen parametrelerde nakil öncesinde istatistiksel fark yoktu. Nakil sonrası ise plazma CS düzeyleri ve H/L oranları deney gruplarında benzerdi, fakat deney gruplarına ait değerler kontrol grubundan anlamlı şekilde düşüktü (Sırasıyla, P<0,001 ve P<0,01).
Sonuç: Sülünlere nakil öncesi bir hafta süreyle oral C vitamini verilmesi, nakil kaynaklı stres yanıtında azalma sağlamaktadır.

Anahtar Kelimeler: C Vitamini, Heterofil/Lenfosit oranı, Kortikosteron, Nakil stresi, Sülün.

ABSTRACT
Objective: In this study, the efficiency of vitamin C in the prevention or reduction of transport induced stress in ring-necked pheasants was investigated.
Material and Method: In the study, a control and two experimental groups consisting of a total of 30 pheasants (15 males and 15 females) at the age of 8-12 months, with body weight of 1140-1525 g, were formed (n=10/group). The experimental groups were given daily doses of 200 (AA1) and 400 (AA2) mg/kg of vitamin C in drinking water, respectively. After one week of treatment, pheasants were exposed to transport stress for two hours. Plasma corticosterone (CS) levels and heterophile/lymphocyte (H/L) ratios were determined before and after transport.
Results: When the values obtained before and after transportation were compared, a significant increase was found in CS values and H/L ratios in the control group after transportation (P<0.001), while a significant increase was found only in plasma CS levels in the AA1 and AA2 groups (P<0.05 and P< 0.001, respectively). There was no statistical difference in the parameters measured in all three groups before transportation. After transportation, plasma CS levels and H/L ratios were similar in the experimental groups, but the values of the experimental groups were significantly lower than the control group (P<0.001 and P<0.01, respectively).
Conclusion: Oral administration of vitamin C to pheasants for one week before transportation provides a decrease in the stress response due to transportation.

Keywords: Corticosterone, Heterophil/Lymphocyte ratio, Pheasant, Transport stress, Vitamin C

INTRODUCTION

Transporting ring-necked pheasants (*Phasianus colchicus*) from rearing facilities to nature is a common practice in many European countries (Draycott et al., 2002; Draycott et al., 2005) and the USA (Schwartzkopf-Genswein et al., 2012), as it is in our country (Annual report, 2020), to protect the natural life and increase the number of birds suitable for hunting. The transportation process increases the stress load in birds for many reasons, such as catching, caged, sudden change in microclimate

conditions, water and feed deprivation, sudden accelerations and decelerations, vibration, unfamiliar voice, restricted floor space, and social perturbation due to high animal intensity. The consequences of the stress during transport of birds were reviewed in detail for poultry especially broilers because different transport technics may cause an increase in mortality, decrease in poultry welfare due to stressful transport, and meat quality (Schwartzkopf-Genswein et al., 2012; Qi et al., 2017; Zaboli et al., 2019).

The effects of stress, at the molecular/cellular or physiological level, are mostly related to oxidative stress and damage to important biological molecules. Therefore, a number of feed-derived and supplemented antioxidants such as vitamins, minerals, amino acids, and phytogenic feed additives are added to minimize these unwanted effects of stress (Saeed et al., 2019).

Vitamin C (chemical names: ascorbate and ascorbic acid [AA]) is a 6-carbon lactone that is synthesized from glucose by poultry and many other animals in kidneys in birds and reptiles, and in the liver in some mammals (Ahmadu et al.,2016). Ascorbic acid is one of the most important antioxidants that can neutralize oxidative stress through an electron donation/transfer process and is involved in the biosynthesis of corticosterone, a hormone that increases energy supply during stress. Birds need more AA during stress because endogenous AA is insufficient to meet the bird's requirements, so adding AA to drinking water or feed helps lower corticosterone levels during stress (McKee and Harrison, 1995). It has been reported that, under a variety of stressful conditions, improved performance resulting from AA use is associated with suppressed stress responses demonstrated by a reduction in plasma adrenocorticotropic hormone (Sahin et al., 2003) and corticosterone (McKee and Harrison, 1995; Mahmoud et al., 2004) levels. Positive effects of ascorbic acid on immune response, feed consumption, live weight gain, rectal and body temperature, fertility, hatchability of fertile eggs, oxidative stress, carcass grade, carcass yield and weight gain have been reported in birds. (Saeed et al., 2019). Therefore, it has been reported that AA can be supplemented to reduce the negative effects of stress due to heat, transportation, and other environmental factors in poultry (Ahmadu et al., 2016).

In poultry, two of the most common physiological parameters of stress are circulating concentrations of corticosterone and the heterophil/lymphocyte (H/L) ratio. Transport stress can activate the hypothalamic-pituitary-adrenal axis and thereafter plasma corticosterone is elevated following a road journey (Kannan et al., 1997). This apparent activation of the hypothalamic-pituitary-adrenal axis is consistent with the observation of post-transport increases in the H/L ratio (Gross and Siegel, 1983; Maxwell, 1993; Mitchell and Kettlewell, 1998; Erisir et al., 2008).

While there are many studies that have revealed that vitamin C can moderate the effect of different stress factors on poultry (Zulkifli et al., 2000; Sahin et al., 2002; Sahin et al., 2003; Mahmoud et al., 2004; Minka and Ayo, 2011; Ghazi et al., 2015; Ahmadu et al., 2016) there are few studies investigating the effects of stress due to handling (Chloupek et al., 2009), transport (Voslarova et al., 2006; Suchy et al., 2007; Voslarova et al., 2012), translocation (Volfova et al., 2022) and other factors (Voslarova et al., 2013) in pheasants. To our knowledge, there is only one study in pheasants where Nowaczewski (2006) showed that supplementation with vitamin C reduced the tonic immobility reaction and CS level in stressed pheasants. Therefore, this study was undertaken to determine the stress-ameliorating effects of vitamin C supplementation in drinking water in response to transportation in pheasants.

MATERIALS and METHODS

Animals and experimental protocol

In total, 30 adults (8-12-months-old) healthy ring-necked pheasants (*Phasianus colchicus*; hereinafter, pheasant) of both sexes were used. The sam-

ple size of this study was determined using G-power software (G* Power 3.1.9.2, Heinrich–Heine–Universität, Düsseldorf, Germany). Based on the result of G*Power, the number of samples was at least eight pheasants for each group. However, 10 pheasants were used per group taking into account the possible losses. Pheasants were obtained from the Gelemen Pheasant Production Station, Samsun, and were brought from the station to the pen (41° 22′ N, 36° 12′ E) within plastic transport cages. This experiment was carried out with an average of 19±1° C outside temperature, 21±1° C inside temperature and 71±7% relative humidity. The birds were kept at a fixed light cycle of 15L:9D to mimic the early June conditions outside during the experiment. This study was approved by the Animal Experimentation Ethics Committee of Ondokuz Mayis University (Approval no: 2016/04).

The pheasants were divided into three groups considering their body weight (BW), with five males and five females in each group. The BW of the birds in the control group (C) and treatment groups (AA1 and AA2) were 1330±89 and (1350±129 and 1349±112 g), respectively. There was no statistical difference among the three groups for BW. All the groups were fed commercial feed obtained from the station to avoid unwanted effects of diet change. All birds were subjected to the adaptation period (a week) before the experiment. During this period, the daily average water consumption of each group was also determined.

Daily drinking water was supplied to the C group without AA supplementation while groups AA1 and AA2 were supplemented with 200 and 400 mg of AA/kg BW, respectively. Ascorbic acid was obtained by DSM Besin Maddeleri Ltd., Istanbul, Turkey. This supplementation was continued for seven days. A dose of AA, recalculated for the total BW of pheasants in each group, was dissolved in a predetermined volume of water in dark coloured bottles.

Pheasants were transported at the end of the supplementation period (day 8) to three consecutive parties to avoid exceeding the processing capacity. At each transport party, an equal number of birds from each group were loaded onto the truck with a crate (W=96 x L=57 x H=27 cm3) at the density of approx. 400 cm2kg-1. The crate was placed in such a way to prevent movement during transit and transported for two hours with an average speed of 60 km/hour. All three journeys were made on the same route.

Blood samples (1 ml) were obtained within 3 minutes to avoid change in monitored stress parameters due to sampling such as catching, handling, bleeding (Owen, 2011). Blood was taken from the brachial vein to tubes containing anticoagulant (EDTA) twice immediately before and after transportation to determine the level of plasma corticosterone and H/L ratio.

The samples were sent to the laboratory from the sampling room (within 30 min after blood collection) in a small styrofoam cooler. After their transfer to the laboratory, the blood smears were prepared using the May-Grunwald-Giemsa stain. The H/L ratios were determined one day later. Blood smears were examined under a microscope at a magnification of 100x with oil immersion and in each smear, heterophils and lymphocytes were counted until the cumulative total reached 100 cells, and then the H/L ratio was calculated.

The remaining blood samples were centrifuged at 10000 rpm for 10 min, plasma was decanted and then stored at -20 °C until corticosterone analyses. Plasma corticosterone levels were determined in duplicate by immunoassay according to guidelines provided by the manufacturer (Enzo Life Sciences, Corticosterone ELISA Kit, ADI-900-097, Lausen, Switzerland). Standards used in the current study were between 32-20000 pg/ml. The intensity of colour was measured at 405 nm with an 8-channel microtitration plate spectrophotometer (DAS, Digital and Analogue Systems, A3, Italy). The results

were calculated by using the 4 parameters logistic curve-fit.

Statistical analysis

Statistical analysis was carried out using the SPSS statistical package (IBM SPSS Statistics, Ver. 21, USA). After the Shapiro-Wilk normality test and homogeneity of variance test, data with homogeneous variances (H/L ratio) were subjected to a one-way ANOVA to assess statistical significance, followed by a Tukey-HSD test for multiple comparisons. Due to the standard error of means exceed to their mean values, data with heterogeneous variances (corticosterone) were executed to GENMOD analysis with linked time function. Differences in corticosterone mean changed over time were analysed with the contrast structure (linear form) of the GENMOD procedure. Data are presented as mean±SD for H/L, and mean, median and their deviation for corticosterone.

RESULTS

Plasma corticosterone concentration was statistically higher after transportation in the control, AA1 and AA2 groups (P<0.001, P<0.05 and P<0.001, respectively) while the H/L ratio was higher only in the control group (P<0,001). When compared groups, plasma corticosterone level and H/L ratio were similar in all three groups before transportation. However, after transportation, both CS and H/L ratio were higher in the control group than the AA administrated groups (P<0.001 and P<0.01, respectively). Experimental groups also were similar to each other after transportation (Table 1).

Table 1. The stress parameters values obtained before and after transport in pheasants

		Groups									
		Control			AA1			AA2			
		Mean	Median	Deviance	Mean	Median	Deviance	Mean	Median	Deviance	P value
Corticosterone[1] (ng/ml)	BT	21.66	12.94	0.5646	24.06	10.60	0.2815	22.79	9.59	0.5864	>0.05
	AT	89.35[a]	96.70		50.20[b]	43.84		52.24[b]	43.79		<0.001
	P value	<0.001			<0.05			<0.001			
		Mean±SD			Mean±SD			Mean±SD			P value
H/L ratio	BT	0.42±0.13			0.40±0.15			0.45±0.18			>0.05
	AT	0.76±0.21[a]			0.52±0.09[b]			0.58±0.10[b]			<0.01
	P value	<0.001			>0.05			>0.05			

DISCUSSION

Road transport represents a critical stage in poultry production, and it is considered one of the main causes of stress. These stress factors include human-induced handling and crating, journey-induced noise, vibration, density, starvation, emotional factors such as unfamiliar sound and environment, and climatic factors such as extreme heat and humidity. The consequences of stress during transport of birds and coping with transport induced-stress were studied mainly in poultry by many researchers and reviewed by many authors (Kannan et al.,1997; Mitchell and Kettlewell, 1998; Zulkifli et al., 2001; Zhang et al., 2009; Vosmerova et al., 2010; Minka and Ayo, 2011; Schwartzkopf-Genswein et al., 2012; Qi et al., 2017). Although there are studies investigating the effects of transportation, there is no publication about alleviating transport-induced stress in pheasants. There-

fore, we investigated whether AA is effective in alleviating stress in pheasants as in other poultry. Our results demonstrate that transportation is a stressful procedure in pheasants, as shown by an immediate increase in monitored parameters in the control group after transportation (Table 1). Plasma corticosterone concentration, which is considered the main indicator of stress in birds, was significantly higher after the travel than before transport in all groups. Although there was a numerical increase in the H/L ratio in all groups after transportation, the increase was statistically significant only in the control group. Considering increases in corticosterone and H/L ratio after transportation, we interpreted these results that transport-induced stress has occurred in all groups at different levels. Our results agreed with early researchers who reported that corticosterone (Suchy et al., 2007; Voslarova et al., 2012) or H/L ratio (Voslarova et al., 2006) was higher in transported pheasants in comparison with the non-transported control pheasants. Voslarova et al. (2006) and Suchy et al. (2007) investigated the effects of transport stress and reduction of floor area (290 and 195 cm^2/kg) on pheasants at 9 weeks of age, transported at different densities for 4 hours, and described changes in some biochemical and hematological parameters. Similarly, stress effects resulting from transport in common pheasant were examined by Voslarova et al. (2012), who observed an increase in the corticosterone concentration.

We compared parameters measured before and after transportation among groups to evaluate the effectiveness of AA. There was no statistical difference before the journey for all the parameters measured. After the journey, all parameters were similar for each experimental group, and they were lower than the control group. According to these results, it can be postulated that AA had a positive effect on reducing stress responses with the indication of decreased plasma corticosterone level and H/L ratio, and this agrees with the conclusions reached by many researchers (Kutlu and Forbes, 1993; McKee and Harrison, 1995; Zulkifli et al., 2001; Sahin et al., 2002; Sahin et al., 2003; Mahmoud et al., 2004; Minka and Ayo, 2011; Ghazi et al., 2015). These researchers used broilers or quails to determine the effectiveness of AA in dealing with stress depending on transportation or high temperature and used plasma corticosterone level, H/L ratio, or other biochemical parameters as stress markers.

The lower values of corticosterone level and H/L ratio recorded in pheasants administered AA following transportation suggested that the AA reduced or eliminated the adverse effects of road transportation stress in pheasants. Kutlu and Forbes (1993) reported that AA reduces the synthesis of corticosteroid hormones in birds. Similarly, Sahin et al. (2003) reported low concentrations of ACTH in quails reared at high temperature and fed a diet supplemented with AA. Ascorbic acid plays an important role in the biosynthesis of corticosterone, a hormone that increases energy supply during stress. AA alleviates the negative effects of stress by reducing the synthesis and secretion of corticosteroids (McKee and Harrison, 1995; Sahin et al., 2003; Mahmoud et al., 2004).

In conclusion, doses of 200 and 400 mg of AA exerted a positive influence on alleviating transport-induced stress in pheasants. It appears advisable to use a dose of 200 mg of AA per kg BW in water for one week before transportation of pheasants.

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Conflict of Interest

The authors declared that there is no conflict of interest.

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Orjinal Araştırma Makalesi/ Original Paper

Deneysel Diyabet Modeli Oluşturulan Ratlarda Gebelik Süresince Hipokampusta Piramidal Nöron Sayısındaki Değişimin Stereolojik Olarak İncelenmesi

Stereological Investigation of Change in Hippocampal Pyramidal Neurons in During Pregnancy in Rats Occurred Experimental Diabetes Models

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ÖZET

Amaç: Diyabetes mellitus, dünya çapında hızla artan insülin eksikliği ya da insülin direnci sebebiyle oluşan karbonhidrat, lipid ve protein metabolizması bozukluğu ile belirgin yüksek mortalite ve morbiditeye sahip endokrin ve metabolik bir hastalıktır. Hipokampustaki nöronal sistem üzerinde de etkileri olduğu çalışmalarda gösterilmiştir. Çalışmamızın amacı deneysel diyabet oluşturulan ve normal sıçanlarda, gebelik döneminin her trimesterinde hipokampustaki piramidal nöron sayısına etkilerini stereolojik yöntemlerle değerlendirmektir.

Materyal ve Metot: Çalışma için sıçanlar rastgele olmak üzere iki gruba ayrıldı. Kontrol grubu(n:18), Diyabetes mellitus grubu(n:18); Streptozotosin (STZ) ile deneysel diyabet oluşturulan Diyabetes mellitus grubuna tek doz 45mg/kg Streptozotosin intraperitoneal (i.p) olarak uygulandı. Kontrol grubuna herhangi bir işlem uygulanmadı. Uygulamadan 72 saat sonra her iki gruptaki sıçanların açlık kan şekerleri ölçüldü. Diyabet grubunda açlık kan şekeri değeri 200 mg/dl üzerinde olanlar diyabet olarak kabul edildi. Vaginal smear ve vaginal plak izlemi yapılarak gebelik tespiti yapıldı. Gebelik trimester dönemleri olan 7, 14 ve 21. günlerde anestezi altında sıçanlardan beyin dokuları çıkarılarak rutin ışık mikroskobik histolojik takip yapıldı. Her iki gruba sayısal yoğunluk hesaplaması amacıyla fiziksel disektör metodu uygulandı. Bunun için 5 µm kalınlığında ilki rastgele olmak üzere sonrakiler her 400µm'de bir ortalama beş çift kesit alındı. Kesitler Hematoksilen-Eozin ile boyandı. Işık mikroskobunda incelenerek, fotoğraflandı. Stereolojik incelemede tarafsız sayım çerçevesiyle nöron sayımı yapıldı. İstatistiksel analizde Mann-Whitney U testi kullanıldı**.**

Bulgular: Stereolojik hesaplamalar sonucunda diyabet ve kontrol grupları arasındaki hipokampal nöron sayısında istatistiksel açıdan anlamlı fark bulundu($p<0.05$). Ancak trimesterler arasında gruplarda herhangi bir istatistiksel fark bulunmadı.

Sonuç: Diyabetin vücutta birçok zararlı etkisi olduğu bilinmekte olup çalışmamızda gebe sıçanlarda hipokampal nöron sayısında anlamlı azalmaya neden olduğu tespit edildi.

Anahtar Kelimeler: Diyabet, Gebelik, Hipokampus, Stereoloji, Streptozotosin.

ABSTRACT

Objective: Diabetes mellitus is an endocrine and metabolic disease increasing world wide with the markedly high mortality and morbidity due to carbohydrate, lipid and protein metabolism disorder caused by insulin deficiency or insulin resistance. Studies have also shown that it has effects on the neuronal system in the hippocampus. The aim of our study is to evaluate the effects of the pyramidal neuron number in the hippocampus in each trimester of pregnancy by stereological methods in experimentally induced diabetes and normal rats.

Material and Method: Rats were randomly divided into two groups for the study. Control group (n:18), Diabetes mellitus group (n:18); experimental diabetes was induced by streptozotocin (STZ). A single dose of 45mg/kg Streptozotocin was administered intraperitoneally (i.p) to the Diabetes mellitus group. No treatment was applied to the control group. Fasting blood glucose of rats in both groups was measured 72 hours after the application. In the diabetes group, those with a fasting blood glucose value above 200 mg/dl were considered as diabetes. Pregnancy was determined by monitoring vaginal smear and vaginal plaque. Routine light microscopic histological follow-up was performed by removing brain tissues from rats under anesthesia on the 7th, 14th and 21st days of pregnancy. Physical dissect or method was applied to both groups for numerical density calculation. For this, an average of five pairs of sections were taken at 5 µm thickness, the first of which was random, and the subsequent ones were every 400 µm. Sections were stained with Hematoxylin&Eosin. Examined and photographed under a light microscope. Neuron counting was performed with an unbiased counting frame in stereological examination. Mann-Whitney U test was used for statistical analysis..

Results: As a result of stereological calculations, a statistically significant difference was found in the number of hippocampal neurons between diabetes and control groups ($p<0.05$). However, there was no statistical difference between the groups between trimesters.

Conclusion: It is known that diabetes has many harmful effects on the body, and in our study, it was determined that there was a significant decrease in the number of hippocampal neurons in pregnant rats.

Keywords: Diabetes, Hippocampus, Pregnancy, Stereology, Streptozotocin.

Atıf Yapmak İçin: Yıldız A, Rağbetli MÇ, Çölçimen N. Deneysel diyabet modeli oluşturulan ratlarda gebelik süresince hipokampusta piramidal nöron sayısındaki değişimin stereolojik olarak incelenmesi. ***Van Sag Bil Derg* 2022, *15*,(2)136-141.** https://doi.org/10.52976/vansaglik.1012527.

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GİRİŞ

Diyabetes mellitus, dünya çapında hızla artan insülin eksikliği ya da insülin direnci sebebiyle oluşan karbonhidrat, lipid ve protein metabolizması bozukluğu ile belirgin yüksek mortalite ve morbiditeye sahip endokrin ve metabolik bir hastalıktır. Hipokampus'un öğrenme ve bellek oluşumunda rol aldığı bilinmektedir. İnsanlarda ve hayvanlarda hipokampus lezyonları, bilgilerin kısa süreli bellekten uzun süreli belleğe aktarılmasında çeşitli sorunlara yol açar ve böylece yeni bilgilerin depolanması engellenmiş olur (Yonguç, 2009). Diyabet birçok organ ve doku üzerinde uzun dönemde olumsuz etkiler oluşturmaktadır. Hipokampustaki nöronal sistem üzerinde de etkileri olduğu çalışmalarda gösterilmiştir. Hipokampus histolojik olarak üç bölüme ayrılmaktadır ve bu üç bölümün tamamına hipokampal formasyon adı verilmektedir. Bilginin kısa süreliden, uzun süreli hafızaya dönüştürülmesinde, hipokampus rol oynar (Tanbek, 2015). Hipokampusun bilhassa davranış oluşturma ve hafıza ile ilişkili fizyolojik olaylarda kayda değer rolü vardır. Amigdala, orbitofrontal korteks ve ön singulat korteksle birlikte hipokampus bilgi işleme sürecinde ve emosyonel bellekle deklaratif bellek oluşumunda rol oynar (Koç Okudur, 2013). Diyabetin hipokampustaki nöronal yapılarda nörotransmitter salgılanması ve nörotransmitterlerin reseptörlerle kombinasyonu düzeyinde yapısal, fonksiyonel ve kimyasal türlü bozulmalara ve nöronal apopitozise sebep olarak bilişsel işlevleri bozduğu yapılan araştırmalarla ortaya konmuştur (Köroğlu ve ark., 2004). Biz de çalışmamızda Diabetes mellitus oluşturulan ve normal sıçanlarda, gebelik döneminin her üç trimesterinde de hipokampustaki piramidal nöron sayısında meydana gelen değişiklikleri stereolojik yöntemlerle değerlendirmeyi amaçladık.

MATERYAL ve METOT

Çalışma için Van Yüzüncü Yıl Üniversitesi Hayvan Deneyleri Etik kurulundan etik onay alındı (24/08/2017, No: 2017/08). Otuz altı adet 2 aylık, yetişkin ortalama 190-250 gr. ağırlığında Wistar Albino cinsi dişi sıçan alındı. Sıçanlar randomize olarak 2 gruba (kontrol ve diyabet) ayrıldı. Deney hayvanları standart kafeslerde, 12/12 ışık/karanlık siklusu, 22±2 ^{o}C sıcaklıkta, standart pellet yem ve musluk suyuyla ad-libitium beslenmeye tabi tutuldular. STZ fresh olarak hazırlanıp 45 mg/kg tek doz intraperitoneal olarak uygulandı ve akabinde 72 saat sonra açlık kan şekeri seviyesi ölçüldü (Kannan ve ark., 2016). 200 mg/dl ve üzerindeki sıçanlar diyabet kabul edildi. Kontrol grubuna herhangi bir işlem yapılmadı. Bundan sonra sıçanların vajina girişine bir damla serum fizyolojik damlatılıp pamuklu çubuk yardımıyla smear alındı. Oda sıcaklığında smearler kurutularak fiksasyon sağlandı. Yüzde birlik toluidin mavisi ile 5 dakika boyanan preperatlar distile suyla yıkandıktan sonra entellan ile kapatıldı. Mikroskopta incelendi (Şekil 1). Diyabet ve kontrol grubundaki sıçanların siklus senkronizasyonu sağlanarak çiftleşeme için bir gece boyunca 3 dişi 1 erkek olacak şekilde kafese konuldu. Vajinal plak tespit edilenler gebe olarak kabul edildi. Çalışmamızda birinci trimester için gebeliğin 7. günü, ikinci trimester için gebeliğin 14.günü, üçüncü trimester için gebeliğin 21. günü seçildi. Her iki gruptan gebeliğin 7. 14. ve 21.günlerinde 6 adet hayvanın anestezi (ketamin, 50 mg/kg) altında beyin dokusu bütün olarak çıkarıldı. Dokular % 10'luk nötral formaldehit solüsyonunda 24 saat tesbit edildi. Rutin ışık mikroskobik histolojik takip yapıldı. Her iki gruba sayısal yoğunluk hesaplanması amacıyla fiziksel disektör yöntemi uygulandı. Parafine gömülen dokulardan mikrotomla 5µm kalınlığında ardışık kesitler alındı. İlki rastgele olmak üzere sonrakiler her 400µm'de bir ortalama beş çift kesit alındı. Kesitler Hematoksilen-Eozin ile boyandı ve entellenla kapatıldı. (Bancroft ve Stevens, 1996; Demir, 2001). Işık mikroskopunda

(Nikon (Y-IM) Eclipse, Japan) 100 'lük objektifte dokular incelendi ve fotoğraflandı. Sayısal yoğunluk hesaplama formülü kullanılarak hipokampusun piramidal hücre tabakasındaki cornu ammnois'in tüm alanlarındaki piramidal nöronlar ayrım yapılmadan sayıma dahil edildi. Stereolojik olarak, Sayısal Yoğunluk Hesaplama formülü kullanılarak tarafsız sayım çerçevesinin alanı bu büyütmede 6500µm olarak ele alındı. Alan örneklemede ise ¼ oranı uygulanarak kareli alan cetvelimizin her dörtte bir alanı sayıma dahil edildi. Sayım yapılırken ilk kesitte gözlenip ikinci kesitte gözlenmeyen nöron çekirdekleri baz alınarak nöronlar sayıldı.

Sayısal Yoğunluk Hesaplama formülü:

$Nv = N/Vref$

Nv: hücrelerin sayısal yoğunluğu (hücre/birim hacim), N: hücre sayısı ve Vref: hipokampusun toplam referans hacmidir (Mayhew ve Gundersen, 1996).

Standart sterelojik yaklaşımda her gruptaki optimum örnek boyutunu belirlemek için hata katsayısı (HK= Coefficient of Error; CE) ve değişim katsayısı (DK= Coefficient of Variation; CV) kullanılır (Gunderson ve Jensen 1987). Çalışmamızın HK ve DK değerleri literatür verileriyle uyumluydu.

İstatistikler minimum, maksimum, standart sapma, medyan ve ortalama değerler olarak değerlendirildi. İstatistiksel analizde Mann-Whitney U testi kullanıldı. Hesaplamalar SPSS istatistik paket programında yürütüldü ve anlamlılık düzeyi %5 olarak kabul edildi.

BULGULAR

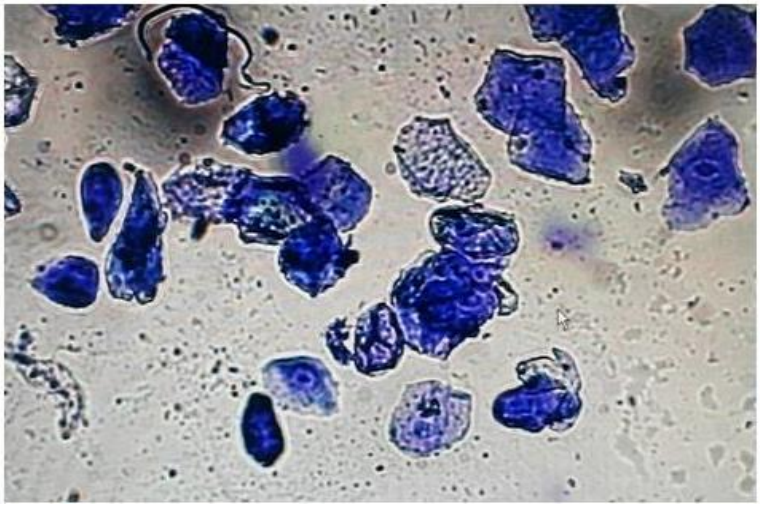
Stereolojik hesaplamalar sonucunda istatistiksel olarak diyabet ve kontrol grupları arasında hipokampal piramidal nöron sayısı bakımından anlamlı fark tespit edildi. ($p<0.05$) (Tablo 1) (Şekil 1) . Ancak trimesterler arasında (I, II. ve III) hipokampal piramidal nöron sayısı açısından anlamlı fark izlenmedi (Tablo 2) (Şekil 2, 3). Sıçanlara ait beyin dokusunda yapılan histopatolojik incelemede gruplar arasında fark izlenmedi.

Tablo 1. Gruplar arası karşılaştırma sonuçları

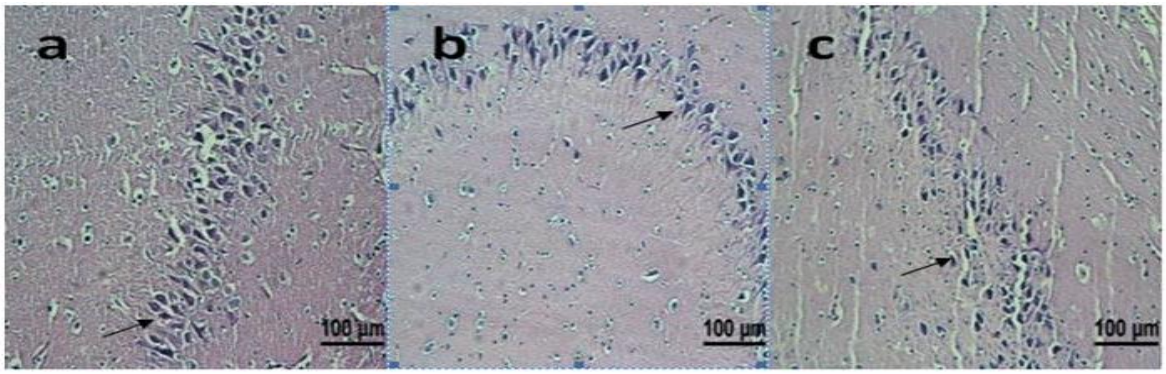
	Grup	Median	Mean	Std. Sap.	Minimum	Maximum	*p.
Hücre Sayısal Yoğunluk (mm^3)	**Kontrol**	569201	571754	77974	465807	704628	0,011
	Diyabet	446038	456828	128145	234876	745890	

Tablo 2. Gruplarda trimesterler arası karşılaştırma sonuçları

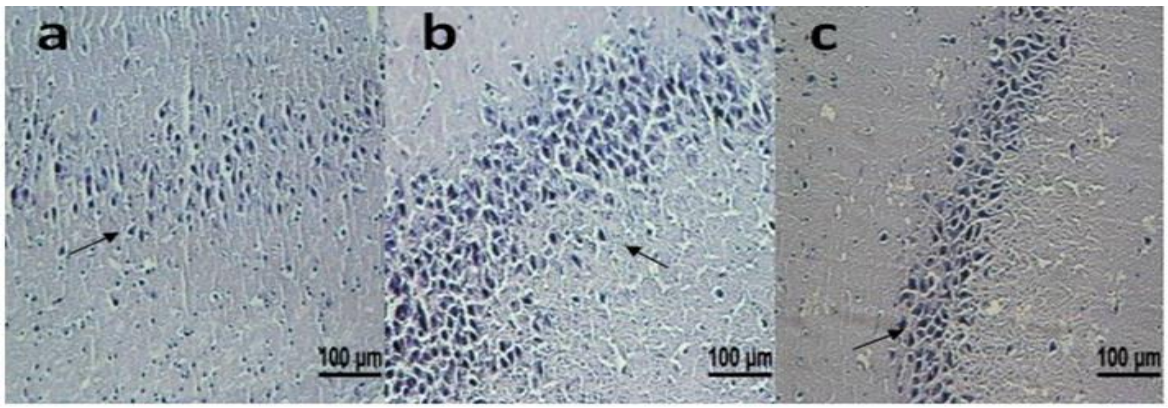
		Kontrol					Diyabet					
	Trimester	Median	Ort.	SS	Min.	Max.	Median	Ort.	SS	Min.	Max.	*p.
Hücre Sayısal Yoğunluk (mm^3)	**T1**	625628	639149	59875	587190	704628	424081	517215	199170	381673	745890	0,513
	T2	536702	549473	90727	465807	645909	425713	391682	108337	234876	480428	0,077
	T3	528471	526639	43506	482246	569201	469752	483302	40146	451684	528471	0,275



Şekil 1. Toluidin mavisi ile boyanmış östrus siklusu



Şekil 2. Diyabet grubu 1. trimester (a) 2. trimester (b) ve 3. trimester (c) piramidal hücrelerin görünümü (siyah ok) (Hematoksilen & Eozin, Scale bar 100 µm)



Şekil 3. Kontrol grubu 1. trimester (a) 2. trimester (b) ve 3.trimester (c) piramidal hücrelerin görünümü (siyah ok) (Hematoksilen- Eozin, Scale bar 100 µm)

TARTIŞMA

Hiperglisemi hafıza ve dikkat açısından bozulmalara sebep olabilir. Kronik hiperglisemi bilişsel bozulmaya ve sinapsal düzenlemede bozulmalara neden olabilmektedir. Hipergliseminin yanı sıra hipoglisemide bilişsel işlevlerde harabiyet yapmakta ve tekrarlayan hipoglisemi atakları bu yıkımı 1,5 – 2 kat artırmaktadır (Ünal ve ark., 2015). Beyin dokusu insülin üretmediği halde hipokampusda insülin reseptörleri tespit edilmiştir. Bu insülin reseptörlerinin beyindeki işlevleri gıda alımını azaltma, bilişsel fonksiyonlar, bellek ve nörodejeneratif bozukluklara sebep olmaktadır. Tip 1 ve Tip 2 Diyabetes mellitusda kognitif işlevlerde azalma olduğu tespit edilmiştir (Ertörer, 2014). Yonguç ve arkadaşlarının (2009) yaptığı çalışmada; STZ ile deneysel diyabet oluşturulan modelde Morris Su Labirenti (MWM) deneyinden ve stereolojik incelemeden elde edilen veriler, STZ ile deneysel diyabet oluşturulan sıçanlarda platformun yerini öğrenmede bozulmalara sebep olduğu ve hipokampusun piramidal katmanındaki toplam nöron sayısını azalttığı görülmüştür. Zhao ve arkadaşlarının (2016) yaptığı başka bir çalışmada STZ ile diyabet oluşturulan ratların hipokampusunda CA1'in kapladığı alanda azalma ve sinaptik yapılarda dejenerasyon saptanmıştır. Onar ve arkadaşlarının (2019) yaptığı çalışmalarında yine STZ kullanılarak oluşturulan diyabetin hipokampusde NLRP3 seviyesini artırarak ve nitrozatif stres oluşumuyla sıçanlarda öğrenme ve hafıza bozukluğuna sebep olduğunu göstermişler. Bizimde çalışmamızda diyabetik gebe sıçanların hipokampal piramidal nöron sayısında kontrol grubuyla karşılaştırıldığında istatistiksel olarak anlamlı fark tespit edildi. Yapılan bir çalışmada kontrolsüz gestasyonel diyabetin postnatal dönemde sıçan yavrularının hipokampal nöronlar üzerinde nörotoksik etki yaptığı görülmüştür (Golalipour ve ark., 2012). Kontrolsüz diyabet gebe sıçanların yavrularında serebral purkinje hücrelerinde tahribata neden olmakta ve bu yavrularda motor ve davranışsal fonksiyonlarda bozulma görülmektedir (Hami ve ark., 2016). Bu çalışmalar diyabetin yavru sıçanlardaki etkilerini göstermekte olup bizim çalışmamızda gebe sıçanların üzerinde olduğu için motor ve davranış fonksiyonları değerlendirilmedi. Sonuçta diyabetin vücudun birçok bölümünde hasara neden olduğu bilinmekte olup yaptığımız çalışmayla gebe sıçanlarda hipokampal nöron sayısında azalmaya neden olduğu tespit edildi ve daha ileri çalışmalarla desteklenmesinin uygun olacağı görüşündeyiz.

Çıkar Çatışması

Yazarlar çıkar çatışması olmadığını beyan eder.

Van Uluslararası Uygulamalı Bilimler Kongresi (24-25 Temmuz 2020/ Van) özet sözlü bildiri olarak sunulmuştur

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Orjinal Araştırma Makalesi/ Original Paper

Relationship Between Skeletal and Dental Malocclusions in the Sagittal Direction in Turkish Orthodontic Patients: A Retrospective Study

Türk Ortodonti Hastalarında Sagital Yönde İskeletsel ve Dental Maloklüzyonların İlişkisi: Retrospektif Bir Çalışma

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ÖZET

Amaç: Bu çalışma iskeletsel ve dental maloklüzyonların sagital yönde uyumunu değerlendirmeyi amaçlamaktadır.

Materyal ve Metot: Van Yüzüncü Yıl Üniversitesi Diş Hekimliği Fakültesi Ortodonti Kliniği'ne başvuran, kraniyofasiyal anomalisi olmayan, daha önce ortodontik tedavi görmemiş ve travma öyküsü olmayan 11-18 yaş arası 230 hasta (erkek, kadın) çalışmaya dahil edildi. Bireyler ANB açılarına göre gruplara ayrıldı. Farklı sagital iskeletsel maloklüzyonlarda molar ilişkiler incelendi. Bilgileri değerlendirmek için tanımlayıcı analiz ve Pearson ki-kare testi kullanıldı. Elde edilen veriler istatistiksel olarak %5 anlamlılık düzeyinde analiz edilmiştir**.**

Bulgular: 12-30 yaş arası 230 kişi ANB açılarına göre gruplara ayrıldı. İskeletsel Sınıf 1 maloklüzyonlu bireylerde molar ilişki en fazla Angle Class II olarak belirlenmiştir, Angle Class IV ise en az görülen ilişkidir. İskeletsel Sınıf 2 maloklüzyonu olan bireylerde molar ilişki en fazla Angle Sınıf II olarak belirlenirken, Angle Sınıf III subdivizyon en az görülen ilişkidir. İskeletsel Sınıf 3 maloklüzyonlu bireylerde molar ilişki en fazla Angle Class III olarak belirlenirken, en az Angle Class IV olarak belirlenmiştir.

Sonuç: Bu çalışmada iskeletsel maloklüzyonlar ile molar ilişkiler arasında anlamlı bir ilişki olduğu gözlendi. Ancak molar ilişkinin iskeletsel maloklüzyon dışında farklı faktörlere bağlı olarak değişebileceği düşünülmektedir.

Anahtar Kelimeler: İskeletsel Maloklüzyonlar, Molar ilişki, Sagital Yön.

ABSTRACT

Objective: This study aims to evaluate the compatibility between skeletal and dental malocclusions in the sagittal direction.

Material and Method: 230 patients (male, female) aged 11-18 years, who applied to Van Yüzüncü Yıl University Faculty of Dentistry Orthodontic Clinic, had nocraniofacial anomaly, had not received orthodontic treatment and had no history of trauma, were included in the study. Individuals were divided into groups according to their ANB angles. The molar relationships in different sagittal skeletal malocclusions were examined. Descriptive analysis and the Pearson chi-square test were used to evaluate the information. The obtained data were statistically analyzed at the 5% significance level.

Results: 230 individuals between the ages of 12-30 were divided into groups according to their ANB angles. In individuals with skeletal Class 1 malocclusion, the molar relationship was Angle Class II at most and Angle Class IV at most negligible. In individuals with skeletal Class 2 malocclusion, the molar relationship was determined as Angle Class II at most, while Angle Class III subdivision and nomolar relationship were observed at least. In individuals with skeletal Class 3 malocclusion, the molar relation was Angle Class III at most, Angle Class IV at least, and nomolar relation.

Conclusion: In this study, it was observed that there was a significant relationship between skeletal malocclusions and molar relationships. However, it is thought that the molar relationship may vary due to different factors other than skeletal malocclusion.

Keywords: Molarrelation, Skeletal Malocclusions, Sagittal Direction.

INTRODUCTION

Orthodontics is a branch of science that deals with correcting dentofacial deformations and malocclusions to achieve optimum aesthetics and function. The aim of orthodontic treatment is not only to achieve functional occlusion. Increasingly, aesthet-

ic-oriented needs have led to a focus on profile aesthetics. Today, facial appearance is why most patients apply for orthodontic treatment (Gomez et al., 2017; Maetevorakul et al., 2016).

Malocclusion is non-normal relations between tooth groups, dental arches, lower jaw, and upper jaw teeth. Classification of occlusion is evaluated in separate dimensions in the spatial plane. The first classification made by Edward H. Angle was made according to the mesiodistal relationship of permanent molars.

In addition to this classification, malocclusion is evaluated sequentially according to whether the lower and upper jaws are relative to the cranial base of the skull in the sagittal direction. Malocclusions are classified as Class I, Class II, or Class III based on the maxillo-mandibular relationship in the sagittal order concerning the skull base (Kozanecka et al., 2016; Ülgen., 2015).

When the literature is examined, many studies examine the prevalence of malocclusion according to race such as Caucasian, Italian, Nigerian, and Black American (Kerosuo, 1990; Ciuffolo et al., 2005; Onyeaso et al., 2002; Garner et al., 1985). In studies conducted, malocclusion prevalences were found to vary between 11% and 93% (Vig and Fields, 2000; Gelgor et al., 2007).

While it is difficult to describe the disparities between the groups studied, it does lead us to believe that these discrepancies may arise as a result of variances in patient registration, ethnic structure, social environment and age groups (Thilander et al., 2001).

Furthermore, evaluating patient groups who are seeking orthodontic treatment is critical in terms of arranging clinical objectives based on the patient population. When looking through the literature, it is clear that there is research that looks at the compatibility and relationship between skeletal and dental malocclusion in the sagittal plane. It's crucial to look at the causes underlying this connection. In orthodontic diagnostic and treatment planning, it's a popular topic whether the dental relationship in the sagittal plane is related to the skeletal relationship. In this context, the study's goal is to determine the sagittal relationship between skeletal and dental malocclusion.

Whether or not the dental relationship is related to the skeletal relationship in the sagittal plane, it is a focal point for orthodontic diagnosis and treatment. The study's goal is to see how skeletal and dental malocclusions interact in the sagittal plane.

MATERIALS and METHODS

In this retrospective study, individuals who applied to Van Yüzüncü Yıl University Faculty of Dentistry Orthodontic Clinic between 2014-2018 without craniofacial anomalies, who did not receive orthodontic treatment, who had no trauma history and no impacted teeth were included. Following the planning of the study, ethics committee approval was obtained from the Clinical Research Ethics Committee (Karar no:2021/02-32). The research was conducted in accordance with the principles of the Declaration of Helsinki. A total of 230 patients, 147 girls, and 83 boys, aged 12-30 years, were randomly selected and included in the study. Intraoral photographs panoramic and cephalometric radiographs of the patients included in the study were examined, and care was taken to ensure that the patients were in the permanent dentition period and did not have congenitally missing or impacted teeth. ANB values of the patients were determined due to lateral cephalometric analysis. Individuals were divided into groups according to ANB angle as skeletal Class 1 (ANB 0°-4°), skeletal Class 2 (ANB>4°), and skeletal class 3 (ANB<0°). According to the Angle Classification, the molar relation values determined as a result of clinical examination and measurements of the patients have been recorded as Class I, Class II, Class III, Class IV, Class II subdivision and Class III subdivision according to the Angle classification(Figure 1). During the clinical examination, the molar relations of the patients were evaluated in centric occlusion and recorded. In

addition, the measurements of the patients were assessed with intraoral-extraoral photographs and dental models, and their molar relations were examined in detail.

Statistical Analysis

The obtained data were transferred to the computer environment, and statistical analysis was performed with the SPSS (Statistical Package for the Social Sciences) 21.0 version package program. Descriptive analyzes and the Pearson chi-square test were used to evaluate the information. The statistical significance level was determined as p=0.05. Ethics committee approval was received for this study from the Van Yüzüncü Yıl University Faculty of Medicine Ethics Committee (03/08/2021, Decision no: 03). The patients were informed in detail about the purpose and process of the study. Patients who voluntarily signed the "informed consent form" approved by the ethics committee were included in the study after obtaining the consent of their parents.

RESULTS

Of the 230 individuals aged 12-30 years included in the study, 147 were female, and 83 were male. When the age distribution and average age of the individuals participating in the study by gender are examined; While the mean age of female patients (n=147) was 15.7 years, the mean age of male patients (n=83) was 14.4. The mean age of all individuals participating in the study was found to be 15.2 years. Molar relationship in 2.6% (n=6) of a total of 230 individuals; While it cannot be detected due to the missing of at least one of the maxillary or mandibular first molars, 23.5% (n=54) Angle Class I, 42.6% (n=98) Angle Class II, 10.4%' (n=24) Angle Class III, 2.6% Angle Class IV, 11.3% (n=26) Angle Class II Subdivision, and 7% (n=16) Angle Class III Subdivision seen. The evaluation of the molar relationship status of the individuals according to the ANB angle is shown in Table 1. Of the individuals, 46.5% (n=107) were skeletal Class I, 30% (n=69) skeletal Class II, and 23.5% (n=54) skeletal Class III. In the right-sided molar relationship evaluation, 30.9% of the patients were Angle Class I, 47.4% Angle Class II, 15.2% and Angle Class III, 6.5% were closing due to missing at least one of the molar teeth observed to be absent. Evaluating the left-sided molar relationship, 29.6% of the patients were Angle Class I, 49.1% Angle Class II, 14.8% Angle Class III, and 2.6% were missing at least one molar tooth, not any relationship. (Table 1)

Considering the distribution of molar relations by gender, 2.7% of female individuals were in the no molar relation group, 23.8% were Angle Class I, 44.9% Angle Class II, 7.5% Angle Class III, It was found that 1.4% was Angle Class IV, 12.2% was Angle Class II Subdivision and 7.5% was Angle Class III Subdivision. In males, 2.4% were in the no molar bite group, 22.9% Angle Class I, 38.6% Angle Class II, 15.7% Angle Class III, 4.8% Angle Class IV, 9.6% Angle Class II Subdivision, and 6.0% Angle Class III Subdivision. (Table 1). No statistically significant difference was found between gender and molar relationship (p>0.05).

When the relations between skeletal malocclusions and molar closure were evaluated, it was observed that the molar relation was the most Angle Class II and the minor Angle Class IV in individuals with skeletal Class 1 malocclusion. In individuals with skeletal Class 2 malocclusion, the molar relationship was determined as Angle Class II at most, while Angle Class III subdivision and no molar relationship were observed at least. In individuals with skeletal Class 3 malocclusion, the molar relationship was found to be Angle Class III at most, while Angle Class IV and molar relationship were found to be the least. The correlation between skeletal malocclusions and molar relationships was statistically significant (p<0.05).

Table 1. Skeletal malocclusion and molar relationship distribution.

		n	%
Gender	female	147	63,9%
	male	83	36,1%
Skeletal malocclusion	Class 1	107	46,5%
	Class 2	69	30,0%
	Class 3	54	23,5%
Right molar relationship	Class I	71	30,9%
	Class II	109	47,4%
	ClassIII	35	15,2%
	No molarrelationship	15	6,5%
Left molar relationship	Class I	68	29,6%
	Class II	113	49,1%
	Class III	34	14,8%
	No molarrelationship	15	6,5%
Molar relationship	No molarrelationship	6	2,6%
	Class I	54	23,5%
	Class II	98	42,6%
	Class III	24	10,4%
	Class IV	6	2,6%
	Class II Subdivision	26	11,3%
	Class III Subdivision	16	7,0%

Figure 1. Angle classification

DISCUSSION

The need for orthodontic treatment rapidly increases daily in many countries and reaches serious numbers (Thilander et al., 2001). In line with this increasing treatment need, many studies have been carried out to determine the prevalence of malocclusions in various societies (Kozanecka et al., 2016; Ülgen, 2015; Kerosuo,1990; Ciuffolo et al., 2005; Onyeaso et al., 2002). However, the fact that different results were obtained even in studies carried out on similar populations reveals how much malocclusions can differ between regions. Studies evaluate the prevalence of malocclusion according to many different ethnic groups in the literature (Kerosuo,1990; Ciuffolo et al., 2005; Onyeaso et al., 2002; Garner and Butt., 1985). The Prevalence of malocclusion varies between 11% and 93% in studies (Garner and Butt., 1985; Vig et al., 2000; Gelgor et al., 2007). Although it is difficult to explain these severe differences between the groups examined, this difference is due to the different patient groups recorded, ethnicity, social. It is thought that it may occur depending on the frame and age group (Thilander et al., 2001). However, the evaluation of patient groups applying for orthodontic treatment is essential in arranging clinical needs by considering the applicant patient population.

Many studies have investigated whether different skeletal malocclusions affect the soft tissue thickness of individuals, but gender differences were not evaluated in every study (Uysal et al., 2009; Kalha et al., 2008; Utsuno et al., 2010a; Utsuno et al., 2010b). Utsuno et al assessed the effect of skeletal malocclusions on soft tissue in women aged 6-16 and 17-33 years (Utsuno et al., 2010a; Utsuno et al., 2010b). This study found no statistically significant difference between gender and molar relationships. Other research explores the distribution of maxillary midline diastema and dental midline deviation in patients with varied skeletal malocclusions. Maxillary midline diastema and dental midline deviation were similar in various skeletal malocclusions (Çınarsoy Ciğerim et al., 2019). In this study, it was observed that there was a significant relationship between sagittal skeletal malocclusions and molar relations.

Zupancic et al., (2008) observed that overjet is a predictive factor of sagittal skeletal relationships in Class II division I anterior relation (Zupancic et al., 2008). In a study looking at the relationship between dental malocclusion and skeletal malocclusion in the sagittal plane in orthodontic patients, the incisal classification was found to be significantly related with WITS evaluation. In contrast, with ANB, the association was marginally significant (Al-Hamlan et al., 2015). In this study, it was observed that there was a substantial relationship between sagittal skeletal malocclusions and molar relations.

In a study examining molar and canine relationships, Class II half and full-step asymmetries were more prevalent than Class III asymmetries in the

molar and canine regions (Behbehani et al., 2012). In this study, in individuals with skeletal Class 1 malocclusion, the molar relationship was found to be Angle Class II at most and Angle Class IV at most negligible. In individuals with skeletal Class 2 malocclusion, the molar relationship was determined as Angle Class II at most, while Angle Class III subdivision and no molar relationship were observed at least. In individuals with skeletal Class 3 malocclusion, the molar relation was Angle Class III at most, Angle Class IV at least, and no molar relation. It has been found that there is a relationship between skeletal malocclusions and molar relationships.

Conclusion

This study is the first study to examine the concordance between sagittal skeletal malocclusions and molar relationships. In this study, it was observed that there was a significant relationship between sagittal skeletal malocclusions and molar relations. However, it is thought that the molar relationship may vary due to different factors other than skeletal malocclusion

Conflict of interest

The authors declare that there is no conflict of interest.

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Orjinal Araştırma Makalesi/ Original Paper

Flexible Üreterorenoskopide Erişim Kılıfının Kullanımı Vazgeçilmez mi?

Is It Essential to Use The Access Sheath In Flexible Urethrorenoscopy?

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ÖZET
Amaç: Çalışmamızda erişim kılıflı flexible üreteroskopi ve erişim kılıfsız Flexible-URS kullanımının etkinlik ve güvenilirliklerini karşılaştırmayı amaçladık.
Materyal ve Metot: Böbrek pelvisinde, orta ve üst kalikste toplam taş yükü 0,8 ile 1,5 cm3 arasında olan ve üreteroskopik taş cerrahisi yapılan toplam 70 vakanın verileri geriye dönük retrospektif olarak değerlendirildi. Üreteral erişim kılıfsız F-URS (n=32) ve üreteral erişim kılıflı F-URS (n=38) uygulanan hastaların verileri retrospektif olarak incelendi. Gruplar arasında stone-free oranları, ameliyat süreleri, floroskopiye maruziyet süresi, kan kaybı ve komplikasyonlar açısından karşılaştırma yapıldı**.**
Bulgular: Toplam taş yükü 1.5 cm3 ve altında olan 70 hastanın 32'inde (%45,7) erişim kılıfsız F-URS yapılırken, 38 (%54,3) hastaya ise erişim kılıflı F-URS yapıldı. Ortalama operasyon süresi erişim kılıfsız F-URS grubunda 98,42±8,12 dk, erişim kılıflı F-URS grubunda ise 101,23±9,08 dk idi ve istatistiksel olarak anlamlı değildi (p=0.303). Ameliyat sonrası 1. gün ve 1. ay takipte stone-free oranları erişim kılıfsız F-URS grubunda sırasıyla %81,48 ve %85,18 iken, erişim kılıflı F-URS grubunda ise %81,25 ve %87,5 olup iki gurup arasında stone-free başarısı yönünden istatiksel olarak anlamlı bir fark bulunmadı (p=0,896 ve p=0,674).
Sonuç: Erişim kılıfsız F-URS ile erişim kılıflı F-URS kıyaslandığında benzer ameliyat sürelerine, benzer başarı ve komplikasyon oranlarına sahiptir.

Anahtar Kelimeler: Böbrek Taşı, Erişim Kılıfı, Flexible, Üreteroskopi.

ABSTRACT
Objective: This study, we aimed to compare the efficacy and safety of F-URS with Access sheat hand F-URS with out Access sheath.
Material and Method: The data of 70 patients who underwent ureteroscopic stone treatment with a total stone load between 0.8 and 1.5 cm3 in the renal pelvis, middle and uppercalyx were evaluated retrospectively. The data of patients who underwent Flex-URS without ureteral Access sheath (n=32) and F-URS with ureteral Access sheath (n=38) were reviewed retrospectively. The groups were compared in terms of stone-free rates, duration of operation, exposure to fluoroscopy, decrease in hemoglobin and complications.
Results: F-URS without Access sheath was performed in 32 (45.7%) of 70 patients with a total stone burden of 1.5 cm3 orless, while F-URS with access sheath was performed in 38 (54.3%) patients. The mean operation time was 98.42±8.12 min in the F-URS without Access sheath group, and 101.23±9.08 min in the F-URS group with the access sheath, and was not statistically significant (p=0.303). The stone-free rates at postoperative 1 day and 1 month follow-up were 81.48% and 85.18% in the F-URS without access sheath group, respectively, while it was 81.25% and 87.5% in the F-URS group with the Access sheath, and stone-free rates were found between the two groups nostatistically significant difference was found in terms of success (p=0.896 and p=0.674).
Conclusion: F-URS without access sheath and F-URS with Access sheath have similar operative times, similar success and complication rates.

Keywords: Kidney Stone, Access Sheath, Flexible, Ureteroscopy.

GİRİŞ

Son yıllarda böbrek taşlarının tedavisinde flexible üreteroskopi (F-URS) giderek önemi artan bir seçenek haline geldi. F-URS işlemi esnasında ağırlıklı olarak kullanılan üreteral erişim kılıfının taşsızlık oranı üzerindeki etkisi ve olası gelişen komplikasyonları üzerinde yapılan çeşitli çalışmalar neticesinde üreteral erişim kılıfsız F-URS gibi alternatif yöntemleri gündeme getirmiştir. Üreteral erişim kılıfları, taşın çıkarılmasını kolaylaştırmak, görüntü kalitesini artırmak ve düşük intrarenal basıncı sağlamak için yaygın olarak kullanılır (Cooper ve ark., 2020). Erişim kılıfı, lazerle parçalanan küçük taş parçalarının irrigasyon sıvısının çıkışıyla pasif olarak ortadan kaldırılmasına izin verme ve böbrek

toplayıcı sisteme çoklu giriş ve yeniden erişim sağlama kolaylığına da sahiptir (Traxer ve ark., 2015). Avantajlarının yanında, erişim kılıfının kullanılması üreter duvarı iskemisine ve üreter yırtıklarına neden olabilir ve potansiyel olarak postoperatif üreteral darlık riskinde artma gibi dezavantajları da olabilir (Kourambas ve ark. 2001; Rehman ve ark., 2003; Auge ve ark., 2004; Stern ve ark., 2007). Yapılan çalışmalarda erişim kılıfsız F-URS'nin taşsızlık başarısı, intraoperatif ve yakın postoperatif komplikasyon açısından erişim kılıflı F-URS sonuçları ile aynı olduğunu bildirmişlerdir (Kourambas ve ark., 2001). Bununla birlikte bazı yazarlar taşsızlık başarısının erişim kılıflı F-URS'de daha yüksek olduğunu bildirmişleridir (L'Esperance ve ark., 2005).

Bu çalışmada, erişim kılıfsız F-URS ile erişim kılıflı F-URS sonuçlarını karşılaştırarak klinik deneyimlerimizi aktarmaya çalıştık.

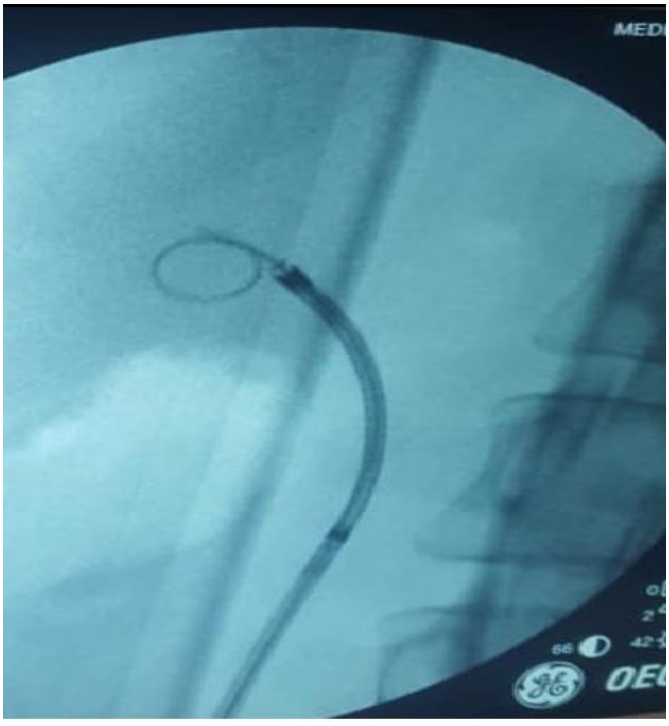
MATERYAL ve METOT

Çalışmamız Eylül 2019 ile Ağustos 2021 tarihleri arasında toplam taş yükü büyüklüğü 0,8 cm3 ile 1,5 cm3 arasında değişen böbrek pelvisi, orta ve üst kaliks taşlarının tedavisi için üreteral erişim kılıfsız F-URS (n = 32) ve üreteral erişim kılıflı F-URS (n = 38) cerrahi işlemi yapılan vakaların verileri retrospektif olarak değerlendirildi. 15 yaşından küçük, soliter böbrekli, at nalı böbrek anomalisi, kaliksiyel kist taşı mevcudiyeti, perkütan cerrahi uygulaması, ESWL uygulaması, geçirilmiş retroperitoneal cerrahi öyküsü, alt kaliks taşı olanlar ve toplam taş yükü 1.5 cm3'den büyük olan vakalar çalışmaya dahil edilmedi. Üst üriner sistem ve hastadaki taşın özellikleri (taş ebatı ve sayısı, taşın bulunduğu konum), yapılan işlemin süresi ve operasyon sonrası bulgular (taşsızlık oranı, hastanede yatış süresi) ile beraber intraoperatif ve postoperatif komplikasyonlar not edildi. Taşın ebadı, kontrastsız üst abdomen tomografisi (BT) ile tespit edilen en uzun çap olarak tanımlandı.

Tüm hastaların ameliyat öncesi tam idrar tetkiki, idrar kültürü, serum hemogram ve biyokimyayı (kreatinin, sodyum, üre, potasyum) içeren labaoratuvar değerleri kaydedildi. Her iki gruba cerrahi işlem öncesi benzer profilaktik antibiyotik tedavisi (seftriakson 1 gr) uygulandı. Gruplar arasında taşsızlık oranları, cerrahi işlem süreleri, floroskopiye maruz kalma süreleri, hemoglobin değerindeki değişim, intraoperatif ve postoperatif komplikasyonlar (Clavien-Dindo sınıflamasına göre), postoperatif analjezik ihtiyacı ve hastanede yatış süreleri bakımından karşılaştırıldı. Bu çalışma Helsinki Deklarasyonu ilkelerine uygun olarak yapılmış olup İstanbul Atlas Üniversitesi etik kurul onayı alınmıştır (Kayıt No: 2019/15-28).

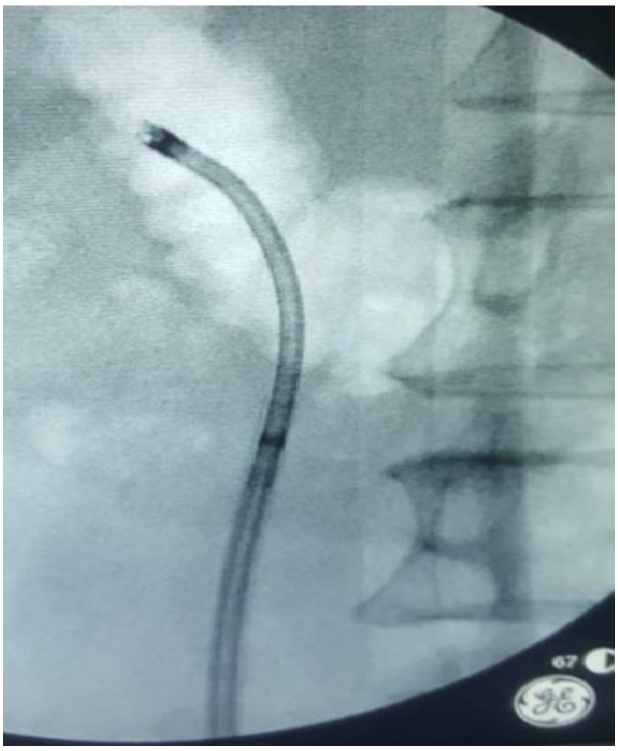
Cerrahi Teknik

Vakaların hepsine genel anestezi altında dorsal litotomi pozisyonunda işlem yapıldı. Bütün vakalara 6F çalışma kanallı semirijid üreteroskopla (Storz, Germany) böbrek pelvisine kadar çıkılarak üreteral aktif dilatasyon yapıldı ve hidrofilik kılavuz tel yerleştirildi. Üreteroskop çıkarıldıktan sonra, erişim kılıfsız hasta gurubunda, hidrofilik kılavuz tel 3.6F çalışma kanallı tek kullanımlık F-URS (Otu, Ningbo Wise OptoMech Technology Corporation, China) içinden geçirilerek böbreğe ulaşıldı (Şekil 1).



Şekil 1. Erişim kılıfsız F-URS

Erişim kılıfı kullanılan guruba ise hidrofilik tel 9.5/11.5F çaplı üreteral erişim kılıfı içinden floskopi eşliğinde üretere yerleştirildi. Ardından iç çapı 3.6 F olan tek kullanımlık F-URS kullanıldı (Şekil 2).



Şekil 2. Erişim kılıflı F-URS

Bazı hastalara İhtiyaç halinde her iki gurupta da üreteral balon dilatasyon kullanıldı. Taşlar, her iki gurupta da holmiyum lazerle (QuantaSystem,Italy) 0.8 ila 1.0 J enerji ayarı ve 6 - 10 Hz hızda 272 veya 365 µm fiber kullanılarak 'tozlanma' modu ile parçalandı. Üreteral erişim kılıfı kullanılan gruba; kılıf yerleştirilmesi, operasyon sonu rezidü taş kontrolü ve double-J stent uygulama esnasında floskopi kullanılırken erişim kılıfı kullanılmayan gruba ise sadece işlem sonu rezidü taş kontrolü ve double-J stent uygulama esnasında floskopi kullanıldı. Litotripsi işleminden sonra tüm vakalara 6.4 F double-J stent implante edildi ve işlemden 1 ay sonra çıkarıldı.

Taşsızlık işlem sırasında floroskopi ve postoperatif 1. gün düz batın grafisi ile öncelikle değerlendirildi. Bütün hastalar postoperatif 1. ayda ultrasonografi ile değerlendirildi ve ultrasonda rezidüel taş tespit edilen hastalara BT yapıldı. 3 mm3'den küçük asemptomatik, obstrüksiyon yapmayan taşlar klinik önemsiz sayılarak göz ardı edildi.

İstatiksel Analiz

Veri toplama işlemleri IBM SPSS 20.0 kullanılarak yapıldı. Değişkenlerin dağılım uygunluğu Shapiro-Wilk testi ile belirlendi ve normal dağılım gösteren değişkenler ortalama ± standart sapma olarak sunuldu. Gruplar arasındaki farklar bağımsız örneklem t testi ile analiz edildi. Kategorik değişkenler frekans ve yüzde olarak sunuldu ve ki-kare testi ile karşılaştırıldı. <0.05'lik bir p değeri istatistiksel olarak anlamlı kabul edildi.

Etik Onam

Çalışmamızda Helsinki bildirgesine uyularak, çalışmamıza katılan tüm olgulardan yazılı onam alınmıştır. Etik Kurul izni Atlas Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulundan 28.01.2022 tarihinde E-22686390-050.01.04-11871 numaralı sayı kararı ile alınmıştır.

BULGULAR

Toplam taş yükü 1.5 cm3 ve altında olan 59 hastanın 27'inde (%45,8) erişim kılıfsız F-URS yapılırken, 32 (%54,2) hastaya ise erişim kılıflı F-URS uygulandı. Yaş, cinsiyet, toplam taş ebadı ve taş tarafı iki grupta da benzer olarak görüldü (sırasıyla p<0.726, p<0.298, p<0.526 ve p<0.815) (Tablo 1).

Operasyon süresi erişim kılıfsız F-URS grubunda 98,42±8,12 dakika (dk), erişim kılıflı F-URS grubunda 101,23±9,08 dk idi ve istatistiksel olarak anlamlı değildi (p= 0.303). İntraoperatif kullanılan floskopi süresi her iki gurupta da benzer olup aralarındaki fark anlamlı bulunmadı (p= 0.313). Cerrahi işlem sonrası 1. gün ve 4. hafta takipte taşsızlık oranları erişim kılıfsız F-URS grubunda sırasıyla %81,48 ve %85,18 iken, erişim kılıflı F-URS grubunda ise %81,25 ve %87,5 olup iki gurup arasında taşsızlık başarısı açısından istatiksel olarak anlamlı bir fark bulunmadı (p=0.896 ve p=0.674).

Tablo 1. Gruplara özgü demografik veriler ve taş özellikleri

Parametreler	Kılıfsız F-URS	Kılıflı F-URS	P-değeri
Hasta sayısı (n, %)	32 (%45,7)	38 (%54,3)	0.726
Yaş (yıl)	44,60±6,35	45,12±7,56	0.298
Cinsiyet (n, %)			
Erkek	19 (%59,4)	23 (%60,5)	
Kadın	13 (%40,6)	15 (%39,5)	
Taş boyutu (mm)	10,20±3,45	11,05±2,37	
Taş tarafı (n, %)			
Sağ	15 (%55,6)	19 (%59,4)	0.526
Sol	12 (%44,4)	13 (%40,6)	0.815

Erişim kılıfsız F-URS grubunda bir hastada (%3,7) ve erişim kılıflı F-URS grubunda iki (%6,25) hastada belirgin üreteral darlığa bağlı böbreğe ulaşılamadı ve bu hastalara double-J stent uygulanarak 3 hafta sonra işlem tekrarı başarılı şekilde gerçekleştirildi. Gruplar hemoglobin düşüşü bakımından karşılaştırıldığında anlamlı farklılık saptanmamış olup hiçbir hastaya kan transfüzyon ihtiyacı olmadı (sırasıyla 0,70 ± 0,41g/dL ve 0,74 ± 0,26 g/dL, p=0.220). Erişim kılıfsız F-URS grubunda iki vakada ve erişim kılıflı F-URS grubunda üç vakada cerrahi işlem sonrası ateş görüldü (p= 0.340). Bu vakalara antipiretiklerle (Clavien 1) müdahale edildi. Erişim kılıfsız F-URS grubunda bir vakada ve erişim kılıfslı F-URS grubunda da bir vakada işlem sonrası narkotik analjezik gereksinimi oldu (p=0.697). Hastanede yatış süresi erişim kılıfsız F-URS grubunda 24,64 ± 4,0 saat ve erişim kılıfslı F-URS grubunda 24,62 ± 5,44 saat idi ve istatistiksel olarak anlamlı farklılık görülmedi (p=0.744). Vakaların hiçbirinde major komplikasyon (Clavien 4-5) görülmedi. İntraoperatif ve postoperatif parametreler Tablo 2'de verilmiştir.

Tablo 2. Gruplara özgü intraoperatif ve postoperatif verilerin karşılaştırılması

Parametreler	Kılıfsız F-URS	Kılıflı F-URS	P-değeri
Operasyon süresi(dakika)	98,42±8,12	101,23±9,08	0.303
Floroskopi süresi (dakika)	1.1±0,12	1.2±0,60	0.413
Taşsızlık (n, %)			
Postoperatif 1. gün	26 (%81,25)	31 (%81,57)	0.896
Postoperatif 1. ay	28 (%87,5)	33 (%86,84)	0.674
Ateş	2 (%6,25)	3 (%7,89)	0.540
Hemoglobin değer kaybı (g/dl)	0,70 ± 0,41	0,74 ± 0,26	0.220
İşlem sonrası narkotik analjezik ihtiyacı (n, %)	1 (%3,12)	1 (%2,63)	0.697
Hastanede yatış süresi (saat)	24,64 ± 4,0	24,62 ± 5,44	0.744

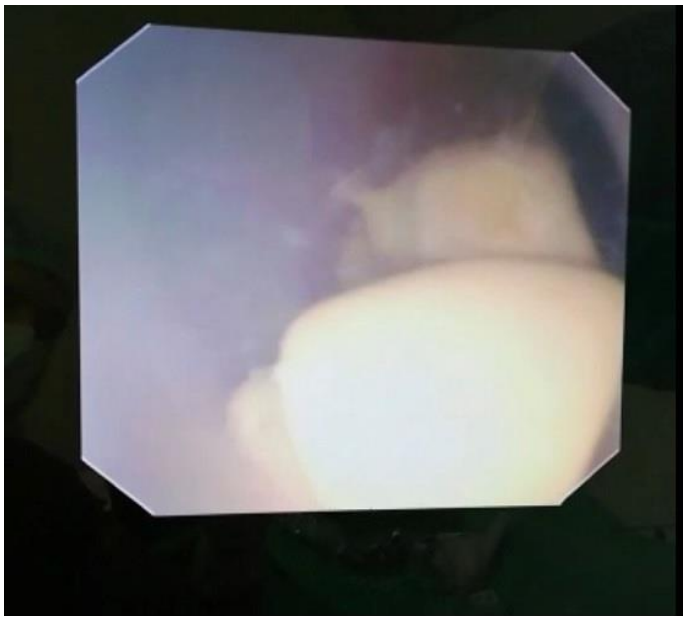
TARTIŞMA

Günümüzde cerrahi araç gereçlerin daha yüksek çözünürlük ve kalitede olması, holmiyum lazerin kullanılması ile endoürolojik cerrahi işlemlerinin endikasyonları da oldukça artmıştır. Böbrek taşlarının tedavisinin başarısında taş boyutu, lokalizasyonu, anatomik yapı, cerrahi yöntem ve cerrahın tecrübesi gibi bir çok etkili faktör söz konusudur. Mevcut olan güncel kılavuzlara göre, 1–2 cm3 böb-

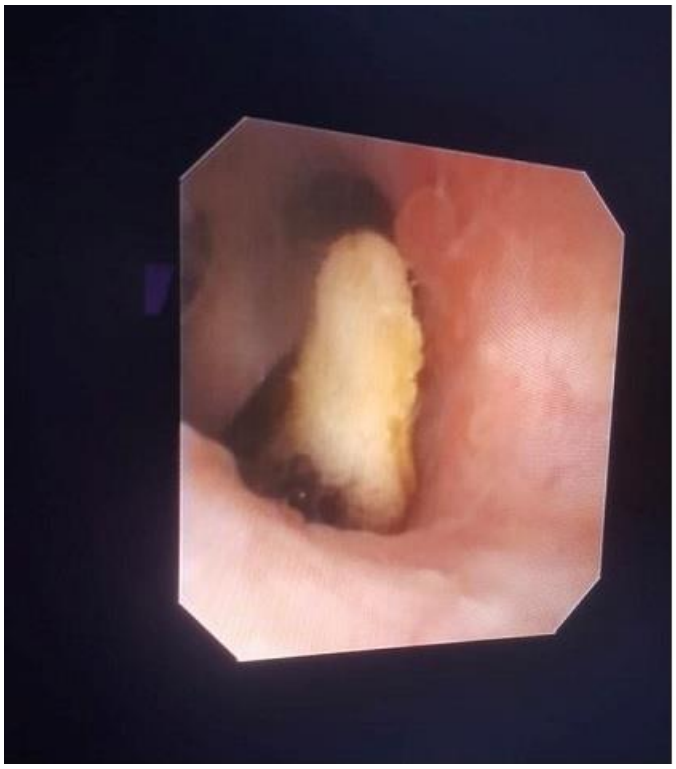
rek alt pol harici taşlarının cerrahi müdahalesinde F-URS hastanın ve cerrahın tercihine göre ilk seçenek olarak uygulanabilir (L'Esperance ve ark., 2005; Turk ve ark., 2015). Çalışmamız böbrek pelvisinde, orta ve üst kaliksinde toplam taş yükü 0,8 ila 1.5 cm3 arasında olan hastalardan oluşmaktaydı.

Endoüroloji alanında F-URS'de kullanılan erişim kılıfı boyutu 12/14F olarak evrensel kabul edilmekle beraber gelişen digital teknoloji neticesinde yeni standart boyutlu 10/12F erişim kılıfları hızlı bir şekilde kullanıma girmiştir (Al-Qahtani ve ark., 2014). Bu da taşsızlık başarı oranı üzerinde etkisi olmamakla beraber, operasyon süresinin kısalmasına ve daha az üreter hasarına neden olduğunu ortaya koymaktadır (Tapiero ve ark., 2014). Shlomi Tapiero ve çalışma arkadaşları, taş boyutunun 15±7 mm3 olduğu çalışmalarında erişim kılıfı boyutu küçüldükçe cerrahi sürenin (16F 139 dk., 14F 118 dk., 11F 92 dk.) istatiksel olarak anlamlı düştüğü ortaya konulmuş olup taşsızlık başarısı oranı üzerinde etkisi olmadığını bildirmişleridir (Tapiero ve ark., 2014). Çalışmamıza dahil edilen erişim kılıflı F-URS hastaların taş boyutu ortalaması 11,05±2,37 mm3 olup cerrahi süre 101,23±9,08 dakika idi ve kullanılan erişim kılıfı boyutu 9.5/11.5F olup 2 hastada uzun segmenter darlığa bağlı olarak böbreğe ulaşılamadı ve hiçbir hastada üreteral hasar görülmedi. Erişim kılıfsız hasta gurubunun taş boyutu ortalaması 10,20±3,45 mm3 ve cerrahi süre ise 98,42±8,12 dakika olup bir hastada aşılamayan darlık nedeni ile böbreğe ulaşılamadı.

Çoğu endoürolog F-URS kullanırken, büyük boyutlu taşların tedavisinde fragmantasyon ve fragmanların çıkarılması yerine böbrek taşlarının 'tozlanmasını' tercih etmektedir (Traxer ve ark., 2015) ve çalışmamızda yer alan her iki guruptaki hastalara 'tozlanma' ile taşlara müdahale ettik. Yine endoürologlar görüntü kalitesi yönünde erişim kılıfının avantaj sağladığını iddia etse de yeni digital teknoloji bu gerçeği değiştirmiş gibi gözükmektedir. Vakalarımızda görüntü kalitesi açısından bir farklılık görmedik (Şekil 3, Şekil 4).



Şekil 3. Erişim kılıflı görüntü



Şekil 4. Erişim kılıflı görüntü

Erişim kılıfının F-URS'de kullanmanın taşsızlık başarısı oranı üzerinde olumlu etkisi olduğunu ortaya koyan çalışmalar olsa da Traxer ve arkadaşlarının 2015 yılında yaptıkları çok merkezli çalışmalarında erişim kılıflı F-URS'nin taşsızlık başarısının erişim kılıfsız F-URS ile aynı olduğunu ortaya koymuştur(Traxer ve ark., 2015). Buna karşı L'Esperance ve

ark. 1997 ve 2003 yılları arasında retrospektif gerçekleştirilen çalışmasında, erişim kılıflı F-URS yapılan 173 hasta ile erişim kılıfsız 83 hastanın taşsızlık başarı oranının sırasıyla %79 ve %67 olarak bildirilmiş olup, erişim kılıfının taşsızlık başarısı üzerinde olumlu etkisi olduğunu ortaya koymuşlardır (p=0.042) (L'Esperance ve ark., 2005). Geraghty ve ark. 2016 yılında yaptıkları çalışmada erişim kılıfı kullanılan hastalarda taşsızlık başarı oranı %81.5 iken erişim kılıfı kullanılmayan gurupta ise taşsızlık oranı %87.5 olarak rapor etmişlerdir (Geraghty ve ark., 2016). Yine bu yönde literatürde, erişim kılıfını kullanmanın taşsızlık başarısı üzerinde etkili olmadığını gösteren çalışmalarla karşılaşmaktayız (Berquet ve ark., 2014; Tapiero ve ark., 2014). Çalışmamız erişim kılıfını kullanmanın taşsızlık başarısı oranı üzerinde etkili olmadığını destekler sonuçtaydı. Operasyon sonrası birinci ayında erişim kılıfı kullanılan hastalardaki taşsızlık başarı oranı %87,5 iken, erişim kılıfsız gurupta ise taşsızlık başarı oranı %86,84 idi (p=0.674).

Gerek intraoperatif ve gerekse postoperatif komplikasyonlar açısından erişim kılıflı ve erişim kılıfsız müdahalede bir fark olmadığı rapor edilmiştir (Tapiero ve ark. 2014; Traxer ve ark., 2015; Geraghty ve ark., 2016). Erişim kılıfı boyutunun gelişen teknolojiye paralel olarak giderek küçülmesi olası komplikasyonları azaltmış gibi anlaşılmaktadır (Tapiero ve ark., 2014). Bunun aksi yönde sonuç bildiren Chen ve ark. 2018 yılında yaptıkları çalışmada, boyutu büyük erişim kılıfının (14F/16F) küçük boyutlu erişim kılıfına (12F/14F) göre postoperatif komplikasyon açısından daha avantajlı olduğunu ortaya koymuşlardır (Chen ve ark., 2018). Yakın zamanda Lima ve arkadaşlarının bildirdikleri çalışmada ameliyat sonrası komplikasyonlar açısından bir fark olmadığını ve erişim kılıfı kullanılan hasta gurubunda sekiz hastada (7 Clavien I/II ve 1 Clavien IVa) ve erişim kılıfı kullanılmayan gurupta ise iki hastada (Clavien I) ameliyat sonrası komplikasyon rapor etmişlerdir (p=0.19) (Lima ve ark., 2020). Çalışmamızın düşük seriye sahip olması, intraoperatif ve postoperatif komplikasyon açısından kısıtlayıcı bir sebep olarak değerlendiriyoruz. Bununla birlikte çalışmamızda postoperatif ağrı, kanama ve hastanede kalış süresi açısından aralarında bir fark olmayıp, erişim kılıfsız gurubunda iki hastada ve erişim kılıflı grubunda ise üç hastada postoperatif ateş görüldü (Clavien I) (p=0.340). Hiçbir hastamızda majör bir komplikasyon ile karşılaşılmadı.

Sonuç olarak, klasik olarak 1.5 cm3 ve daha küçük böbrek taşlarında erişim kılıflı F-URS uygulanan standart cerrahi bir teknik olmasına rağmen, erişim kılıfsız F-URS seçilmiş olgularda erişim kılıflı F-URS kadar etkin ve güvenli olarak uygulanabilir. Erişim kılıfsız F-URS ile erişim kılıflı F-URS kıyaslandığında benzer ameliyat sürelerine, benzer başarı ve komplikasyon oranlarına sahiptir

Çıkar Çatışması

Yazarlar çıkar çatışması olmadığını beyan eder.

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Vaka Sunumu/ Case Report

Gluteal Abscess After Intramuscular Injection

Kas İçi Enjeksiyon Sonrası Gluteal Apse

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ÖZET
40 yaşında bayan hasta kas içi enjeksiyon sonrası gluteal ağrı şikayeti ile başvurdu. Hastanın ilk değerlendirmesinde sadece gluteal bölgede apse olmayan selülitli geniş bir alan vardı. Hastanın takibinin ikinci gününde ultrasonografide gluteal apse saptandı ve apse drene edilerek nekrotik doku debride edildi. Yara temizliği 10 gün boyunca günlük olarak yapıldı. Daha sonra yara, dikişlerle kısmen kapatıldı. Kalan yara ikincil iyileşme için bırakıldı. İlk ameliyattan sonraki 21. günde yara tamamen iyileşti.

Anahtar Kelimeler: Apse, Drenaj, Yara.

ABSTRACT
A 40-year-old female patient presented with the complaint of gluteal pain after an intramuscular injection. In the patient's initial evaluation, there was only a large area with cellulite in the gluteal region without an abscess. On the second day of the patient's follow-up, a gluteal abscess was detected on ultrasonography, and the abscess was drained and necrotic tissue debrided. Wound cleaning was done daily for 10 days. Then, the wound was partially closed with sutures. The remaining wound was left for secondary healing. The wound healed completely on the 21st day after the first operation.

Keywords: Abscess, Drainage, Wound.

INTRODUCTION

Intramuscular injection is a method frequently used by doctors as it provides a practical and rapid treatment response. Regardless of the injection area, two important points to be considered at intramuscular injection are to avoid direct damage to neurovascular structures and to inject intramuscularly as much as possible (Filinte et al., 2010). Due to a large amount of muscle tissue, intramuscular injection is most commonly applied to the gluteal region. In some cases, deltoid muscles are also where the injection is used.

A gluteal abscess is one of the most important complications after gluteal injection (Mishra and Stringer, 2010). A gluteal abscess occurs due to injections not made by the rules of asepsis. However, abscesses seen at the intramuscular injection site are usually sterile abscesses, and apart from the local trauma caused by the injection, the irritation properties of the drug are thought to cause abscess and necrosis. When the injected drug is released into the subcutaneous tissue instead of the muscle, its absorption is delayed, and thus more tissue reactions are observed (Kim et al., 2017).

In this case report, a gluteal abscess's diagnostic and treatment process occurred after intramuscular injection was presented.

Case presentation

A 40-year-old woman was admitted to the emergency department of Igdir State Hospital in November 2019 with gluteal pain for five days. In her anamnesis, the patient stated that a myorelaxant injection was administered in another health institution 5 days ago due to left leg sciatic pain. The patient without a history of surgery had only hypertension controlled with anti-hypertensive drugs. On evaluation, the vital findings of the patient were as follows: blood pressure: 124/75 mm Hg, the pulse rate: 108 beats per minute, oxygen saturation on room air:

97%, and body temperature: 37.9o Celsius. On abdominal physical examination, there was no pathology. In addition, there was an area with cellulitis around the injection orifice.

There was no laboratory pathology except a high C-reactive protein (CRP) level (9.58 mg/L) and elevated leukocyte count (12.1x103/mm3). On superficial ultrasonography (USG), there was no abscess area but an area with cellulitis. A computed tomography (CT) was planned for the patient to rule out the possibility of a deep-located abscess. There was no definite abscess on the CT scan (Figure 1).

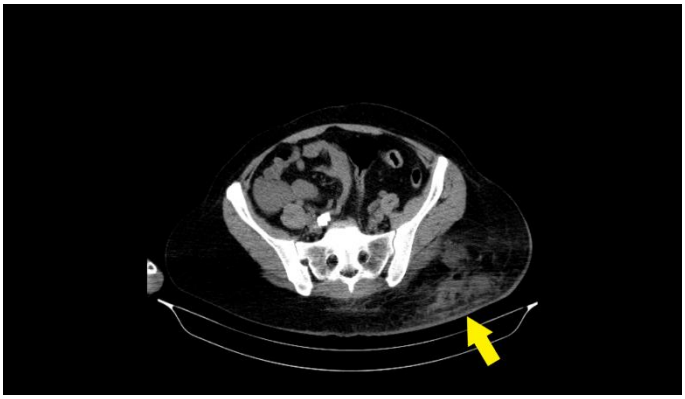

Figure 1. A 40-year-old woman was admitted to hospital with gluteal pain after intramuscular injection. A yellow arrow shows an area with gluteal infection .

Therefore, the patient was admitted for follow-up with a pre-diagnose of cellulitis, and treatment was begun using ampicillin-sulbactam 1000 mg intravenously every 12 hours and metronidazole 500 mg/100 ml every 8 hours. Two days after admission, her vital findings were as follows: blood pressure: 132/80 mm Hg, the pulse rate: 118 beats per minute, oxygen saturation on room air: 97%, and body temperature: 38.5o Celsius. At control superficial USG, there was a deeply-located abscess of 28*26 millimetres. Therefore, surgical abscess drainage was planned.

Abscess drainage was performed under general anaesthesia. Approximately 200 cc of purulent fluid came from the abscess area. A sample was taken from the abscess material and sent for culture. All necrotic tissue was removed until the clean surgical margin was reached (Figure 2). The operation area was cleaned with a mixture of hydrogen peroxide and povidone-iodine. According to the abscess culture results, ampicillin-sulbactam treatment was stopped, and piperacillin-tazobactam 4.5 grams every 6 hours vial was started. Wound cleaning was performed under sedation for 10 days. Afterwards, the wound was partially closed with sutures (Figure 3). Antibiotherapy was administered for 14 days. The wound was completely healed on the 21st day after the first surgery.

Figure 2. The image after abscess drainage and removal of all necrotic tissues.

Figure 3. The image of the wound after partial closure with sutures.

DISCUSSION

The incidence of complications after intramuscular injection varies between 0.4% and 19.3% (Mayrink et al., 2003). Problems arising from the injection are either due to local trauma caused by the injection itself or to the damaging properties of the drug. Complications after intramuscular injection are bleeding, hematoma formation, nerve damage, chronic pain, abscess formation, tissue necrosis, scar formation, joint contracture, and tumour (Treadwell, 2003).

Soft tissue infections or abscesses can be seen after gluteal injections. Patients initially present with symptoms such as erythema, oedema and pain at the injection site, which are cellulitis symptoms, and abscess formation occurs when the infection progresses. But, patients who presented to the hospital late may present with an abscess clinic.

In the diagnosis of abscess, infective laboratory parameters such as high white blood cell count and c-reactive protein level are essential in showing the disease's severity (Puthezhath et al., 2010). In addition, imaging tools such as superficial USG and CT are helpful for diagnosis. The primary purpose of imaging tools is to show the presence of an abscess in the injection area. Computed tomography can be beneficial in cases where no abscess is seen on USG and a deep-located abscess is considered. In our patient, she was admitted to the hospital with gluteal pain and erythema. Inflammatory parameters of the patient were high, and on superficial USG and CT scan, no abscess focus was seen.

In treating gluteal area infections, it is essential to perform abscess drainage as the first step in patients with abscesses. However, in patients without abscesses, antibiotherapy is the first step approach. The main microbial agents of gluteal area infections are Staphylococcus aureus and beta-hemolytic streptococcus (Bowler et al., 2001). Suitable anti-microbial therapy should be started, and the duration of antibiotherapy should be extended according to the patient's clinic (Jeng et al., 2010). In patients with worsening vital signs and increased infective parameters during follow-up, the possibility of abscess should be considered, and a diagnosis should be made with imaging tools if necessary. Since her vital signs deteriorated, control USG was taken in our patient, and the abscess was drained when an abscess was detected USG.

The primary purpose of the surgical treatment of abscesses is to open and drain all the abscess pouches and remove the necrotic tissues from the body. In addition, another critical issue is the culture examination of the abscess material and the revision of antibiotic therapy according to the culture result. The duration of antibiotic treatment should be adjusted according to the patient's clinic and the infective state of the wound. In our case, repeated surgical drainages and debridements may be required in large abscesses. Another option is to treat the wound with negative-pressure wound therapy (NPWT). The number of NPWT sessions is determined depending on the closure rate and size of the wound (Rashid et

al., 2020). However, primary closure should be performed after the wound is followed up with secondary healing at the places where NPWT is inaccessible.

Conclusion

Gluteal abscess after intramuscular injection is a severe problem for patients and doctors. Early diagnosis and drainage are essential for gluteal abscess. Depending on the size of the abscess and the wound width, appropriate antibiotic therapy after drainage is the continuation of the treatment. The wound can be closed primarily or left for secondary healing at surgical treatment.

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Vaka Sunumu/ Case Report

Üç Köklü Mandibular 3. Molar Diş: Nadir Bir Anatomik Varyasyon

Three Rooted Mandibular 3.Molar Tooth: A Rare Anatomic Variation

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ÖZET
Diş hekimleri, klinikte diş tedavileri sırasında dişin anatomik yapısıyla ilgili çeşitli varyasyonlarla karşılaşabilirler. Süper nümerer diş; en sık görülen varyasyonlardan biri olmasına rağmen, azı dişlerinde fazla kök bulunması anatomik kök varyasyonunun ilginç bir örneğidir. Mandibular azı dişleri genellikle 2 ayrı köke (mesial ve distal) sahiptir. Çok nadiren ilave bir üçüncü kök (süper nümerer kök) görülür. Bu makalenin amacı, diş hekimliği kliniğinde dikkat edilmesi gereken önemli bir varyasyon olan mandibular 3. molar dişteki üç kök varlığını ayrıntılı bir şekilde tanımlayarak, bu tip olgularla karşılaşma ihtimalini aktif olarak çalışan diş hekimlerine sunmaktır.

Anahtar Kelimeler: Üçüncü Azı dişi, Anatomik varyasyon, Diş kökü.

ABSTRACT
Dentists may encounter various variations related to the anatomical structure of the tooth during dental treatments in the clinic. Super numerary tooth; although it is one of the most common variations, the presence of excess roots in molars is an interesting example of anatomical root variation. Mandibular molars usually have two roots (mesial and distal). Very rarely an additional third root (super numerary root) is seen. The purpose of this article is to present a case of variation defined by the presence of three roots in the mandibular 3rd molar tooth, which is an important variation that should be considered in the dentistry clinic.

Keywords: Third Molar, Anatomicvariation, Toothroot.

GİRİŞ

Literatürde ilk olarak 1844'te Carabelli (Carabelli ve ark., 1844) tarafından Radix entomolaris" (RE) ek bir üçüncü kök olarak belirtilmiştir ve "ekstra üçüncü kök" veya "dil dışı kök" gibi çeşitli terimlerle tanımlanmıştır" (De Moor ve ark., 2004). Radix paramolaris (RP) "meziyobukkal kök" olarak bilinir (Carlsen ve Alexandersen, 1991) ve ilk kez Bolk (Bolk, 1915) tarafından 1915'te tanımlanmıştır.

RE ve RP kök komplekslerinin tanımlanması ve diş morfolojisi Carlsen ve Alexandersen tarafından açıklanmıştır (Bolk, 1915; Carlsen veAlexandersen, 1990, 1991). RE distolingual olarak koronal üçüncüsü tamamen veya kısmen distal köke sabitlenmiş olarak bulunur. Genellikle distobukkal veya mezial kökünden daha küçük ve daha kavisli görünür ve diğer iki kökle aynı enine düzlemde bulunur. Bu, diş hekimlerinin RE'li bir molar için kanal tedavisi ve /veya ekstraksiyonu düşünürken dikkat etmeleri gerektiğini göstermektedir. RE'nin boyutu, kısa bir konik uzantıdan normal uzunluktaki olgun bir köke ve kök kanalına kadar değişebilir (Bolk, 1915; Carlsen ve Alexandersen, 1990, 1991; De Moor, et al., 2004). Bu üçüncü kök enine kesitlerde distal kökten daha daireseldir. Çoğu durumda pulpa radyografik olarak görülebilir. RE'nin apikal üçte ikisinde, var olan eğime ek olarak mesial veya distal yönelimli bir eğim görülebilir. Tratman, RE'nin sadece distal kökün bir bölümü olmadığını, daha ziyade ayrı bir apekse sahip gerçek bir ekstra kök olduğunu belirtmiştir (Tratman, 1938). RP, mesial köke göre bukkal olarak görülür ve mesial kök ile ayrı veya kaynaşmış olarak bulunabilir. RP'nin boyutları, bir kök kanalı olan "olgun" bir kökten kısa bir konik uzantıya kadar değişebilir (Carlsen ve Alexandersen, 1991). Bu üçüncü kök, diğer köklerden ayrı

olmak üzere bukkal veya mezial kök olarak iki şekilde bulunur (Carlsenve Alexandersen, 1991).

Klinik tanı konmasında; distolingual / mesiyobukkal kökü olan bir azı dişinin minesi ile iki normal kökü olan normal bir azı dişindeki minenin yapısının çok benzer olduğu dikkate alınmalıdır (Calberson ve ark., 2007). Bu nedenle, RE / RP'nin tanımlanması sadece kronun klinik muayenesi ile gerçekten mümkün değildir. Literatürde, periodontal hastalık ile köklerin servikal morfolojisinin klinik gözlemi ve analizinin RE'nin tanımlanmasını kolaylaştırdığı bildirilmiştir. Ayrıca, fazladan bir tüberkulum paramolare veya daha belirgin bir oklüzal distal veya distolingual lobun varlığının, servikal bir çıkıntı veya dış bükeylik ile kombinasyon halinde ek bir kökün varlığına işaret edebileceği bildirilmiştir (Calberson ve ark., 2007). Endodontik tedaviden önce RE veya RP teşhisi konulması sayesinde, pulpa odası açıldıktan sonra hekimi neyin bekleyeceği veya hekimin nereye bakacağı daha net bilinir.

Radyografik teşhis; mandibularmolar dişlerde köklerin anatomik varyasyonları, radyografiler dikkatlice okunarak belirlenebilir. RE / RP çoğunlukla diğer iki kökle aynı bukkolingual düzlemde yer aldığından, ameliyat öncesi radyografide her iki kökün üst üste binmesi yüzünden tanı konulmayabilir (Carslen ve Alexandersen, 1991; De Moor ve ark., 2004; Calberson ve ark., 2007) .Ingle ve ark. (Ingle JL, 2002) dişin anatomisine ilişkin temel bilgileri elde etmek için standart bukkolingual projeksiyondan sonra aynı düzlemde çekilen biri mesial taraftan 20° açı ile ve diğeri distalden 20° açı ile alınan pozlamayı kullanarak ilgili dişin kapsamlı bir radyografik çalışmasını önermiştir. Loh (Loh, 1990) , RE/RP'nin geleneksel şekilde çekilen periapikal radyografilerde normalde görünmediğini iddia etmiştir. Röntgenin maruz kalma süresinin ve dozunun ayarlanması ve ana ışının açılandırılması (daha büyük distobukkal/mesiyal kökün üst üste gelmesini önlemek için), RE/RP'nin daha belirgin olmasına yardımcı olabilir, ancak radyografilerin doğru yorumlanması eğitimli bir göze bağlıdır (Loh, 1990). Walker ve Quackenbush tarafından 1985'de yapılan bir çalışmada panoramik radyografilerin yaklaşık % 90 doğruluk oranıyla sonuçlandığı raporlanmıştır (Walker ve Quackenbush, 1985).

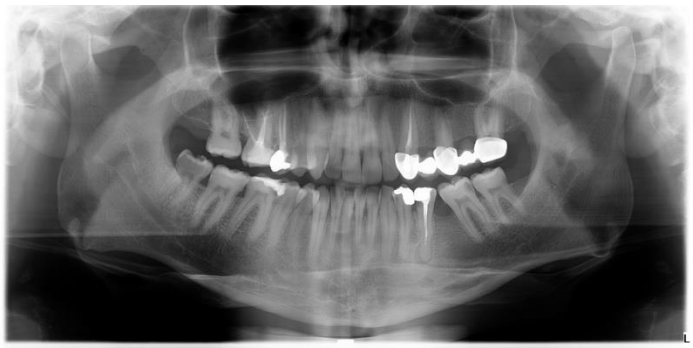
Bu makalenin amacı, diş hekimliğinin klinik uygulamaları sırasında karşılaşılması muhtemel önemli bir varyasyon olan mandibular 3. molar dişteki üç kök varlığını ayrıntılı bir şekilde tanımlamak ve klinikte çalışan diş hekimlerine bu tip olgularla karşılaşma ihtimalini sunarak literatüre katkı sağlamaktır.

OLGU SUNUMU

Bu olgu, 30 yaşındaki erkek hasta, sürekli devam eden şiddetli ağrı şikâyeti ile kliniğimize başvurdu, hastanın sistemik anamnezinde herhangi bir hastalığa rastlanmadı. Oral hijyeninin yetersiz olduğu gözlenen ve sigara kullanan erkek hastanın; ekstraoral (ağız dışı) bulgularında herhangi bir anomali tespit edilmedi. Ağız içi muayenesinde ağız içi kamera (Dentaline DP -70, made in Japan) ile sağ mandibular bölge 3. molar dişte aşırı kron harabiyeti olduğu tespit edildi (Şekil 1).

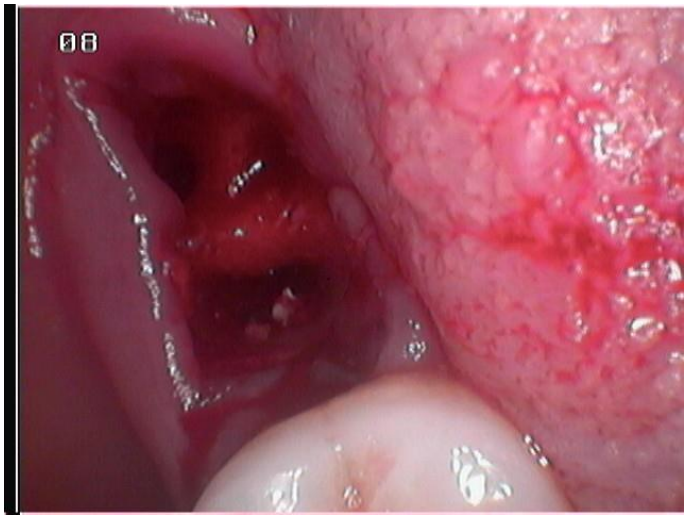
Şekil 1. Ağız içi muayene görüntüsü

İlgili dişin periodontal muayenesinde herhangi bir mobilite ve patolojik cebe rastlanmadı. Tüm çeneden alınan panoromik röntgen filminde sağ mandibular 3. molar dişin 2 köklü olduğu tespiti sonucu dişin çekimine karar verildi (Şekil 2).



Şekil 2. Panoromik film.

Alınan anamnez sonucu, hastaya Ultracain D-S 40 mg anestezik solusyon, mandibular blokaj olarak uygulanmış ve uyuşmanın sağlanmasından sonra elevatör ile diş yükseltilmiş, alt molar davyesi ile diş çekimi gerçekleştirilmiştir. Çekim sonrası ağız içi kamera ile alınan görüntüde çekim soketinde 3 kök olduğu tespit edilmiştir (Şekil 3). Çekilen dişin son derece net ayrı 3 köklü olması, özellikle mandibular 3. molar dişte gözlenen nadir bir varyasyondur (Şekil 4). Tüm işlemler ve olgunun, bilimsel ortamda paylaşımı için hastaya bilgilendirilmiş onam formu imzalatılmış ve onam alınmıştır.



Şekil 3. Çekim sonrası ağız içi kamera görüntüsü

Şekil 4. Diş çekim sonrası görüntüsü.

TARTIŞMA

Ekstra kök (RE) varlığının, alveollere daha fazla bağlanma yüzey alanı sağlayarak azı dişlerinin stabilitesine katkıda bulunduğu varsayılmaktadır (Mayhall, 1981; Walker ve Quackenbush, 1985; Loh, 1990). Stabilitenin artması yapılacak protezlerin tutuculuğuna pozitif etki yapar, özellikle hareketli protezlerin tutuculuğunda hasta memnuniyetini artırır. Sabit protezlerde (kompleks köprü) gelen kuvvetin dağılımına pozitif katkıda bulunarak köprünün stabilitesi ve protezlerin daha uzun süre kullanılması bakımından son derece önemlidir.

Endodontik tedavi, tüm pulpa boşluğunun mekanik ve kimyasal debridmandan (ölü, hasarlı veya enfekte dokunun tıbbi olarak çıkarılmasıdır) temizlenmesi ve ardından hermetik dolgu materyali ile tam tıkanmanın sağlanmasıdır. Tespit edilemeyen kök kanalları ve ekstra kanallar endodontik tedavinin başarısızlığında en sık görülen sebeplerden biridir (Anand, 2016). Dişin tüm kanallarının başarılı endodontik tedavisi için dikkatli radyografik tanı çok önemli bir rol oynar. Farklı açılarda alınan radyografiler, bir dişin anatomisi ile ilgili temel bilgileri ortaya çıkarır ve böylece ekstra kanallar/kökler gibi herhangi bir anormal anatomiyi tespit etmeye yardımcı olabilir (De Moor ve ark., 2004). Bununla birlikte, geleneksel radyografideki önemli bir kısıtlama, üç boyutlu bir nesnenin iki boyutlu görüntüsünü üreterek üstteki yapının üst üste binmesine neden olmasıdır. Kök kanallarının morfolojik yapısını ve aralarındaki ilişkileri daha detaylı anlamak için daha gelişmiş tanı araçlarına ihtiyaç vardır. Son zamanlarda, konik ışınlı bilgisayarlı tomografi (CBCT), karmaşık kök anatomisine sahip dişlerin teşhisine

yardımcı olmak için yararlı bir araç olarak ortaya çıkmıştır (Gopikrishna, 2008; Aggarwal, 2009). RE/RP büyük bir endodontik zorluk teşkil eder; çünkü gözden kaçırılan extra (fazla) kök kanalı nedeniyle yetersiz gerçekleştirilen pulpa ekstirpasyonu tedavi başarısızlığına neden olabilir. Hasta uygulanan tedavi sonrası ağrı hissi ve/veya sekonder bir kök enfeksiyonu ile karşılaşabilir.

Cerrahi tedavi öncesi RE/RP tespitinin tam ve doğru olarak yapılması işleme girecek olan hekimin uygulamasını kolaylaştırarak cerrahi işlem esnasında ve sonrasında oluşabilecek travma ve komplikasyonları engeller.

Sonuç olarak bu olgu sunumu diş hekimlerine, Dişlerin anatomik kök yapıları ve sayılarında varyasyon olabileceği. Extra (fazla) köklerin ve kanalların dental işlemler öncesi tespiti komplikasyonların önlenmesi açısından fayda sağlayabilir.

Çıkar Çatışması

Yazarlar çıkar çatışması olmadığını beyan eder.

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Derlem/ Review

Saponin Bileşeninin Biyolojik Aktiviteleri, Kullanım Alanları ve Etkileri

The Biological Activities, Applications and Effects of Saponin Component

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ÖZET
Tarih boyunca bitkiler insanlar tarafından birçok hastalığın tedavisinde kullanılırken, son yıllarda yapılan çok sayıdaki *in vivo, in vitro* ve *in silico* çalışmalarda, bitkilerin yapısında tıbbi olarak yararlı etkiler gösteren çeşitli bileşenler olduğu bilimsel olarak da ortaya konmuştur. Saponinler, geniş bir farmakolojik ve endüstriyel potansiyele sahip olan bitkilerin sekonder metabolit ürünleridir. Uzun yıllar boyunca saponinlerin sağlığa zararlı etkilerinin olduğu düşünülmüş olmasına rağmen, yapılan çalışmalarda uygulama dozu ve uygulama sıklığına bağlı olarak yararlı etkilerinin olabileceği belirlenmiştir. Farmakolojik araştırmalar, saponinlerin antidiyabetik, sitotoksik, antibakteriyel, kolesterol düşürücü, antifungal ve anti-inflamatuar aktiviteler sergilediğini ve birçok farklı alanda faydalı olduğunu ortaya koymuştur. Oluşturulan bu derleme, saponin bileşeni hakkında bilgi vermek ve bu bileşeninin biyolojik aktiviteleri ile saponin içeren bitki ve gıdaların kullanımının sağlık üzerinde meydana getirdiği etkiler, yapılan bilimsel çalışmalar örnek gösterilerek açıklanmak üzere hazırlanmıştır.

Anahtar Kelimeler: Biyolojik aktivite, Sağlığa etki, Saponin.

ABSTRACT
While plants have been used by humans as a remedy for many diseases through out history; in recent years, many *in vivo, in vitro*, and *in silico* studies have scientifically demonstrated that there are various components in thes tructure of plants that have beneficial medicinal effects. Saponins are secondary metabolite products of plants with wide pharmacological and industrial potentials. Although saponins have been thought to have harmful effects on health for many years, it has been decided that there may be beneficial effects depending on the application dose and application frequency. Pharmacological studies have revealed that saponins exhibit antidiabetic, cytotoxic, antibacterial, cholesterol-lowering, antifungal and anti-inflammatory activities and are useful in many different areas. This review was created to give information about the saponin component and to explain the biological activities of this component and the effects of the use of saponin-containing plants and foods on health, by showing examples of different scientific studies.

Keywords: Biological Activity, Effect on Health, Saponin.

GİRİŞ

Saponin ismi "sapo" kelimesinden türetilmiş olup Latincede sabun anlamındadır. Birçok bitki, büyüme ve gelişmesinin farklı aşamalarında çevreden gelebilecek zararlı etkenlere karşı saponin sentezlemektedir. Bitkinin büyüme ve üremesinde etkisi olmayan saponinler ise güçlü antimikrobiyal aktiviteleri ile bitkiyi böcekler ve mikroorganizmalara karşı korumaktadır (Küçükkurt ve Fidan, 2008).

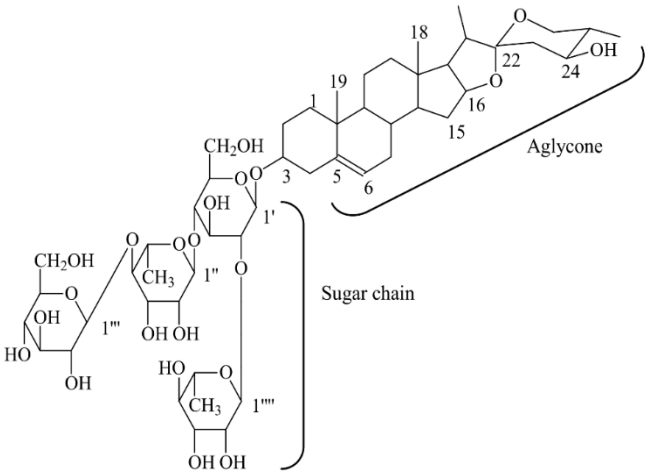
Doğada birçok bitki yüksek oranda saponin içermektedir ve acı tada sahip olmaları nedeniyle çok azı insan ve hayvanlar tarafından tüketilebilmektedir. Nohut, yonca filizleri, patlıcan, bakliyat, özellikle soya fasulyesi ve kuşkonmaz ayrıca beyaz fasulye, ıspanak, bakla, pancar, sarımsak ve yulaf saponinlerin en zengin kaynaklarıdır (Tablo 1). Bununla birlikte saponinlerin sadece bitkilerde bulunduğu düşünülürken, Echinodermata (derisidikenliler), Holothuroidea (deniz hıyarı), Asteroitae (deniz yıldızı) gibi bazı deniz hayvanlarının vücutlarında da saponinlerin bulunduğu bildirilmiştir (Osbourn, 2003).

Yucca schidigera bitkisi dünyada ticari olarak en fazla kullanılan steroidalsaponin (%9-10) kaynaklarından biridir (Piacente ve ark., 2004). Ayrıca *Quillaja saponaria* ağacının %10 oranında triterpenoid saponin içerdiği ve saponinlerinin bidezmozidal yapıda

olduğu bildirilmektedir (Cheeke, 2001). *Y. schidigera* ve *Q. saponaria* bitkilerinin Amerikan Gıda ve İlaç Dairesi (FDA) tarafından GRAS (Genel olarak güvenilir-zararsız kabul edilen) etiketine sahip olmaları sayesinde ekstraktları gıda, farmakoloji ve kozmetik endüstrisinde kullanılmaktadır.

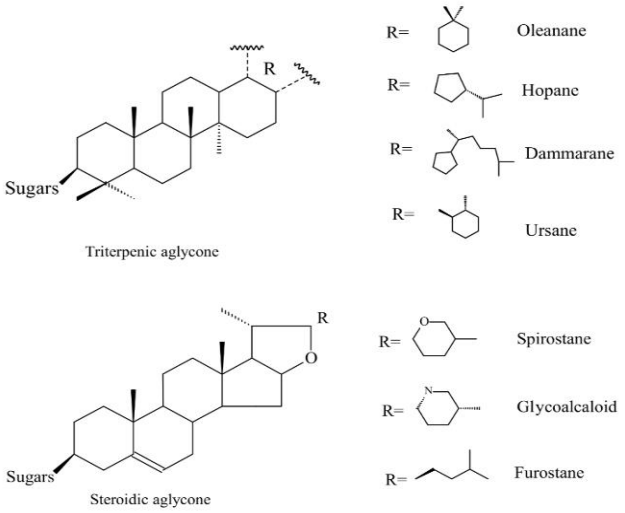
Saponinlerin Sınıflandırılması

Saponinlerin yapısında glikon ve aglikon (sapogenin) adı verilen iki farklı form bulunmaktadır (Şekil 1).



Şekil 1. Saponin kimyasal yapısı (Chaieb, 2010)

Aglikonun kimyasal yapısındaki farklılığa göre de steroidal veya triterpenoidal saponinler olarak iki gruba ayrılmaktadır (Şekil 2). Steroidal saponinler 6 halkadan oluşan 27 C'lu bileşiklerdir (Vincken ve ark., 2007). C3'te her zaman bir –OH grubu bulunmaktadır.



Şekil 2. Steroidal ve triterpenoidsaponinlerin yapısı (Chaieb, 2010)

Triterpenik saponinler; Caryophyllaceae, Hippocastanaceae, Polygonaceae gibi çift çenekli bitki ailelerinde sentezlenen (Rao ve Sung, 1995) ve bitkilerin sitozollerinde ve plastidlerinde üretilen lipofilik maddelerdir. Triterpenler doğada serbest halde bulunabildikleri gibi, ester ya da glikozitleri şeklinde de bulunabilirler. Bir veya daha fazla şeker zincirine sahiptirler. Şekerli bileşenleri glikon olarak adlandırılır. Saponin glikozitlerinde şeker kısmı

genellikle monosakkarit taşıyan, düz veya dallanmış oligosakkaritlerden oluşmaktadır.

Diğer taraftan hem steroidal saponinler hem de triterpenik saponinler sahip oldukları karbonhidrat zinciri sayısına göre iki farklı gruba ayrılabilirler. Bisdezmozidik saponinler iki karbonhidrat zinciri, monodezmozidik saponinler ise tek karbonhidrat zinciri taşımaktadırlar.

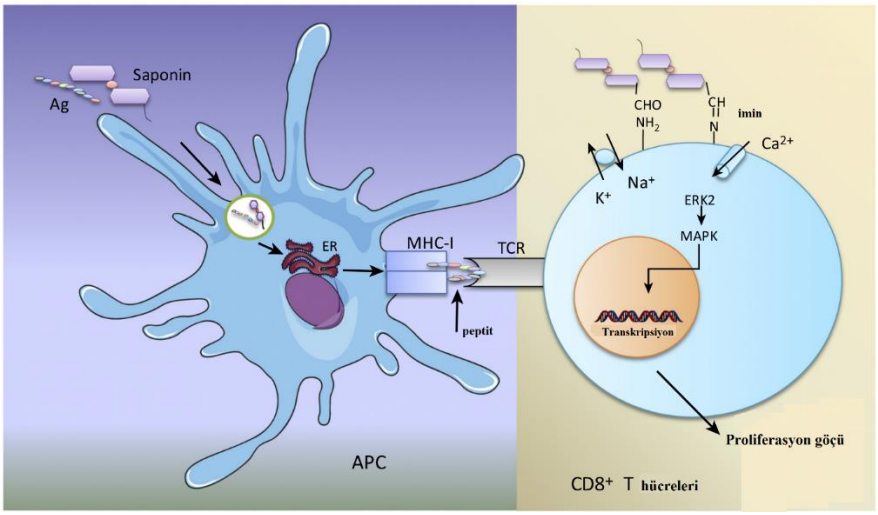
Saponinlerin Biyolojik Aktivitesi

Saponinlerin biyolojik etkilerinin çoğu hücre membranında por oluşturma ve gözeneklerin formunu ayarlama özelliklerine bağlı olarak gerçekleşmektedir. Membran sterolleri (özellikle kolesterol) ile aglikon kısmın afinitesine göre kompleks oluşturabilmektedirler. Ayrıca hidrofobik aglikon, membranda bilayerin hidrofobik iç kısmına yerleşebilmektedir. Bu etkileri sayesinde membran proteinlerinin çevresindeki lipitlerin değişimine neden olabilmektedir (Francis ve ark., 2002). Saponinlerin membran geçirgenliğine etkisi, savunma sistemini uyarması, antikanserojenik özelliklere sahip oldukları ve ayrıca hayvanlarda büyümeyi ve üremeyi etkilediği saptanmıştır. Yapılarının farklılığı ile protozoanlara karşı öldürücü özelliğinin bulunduğu, antioksidan özellik gösterdiği, sindirimde proteinleri, midede vitamin ve mineralleri bozduğu, hipoglisemi, antifungal ve antiviral etki gösterdiği bildirilmiştir (Öztaşan ve ark., 2004). Saponinlerin kuvvetli derecede antifungal aktivite göstermekle birlikte antifungal aktivitelerini, mantar membranlarındaki sterollerle kompleks oluşturması sonucunda hücredeki membran bütünlüğünün kaybolması ile gerçekleştiği belirlenmiştir (Morrissey ve Osbourn, 1999). Saponinler ile bitkiye saldırıda bulunan mikroorganizmaların hücre zarı arasındaki kompleks oluşumunun gerçekleşmesi ile mikroorganizmaların hücre bütünlüğü bozulmakta ve hücre görevini yapamaz hale gelmektedir.

Saponinlerin hücre zarındaki sterollerle kompleks oluşturup antimikrobiyal aktivite göstermesinde, bu moleküllerin sahip olduğu şeker moleküllerinin kritik rol oynadığı ifade edilmiştir (Morrissey ve Osbourn, 1999).

Aldehit içeren saponinler iki farklı mekanizma ile biyolojik aktivite gösterir. Birincisi, majör histokompatibilite kompleksi (MHC) antijenlerinin antijen sunan hücre (APC)'ler tarafından bir lipit gövdesinin oluşturulmasıdır. İkincisi ise, T hücre reseptör (TCR)'lerinde bulunan amino asitler ile etkileşime girerek T hücrelerinin doğrudan aktivasyonudur. Bu etkileşim adımlarını ERK2, MAPK ve transkripsiyon faktörlerinin aktivasyonu takip eder ve bu durum sitokin salınımına ve hücre çoğalmasına, yer değiştirmesine ve farklılaşmasına yol açar (Bonam ve ark., 2017) (Şekil 3).

Saponinlerin bazı mantarlara karşı önemli derecede aktivite göstermesine rağmen bazı mantarlara karşı aktivite göstermediği belirlenmiştir. *Septorialycopersici, Botrytiscinerea*ve *Fusarium oxysporum* f.sp. *lycopersici* mantar hücreleri ile yapılan bir araştırmada, bu mantarların saponin molekülünde bulunan şeker zincirindeki şeker molekülleri arasındaki glukozidik bağları kıracak enzimlere sahip olduğu saptanmıştır. Böylece şeker zincirinin yapısının bozulması ile antifungal aktivitede büyük oranda azalma meydana geldiği bildirilmiştir (Kumari ve Kohli, 1987). Yapılan bir diğer çalışmada, saponin çözeltisinin HIV replikasyonunu engellediği belirlenmiştir. Bu bileşenlerin etki mekanizması hakkında çok az bilgi mevcut olmasına rağmen biyolojik aktivitenin virüs membranı ile saponin bileşiğinin spesifik olmayan etkileşimi sonucu virüs replikasyonunun başlangıç basamağının gerçekleşmemesinden kaynaklandığı belirtilmiştir (Kazuhiro ve ark., 1991). Ayrıca membranolitik etkisi nedeniyle saponinlerin, bağırsak hücrelerinde kolesterol kaybının artışına neden olduğu belirtilmektedir (Morehouse ve ark., 1999).



Şekil 3. Saponinlerin etki mekanizmaları (Bonam ve ark., 2017)**CD8⁺ T cells:** Sitotoksik T hücreleri, **ER:** endoplazmik retikulum (endoplasmicreticulum), **ERK2:** hücre dışı sinyalle düzenlenen kinazlar (extracellularsignal-regulatedkinases), **MAPK:**mitojenle aktive olan protein kinaz (mitogen-activated protein kinase).

Saponinlerin immun sistem üzerine etkisi incelendiğinde, düşük dozlarda kullanımının bağışıklık sistemini uyardığı ve antijenlere karşı antikor üretimini artırarak aşıda bağışıklığı artırıcı etkiye (adjuvant etki) sahip olduğu bildirilmiştir (Ratnapriya ve ark., 2019). Saponinler ayrıca eritrositleri parçalama özelliğine de sahiptir. Bu işlev, ilaçlarda veya bitki ekstraktlarında saponinlerin varlığını tespit etmek için hemolitik analizlerin geliştirilmesine yardımcı olmuştur. Hemolitik özellikler genellikle saponinler ile eritrosit membranın sterolleri arasındaki etkileşime dayandırılmaktadır. Sonuç olarak membran patlamakta, geçirgenlikte artışa ve hemoglobin kaybına neden olmaktadır. Baumann ve ark. (2000) tarafından, saponinlerin hemoliz yoluyla insan eritrositlerinin zar yapısı üzerindeki etkisinin araştırıldığı çalışmada, saponin ile parçalanmış eritrositlerde saponin hasarının geri döndürülemez olduğu görülmüştür. Tablo 2'de saponinlerin yukarıda belirtilen biyolojik aktivitelerinin yanı sıra belirlenen diğer bazı özellikleri özetlenmiştir.

Saponin İçerdiği Bilinen Bitkilerin Kullanım Alanları ve Oluşturduğu Biyolojik Etkiler

Caryophyllaceae ailesinden çok yıllık bir bitki olan *Silene cucubalus* halk arasında saç bakımında ve deterjan olarak kullanılmakta ve kırsal kesimlerde bu bitkinin kaynatılmasıyla elde edilen özüt; yaralanmaların, uyuzun ve deri enfeksiyonlarının tedavisinde kullanıldığı belirtilmiştir (Bellakhdar, 1997). Araliaceae ailesinin en belirgin üyesi ginseng'in (*Panax ginseng* C. A. Mayer) Uzak doğu tıbbında 5000 yıldan daha fazladır kullanıldığı ve Panax türlerinin zihinsel fonksiyonların artmasında, metebolik fonksiyonların uyarılmasında, sağlığın güçlendirilmesinde kullanıldığı bildirilmiştir (Duke, 1985). Bunun yanı sıra ginseng saponinlerinin cilt kanserine karşı etkili olduğu ifade edilmiştir (Keum ve ark., 2000). Bir diğer çalışmada, ginsenoside Rg3'ün insan prostat kanseri hücrelerinde ve kolon kanseri hücrelerinde NF-κB sinyalini inaktive ederek önemli terapötik etkiler gösterdiği rapor edilmiştir (Kim ve ark., 2010).

Saponince zengin *Picrasma javanica* adlı bitki halk tedavisinde geleneksel olarak mide ağrısının giderilmesinde, iltihapların iyileştirilmesinde ve ateş düşürücü olarak kullanılmaktadır (Khan ve ark., 2001). *Oxtropis myriophylla'*nın ise ateş düşürücü olarak, kanamayı kontrol altına almak, kızamıkçığın tedavisi, grip tedavisi, boğaz ağrısının ve şişliğinin giderilmesinde kullanıldığı bildirilmiştir (Masafumi ve ark., 2002).

Dünyanın yarı ılıman bölgesinde yetişen *Tribulus terrestris* adlı bitki; halk arasında idrar yolları, böbrek, karaciğer ve göz hastalıkları tedavisinde kullanılmaktadır (Sun ve ark., 2002). İzgür ve İlhan (2002) tarafından, hayvanlarda görülen vücut sıcaklığının yükselmesi, dalağın şişmesi, kanın pıhtılaşmaması ile karakterize edilen şarbon (antraks) hastalığına karşı, Türkiye'de üretilen antraks aşısında %0.1-0.5 oranında saponin içerdiği bildirilmiştir.

Saponinlerin antihipertansif etkisinin araştırıldığı birçok çalışmada, saponin ekstraktının hipertansif ratlarda kan basıncını önemli bir şekilde azalttığı belirlenmiştir (Jeon ve ark., 2000; Zaoui ve ark., 2000). Saponinlerin bu etkisinin diüretik (Zaoui ve ark., 2000), nitrik oksit (NO) üretiminin stimulasyonu (Jeon ve ark., 2000) ve anjiotensin dönüştürücü enziminin inhibisyonu (Dongma ve ark., 2002) ile oluştuğu saptanmıştır.

Protopanaxatriol saponin (PPT), önemli ölçüde anti-kanser, anti-diyabet ve anti-anemi etkilere sahiptir, ancak bağırsak bakterileri üzerindeki etkisi nadiren incelenmiştir. Yapılan bir çalışmada, PPT'nin antibiyotikle tedavi edilen farelerde bağırsak sağlığını iyileştirme yeteneğine sahip olup olmadığı geniş spektrumlu bir antibiyotik olan sefalosporin kullanılarak araştırılmıştır. Sonuçlar, PPT'nin bağırsak mikrobiyotasının bileşimini iyileştirdiğini, kısa zincirli yağ asitlerinin yanı sıra reseptör proteinleri ve sıkı bağlantı proteinlerinin konsantrasyonunu arttırdığını ve proinflamatuar sitokinleri azalttığını göstermiştir. Bu bulgular, PPT'nin bağırsak mikroorganizmaları üzerinde koruyucu bir etkiye sahip olduğunu ve antibiyotikle tedavi edilen farelerde bağırsak bariyerinin bütünlüğünü arttırdığını ve ayrıca kolonik iltihabı hafiflettiğini göstermektedir (Zhang ve ark., 2019). Bir başka çalışmada ise kinoa, mercimek ve çemen otunun saponin açısından zengin ekstraktlarının insan bağırsak mikrobiyotası tarafından sapogeninlere dönüşümü, seçilmiş bağırsak bakterilerinin büyümesi üzerinde modülatör bir etki sergilediği belirlenmiştir (Hierro ve ark., 2020).

Sevimli-Gür ve ark. (2011) tarafından *Astragalus* türlerinin yara iyileştirici olarak kullanımı araştırılmıştır. Çalışmada majör saponinler kullanılmış ve Astragalozit IV (Ast IV), Siklokantozit E ve Astragalozit IV'ün aglikonu olan sikloastragenol isimli bileşiklerin çok düşük dozlarda dahi aktivite gösterdiği saptanmıştır. Ratlarda alzheimer modeli oluşturularak yapılan bir başka çalışmada Ast IV'ün antiapoptotik etkiye sahip olduğu belirlenmiş olup bu molekülün nöroprotektif etkiye sahip olduğu öne sürülmüştür (Yin ve ark., 2010). Ayrıca, Ast IV'ün bir nöral koruyucu ajan olduğu kanıtlanmış ve parkinson hastalığının tedavisinde potansiyel bir ajan olarak önerilmiştir (Horo ve ark., 2010).

Birkaç *Astragalus* türünün kökleri geleneksel tıpta nefrit, diyabet, lösemi, rahim kanseri ve terleme önleyici, diüretik ve tonik tedavisi için kullanılmaktadır (Calis ve ark., 2008). Avicin D'nin, mitokondrinin hasarı ve çeşitli pro-survival ve antiapoptotik proteinlerin aşağı regülasyonu yoluyla intrinsikkaspaz yolunu aktive ederek lösemi ve lenfoma hücrelerinin apoptotik hücre ölümünü indüklediği belirlenmiştir (Gaikwad ve ark., 2005).

Saponin içeren gıda tüketiminin diyabet üzerine etkisinin değerlendirildiği çalışmalarda, saponinlerin sadece hipoglisemik etkisi olmayıp aynı zamanda plazma trigliseridi de azalttığı ifade edilmiştir (Patel ve ark., 2015; Smith ve Adanlawo, 2015). Yapılan bir başka çalışmada, *Polysciasfruticosa* yapraklarından izole edilen büyük bir saponin olan 3-O-[β-d-glukopiranozil-(1→4)-β-d-glukuronopiranosil] oleanolik asit 28-O-β-d-glukopiranozil esterin (PFS)'nin α-amilaz ve α-glukozidaz inhibisyonu ile

farelerde tokluk kan şekeri seviyesini düşürme potansiyeli değerlendirilmiştir. Enzim inhibisyon deneylerinde PFS'nin, α-amilaz ve α-glukozidazı güçlü bir şekilde inhibe ettiği belirlenmiştir. Sükroz tolerans testinde, sıçanlara 100 mg/kg vücut ağırlığında uygulanan PFS'nin tokluk kan şekeri seviyesini önemli ölçüde azalttığı saptanmıştır. Bu bulgular, *P. fruticosa* yapraklarının ve başlıca saponin PFS'nin diyabeti ve komplikasyonlarını önlemede ve tedavi etmede kullanılabileceğini ortaya koymuştur (Luyen ve ark., 2018). Patel ve ark. (2015), *Bryonia laciniosa*'nın tohumlarından elde edilen saponinlerin diyabetik sıçanlarda kan glikoz düzeyini düşürdüğünü belirlemişlerdir. Aynı çalışmada, sıçanlarda kolesterol ve trigliseridler de dâhil olmak üzere çeşitli lipid parametrelerinin düştüğü de tespit edilmiştir (Patel ve ark., 2015). Farklı bir çalışmada, *Tithonia diversifolia* yaprağından (STD) elde edilen saponinlerin (20-100 mg/kg dozlarında) alanin aminotransferaz (ALT), aspartat aminotransferaz (AST), alkalen fosfataz (ALP) ve gama glutamil transferaz (GGT) enzimlerinde ve karaciğer, kalp ve böbrek aktivitesinde hafif bir artışa neden olduğu rapor edilmiştir. Ayrıca aynı çalışmada yüksek yoğunluklu lipoprotein (HDL), beyaz kan hücresi ve lenfositte eş zamanlı bir artışla trigliseritler, düşük yoğunluklu lipoprotein (LDL), kolesterol, kreatinin, üre, laktat dehidrogenaz (LDH), PCV (sıkıştırılmış eritrosit hacmi) ve hemoglobin seviyesinde önemli bir azalma belirlenmiştir. Elde edilen sonuçlar, incelenen dozlarda normal sıçanlarda STD'nin bağışıklık tepkisini arttırmada, kolesterol ve trigliseritleri azaltmadaki önemini göstermiştir (Ejelonu ve ark., 2017). Birçok çalışmada saponinlerin obeziteye karşı çeşitli faydalı etkiler sergilediği bildirilmiştir (Kuate ve ark., 2015; Hierro ve ark., 2018). Oishi ve ark. (2007), *Momordica charantia* L. 'daki (kudret narı) saponin fraksiyonunun antiobezite potansiyelini değerlendirerek, farelere mısır yağı yüklemesinden sonra pankreas lipaz aktivitesini ve ayrıca serum nötr yağ seviyesinin yükselmesini engelleyebildiğini saptamışlardır.

Küçükkurt ve ark. (2008) tarafından yapılan çalışmada saponin içeren bitkilerin, antioksidan gücü artırmada ve oksidatif stres düzeyini azaltmada olumlu etkilere sahip olduğu belirlenmiştir. Bir diğer çalışmada, *Garcinia kola* kökünden elde edilen saponin özütünün, parasetamol-indüklü hepatotoksisitede yükselmiş karaciğer enzimlerini önemli ölçüde düşürdüğü belirlenmiştir. Aynı çalışmada *Garcinia kola* kökünden elde edilen saponin ekstraktının, hepatositik hücre zarının yapısal bütünlüğünün korunmasını ve hasarlı karaciğerin yenilenmesini sağladığı gösterilmiştir (Smith ve Adanlawo, 2015).

Deniz hıyarı saponininin hipoglisemik bir ajan olarak anormal biyokimyasal parametreleri normalleştirme potansiyeline sahip olduğunu ve pankreas dokularının adacık hücrelerinin normal histolojik yapısını korumaya yardımcı olduğu belirlenmiştir (El Barky ve ark., 2016). Bazı saponin türlerinin potansiyel antitümör aktiviteye sahip olduğu da bildirilmiştir (Facioni ve ark., 2018). Mudryj ve ark. (2014), saponin tüketiminin kanser riskine karşı korumayı artırdığını, kan şekeri ve kolesterol seviyesini düşürdüğünü saptanmıştır. Vinarova ve ark. (2015), *Quilla jasaponaria* ekstraktının kolestrol ve doymuş yağ asitlerinin biyolojik olarak erişilebilirliği üzerindeki etkisini incelemiş ve hem *in vitro* hem de *in vivo* deneylerde güçlü hipokolesterolemik etkilere sahip olduğunu, bu etkilerinde bitkinin saponin bileşenleri içermesinden kaynaklandığını ifade etmişlerdir.

Tüm bu sağlığa faydalı etkilerinin yanı sıra saponin içeren bileşenler böceklerde, yumuşakçalarda ve balıklarda toksik etki göstermektedir. Sıcakkanlı hayvanlarda ise toksisiteleri; saponinin kaynağına, kompozisyonuna ve konsantrasyonuna bağlıdır. Ayrıca canlının saponine hangi yola maruz kaldığı da önemlidir. Saponinler intravenöz verildiğinde kanın hemoliz olmasına neden olduğu bildirilmiştir (Francis ve ark., 2002). Bu nedenle anti besinsel faktör olarak yüksek miktarda tüketildikleri zaman toksik etkilere neden olabilen saponinlerin, biyolojik etkileri daha çok sindirim kanalında görüldü-

günden düşük oranda kullanımının sağlık üzerine faydalı olabileceği belirtilmektedir (Eryavuz ve Dehority, 2004).

SONUÇ

Kullanım miktarına bağlı olarak sağlık üzerinde meydana getirdiği etkilerde değişiklik gösteren saponin içerikli bileşikler gerek farmakolojik gerekse geleneksel tıpta çeşitli hastalıkların tedavisinde kullanım olanağı bulunan sekonder metabolitlerdir. Çeşitli bitkilerin yapılarında doğal olarak bulunan ve her geçen gün yeni bir formunun izole edildiği saponin bileşiklerinin hastalıkların tedavisinde meydana getirdiği etkilerin oluşum mekanizmalarının aydınlatılmasına yönelik yapılacak olan *in vivo* ve *in vitro* çalışmalara daha fazla ihtiyaç duyulması ve bu bileşenin sağlık üzerinde meydana getirdiği etkilerin gün geçtikçe daha fazla ilgi ve merak konusu olması, bu alanda yapılacak olan çalışmaların gerekliliğini ortaya çıkarmaktadır. Sonuç olarak, saponinlerin fizikokimyasal, biyokimyasal ve farmakolojik etkinliklerinin sağlık üzerinde olumlu etkiler sağlayabileceği ve bunun etki şekline, doza ve maruziyet süresine göre değişiklik gösterebileceği söylenebilir.

Çıkar Çatışması

Yazarlar çıkar çatışması olmadığını beyan eder.

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