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Can nasal septum deviation be one of the factors affecting diabetic retinopathy?

Nazal septum deviasyonu, diyabetik retinopatiyi etkileyen faktörlerden biri olabilir mi?

Erdoğan Yaşar [1], Serkan Kayabaşı [2]

[1] Aksaray University, Medicine Faculty, Department of Ophthalmology, Aksaray, Turkey
[2] Aksaray University, Medicine Faculty, Department of Otorhinolaryngology, Aksaray, Turkey

ORCID ID of the author(s)
EY: 0000-0001-5129-9397
SK: 0000-0002-5292-5940

Corresponding author/Sorumlu yazar:
Erdoğan Yaşar
Address/Adres: Aksaray Üniversitesi, Tıp Fakültesi, Göz Hastalıkları Anabilim Dalı, Aksaray, Türkiye
E-mail: dr.e.yasar@gmail.com

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Abstract

Aim: Information on the extraocular causes of diabetic retinopathy is limited. Therefore, when researching etiology in a patient with diabetic retinopathy, if glucose, blood pressure and cholesterol are normal, other reasons must be investigated. Our aim was to evaluate the effect of nasal septum deviation (NSD) on the presence and severity of diabetic retinopathy in patients with diabetes mellitus.

Methods: This prospective case-control study included 100 eyes of 50 patients with only diabetes mellitus (DM+ NSD-, control group) and 120 eyes of 60 patients with DM and nasal septum deviation (DM+NSD+, NSD group). After evaluation of NSD patients using a nasal obstruction symptom evaluation scale (NOSE scale), 22 patients were classified as mild, 21 as moderate, and 17 as severe. Anterior segment and dilated fundus examinations were performed in all patients. Diabetic retinopathy (DR) was classified as mild, moderate, and severe non-proliferative DR and proliferative DR (PDR).

Results: The mean age of patients in the NSD and control groups was 58.7 (15.2) years (range: 41–69) and 59.6 (8.1) years (range: 44–67), respectively. The prevalence of DR and PDR were 70% (n=14) and 30% (n=6), respectively, in the severe NSD group (P=0.045 and P=0.035, respectively). The relationship between PDR and other factors in patients with NSD were evaluated, and a correlation was detected with DM duration (P=0.024, OR=1.272), HbA1c (P=0.032, OR=3.085), and NOSE scale severity (P=0.040, OR=2.566).

Conclusion: The results of the present study show an increased risk of DR and PDR in patients with severe NSD. In addition to other risk factors in PDR etiology, NSD should also be considered.

Keywords: Diabetic retinopathy, Proliferative diabetic retinopathy, Nasal septum deviation, Hypoxia

Öz

Amaç: Diyabetes Mellituslu hastalarda nazal septum deviasyonunun diyabetik retinopatinin varlığı ve şiddeti üzerine etkisini değerlendirmek.

Yöntemler: Bu prospektif vaka kontrol çalışmasına Diabettes Mellitus (DM) olan 50 hastanın 100 gözü ve nazal septum deviasyonu (NSD) olan DM'li 60 hastanın 120 gözü (kontrol grubu) dahil edildi. NSD hastaları burun tıkanıklığı semptom değerlendirme ölçeği (NOSE ölçeği) ile değerlendirme sonrası hastalar; 22 hafif, 21 orta ve 17 ağır evre olarak sınıflandırıldı. Tüm hastalara ön segment ve dilate fundus muayenesi yapıldı. Diyabetik Retinopati(DR);hafif, orta, şiddetli non-proliferatif DR ve proliferatif DR olarak sınıflandırıldı.

Bulgular: NSD grubundaki hastaların yaş ortalaması 58,7 (15,2) (dağılım, 41-69) ve kontrol grubundaki hastaların yaş ortalaması 59,6 (8,1) (dağılım, 44-67) idi. DR prevalansı şiddetli evre NSD grubunda %70 (n=14), proliferatif DR prevalansı %30 (n=6) idi ve aradaki fark anlamlı bulundu (sırasıyla P=0,045, P=0,035). Proliferatif DR ile NSD hastalarındaki diğer faktörler arasındaki ilişki değerlendirildi ve DM süresi (P=0,024, OR=1,272), HbA1c (P=0,032, OR=3,085) ve NOSE skalası şiddeti (P=0,040, OR= 2,566) arasında pozitif ilişki saptandı.

Sonuç: Sonuçlarımız ağır tip NSD hastalarında artmış DR ve proliferatif DR riskini göstermektedir. Bu nedenle PDR etiyolojisinde diğer risk faktörlerine ek olarak NSD de düşünülmelidir.

Anahtar kelimeler: Diyabetik retinopati, Proliferatif diyabetik retinopati, Nazal septum sapması, Hipoksi

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Introduction

Diabetic retinopathy (DR) is a progressive disease of retinal vessels due to chronic hyperglycemia (retinal vascular capillary occlusion, vascular hyperpermeability, and neovascularization) [1]. Diabetes mellitus (DM) is a serious microvascular complication that threatens visual acuity and is one of the leading causes of blindness [2]. The prevalence of DR is about 35% in individuals with DM, and it is diagnosed in about 60% individuals who have had diabetes for 20 years [3-5]. The duration of DM and the severity of hyperglycemia are the main risk factors associated with retinopathy [6-7]. DR can be classified as non-proliferative DR (NPDR) and proliferative DR (PDR) depending on the presence or absence of neovascularization (NV) because of development and progression of DR [8]. The main factor in the etiology of PDR is the development of hypoxia [9-10].

Nasal septum deviation (NSD) is the displacement of the nasal septum from the midline to the right or left. NSD is the most common anatomical cause of nasal congestion [11]. Chronic alveolar hypoxia, which occurs in patients with NSD, arises due to decreased airflow obstruction in the upper respiratory tract, increased pulmonary vascular resistance, and insufficiency to regulate movements of the thorax via reflexes [12-13]. Although the prevalence of NSD can reach up to 80%, only some individuals are affected by nasal congestion [14]. Therefore, NOSE survey, a specific and reliable tool for assessing nasal congestion in adults, is used [15-16].

To the best of our knowledge, the relationship between DR and NSD, which can cause hypoxia, has not been studied to date. Therefore, we aimed to investigate the relationship between the presence and severity of DR and NSD.

Materials and methods

This prospective study included 120 eyes of 60 DM patients with NSD (DM+NSD+, NSD group) who presented to the ENT outpatient clinic between March and September 2019 and 100 eyes of 50 DM patients without NSD (DM+ NSD-, control group) who were evaluated at the eye clinic. All study procedures were conducted in accordance with the Helsinki Declaration. Ethics Committee approval was granted by Aksaray University Ethics Committee with the number 2019/44, and informed consent forms were received from all patients prior to their participation.

The study group comprised 50 patients without NSD and 60 patients aged>18 years who were diagnosed with NSD by endoscopic and/or radiological imaging. Patients with NSD were classified into the following three groups as evaluated by the nasal obstruction symptom evaluation (NOSE) scale: Mild cases (n=22), moderate cases (n=21), and severe cases (n= 17). The NOSE scale mainly focuses on nasal congestion and provides an assessment before and after the treatment [15-16]. The NOSE scale consists of 0–4 points (0: Not a problem; 1: Very mild problem; 2: Moderate problem; 3: Fairly bad problem; and 4: Severe problem). NOSE [16] was used to assess the following symptoms: Swelling or fullness in the nose, nasal congestion, difficulty in breathing and sleeping, and not being able to comfortably breathe during exercise or exertion. Each question was scored using the 5-point Likert scale, and finally scored between 0 and 100 points in total. Higher NOSE survey scores correspond to more severe nasal congestion. Patients who had previously undergone nasal surgery, those with nasal polyps or chronic sinusitis, those scheduled to undergo rhinoplasty surgery, those with craniofacial anomalies, and those with active upper respiratory tract infection were excluded from the study.

The criteria for exclusion for both groups included known hypertension, hypercholesterolemia, coronary artery disease, heart failure, metabolic syndrome, obstructive sleep apnea syndrome, smoking and alcohol consumption, pregnancy, the presence of anterior segment pathologies (central corneal pathology, iris pathology, pupil disorders, intensive cataract, and uveitis) that prevent imaging of the retina as well as known or previous non-diabetes retinal vascular diseases.

Patients' data, such as gender, age, diabetes duration, glycosylated hemoglobin (HbA1c) level, and treatment type were recorded. After routine anterior segment examination with slit lamp biomicroscopy, the pupils of both eyes were dilated with a drop of mydriatic eye drops (0.1% tropicamide). Fundus examination was performed after 30 minutes of rest, by the same ophthalmologist using a 78D Volk lens.

DR was classified according to the International Clinical Diabetic Retinopathy (DR) Disease Severity Scale as mild NPDR (microaneurysm only), moderate NPDR (more than just microaneurysm, but less than severe NPDR), severe NPDR (severe intraretinal hemorrhages and microaneurysms in each of the four quadrants, precise venous beading in two or more quadrants, and moderate IRMA in one or more quadrants), and PDR (one or both of the following: Neovascularization, vitreous/preretinal hemorrhage). The degree of retinopathy was assessed for each eye and individual classification was made with regards to the worse eye. Fundus fluorescein angiography was performed when neovascularization was unclear.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) 23.0-Windows (SPSS Inc., Chicago, IL) was used for statistical analysis. The normality of distribution of quantitative data was evaluated using Shapiro–Wilk test. Independent sample t-test (for normal distribution) and Mann–Whitney's (for non-normal distribution) test were used to compare the means of quantitative variables. Chi-square test was performed to compare the means of categorical variables. Binomial logistic regression analysis was performed to calculate the odds ratios of the relationship between descriptive variables. Values of $P < 0.05$ were considered statistically significant.

Results

The mean age of patients in NSD group was 58.7 (15.2) (range: 41–69) years, and the group comprised 36 female and 34 males. The mean age of the patients in the control group was 59.6 (8.1) (range: 44–67) years, and the group comprised 27 women and 23 men. No significant difference was observed between the groups in terms of mean age and gender ratio ($P>0.05$).

Comparisons among the mild, moderate, and severe cases in the NSD group determined by the NOSE scale and the control group in terms of DR, NPDR, PDR, HbA1c, and DM

duration are shown in Table 1. No differences were observed between the mild and moderate groups and the control group in terms of DR, NPDR, PDR, HbA1c, and DM duration (P<0.05). The prevalence of DR was 70% (n=14) in the group with severe cases, and 40% (n=20) in the control group. The deference was higher in DR group (P=0.045). The prevalence of PDR was 30% (n=6) in the group with severe cases and 8% (n=4) in the control group, and the deference was higher in PDR group (P=0.035). No differences were observed between the two groups in terms of NPDR, HbA1c, and DM duration (P>0.05).

Table 1: The comparison of control group and nasal septum deviation stage groups in terms of diabetic retinopathy

Parameters	Control group Mean(SD)	Mild Group Mean(SD)	*P*-value	Moderate Group Mean(SD)	*P*-value	Severe Group Mean(SD)	*P*-value
HgA1C	8.9(1.3)	8.8(1.2)	0.781	9.1(1.2)	0.586	8.7(1.6)	0.543
DM duration	11.8(4.4)	12.1(3.9)	0.199	11.4 (3.9)	0.148	12.2(3.9)	0.169
DR %(n)	44(22)	40(8)	0.784	45(9)	0.923	70(14)	0.045
NPDR %(n)	36(18)	35(7)	0.912	40(8)	0791	40(8)	0.791
PDR%(n)	8(4)	5(1)	0.406	10(2)	0.838	30(6)	0.027

DM: Diabetes Mellitus, DR: Diabetic Retinopathy, NPDR: Non-proliferative Diabetic Retinopathy, PDR: Proliferative Diabetic Retinopathy, mean: mean, SD: Standard Deviation

Factors affecting the presence of PDR, NPDR, and DR in patients with NSD were evaluated by binominal logistic regression (Table 2). A positive relationship was observed between DM duration (P=0.024, OR=1.272), HbA1c (P=0.032, OR=3.085), and NOSE (P=0.040, OR=2.566) in the PDR group, and no relationship was found between PDR, age, gender, and nasal septum lateralization (right/left; P>0.05). In the NPDR group, there were a positive relationship between DM duration (P=0.005, OR=1.573) and HbA1c (P=0.007, OR=2.969), and no relationship between NPDR and NOSE scale severity, nasal septum lateralization (right/left), age, and gender (P>0.05). In the DR group, there was a positive relationship between DM duration (P=0.014, OR=1.152), HbA1c (P=0.001, OR=2.621), and NOSE scale severity (P=0.040, OR=2.586), and no relationship between DR and nasal septum lateralization (right/left), age, and gender (P>0.05).

Table 2: The factors affecting the severity of diabetic retinopathy in patients with nasal septum deviation

Parameter	PDR		NPDR+		DR	
	P-value	OR	p-value	OR	*P*-value	OR
Age	0.186	-	0.204	-	0.259	-
Gender	0.524	-	0.356	-	0.429	-
DM duration	0.024	1.272	0.005	1.573	0.014	1.152
HgA1C	0.032	3.085	0.007	2.969	0.001	2.621
NOSE severity	0.040	2.566	0.254	-	0.040	2.586
NSL	0.356	-	0.439	-	0.643	-

DM: Diabetes Mellitus, DR: Diabetic Retinopathy, NPDR: Non-proliferative Diabetic Retinopathy, PDR: Proliferative Diabetic Retinopathy, mean: mean, SD: Standard Deviation, NOSE: Nose Obstruction Symptom Evaluation, NSL: Nasal Septum Lateralization, OR: Odds Ratio

Discussion

Diabetic retinopathy, which is a complication of diabetes, is usually associated with hyperglycemia or hypoglycemia [1]. However, in some cases, although glucose is normal, diabetic retinopathy may occur due to secondary causes. Commonly known secondary causes are HT and hypercholesterolemia, and researches on other causes are still ongoing [6]. The main result of this study is that PDR and total DR rates were higher in patients with severe NSD than in controls.

DM duration and severity of hyperglycemia (HBA1c) are the main risk factors for DR in various studies [6-7]. In the present study, similar to the literature, HbA1c and DM duration correlated with PDR and NPDR. Other risk factors for DR include hypertension, hypercholesterolemia, coronary artery disease, heart failure, abdominal obesity, obstructive sleep apnea, smoking, alcohol use, ethnicity, and the age of onset [16-25]. In the present study, no comparison could be made as these associated diseases were determined as exclusion criteria so that diabetic retinopathy is not affected. To the best of our knowledge, there is no study investigating the relationship between NSD and DR in the literature.

Diabetic retinopathy can be classified as non-proliferative and proliferative. The earliest clinical signs of non-proliferative diabetic retinopathy are retinal hemorrhages and microaneurysms. The development of venous beading, cotton wool spots, and intraretinal microvascular abnormalities are hallmarks of progressive capillary perfusion. Neovascularization on the surface of the optic disc and retina indicates the presence of proliferative diabetic retinopathy with more retinal ischemia [26]. The key factor in the etiology of PDR is the development of hypoxia, which is considered important for the release of growth factors that increase the permeability of the retinal vessels and stimulate neovascularization [9-10].

Pathological ocular angiogenesis in diabetic retinopathy is regulated by vascular endothelial growth factor-A (VEGF-A). In the retina, VEGF-A is released by ganglion cells, Müller cells, and retinal pigment epithelial cells [27]. High affinity VEGF receptors have been shown in retinal endothelial cells and pericytes. Hypoxia is the main regulator of VEGF-induced ocular neovascularization via hypoxia-inducible factor-1 [28]. Secondary to induction of VEGF by hypoxia, angiogenesis can be controlled by angiogenic inducers and inhibitors. VEGF is an important growth factor, especially for angiogenesis due to hypoxia, and is associated with the formation of new pathological vessels [27-28]. This new vessel formation becomes pathological as they are fragile and permeable. New vessels rupture and grow along the surface of the retina and towards the posterior hyaloid face. However, these delicate vessels are easily disrupted by vitreous traction, resulting in bleeding into the vitreous space or preretinal space. Intravitreal hemorrhage and tractional retinal detachment may occur in these pathological new vessels [29]. In the present study, proliferative DR may have occurred because of hypoxia induced by a severe NSD with a similar mechanism.

Nasal septal deviations play a critical role in nasal obstruction and chronic alveolar hypoxia occurs in patients with NSD, especially in patients in severe stage, because of a decrease in airflow obstruction in the upper respiratory tract, an increase in pulmonary vascular resistance, and the inability of the chest to regulate movements through reflexes [11-13]. In our study, we think that in patients with severe stage nasal septum deviation, retinal hypoxia and ischemia may have occurred with a similar mechanism.

When PDR is detected, the causes that will cause retinal ischemia are considered first. Diabetes-related causes are always insufficient to explain the etiology. Other systemic diseases that can cause ischemia and hypoxia in the retina should also be considered. This study will contribute to the literature by showing that NSD should also be taken into account in addition to other risk factors in the etiology of PDR. We concluded that

patients with treatment-resistant PDR should be assessed by otolaryngologists in terms of severe NSD that may cause hypoxia after other secondary causes are excluded. Studies with a larger number of patients are needed to investigate to what extent NSD can affect the development and progression of PDR.

Limitations

Limitations of this study include the fact that oxygen saturation was not measured in patients with NSD, the study was conducted only according to the severity assessment of the NOSE Scale. The other limitation of study was the relatively low number of patients.

Conclusion

The present study has demonstrated that patients with NSD who are severely affected based on NOSE scale severity are at risk for diabetic eye complications (DR, PDR), but those with mild to moderate NSD are not at such risk. In view of NSD-related effects, it was found that PDR increased by about 2.5 times with NOSE scale severity. Ophthalmologists and otolaryngologists should be informed about this in patients with DM. Studies with a larger number of patients are needed to investigate to what extent NSD can affect the development and progression of PDR.

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