

ARAŞTIRMAMAKALESİ/ORIGINALRESEARCH

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Tip 2 Diyabetik Hastalarda Serum Prostat Spesifik Antijenin Değerlendirilmesi

The Assesment of Serum Prostate Specific Antigen in Type 2 Diabetic Patients

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ÖZET

GİRİŞ ve AMAÇ: Prostat kanseri riski dolaşımdaki yüksek insülin seviyesi ve insülin rezistansı ile artış gösterir. Diyabet hastalarında düşük insülin seviyelerinden dolayı riskin azaldığına dair bazı çalışmalar vardır. Bu çalışmada diyabetik 50 yaş ve üstü erkeklerde serum Prostat Spesifik Antijen (PSA) düzeylerinin incelenmesi hedeflenmiştir.

YÖNTEM ve GEREÇLER: Çalışma; Mart 2008 ve Kasım 2008 tarihleri arasında Düzce Üniversitesi Dahiliye polikliniğine başvuran 50 yaş ve üstü 137 (67 vaka, 70 kontrol) erkek hastada yapıldı. Vaka grubu ve kontrol grubu yaşlara göre üçe ayrıldı. PSA değerleri bu yaş grupları arasında karşılaştırıldı. Ayrıca diyabetin tanı süresine göre hastalar üç gruba ayrılıp serum PSA değerleri karşılaştırıldı.

BULGULAR: Diyabetik 50-59 yaş grubunda ortalama serum PSA değeri 0.76 ± 0.35 ng/mL olup aynı yaş grubundaki non-diyabetiklerin ortalama PSA değerinden (1.08 ± 0.75 ng/mL) daha düşük bulundu. 60-69 yaş gruplarında benzer şekilde diyabetik hastaların serum PSA değerleri non-diyabetiklere göre anlamlı derecede düşük bulundu. >70 yaş grupları arasında ve diyabetin sürelerine göre olan gruplar arasında PSA değerleri arasında anlamlı fark bulunmadı.

TARTIŞMA ve SONUÇ: Diyabetik 50-59 yaş ve 60-69 yaş gruplarında serum PSA değerlerini diyabetik olmayanlara göre anlamlı şekilde düşük bulduk. Diyabetin süresi ile PSA arasında istatistiksel anlamda fark bulamadık. Sonuç olarak diyabetiklerde prostat kanseri riskinin diyabet olmayanlara göre daha düşük olduğunu düşünüyoruz.

Anahtar Kelimeler: diyabetes mellitus, psa, prostat kanseri

ABSTRACT

INTRODUCTION: Risk of the prostate cancer is associated with high insulin levels in circulation and insulin resistancy. There are some studies that suggested lower risk in diabetics due to decreased insulin levels. In this study we aimed assesment of serum Prostate Specific Antigen (PSA) levels in diabetic men age of 50 and over.

METHODS: 137 patients age over 50 years (67 case, 70 control) admitted to Duzce University School of Medicine outpatients clinic from March 2008 to November 2008 have been included in this study. Case and control groups were divided three groups as their age. PSA values were compared between in these age groups. Moreover, case group were divided three groups as their diagnosed diabet time and these group's PSA values were compared.

RESULTS: Serum mean PSA values of diabetic patients age of 50-59 years was 0.76 ± 0.35 ng/mL and it was found lower than same age group of non-diabetic patient's serum PSA values (1.08 ± 0.75 ng/mL). Similary in age groups of 60-69 years, diabetic patient's PSA values were found significantly lower than non-diabetic patient's PSA values. Between over age of 70 years groups and between diagnosed time of diabet groups, serum PSA values were not found significantly different.

DISCUSSION AND CONCLUSION: We found serum PSA levels sigificantly lower in diabetic groups than non-diabetic groups age of 50-59 years and 60-69 years. We couldn't find istically difference between PSA and diagnosed time of diabet. Consequently, prostate cancer risk may be lower in diabetic patients than non-diabetics.

Keywords: diabetes mellitus, psa, prostate cancer

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INTRODUCTION

Type 2 Diabetes Mellitus (DM) is a complex metabolic disease with insulin resistance and hyperinsulinemia at the onset. However, later in the disease, the pancreas loses its ability to synthesize insulin due to damage to the pancreatic β cells. The risk of prostate cancer (PC) increases with high circulating insulin levels and insulin resistance (1). In conclusion, it has been hypothesized that the risk may increase in men newly diagnosed with diabetes, but that the risk may decrease as insulin levels decrease during the course of diabetes (2)

Many epidemiological studies have investigated the relationship between diabetes and PC. Four of the five large studies have found a risk reduction of approximately 10% to 40% (3-7). In some small-scale studies, different results were obtained (8-9). The hypothesis of a relationship between diabetes and PC may reveal different results in terms of the time of diagnosis of diabetes. In three studies on this subject; In the Health Professionals Follow-up cohort study, the incidence of PC was higher in men newly diagnosed with diabetes (5). Diabetes diagnosis time was found to be insignificant with the relationship between diabetes and PC in the Physicians' Health study (6). In contrast, in the Cancer Prevention cohort study, the incidence of PC was significantly higher in people with diabetes diagnosed for 5 years or more (7).

The Prostate specific antigen (PSA) is a serine protease produced in malignant and nonmalignant epithelial cells. It is a useful marker recommended for PC screening in men aged 50 years and older. PSA is prostate specific, not PC specific and measured by radioimmunoassays. Its normal value is 0-4 ng/mL. Men with a PSA value between 4 and 10ng/mL who cannot be attributed to any cause may have a 30% risk of developing PC, and men with a PSA value above 10ng/mL may have a 50% risk of developing PC (10). Low testosterone and Insulin-like growth factor (IGF-1) levels in diabetic men may affect serum PSA levels (11).

In this study, it was aimed to examine the serum PSA levels in diabetic and non-diabetic men aged 50 and over, and also according to the differences in the duration of diabetes diagnosis.

MATERIAL AND METHODS

This study was performed on 137 (67 cases, 70 controls) male patients aged 50 years and older who applied to Düzce University Internal Medicine outpatient clinic between March 2008 and November 2008. The case group consisted of patients diagnosed with diabetes before or newly diagnosed with diabetes. The control group consisted of patients without diabetes, impaired

fasting glucose and impaired glucose tolerance. Patients with benign prostatic hyperplasia, prostatitis and PC which could change serum PSA value, were not included in either group. Patients with serum PSA values higher than the upper limit of their age group were also excluded from the study.

In order to compare the PSA values between the diabetes and control groups, both groups were divided into three groups as 50-59 years old, 60-69 years old and 70 years old and above.

Diabetes diagnosis times of the patients were recorded in order to compare serum PSA values according to the duration of diabetes diagnosis in the case group. The diagnosis period groups were formed as 0-5 years, 6-10 years and > 10 years. The serum PSA values of these groups were compared among themselves. Diabetes patients included in the study were not divided into different categories in terms of their use of diet, oral anti-diabetic drugs or insulin for diabetes regulation, and it was shown that they did not affect serum PSA values in previous studies. Likewise, blood HbA1c levels of diabetic patients were ignored in our study, since they did not show any significance in terms of PSA levels (11-12).

The PSA values were measured in serum samples with solid phase bilateral chemiluminescent enzyme immunometric measurement method, in Immulite 2000 device, using Immulite 2000 PSA kits, with a sensitivity of 0.02ng/ml.

This study was presented as a graduation thesis in Düzce University, Department of Internal Medicine in 2009.

Statistical Analysis

In this study, statistical analyzes were performed with SPSS (Statistical Package for Social Sciences) for Windows 15.0 package program. The results of all parameters belonging to the groups were given as mean \pm standard deviation. Independent T-test was used when comparing PSA values in diabetes and control groups, which were divided into 3 groups according to age. PSA values according to diabetes diagnosis time were compared with Anova test. Results were evaluated at the significance level $p < 0.05$.

RESULTS

In our study, serum PSA values of diabetic and non-diabetic male patients aged 50 and over were compared according to age groups. The study consisted of 67 diabetic patients and a control group of 70, and the groups were divided into three groups according to their age.

The mean PSA value of the diabetes group aged 50-59 years consisting of 27 people was 0.76 ± 0.35 ng/mL, and the PSA value of the control age group

consisting of 28 people was 1.08 ± 0.75 ng/mL. There was a statistically significant difference between them ($p < 0.05$).

The mean PSA value of the diabetes group consisting of 23 people aged 60-69 was 1.17 ± 0.43 ng/mL, and the PSA value of the control group consisting of 23 people was 1.77 ± 1.15 ng/mL, and there was a significant difference between them ($p < 0.05$). The PSA value in the diabetes group of 17 people aged 70 and over was 1.87 ± 1.15 ng/mL, and although it was lower than 1.91 ± 1.46 ng/mL in the control group of 19 people, there was no statistically significant difference between them ($p > 0.05$). (Table 1, Figure 1)

Table 1. Parameters of the Groups According to Age Distribution

Age	Diabetic group (n=67) PSA (ng/mL)(Average \pm SD)	Control group (n=70) PSA(ng/mL) (Average \pm SD)	P value
50-59	0.76 \pm 0.35	1.08 \pm 0.75	0.04
60-69	1.17 \pm 0.43	1.77 \pm 1.15	0.03
>70	1.87 \pm 1.15	1.91 \pm 1.46	0.09

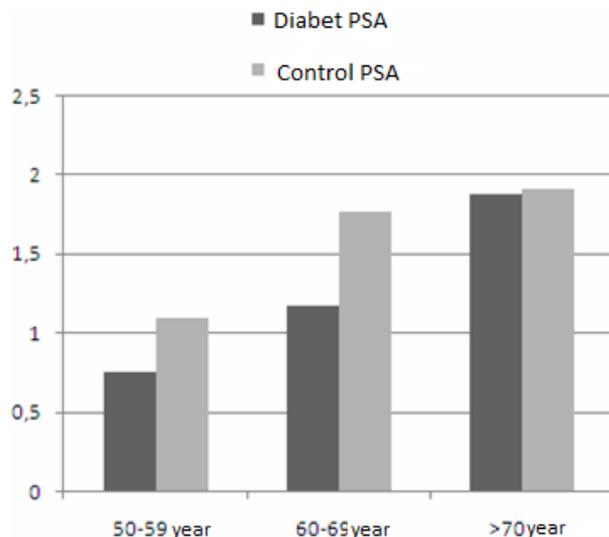


Figure 1 . Parameters of the Groups According to Age Distribution

We divided the diabetic patients into three groups according to the duration of diabetes diagnosis. Groups were formed as 0-5 years, 5-10 years and >10 years. The mean PSA value of those with diabetes for 0-5 years was 1.3 ± 0.95 ng/mL, and there was no significant result when compared with the PSA values (0.95 ± 0.81 ng/mL) of those with diabetes for 5-10 years ($p > 0.05$). Again, when the PSA value of those with diabetes for 0-5 years was

compared with the PSA value of those with diabetes for >10 years (1.43 ± 0.98 ng/mL), no statistically significant results were found ($p > 0.05$). When the PSA value (0.95 ± 0.81 ng/mL) of those with diabetes for 5-10 years was compared with the PSA value (1.43 ± 0.98 ng/mL) of those with diabetes for >10 years, no significant results were found ($p > 0.05$). (Table 2).

Table-2 PSA Levels in Patients According to the Duration of Diabetes

Diabetes duration	PSA (ng/mL)	p value
< 5 year (n=26)	1.33\pm0.95	p>0.1
5-10 year (n=22)	0.95\pm0.81	
< 5 year (n=26)	1.33\pm0.95	P>0.9
>10 year (n=19)	1.43\pm0.98	
5-10 year (n=22)	0.95\pm0.81	P>0.2
>10 year (n=19)	1.43\pm0.98	

DISCUSSION

Studies have shown that the risk of many cancers such as colon, liver and pancreas increases in type 2 DM patients (13-14). In addition, recent studies have reported that the risk of PC is reduced in male patients with diabetes (15-16). In this study, we also found data suggesting that serum PSA values may decrease and therefore the risk of PC may be lower in patients with diabetes.

While genetic factors (having the HPC1 gene) and defects in the X chromosome (such as increase in 7p, 7q, decrease in 8p, 10q) are involved in the mechanism of PC, serum androgens (testosterone, Dihydro testosterone (DHT)), hyperinsulinemia and IGF-1 are other factors that may contribute. An excessively increased defect in the conversion of testosterone to DHT in the prostate tissue and the binding of DHT to the androgen receptor to increase cell proliferation and DNA synthesis predispose to PC. Insulin increases the testosterone level and IGF-1 level in the body through various mechanisms. IGF-1 inhibits cell apoptosis and can increase cell proliferation by binding to the androgen receptor in the prostate independently of androgens (17). In a study by Par stattin et al., a significant correlation was found between high serum IGF-1 levels and PC (18). Similarly, in a study conducted by Steven E. Oliver et al. in people without PC, a positive correlation was shown between IGF-1 and PSA (19).

When interpreting serum PSA values, values that

are considered normal for age should be known. Values of 0-3.5 ng/mL between the ages of 50-59, 0-4.5 ng/mL between the ages of 60-69, and 0-6.5 ng/mL for those aged 70 and above are considered normal limits. For this reason, in our study, comparisons were made by dividing into age groups. In a study by Michiaki Fukui et al., including 224 diabetic and 1293 healthy people, the case group was divided into 4 groups as 40-49 years old, 50-59 years old, 60-69 years old and >70 years old. Serum PSA values were found to be significantly lower ($p<0.05$) in the other age groups, excluding the 40-49 age group, compared to the control groups (12).

In our study, PSA values in the 50-59 age group and 60-69 age group were found to be statistically significantly lower than the control group ($p=0.04$, $p=0.03$, respectively). Although the PSA value (1.87 ng/L) of the case group aged >70 years was lower than the control group (1.91 ng/mL), it was not statistically significant ($p=0.09$). The low number of patients aged >70 years ($n=17$) may have been insufficient in the statistical evaluation, and the wider range of serum PSA values in patients over 70 years of age may have revealed this result.

Because of insulin resistance and hyperinsulinemia in the early stages of type 2 DM, serum testosterone and IGF-1 levels, which pose a risk for PC, may be high. In the later stages of the disease, insulin levels decrease due to pancreatic β -cell losses, and as a result, blood testosterone and IGF-1 levels decrease, Sex hormone binding globulins amount may increase and free androgen fractions may decrease (14). There are different opinions as to whether patients using insulin, when insulin levels are low or oral antidiabetic drugs are contraindicated, are at risk for PC. In a study by Velicer et al., it was stated that diabetic patients using insulin have a lower risk of PC than non-diabetics (hazard ratio 0.49, 95% confidence interval 0.26-0.92) (5). However, in the study conducted by Michiaki Fukui et al., no risk reduction was found in patients using insulin (12). Likewise, in the study of Pierce BL et al., no significant results were found between insulin use and risk (20).

Diagnosis period of diabetes may reveal different results in terms of PC risk. In a study by Rodriguez et al., it was stated that there is an increased risk in the first 3 years of diabetes diagnosis, and a significant decrease in risk after 4 years (15). In a study by Giovannuci et al. involving 47,781 documented PC cases, it was reported that the risk did not decrease in the first 5 years of diabetes diagnosis, but decreased significantly in the next 5 years and 10 years (5). Similarly, in the study conducted by David M Werny et al, it was

determined that there was a reduced risk in those with diabetes diagnosis for more than 10 years, and serum PSA values decreased in the course after the onset of diabetes (11). On the other hand, in the first of 2 case-control studies based on hospital records conducted by Tabloni A et al. it was found that those with diabetes diagnosis for 5 years did not have a significant risk for PC compared to those with diabetes at 5-9 years and >10 years, in the second, it was stated that PC was not associated with the duration of diagnosis of diabetes (9-21). In our study, there was no statistically significant difference between serum PSA values (1.33 ng/mL) in patients with diabetes diagnosis in the first 5 years and PSA values (0.95ng/mL) in patients with 5-10 years of diagnosis ($p>0.05$), however, we observed that the serum PSA value tended to decrease.

We measured the highest PSA values (1.43 ng/mL) in our group with diabetes diagnosis >10 years, and when we compared it with the other 2 groups, we found that there was no significant difference with both ($p>0.05$). As a result, we concluded that the duration of diagnosis of diabetes is not related to PC.

We did not include prostate biopsy results to our study because of inefficient data so this may be a kind of reason about study limitation. And also it was a retrospective study only includes Turkish population.

Conclusion

As a result of our study, we found PSA values to be significantly lower in diabetic male patients compared to non-diabetic patients. These results show us that diabetic patients have a lower risk of PC than those without diabetes, but the conflicting results in other studies show that more studies are needed to elucidate the relationship between diabetes and PC.

Ethics Committee Approval: This study was a graduating thesis in 2009. There was no need for ethics committee approval

Conflict of Interest: The Authors declare that there is no conflict of interest between them

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Informed Consent: This study is a retrospective study

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