The effects of cigarette smoking on prostate-specific antigen in two different age groups

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Abstract

Background: We investigate the effects of cigarette smoking on prostate-specific antigen (PSA) using 2 different age groups.
Methods: The study was carried out between January 2007 and October 2011 with men; the 2 sets of age groups were: 25 to 35 years and 50 to 70 years old. The participants were divided into 4 groups. Of the 25 to 35 age range, smokers were Group 1, and non-smokers were Group 2; of the 50 to 70 age range, smokers were Group 3 and non-smokers Group 4. In addition, for the 50 to 70 age group, the International Prostate Symptom Score was completed, digital rectal examination was performed, and transabdominal prostate volume was measured. We wanted to see whether prostate-specific antigen (PSA) levels showed a difference between the 2 age groups.
Results: There were 114 patients in Group 1, 82 in Group 2, 90 in Group 3, and 102 in Group 4. The mean PSA level was 0.7 ± 0.28 ng/mL for Group 1, and 0.6 ± 0.27 ng/mL for Group 2 ($p = 0.27$), and there was no statistically significant difference between the 2 groups. The mean PSA was 2.5 ± 1.8 ng/mL for Group 3, and 2.1 ± 2.0 ng/mL ($p = 0.59$) for Group 4, and there was no statistically significant difference between the these 2 age groups.
Interpretation: Cigarette smoking effects various hormone levels. Different from previous studies, the PSA level was higher in smokers compared to nonsmokers, although it was not statistically significant. Our study is limited by the small numbers in our study groups and the lack of PSA velocity data.

Introduction

Prostate cancer is the most common cancer and the second leading cause of cancer-related deaths affecting men in the United States. It is estimated that 241 740 patients will be diagnosed with, and 28 170 will die of prostate cancer in 2012.[1] After the introduction of the prostate-specific antigen (PSA) testing for diagnosis, the number of patients detected at an early stage significantly increased.[2] However, PSA is not a specific marker for prostate cancer, PSA also increases in benign prostatic hyperplasia (BPH) and prostatitis; therefore, elevated PSA levels in such cases may lead to unnecessary prostate biopsies.[3]

Cigarette smoking is a major risk factor for many cancers. Some studies do not indicate a direct correlation between current smoking and prostate cancer.[4-6] Yet, other studies report a decrease in the risk of developing prostate cancer in smokers; cigarette smoking is known to cause high-grade cancers and can increase the risk of death from prostate cancer.[7,8]

Cigarette smoking may affect certain hormone levels. Testosterone, dihydrotestosterone (DHT), androstenedione, dihydroepiandrosterone (DHEA), dihydro-epiandrosterone sulfate (DHEAS), cortisol and sex hormone-binding globulin (SHBG) levels are higher and estradiol levels are significantly lower in smoking men compared to non-smokers.[9-11]

Various studies have examined the effects of cigarette smoking on PSA, but were mostly carried out in the older men.[3,12-15] PSA increases in age-related diseases, such as BPH. For this reason, with the aim of investigating the effects of smoking on PSA levels, we designed this present study in young patients to exclude age-related effects, and also in patients over 50 years old in which PSA was used as a screening test.

Methods

The study was conducted between January 2007 and October 2011 with consenting men. The participants were primarily divided into 2 groups according to age range: one group between 25 and 35 years old and the other between 50 and 70 years old. Later, the participants were reclassified according to their smoking status into 4 groups. Smoking

status was defined as a history of smoking more than 10 cigarettes per day for at least 1 year. Of the 25 to 35 age range, smokers were Group 1, and non-smokers were Group 2; of the 50 to 70 age range, smokers were Group 3 and non-smokers Group 4. The younger men were chosen among follow-up patients who applied for routine controls for nephrolithiasis, whereas older men were chosen among 50- to 70-year-old men who applied to the urology outpatient clinic for complaints related to BPH. Blood samples of all the participants were collected at the same time. For all the patients, medical history was taken, and physical examination, urinalysis, and urinary tract ultrasonography were performed. Additionally, for patients in the 50 to 70 range, the International Prostate Symptom Score (IPSS) was completed, digital rectal examination (DRE) was performed and prostate volume was measured by transabdominal ultrasonography. We excluded patients who reported any previous prostate or urethral surgery and prostate cancer, who had urinary tract infection, suspicious nodules detected in DRE, urethral catheters, sexual relationships in the last 24 hours, and ex-smokers.

Evaluations were performed by the same team. Written informed consent was obtained from each patient and Institutional Review Board approval was obtained from the local Ethics Committee. Independent sample t-test method was used for statistical analysis and $p < 0.05$ was considered significant.

Results

There were 114 patients in Group 1, 82 in Group 2, 90 in Group 3, and 102 in Group 4.

Groups 1 and 2

The mean age was 29.6 ± 3.1 for Group 1, and 30.2 ± 3.0 for Group 2 ($p = 0.2$), and no significant difference was found between the 2 groups. Sociocultural levels of the 2 groups were also similar. The mean PSA level was 0.7 ± 0.28 ng/mL for Group 1, and 0.6 ± 0.27 ng/mL for Group 2 ($p = 0.27$), respectively, and the difference between the 2 groups was not statistically significant (Table 1).

Groups 3 and 4

In Group 3 and Group 4, the mean age was 57.7 ± 4.3 for Group 3, and 59.0 ± 5.8 ($p = 0.09$) for Group 4 ($p = 0.09$).

Table 1. Comparison of outcomes of Group 1 and Group 2

	Group 1 (n=114)	Group 2 (n=82)	*p* value
PSA (ng/mL)	0.7 ± 0.28	0.6 ± 0.27	0.27
Age	29.6 ± 3.1	30.2 ± 3.0	0.2

PSA: prostate-specific antigen.

The mean IPSS was 15.5 ± 7.6 for Group 3, and 14.6 ± 7.9 for Group 4 ($p = 0.26$), the mean prostate volume was 45.3 ± 15.5 mL for Group 3, and 46.9 ± 18.9 mL for Group 4 ($p = 0.51$); no statistically significant difference could be determined between the 2 groups. Again, Group 3 and Group 4 were similar in terms of sociocultural levels. The mean PSA was 2.5 ± 1.8 ng/mL for Group 3, and 2.1 ± 2.0 ng/mL ($p = 0.59$) for Group 4, and there was no statistically significant difference between the 2 groups (Table 2).

Discussion

After the introduction of PSA as a screening test, the detection rate of prostate cancer in early stages has considerably increased. Until recently, PSA levels of 4.0 ng/mL have been used as the threshold to undergo prostate biopsy. Then, some authors indicated that similar detection rates could be achieved with PSA levels of 2.5 to 4.0 ng/mL and 4.0 to 10.0 ng/mL, thus they suggested using 2.5 to 4.0 ng/mL as the lower PSA limits to undergo prostate biopsy.[16-18] As a consequence, the number of prostate biopsies increased by lowering the threshold value of PSA. On the other hand, PSA is not cancer-specific; PSA is influenced by various factors and because of complications, such as infection and hematuria, unnecessary biopsies should be avoided where possible.

Cigarette smoking affects the levels of various hormones; PSA is also a molecule that can be easily affected by several factors. In the studies that have investigated the relationship between cigarette smoking and PSA, a clear mechanism could not be exactly clarified. In their study with men between the ages of 40 and 69, Gray and colleagues reported significantly lower free PSA (fPSA) and fPSA% values in smokers than in non-smokers, but total PSA (tPSA) did not show such a difference.[3] Crystal and colleagues have also found the level of PSA significantly lower in smokers compared to non-smokers in men over 55.[12] Escandriolo and colleagues have allocated patients to 2 groups: (1) prostate tumour (PT), those who have been histopathologically diagnosed as benign prostate hyperplasia or prostate adenocarcinoma, and (2) prostate control group (PC), those who were not histopathologically diagnosed. The level of PSA was significantly higher in smokers than in non-smokers in the PT group; on the contrary, the level was significantly lower in non-smokers in the PC group.[13] Gelmann and colleagues

Table 2. Comparison of outcomes of Group 3 and Group 4

	Group 3 (n=90)	Group 4 (n=102)	*p* value
PSA (ng/mL)	2.5 ± 1.8	2.1 ± 2.0	0.59
Age	57.7 ± 4.3	59.0 ± 5.8	0.09
IPSS	15.5 ± 7.6	14.6 ± 7.9	0.26
Prostate volume (mL)	45.3 ± 15.5	46.9 ± 18.9	0.51

PSA: prostate-specific antigen; IPSS: International Prostate Symptom Score.

have studied PSA levels of men over the age of 55 and found significantly lower PSA levels in smokers compared to non-smokers.[14] The underlying reasons for low PSA levels could not be clearly explained. Cigarette smoking was suggested to affect various hormone levels, and such endocrine disturbances may eventually change PSA levels. Again, Li and colleagues have found significantly lower PSA levels in smokers than in non-smokers in men over 40. They have suggested that SHBG levels increased in smokers, which in turn reduced the PSA levels.[15]

In our study, younger and older smokers displayed higher PSA levels compared to non-smokers, although the difference was not statistically significant. Previous studies could not reveal any clear information explaining lower PSA levels detected in smokers. Plausible mechanisms through which cigarette smoking may affect PSA levels are not exactly recognized.

Interestingly, we suggest that the PSA level should be high in smokers. Androgen deficiency is characterized by a decrease in prostate volume and serum PSA level.[19] Jin and colleagues have reported significantly lower testosterone and PSA levels in patients who were given androgen replacement therapy for androgen deficiency compared to patients with androgen deficiency who were not given androgen replacement therapy and also compared to healthy men.[20] Testosterone stimulates efficiency of prostatic epithelial cells which synthesize and secrete PSA. Because cigarette smoking also increases the level of PSA, increased testosterone levels should be expected to cause higher levels of serum PSA levels. Testosterone is converted to dihydrotestosterone (DHT) by the enzyme 5α-reductase and DHT is a more potent hormone compared to testosterone. Prostate requires different hormones, such as testosterone and DHT, to grow and maintain this growth. 5α-reductase inhibitors, such as finasteride, can reduce blood PSA level by 50%.[21] The decrease in DHT will then lead to a drop in PSA level, in contrast, PSA would be expected to increase in smokers as a result of increased DHT. Additionally, α1-antitrypsin is a plasma protein that is produced in the liver and inhibits serine proteases. A deficiency of α1-antitrypsin may lead to pulmonary emphysema, especially in smokers,[22] suggesting that cigarette smoking may affect α1-antitrypsin functions and the level of PSA, which is a serine protease. Moreover, the absence of lower urinary tract symptoms in the younger patients provides an opportunity to evaluate the relationship between cigarette smoking and PSA more clearly. Nevertheless, PSA levels were below the mean values that can pose risks of prostate cancer in the elderly group, and this is significant because in this age group PSA is affected less due to relatively complex oncological mechanisms. Contrary to the data of previous studies, we argue that PSA levels may be higher in smokers than in non-smokers.

This study was carried out in 2 different age groups and interestingly they displayed similar results; we consider these components as the strengths of our study. To the best of our knowledge, this is the first study investigating the effects of smoking on PSA in the 25 to 35 age group. Diseases that develop progressively with advancing age, such as prostate cancer, BPH and prostatitis, were ruled out and only the effects of smoking on PSA were investigated. Furthermore, by including patients from the 50 to 70 age group, we were able to obtain more robust results. Our results supported our theories, and accordingly, PSA level was found higher in smokers than in non-smokers. Our study, however, is limited by the small numbers in our study groups and the lack of PSA velocity data.

Conclusion

Smoking causes many cancers; it also affects the levels of various hormones. Today, PSA is a widely used molecule to screen men for prostate cancer. Nevertheless, it is not cancer-specific and is affected by several factors, and therefore leads to numerous unnecessary biopsies. The relationship between PSA and smoking is not yet clearly established. We obtained different results compared with previous studies. Thus, further studies are required with more patients and longer follow-up periods.

Competing interests: Dr. Koc, Dr. Akgul, Dr. Yilmaz, Dr. Dirik, and Dr. Un all declare no competing financial or personal interests.

This paper has been peer-reviewed.

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