ORIGINAL RESEARCH

ARE CIGARETTE SMOKING, ALCOHOL CONSUMPTION AND HYPERCHOLESTEROLEMIA RISK FACTORS FOR CLINICAL BENIGN PROSTATIC HYPERPLASIA?

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ABSTRACT

Objective: Benign prostatic hyperplasia (BPH) a histopathological term, indicates the benign morphological enlargement of the prostate gland. Clinical BPH refers to the presence of lower urinary tract symptoms (LUTS) and BPH in men. Clinical BPH is a common disease of the elderly male population with an incidence reaching nearly % 70 after the age of 60 years. Different studies have been performed to identify the risk factors for clinical BPH including age, obesity, hypertension, diabetes, vasectomy, sexual activity, physical activity, alcohol consumption, cigarette smoking, caffeine consumption, hormonal status and hyperlipidemia. However, the potential role of the afore-mentioned risk factors in the pathogenesis of clinical BPH is not clarified yet. In this study we investigated whether certain risk factors such as hypercholesterolemia, cigarette smoking and alcohol consumption play a role in the occurrence of clinical BPH.

Methods: Between 1997 and 2000 a total of 142 patients admitted to the outpatient clinic with lower urinary tract symptoms (LUTS) were included in this prospective study. The International Prostate Symptom Score (IPSS) was administered to all patients by the primary physician and history of cigarette smoking and alcohol consumption was noted. On the day of examination, fasting blood samples were collected for serum cholesterol and PSA. All patients underwent uroflowmetric analysis. Patients with benign prostatic enlargement in digital rectal examination and with an IPSS>7 and a maximum flow rate < 10 ml/sec were considered as having clinical BPH. The r esults were analysed by student t test, Chi square test or ANOVA where appropriate.

Results: Ninety-seven (%68.3) patients were found to have clinical BPH whereas 45 (31.7%) patients were not diagnosed as clinical BPH. The mean serum cholesterol level of the patients with and without clinical BPH was 226 mg/dl and 224 mg/dl, respectively (p>0.05). Thirty-four (35.1%) patients with clinical BPH were regular smokers whereas 25 (55.6%) patients without BPH were smokers (p=0.047). The ratio for alcohol consumption was 6% in clinical BPH patients and 13.3% of the patients without clinical BPH (p=0.041). According to PSA values, 23 (23.8%) patients who had clinical BPH had PSA>4ng/ml whereas 7 (15.6%) patients without clinical BPH had PSA>4ng/ml (p>0.05).

Conclusion: Our results indicate a protective effect of cigarette smoking and alcohol consumption in the occurrence of clinical BPH whereas serum cholesterol and PSA levels did not reveal a significant effect on the occurrence of clinical BPH.

Keywords: Prostate hyperplasia, Cigarette, Alcohol, Cholesterol

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SİGARA VE ALKOL KULLANIMI, VE HİPERKOLESTEROLEMİ KLİNİK BENİN PROSTAT HİPERPLAZİSİ İÇİN RİSK FAKTÖRLERİ MİDİR?

ÖZET

Amaç: Benin prostat hiperplazisi (BPH), histopatolojik bir terim olup, prostatın iyi huylu morfolojik büyümesi anlamına gelmektedir. Klinik BPH ise erkeklerde BPH ile birlikte ona bağlı olduğu düşünülen alt üriner sistem semptomlarının bulunması olarak tanımlanır. Klinik BPH, yaşlı erkek popülasyonunda oldukça sık karşılaşılan ve 60 yaş üzeri hastalarda % 70'lere varan insidansa sahip olan bir hastalıktır. BPH gelişiminde, risk faktörü olabileceği düşünülen, yaş, obesite, hipertansiyon, diyabet, vazektomi, seksüel aktivite, fiziksel aktivite, alkol kullanımı, kafein kullanımı, hormonal faktörler ve hiperlipidemi hakkında değişik çalışmalar yapılmıştır. Ancak, bu risk faktörlerinin klinik BPH patogenezindeki rolü henüz tam olarak aydınlatılamamıştır. Bu çalışmada, hiperkolesterolemi, sigara ve alkol kullanımı gibi risk faktörlerinin klinik BPH gelişimindeki önemi araştırılmıştır.

Yöntem: Bu prospektif çalışmaya, 1997-2000 yılları arasında polikliniğimize alt üriner sistem şikayetleri ile başvuran toplam 142 hasta alındı. Her hastanın sigara ve alkol kullanma hikayeleri alınarak çalışmayı yürüten hekim tarafından yüz yüze görüşme yapılarak uluslararası prostat semptom skoru formu (IPSS) uygulandı. Muayene gününde ayrıca total kolesterol ve PSA analizi amacıyla hastalardan açlık kanı alındı ve ardından tüm hastalara üroflovmetrik analiz yapıldı. Parmakla rectal muayenede prostatta benin büyüme tespit edilen, IPSS>7 ve maksimum akış hızı <10 ml/sn. olan hastalara klinik BPH tanısı konuldu. Çalışmada tespit edilen sonuçlar student t testi, ki-kare testi ve ANOVA ile analiz edildi.

Bulgular: Hastaların 97'sinde (%68.3) klinik BPH tespit edilirken 45 (%31.7) hastanın bulgularının klinik BPH ile uyumlu olmadığı gözlendi. Klinik BPH'sı olan hastaların ortalama serum kolesterol seviyesi 226 mg/dl iken, klinik BPH'sı olmayan hastalarda 224 mg/dl olarak tespit edildi (p>0.05). Klinik BPH tanısı alan hastaların 34'ü (%35.1) sigara kullanırken 63 (%64.9) hasta sigara kullanmamaktaydı (p=0.047). Alkol kullanımı sorgulandığında klinik BPH'sı olan hastaların % 6'sı alkol kullanırken, klinik BPH'sı olmayan hastaların %13.3'ü alkol kullanmaktaydı (p=0.041). PSA değerlerine bakıldığında, klinik BPH tespit edilen hastaların 23'ünde (%23.8) PSA>4ng/ml iken klinik BPH'sı olmayan hastaların 7'sinde (%15.6) PSA>4ng/ml olarak tespit edildi (p>0.05).

Sonuç: Çalışma grubumuzda sigara veya alkol kullanan hastalarda klinik BPH görülme sıklığı anlamlı olarak düşük tespit edildiğinden, bu çalışmada sigara ve alkol kullanımının klinik BPH gelişiminde koruyucu etkiye sahip olabileceği düşünüldü. Serum kolesterol ve PSA seviyelerinin ise, klinik BPH gelişiminde anlamlı bir etkiye sahip olmadığı gözlendi.

Anahtar Kelimeler: Benin prostat hiperplazisi, Hiperkolesterolemi, Sigara ve alkol kullanımı

INTRODUCTION

BPH is a common disease and a major cause of morbidity in elderly men which may lead to bladder outflow obstruction and LUTS. Nearly 70 % 60-70 year- old men have LUTS related to BPH and 25-30% of the men have had surgical treatment by the age of 80 years[1]. So far, two factors are established which are mandatory for the occurrence of BPH: Age and a testis with normal testosterone production[2]. Several studies have been performed to identify additional risk factors, especially for clinical BPH including age, obesity, hypertension, diabetes, vasectomy, sexual activity, physical activity, alcohol consumption, cigarette smoking, caffeine consumption, hormonal status and hyperlipidemia. However, any additional strong risk factors have yet to be identified.

BPH is more common in North America and in Europe than in Asia[3]. The incidence of BPH is also low in vegetarian men[4]. The reason for this finding may be related with diet since Asian and vegetarian men have low-fat and high fibre diets which lower the blood cholesterol level and provide pyto-estrogens that are proposed to be preventive against BPH. It is also notable that the lower incidence of clinical BPH in Asian men increases in immigrant generations after they have started to live in North America.[4]. This phenomenon is thought to be due to a high fat diet, since in another study it was shown that there is a relation between a high fat diet and BPH[5].

There are also conflicting results concerning the effect of cigarette smoking and alcohol consumption on BPH. Although cigarette smoking and moderate alcohol consumption was found to be protective against BPH, some studies showed

that these extrinsic factors had no effect on BPH[6,7]. The aim of our study was to evaluate the relation between hypercholesterolemia, cigarette smoking, alcohol consumption and clinical BPH.

METHODS

Between 1997 and 2000 a total of 142 patients over 45 years of age admitted to our outpatient clinic with LUTS were included in this prospective study. All patients underwent routine urological assessment including history, physical examination, urine analysis and cultures, and serum PSA levels. Patients with suspected prostate cancer after digital rectal examination and/or a PSA> 4 ng/ml were sent to prostate biopsy. Patients with urinary tract infections and/or other significant urological conditions such as, urolithiasis, prostate or bladder cancer were excluded from the study. The IPSS was administered to all patients by the primary physician and histories of cigarette smoking and alcohol consumption were noted. We defined clinical BPH as patients who have an IPSS >7 with an enlarged prostate detected in digital rectal examination and found to have a maximum flow rate (Q max) <10 ml/sec in uroflowmetric studies. Smokers were defined as the patients who regularly smoke one or more cigarettes per day. Alcohol consumers were defined as patients who drank one or more glasses of alcohol more than 2 days per week. On the day of examination, fasting blood samples were collected for serum cholesterol and PSA measurements and then, all patients underwent uroflowmetric studies. The statistical analysis was performed with unpaired student t-test, Chi square test or ANOVA test where appropriate.

RESULTS

The mean age of the whole study group was 67.3 years (45-89 years) and the mean PSA value was 2.94 ng/ml (0.1-15.1 ng/ml). Patient's IPSS ranged between 2-35 (mean: 19.3), Q max between 2-28 ml/sec (mean 9.4 ml/sec) and total cholesterol 82-461 mg/dl (mean: 226 mg/dl). Overall, 54 (38%) and 88 (62%) of the patients were smokers and non-smokers, respectively, whereas only 12 (8.4%) patients were alcohol consumers as defined previously. In the whole study group, 97 (68.3%) patients were found to have clinical BPH whereas 45 (31.7%) patients did not. The mean age of the patients with and without clinical BPH was 67.3 (50-78 years) and 66.9 (45-89) years, respectively. So, both groups were identical in terms of the age of the patients. As illustrated in Table I, the severity of the symptoms increased with the increasing age (student's t test, $p=0.021$), but there was no statistically significant relation between the age and Q max value of the patients (student's t test, $p>0.05$).

However, when patients with clinical BPH were considered we only found a statistically significant difference between patients <50 and >50 years of age in terms of IPSS (student's t test, $p<0.01$) whereas there was no significant difference in other age groups in terms of IPSS and there was no significant difference in terms of Q max values in all age groups (student's t test, $p>0.05$) (Table II).

The mean serum cholesterol level of the patients who did not have clinical BPH was 224 mg/dl and in comparison similar to 226 mg/dl found in patients with clinical BPH. (ANOVA, $p>0.05$). We grouped the patients according to serum total cholesterol level into 3 groups: In group 1, there were patients with normal total cholesterol level (<200mg/dl), in group 2, there were patients with mild hipercholesterolemia (200mg/dl-250mg/dl) and in group 3 there were patients with moderate-severe hipercholesterolemia (>250mg/dl). There was no statistically significant difference between the 3 groups in terms of IPSS, Qmax values and the ratios of the clinically BPH patients, (ANOVA, $p>0.05$) (Table III).

When patients with clinical BPH were analysed in terms of smoking we found that 65% (13/20) patients in the age range between 40 and 59 years were smokers versus 27% (21/77) of patients aged 60 and older ($p<0.05$) whereas for patients without clinical BPH

In patients with clinical BPH, 34 (35.1%) patients were smokers whereas 63 (64.9%) patients were non-smoker. In contrary, in patients without clinical BPH, the majority (n=25, 55.6%) of the patients were smokers versus 20 patients (44.4 %) who were non-smokers. There was a statistically significant difference between patients with and without clinical BPH in terms of the incidence of smoking (chi square, $p=0.047$) (Table IV). The ratio of alcohol consuming patients was more than twice as high in the presence of clinical BPH when compared to patients without clinical BPH (6.2 % and 13.3% patients with and without clinical BPH, respectively (chi square, $p=0.027$) (Table IV). We also compared the relation between smoking and alcohol consumption according to the age groups of the patients.(Table V)

As shown in table IV, the ratio of patients with a serum PSA level>4 ng/ml was similar in two groups of patients with and without clinical BPH (23.8% versus 15.6%, respectively, student t test p>0.05). Likewise, there was no statistically significant difference between patients with and without clinical BPH patients in terms of mean PSA values (2.91ng/ml versus 2.79ng/ml student t test p>0.05).

Table I: The relation between the age groups and clinical BPH, IPSS, Q max value of the whole study group.

Age of pts.(years)	40-49	50-59	60-69	70-79	>80
Mean IPSS ψ	17.6	18.6	19.0	19.6	20.3
Mean Q max ψψ	10.1	9.1	9.8	8.9	10.1
% clin BPH (n)	40 (2)	72 (18)	62.8 (27)	71.7 (38)	75 (12)
Number of pts (%)	5 (3.5)	25(17.6)	43 (30.3)	53(37.3)	16(11.3)

ψ p<0.05 Statistically significant relation between symptom severity and age
ψψ p>0.05 No statistically significant relation between Q max and age

Table II: The relation between the age groups, IPSS and Q max of the patients with clinical BPH

Age of pts.(years)	40-49	50-59	60-69	70-79	>80
Mean IPSS ^	17.5	21.1	21.4	21.6	21.1
Mean Q max ^^	7	6.6	6.7	6.7	7.5
Number of pts (%)	2 (2)	18(18.6)	27 (27.8)	38(39.2)	12(12.4)

^ p<0.05. Statistically significant relation between mean IPSS and age of patients with clinical BPH only in the subgroup <50 and >50 years of age.
^^ p>0.05 No statistically significant relation between age and mean Q max values in patients with clinical BPH and

Table III: Mean age, Q max and IPSS levels of the study population grouped according to cholesterol levels.

	<200mg/dl		200-250 mg/dl		>250 mg/dl	
	Clin BPH (+)	Clin BPH(-)	Clin BPH (+)	Clin BPH(-)	Clin BPH (+)	Clin BPH(-)
Mean age	67.7	66	68.4	65.5	67.8	67
Mean Q max	7.3	13.3	6.7	15.5	6.5	15.6
Mean IPSS	20.5	13.3	20.8	14.3	22.9	16
Number of pts (%)	28 (19.7)	11(7.7)	33(23.2)	23(16.3)	36(25.4)	11(7.7)

p>0.05. No statistically significant relation between hypercholesterolemia and clinical BPH.

Table IV: The relation between the cigarette smoking, alcohol intake and the presence of clinical BPH.

	Clinical BPH (+)	Clinical BPH (-)
Age (years)	67.3	66.9
Smoker (%) *	34 (35.1)	25 (55.6)
Non-smoker (%)	63 (64.9)	20 (44.4)
Alcohol intake (+) (%) **	6 (6.2)	6 (13.3)
Alcohol intake (-) (%)	91 (93.8)	39 (86.7)
PSA>4ng/ml (%) ***	23 (23.8)	7(15.6)
Mean PSA (ng/ml)	2.91	2.79
Total	97	45

* p< 0.05. Statistically significant relation between smoking and clinical BPH.
** p< 0.05. Statistically significant relation between alcohol intake and clinical BPH.
*** p> 0.05 No statistically significant relation between PSA value and clinical BPH.

Table V: The relation between cigarette smoking and alcohol intake and the presence of clinical BPH according

	40-49 years		50-59 years		60-69 years		70-79 years		>80 years	
	Clin BPH (+)	Clin BPH (-)	Clin BPH (+)	Clin BPH (-)	Clin BPH (+)	Clin BPH (-)	Clin BPH (+)	Clin BPH (-)	Clin BPH (+)	Clin BPH (-)
Cigarette(+)	2	2	11	3	6	9	13	8	2	3
Cigarette(-)	0	1	7	4	21	7	25	7	10	1
Alcohol (+)	0	1	1	1	2	2	3	2	0	0
Alcohol (-)	2	3	17	6	25	14	35	13	12	4

DISCUSSION

BPH is a common cause of morbidity in elderly patients and may be defined as a biological response of prostate to aging. The direct relation between BPH and aging was documented in different series [2,8]. The present study has also revealed a direct relation between age and the incidence of clinical BPH. Thus, the aging process is one of the most important risk factors for BPH. Another well-known risk factor for BPH is the presence of androgens in the circulation. It has been illustrated that BPH does not occur in men who were castrated before puberty and is very rare in men who were castrated before 40 years[2] of age.

Therefore, it is logical to investigate the potential role of many other extrinsic or intrinsic risk factors that may cause abnormality in hormonal status such as cigarette smoking, alcohol consumption, obesity, hypercholesterolemia, physical activity. For example, one of the factors that affect the hormonal status is cigarette smoking. Field et al, demonstrated that cigarette smoking increases the dehydrotestosterone level which stimulates the prostate gland and proposed that this may increase the risk of BPH [9]. But, Matzkin et al, reported no difference in prostate volume among smoker and non-smoker patients [6]. On the other hand, some epidemiological studies have found evidence of a lower risk of BPH in cigarette smokers [2,6,7]. Meigs et al followed 1709 men aged between 40-70 years for 9 years and observed that men who smoked had %50 less clinical BPH during the follow-up period [2]. Although Seitter et al found no relation between smoking and BPH [10,] there is growing evidence in the literature for a weak protective effect of cigarette smoking in the occurrence of BPH. In our study, we also found a statistically significant protective effect of cigarette smoking on clinical BPH (p=0.047). This protective effect can be related with the hormonal effects of cigarette smoking or another possible mechanism to explain the protective effect of cigarette smoking in developing clinical BPH may be the nicotinergic effect[7].

Another risk factor evaluated in this study was alcohol consumption. Gordon et al reported that high levels of alcohol consumption cause a decrease production and increase the metabolism of testosterone [11]. Morrison proposed that daily beer intake lowered the risk of clinical BPH and in this study; the relative risk of clinical BPH in alcohol consumers was calculated as 0.61[8]. In another study, Gass et al evaluated a total of 882 men aged between 65-80 years and reported that patients who had regular alcohol intake had % 20 less clinical BPH [12]. These results were similar to our study in that we also found a statistically significant protective effect of alcohol consumption against clinical BPH (p=0.041).

It is an interesting finding that BPH incidence is lower in Asian countries than in Western countries whereas Asian immigrants in the United States have the same incidence of clinical BPH as their white American counterparts[4]. Dietary factors seem to explain this phenomenon since Asian people consume more low-fat, high-fiber diets than Western people. In different series, it was shown that high energy and animal product diets increase the risk of BPH while fruit and vegetable based diets have a protective effect against BPH[13]. Lagiou et al dictated that there is a positive association of BPH risk with butter, margarine and seed oils which can increase serum cholesterol levels[13]. It was shown that high fat diet causes an elevation at plasma testosterone level and might be associated with BPH[5]. In a prospective follow-up study, Meigs et al reported a double risk of BPH in patients with coronary heart disease[2]. So, hypercholesterolemia which can be seen in patients who consume high animal

product diet and have coronary heart disease is thought to be a risk factor for BPH. Kitagawa et al showed a correlation between serum fat content and prostatic growth so they suggest that there may be an association between BPH and abnormal lipid metabolism[14]. Hammarsten et al examined 158 patients with BPH and found a statistically significant relation between BPH and low HDL/cholesterol ratio[15]. Indeed we could not find a statistically significant relation between total cholesterol level and clinical BPH ($p>0.05$).

In our study, we found that cigarette smoking and alcohol consumption appear to have significant protective effects against clinical BPH. The pathophysiological mechanism behind this finding remains to be clarified by further studies. The present study did not reveal a significant relation between total cholesterol or PSA levels and the presence of clinical BPH. However, studies with larger population samples are needed to further explore this issue.

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