Smoking and Lower Urinary Tract Symptoms

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Purpose: Pharmacologic effects of nicotine are multifaceted and complicated. Despite numerous studies, the effect of smoking on lower urinary tract functions, have not been yet studied in detail. In this study, we aimed to investigate the effects of smoking addiction on lower urinary tract and sexual functions on the basis of respiratory functions.

Materials and Methods: A total of 186 male patients who have been evaluated between May 2014 and January 2015 were recruited in this study. Smoking history, respiratory symptoms, respiratory function tests, uroflowmetry parameters relating to lower urinary tract symptoms (LUTS), prostate volume, post-voiding residual urine volume and sexual functions of patients have been retrospectively investigated.

Results: We determined that as the mean number of cigarettes smoked daily increases, post-void residual urine volume and International Prostate Symptom Score (IPSS) also increase. Moreover in accordance with this finding, mean urinary flow rates and quality of life scores were statistically significantly decreased. In smoking addicts who have high mean package/year, post-void residual urine volume and IPSS levels were increased but proportionately maximum urinary flow rate and average urinary flow rate plus quality of life scores were found to be statistically significantly decreased. In patients with forced expiratory volume in first second:forced vital capacity (FEV1/FVC) ratio less than 80%, mean urinary flow rates were found to be statistically significantly low. Also, we determined that in smoking addicts who have high mean package/year, erectile functions were statistically significantly impaired.

Conclusion: We showed negative impacts of smoking addiction on LUTS, patient's quality of life, and sexual functions.

Keywords: risk factors; smoking; adverse effects; lower urinary tract symptoms; etiology; urinary bladder.

INTRODUCTION

World Health Organization (WHO) defines the smoking addiction as 'world's fastest growing and longest epidemic.[1] Cigarette smoking is associated with increased peripheral vascular disease and erectile dysfunction (ED). Smokers have increased risk for both pulmonary and cardiac complications.[2] Pharmacologic effects of nicotine are multifactorial and complicated. Nicotine might induce a contraction through an interaction with nicotinic receptors located on the terminal nerves of, possibly, (i) parasympathetic cholinergic, (ii) sympathetic non-adrenergic and (iii) non-sympathetic purinergic nerves in guinea-pig detrusor preparations. In addition a portion of the contraction is due to the purine nucleotide released which may be potentiated by intramural prostaglandin(s). Parasympathetic cholinergic output might be modulated by an unknown excitatory substance released by nicotine from sympathetic nerve.[3] Despite numerous studies, those investigate effects of smoking on different organs and systems, the effect of smoking on lower urinary tract functions, have not been yet studied in detail. Some researchers suggested that the current cigarette smoking was not consistently associated with the lower urinary tract symptoms (LUTS) and the possible association in former smokers warrants further investigation.[4-6] In this study, we aimed to investigate the effects of smoking addiction on lower urinary tract and sexual functions on the basis of spirometry parameters.

Table 1. Characteristics of study patients.

Characteristics	Values*
Age (years)	61.1 ± 8.9 (30-82)
Smoking, no.	
Daily	20.9 ± 9.6 (1-60)
Pack/year	28.6 ± 20.4 (1-120)
Pulmonary function test results, (%)	
FEV1 (mL)	2809 ± 870 (96.9 ± 30.9)
FVC (mL)	3421 ± 986 (95.4 ± 30.5)
FEV1/FVC	86.4 ± 47.3
Uroflowmetry results	
Qmax (mL/s)	20.5 ± 7.8 (7-54)
Qave (mL/s)	10.4 ± 4.5 (3.3-32)
QoL	2.2 ± 1.3 (0-6)
IPSS	15.1 ± 4.9 (1-29)
Serum PSA levels (ng/mL)	1.6 ± 1.4 (0.1-10.3)
PVR, mL	30.2 ± 36.6 (0-212)
Prostate volume (mL)	44.6 ± 19.2 (12-139)
Erectile dysfunction, no. (%)	
Severe	44 (24.2)
Moderate	48 (26.4)
Mild to moderate	29 (15.9)
Mild	23 (12.6)
None	38 (20.9)

Abbreviations: ED, erectile dysfunction; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; IIEF, International Index of Erectile Function; IPSS, International Prostate Symptom Score; PSA: prostate specific antigen; PVR, post voiding residual urine volume; QoL, quality of life.

* Data are presented as mean ± SD (min-max).

MATERIALS AND METHODS

Study Population

A total of 186 male patients who have been admitted to Samsun Training and Research Hospital and Samsun Gazi State Hospital between May 2014 and January 2015 were recruited in this study. Data regarding smoking history, respiratory symptoms, respiratory function tests, and uroflowmetry parameters relating to LUTS, prostate volume, post-void residual urine volume and sexual function of patients were gathered from the medical records. Urine analysis has also been performed for excluding bladder cancer. Smoking history of patients were evaluated as pack/year and stick per day. In pack / year group, patients were categorized into 2 subgroups as low smoking group (smoked less than 28.6 pack / year) and high smoking group (smoked more than 28.6 pack / year). Patients were also classified as light smoker (< 20.9 daily cigarettes) and heavy smoker (> 20.9 daily cigarettes). The study was performed in accordance with the ethical principles in the Good Clinical Practice guidelines, in addition to applicable local regulatory requirements and the study protocol was approved by local ethics review boards. All the patients read the patient information form about the study procedure and written informed consents were obtained.

Evaluations

Spirometry was performed for evaluation of respiratory functions. International Prostate Symptom Score (IPSS) and International Index of Erectile Functions (IIEF) questionnaires were used for evaluation of LUTS and erectile function, respectively. Average urinary flow rate (Qave), maximum urinary flow rate (Qmax) and urination time were measured using uroflowmetry. Prostate volume and post-voiding residual urine vol-

Table 2. The relationship between daily cigarette consumption with QoL, uroflowmetry and urological parameters.

Characteristics	Low Group (Daily Cigarette)	High Group (Daily Cigarette)	P Value*
QoL	2.7 ± 1.6	2.1 ± 1.2	.01
IPSS	12.8 ± 4.8	15.7 ± 47	.00
Urine volume (mL)	294 ± 184	303 ± 178	.849
Qmax (mL/s)	19.6 ± 7.9	20.7 ± 7.8	.49
Qave (mL/s)	10.7 ± 5.9	10.4 ± 5.2	.04
Voiding time (s)	59.9 ± 12.2	37.3 ± 16	.03
Serum PSA level (ng/mL)	1.57 ± .9	1.7 ± 1.5	.59
PVR (mL)	14.4 ± 27.1	34.4 ± 27.7	.00
Prostate volume (mL)	41.1 ± 22.2	45.5 ± 22.3	.21

Abbreviations: IPSS, International Prostate Symptom Score; PSA, prostate specific antigen; PVR, post voiding residual urine volume; Qave, average urine flow per second; Qmax, maximum urine flow per second; QoL, Quality of life.

* Data are presented as mean ± SD.

Table 3. The relationship between pack/year smoking status with QoL, uroflowmetry and urological parameters.

Characteristics	Low Group (pack/year)	High Group (pack/year)	P Value*
QoL	1.9 ± 1.2	2.6 ± 1.3	.00
IPSS	13.9 ± 4.9	16.7 ± 4.5	.00
Flowvolume (mL)	329 ± 206	274 ± 149	.24
Qmax (mL/s)	22.3 ± 8.1	18.2 ± 6.7	.00
Qave (mL/s)	11.3 ± 4.7	9.3 ± 4	.00
Voiding time (s)	44.5 ± 71.4	37.6 ± 16.8	.42
Serum PSA level (ng/mL)	1.4 ± 1.2.	1.9 ± 1.6	.04
PVR (mL)	22.3 ± 29.5	40.7 ± 42.3	.00
Prostate volume (mL)	42.6 ± 16.4	47.2 ± 22.3	.11

Abbreviations: IPSS, International Prostate Symptom Score; PSA, prostate specific antigen; PVR, post voiding residual urine volume; Qave, average urine flow per second; Qmax, maximum urine flow per second; QoL, Quality of life.
* Data are presented as mean ± SD.

ume (PVR) were calculated tridimentionally by using suprapubic ultrasound.

Statistical Analysis

Results were analyzed using the Statistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 17.0. Results are presented as mean ± standard deviation and $P < .05$ was considered as statistically significant. Descriptive data were compared using the unpaired Student t-test and Pearson chi-square test.

RESULTS

One hundred and eighty-six male patients were enrolled in to the study. The characteristics of patients are presented in **Table 1**. Mean age of patients was 61.1 ± 8.9 years. Mean duration of smoking addiction was 28.6 ± 20.4 years; mean number of cigarettes smoked were 20.9 ± 9.6 daily. Results of respiratory test functions for forced expiratory volume in first second (FEV1)/forced vital capacity (FVC) (FEV1/FVC) ratio were 2809 ± 870 mL (96.9% ± 30.9%), 3421 ± 986 mL (95.4% ± 30.5%), and 86.4% ± 47.3%, respectively. Mean IPSS was 15.1 ± 4.9; Quality of Life (QoL) score was 2.28 ± 1.3. Number of patients according to their IIEF score for severe, moderate, mild to moderate, and mild ED and without ED were 44 (24.2%), 48 (26.4%), 29 (15.9%) and 38 (20.9%), respectively. Mean PVR was 30.2 ± 36.6 mL, and mean serum prostate specific antigen (PSA) level was 1.6 ± 1.4 ng/mL. Regarding to uroflowmetry parameters, mean Qmax was 20.5 ± 7.8 mL/s and mean Qave was 10.4 ± 4.5 mL/s. Evaluation of relationship between smoking addiction level with QoL and uroflowmetry parameters demonstrated that PVR and IPSS were statistically significantly high ($P = .00$) but Qave ($P = .04$) and QoL ($P = .01$) were statis-

Table 4. The relationship between pulmonary function test results with QoL, uroflowmetry and urological parameters.

Characteristics	FEV1/FVC < 80%	FEV1/FVC ≥ 80%	P Value*
QoL	2.3 ± 1.2	2 ± 1.2	.28
IPSS	15.5 ± 4.4	15 ± 4.7	.49
Flowvolume (mL)	277.9 ± 222.1	306.8 ± 175.3	.64
Qmax (mL/s)	19.3 ± 7.7	21.8 ± 7.8	.08
Qave (mL/s)	9.6 ± 4.3	11.3 ± 4.7	.03
Voiding time (s)	39.5 ± 19.5	35.9 ± 15.2	.20
Serum PSA level (ng/mL)	1.9 ± 1.6	1.5 ± 1.4	.16
PVR (mL)	28.4 ± 34.4	31 ± 36.6	.69
Prostate volume (mL)	48.9 ± 22.9	41.9 ± 16.1	.03

Abbreviations: IPSS, International Prostate Symptom Score; PSA, prostate specific antigen; PVR, post voiding residual urine volume; Qave, average urine flow per second; Qmax, maximum urine flow per second; QoL, Quality of life; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.
* Data are presented as mean ± SD.

Table 5. The relationship between erectile function with daily cigarette consumption, pack/year smoking status and pulmonary function test results.

Characteristics	Severe ED	Moderate ED	Mild to Moderate ED	Mild ED	No ED	P Value
Daily Smoke, no. (%)						
Low group	6 (15.8)	9 (23.7)	5 (13.1)	4 (10.5)	14 (36.8)	.11
High group	37 (26.2)	38 (26.9)	23 (16.3)	19 (13.4)	248 (17.0)	
Pack/year,no. (%)						
Low group	15 (14.7)	29 (28.4)	16 (15.6)	17 (16.6)	25 (24.5)	.01
High group	28 (36.3)	18 (23.3)	12 (15.5)	6 (7.7)	13 (16.8)	
FEV1/FVC, no. (%)						
< 80%	15 (33.3)	11 (24.4)	7 (15.5)	7 (15.5)	5 (11.1)	.38
≥ 80%	21 (20.1)	26 (25)	19 (18.2)	16 (15.3)	22 (21.1)	

Abbreviations: ED, erectile dysfunction; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

tically significantly low in heavy smoker group (**Table 2**). When correlation between smoking addiction level (mean smoked package/year) and QoL with uroflowmetry parameters were evaluated, QoL and Qmax values were found to be statistically significantly low ($P = .00$), in contrast PVR and IPSS values were statistically significantly high ($P = .00$) in heavy smoker group (**Table 3**). Qave values of patients with FEV1/FVC ratio less than 80%, were statistically significantly low ($P = .04$) (**Table 4**). When correlation between erectile functions and mean number of cigarettes smoked daily were compared with those who have FEV1/FVC ratio less than 80%, erectile function was statistically significantly lower ($P = .001$) in heavy smoker group (**Table 5**).

DISCUSSION

Because studies comparing the correlation between smoking addiction level, respiratory function test parameters and LUTS are lacking, the discussion part of this article is limited. When we investigated the correlations between smoking addiction levels and QoL with uroflowmetry parameters, we determined that as the mean number of cigarettes smoked daily increases, PVR and IPSS values increase. Also in accordance with this finding, mean urinary flow rates and QoL scores were statistically significantly decreased. In smoking addicts who have high mean package/year ratio, PVR and IPSS levels and proportionately Qmax and Qave plus QoL scores were found to be statistically significantly decreased. In a study with similar setting to ours, it has been reported that in 40-75 years age group, inpatients with ≥ 35 cigarettes smoked daily, development of benign prostate hyperplasia is statistically significantly higher.[7] The main reason attributed to this increase was elevated serum testosterone levels in heavy smokers.

In patients with FEV1/FVC ratio less than 80%, mean urinary flow rates were found to be statistically significantly low. We reported a parallel reduction in air flow rate and mean urinary flow rate. We hypothesize that stimulating and inhibitory effects of nicotine might be the cause of this reduction. In a study that analyzed the effects of nicotine on detrusor muscles in rats, the authors have shown stimulating effects of nicotine onmuscarinic (M_1) receptors and inhibitory effects on M_2 receptors at synaptic junctions.[7] In addition, we determined that in smoking addicts who have high mean package/year, erectile function was statistically significantly impaired. Numerous studies have investigated the association between cigarette smoking and ED, and it has been reported that smoking nearly double the risk of moderate or severe ED at a ten years follow up.[8] At another study in men aged 30-79 years old, it has been shown that, risk of ED has increased 2.3-fold in men with history of 20 package/year of smoking.[9] In concordance with our study, it has been reported that there is a statistically significant correlation between cigarette smoking and ED development, and this correlation becomes stronger as the mean number of cigarettes smoked daily increases.[10]

CONCLUSIONS

In conclusion, as with other studies in which the effects of cigarette smoking on LUTS have been investigated, we also showed negative impacts of smoking addiction on LUTS, patient's QoL and sexual functions. In this study, interestingly we would like to express that we determined a statistically significant relationship between spirometry and uroflowmetry parameters in smoking addicts.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. World Health Organization. A WHO / The Union monograph on TB and tobacco control: joining forces to control two related global epidemics [WHO/HTM/TB/2007.390] Geneva: World Health Organization; 2007.

2. Kendirci M, Nowfar S, Hellstrom WJ. The impact of vascular risk factors on erectile function. Drugs Today. 2005;41:65-74.

3. Hisayama T, Shinkai M, Takayanagi I, Toyoda T. Mechanism of action of nicotine in isolated urinary bladder of guinea-pig. Br J Phar. 1988;95:465-72.

4. Rohrmann S, Crespo CJ, Weber JR, Smit E, Giovannucci E, Platz EA. Association of cigarette smoking, alcohol consumption and physical activity with lower urinary tract symptoms in older American men: findings from the third National Health and Nutrition Examination Survey. BJU Int. 2005;96:77-82.

5. Mehraban D, Naderi GH, Yahyazadeh SR, Amirchaghmaghi M. Sexual dysfunction in aging men with lower urinary tract symptoms. Urol J. 2008;5:260-4.

6. Akil IO, Ozmen D, Cetinkaya AC. Prevalence of Urinary incontinence and lower urinary tract symptoms in school-age children. Urol J. 2014;11:1602-8.

7. Onoue S, Yamamoto N, Seto Y, Yamada S. Pharmacokinetic study of nicotine and its metabolite cotinine to clarify possible association between smoking and voiding dysfunction in rats using UPLC/ESI-MS. Drug Metab Pharmacokinet. 2011;26:416-22.

8. Somogyi GT, de Groat WC. Evidence for inhibitory nicotinic and facilitatory muscarinic receptors in cholinergic nerve terminals of the rat urinary bladder. J Auton Nerv Syst. 1992;37:89-97.

9. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and physiological correlates: results of the Massachusetts male ageing study. J Urol. 1994; 151:54-61

10. Kupelian V, Link CL, McKinlay JB. Association between smoking, passive smoking and erectile dysfunction: Results from Boston Area Community Health (BACH) Survey. Eur Urol. 2007;52:416-22.