Urolithiasis and smoking

Mehmet Rami Helvaci (1)
Orhan Ayyildiz (1)
Mustafa Cem Algin (2)
Yusuf Aydin (1)
Abdulrazak Abyad (3)
Lesley Pocock (4)

(1) Specialist of Internal Medicine, MD
(2) Specialist of General Surgery, MD
(3) Middle-East Academy for Medicine of Aging, MD
(4) medi-WORLD International

Corresponding author:
Mehmet Rami Helvaci, MD
07400, ALANYA, Turkey
Phone: 00-90-506-4708759
Email: mramihelvaci@hotmail.com

Received: August, 2018; Accepted: October 2018; Published: November 1, 2018
Citation: Helvaci M. R. et al. Urolithiasis and smoking. World Family Medicine. 2018; 16(10): 9-13.
DOI: 10.5742MEWFM.2018.93507

Abstract

Background: Urolithiasis and smoking are common pathologies in society. We tried to understand whether or not there is a significant relationship in between.

Methods: Consecutive patients with urolithiasis were collected into the first, and age and sex-matched controls were collected into the second, groups.

Results: Fifty-one patients with urolithiasis and 66 controls were studied, in total. When we looked at the urolithiasis patients, 56.8% of them (29 patients) were female with a mean age of 47.2 ± 12.7 (22-70) years. Interestingly, although the lower prevalence of smoking in females in the population, the prevalence of smoking was significantly higher in the urolithiasis group, here (45.0% versus 30.3%, $p<0.05$). On the other hand, there was non-significant difference according to the mean body weight between the groups (77.3 versus 76.4 kg, $p>0.05$).

Conclusion: Several toxic substances found in cigarette smoke get into the circulation by means of the respiratory tract, and cause a low-grade vascular endothelial inflammation all over the body including the gastrointestinal and urinary tracts. The low-grade vascular endothelial inflammation eventually terminates with an accelerated atherosclerosis and relative immunosuppression. The prolonged vascular endothelial inflammation, accelerated atherosclerosis, relative immunosuppression, and sympathetic nervous system activation may induce motility, absorption, and infectious problems in the gastrointestinal and urinary tracts; those may terminate with urolithiasis in smokers.

Key words: Urolithiasis, smoking, chronic endothelial inflammation, accelerated atherosclerosis, early aging

Introduction

Urolithiasis is a common pathology in society, and the lifetime risk of urolithiasis is 12-15% for a white man and 5-6% for a white woman with an up to 50% of lifetime recurrence ratio (1). We detected the prevalence of urolithiasis as 13.7% in women and 15.2% in men among the patients applying to internal medicine polyclinic (2). Approximately 80% of the stones are composed of calcium oxalate (CaOx) and calcium phosphate, and CaOx is the main constituent of them. Beside that, 10% of struvite (magnesium ammonium phosphate produced during infection with bacteria that possess the enzyme, urease) and 9% of uric acid stones are seen. The majority of the CaOx stone formers do not suffer from any systemic disease (3), and the minority of the patients have primary hyperparathyroidism or hyperoxaluria secondary to bowel disease (enteric hyperoxaluria) or genetic disorders of oxalate metabolism (primary hyperoxaluria). Although the relatively higher prevalence of urolithiasis in society, there is not any known exact underlying cause of it. There are just some reported systemic illnesses associated with an increased risk of urolithiasis in the literature. For example, patients with chronic diarrheal illnesses such as ulcerative colitis and Crohn's disease can develop enteric hyperoxaluria; those result with an increased risk of renal stones (4). Oxalate may be the primary problem in such patients, since excess oxalate is absorbed through the inflamed bowel wall. Similarly, a low-grade inflammation induced increased absorption of oxalate may be the primary mechanism of urolithiasis in irritable bowel syndrome (IBS), since it was shown in the above study that there is a significant relationship between urolithiasis and IBS (2). Although indirectly, increased oxalate absorption induced urolithiasis has also been shown previously (5, 6). On the other hand, smoking is a well-known cause of chronic vascular endothelial inflammation all over the body. We tried to understand whether or not there is a significant relationship between urolithiasis and smoking in the present study.

Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Mustafa Kemal University between August 2008 and January 2009. Consecutive patients were taken into the study and patients above the age of 70 years were excluded to avoid debility induced weight loss in elders. Their medical histories including smoking habit were learnt, and current smokers for the last six-months and cases with a history of five pack-years in the past were accepted as smokers. A routine check up procedure including hematologic and biochemical tests, urinalysis, and an abdominal X-ray graphy in supine position was performed, and patients with devastating illnesses including type 1 diabetes mellitus (DM), malignancies, acute or chronic renal failure, cirrhosis, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on body weight. An additional intravenous pyelography was obtained just in suspected cases from urolithiasis at the moment as a result of the urinalysis and abdominal X-ray graphy. So urolithiasis was diagnosed either by medical history or as a result of current laboratory tests. Eventually, cases with urolithiasis were collected into the first, and age and sex-matched controls were collected into the second groups. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

Fifty-one patients with urolithiasis and 66 controls were studied, totally. When we looked at the urolithiasis patients, 56.8% of them (29 patients) were female with a mean age of 47.2 ± 12.7 (22-70) years. Interestingly, although the lower prevalence of smoking in females in the population, the prevalence of smoking was significantly higher in the urolithiasis group, here (45.0% versus 30.3%, $p<0.05$). On the other hand, there was nonsignificant difference according to the weight in between (77.3 versus 76.4 kg, $p>0.05$).

Table 1: Characteristic features of the study cases

Variables	Cases with urolithiasis	*p*-value	Control cases
Number	51		66
Female ratio	56.8% (29)	Ns*	56.0% (37)
Mean age (years)	47.2 ± 12.7 (22-70)	Ns	45.6 ± 13.1 (20-67)
Mean body weight (kg)	77.3 ± 16.5 (45-114)	Ns	76.4 ± 12.2 (50-98)
Prevalence of smoking	***45.0%*** (23)	***<0.05***	***30.3%*** (20)

*Nonsignificant ($p>0.05$)

Discussion

Smoking may be found among one of the most common causes of vasculitis in the world. It is a major risk factor for the development of atherosclerotic endpoints including coronary artery disease (CAD), peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), cirrhosis, chronic renal disease (CRD), stroke, cancers, early aging, and premature death (7, 8). Its atherosclerotic effects are the most obvious in Buerger's disease. It is an obliterative disease characterized by inflammatory changes in small and medium-sized arteries and veins, and it has never been reported in the absence of smoking in the literature. Although there are well-known strong atherosclerotic effects of smoking, some studies reported that smoking in humans and nicotine administration in animals are associated with a decreased body mass index (BMI) (9). Evidence revealed an increased energy expenditure during smoking both on rest and light physical activity (10), and nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (11). According to an animal study, nicotine may lengthen intermeal time and simultaneously decreases amount of meal eaten (12). Additionally, BMI seems to be the highest in former, the lowest in current and medium in never smokers (13). Smoking may be associated with postcessation weight gain but evidence suggests that risk of weight gaining is the highest during the first year after quitting and declines over the years (14). Similarly, although the CAD was detected with similar prevalence in both genders in a previous study (15), prevalence of smoking and COPD were higher in males with CAD against the higher prevalence of BMI, white coat hypertension (WCH), low density lipoprotein cholesterol, triglyceride, hypertension (HT), and DM in females with CAD as the other atherosclerotic risk factors. This result may indicate both the strong atherosclerotic and weight decreasing roles of smoking (16). Similarly, the incidence of a myocardial infarction is increased sixfold in women and threefold in men who smoke at least 20 cigarettes per day compared to the never smoked cases (17). In other words, smoking is more dangerous for women regarding the atherosclerotic endpoints probably due to the higher BMI and its consequences in them. Parallel to the above results, the proportion of smokers is consistently higher in men in the literature (8). So smoking is probably a powerful atherosclerotic risk factor with some suppressor effects on appetite. Smoking-induced weight loss may be related with the smoking-induced vascular endothelial inflammation all over the body, since loss of appetite is one of the major symptoms of inflammation in the body. Physicians can even understand healing of their patients from their returning appetite. Several toxic substances found in cigarette smoke get into the circulation by means of the respiratory tract, and cause a low-grade vascular endothelial inflammation all over the body until clearance from the circulation. But due to the repeated smoking habit of the individuals, the clearance process never terminates. So the patients become ill with loss of appetite, permanently. In another explanation, smoking-induced weight loss is an indicator of being ill instead of being healthy (11-13). After smoking cessation, normal appetite comes back with a prominent weight gain in the patients but the returned weights are their physiological or 'actual' weights. On the other hand, smoking as a pleasure in life may also show the weakness of volition to control eating so it comes with additional weight excess and its consequences. Similarly, prevalence of HT, DM, and smoking were the highest in the highest triglyceride having group as another significant component of the metabolic syndrome (18).

There may be several mechanisms increasing the incidence of urolithiasis in smokers. First of all, smoking may cause a chronic low-grade inflammation in the gastrointestinal tract epithelium by disturbing the normal balance between intestinal flora and circulatory defence mechanisms. The low-grade inflammation induced increased absorption of oxalate, as in chronic diarrheal illnesses, may be the development mechanism of urolithiasis in smokers. Smoking induced sympathetic nervous system activation may cause motility disorder that may aggravate this instability, since diarrheal losses induced lower urinary pH and citrate levels increase urinary CaOx and uric acid supersaturations since citrate may inhibit calcium crystallization by binding to it. Secondly, accelerated atherosclerosis may disturb both gastrointestinal and urinary tracts' epithelial functions for absorption and excretions of elements, so facilitating directly a stone or just a nidus formation for stone. Even the accelerated atherosclerosis induced electrolyte imbalance in urine may facilitate urolithiasis. Thirdly, immunosuppression secondary to accelerated atherosclerosis induced urinary tract infections may cause urolithiasis since some types of bacteria can provoke urinary supersaturation and modify the environment thus leading to formation of crystal deposits that may be a factor promoting urolithiasis. In fact, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced during infection with bacteria that possess the enzyme, urease. Lastly, accelerated atherosclerosis induced glomerular dysfunctions may alter urinary contents, facilitating urolithiasis. So there may be hundreds of mechanisms with variable priorities for urolithiasis in smokers, thus the result of the study should not be surprising.

It is a well known entity that excess weight causes a high cost on physical health even in early decades. Persons with excess weight have a higher prevalence of elevated blood pressure than lean persons, and well-known complications of HT are left ventricular hypertrophy, CAD, heart failure, chronic renal failure, and stroke (19, 20). Similarly, atherogenic dyslipidemia is commonly seen in cases with excess weight, and it is characterized by increased levels of triglycerides and/or low density lipoprotein cholesterol, or a decreased level of high density lipoprotein cholesterol in serum (19). On the other hand, excess weight is accompanied by a large number of coagulation and fibrinolytic abnormalities suggesting that it induces a prothrombotic and proinflammatory state (21). The low-grade chronic vascular endothelial inflammation is characterized by lipid-induced injury that initiates invasion of macrophages followed by proliferation of smooth muscle

cells, endothelial dysfunction, and increased atherogenicity (22, 23). As a supporting evidence of the role of inflammation in atherosclerosis, elevations of serum C-reactive protein (CRP) carry predictive power for the development of major cardiovascular events (24). In particular, excess weight is considered as a strong factor for controlling of circulating CRP concentrations because adipose tissue is involved in the regulation of cytokines (25), so individuals with excess weight have elevated levels of CRP (26). Furthermore, excess weight is highly correlated with dietary intake of increased calories and fat, both of which have been linked to several types of cancer including breast, colon, and prostate (27). Although excess weight is associated with an increased risk of all-cause mortality (28), there was no significant difference according to the mean body weight between the urolithiasis patients and control cases in the present study.

Due to the prolonged survival of human beings, systemic atherosclerosis probably will be the main health problem all over the world in this century, and its associations with sedentary life style, excess weight, smoking, and alcohol are researched under the title of metabolic syndrome in the literature, extensively (29, 30). The syndrome is characterized by a low-grade inflammatory process on vascular endothelium initiated in early years of life (31). The syndrome includes sedentary life style, overweight, WCH, impaired fasting glucose, impaired glucose tolerance, hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, smoking, alcohol, and chronic infections and inflammation for the development of irreversible consequences including obesity, HT, DM, COPD, cirrhosis, CRD, PAD, CAD, stroke, early aging, cancers, and premature death (32, 33). In another perspective, the metabolic syndrome may be the most significant disease of human life decreasing its quality and duration at the moment. The syndrome has become increasingly common all over the world, for example 50 million people in the United States are affected (34). Metabolic syndrome can be slowed down with appropriate non-pharmaceutical approaches including lifestyle changes, diet, and exercise in early years of life (35). If not, the syndrome induced accelerated atherosclerotic process all over the body may be the leading cause of early aging and premature death for both genders. For example, CAD and cancers are the leading causes of death in developed countries. Similarly, although the well-known mutagenic effects of smoking, its role in cancers may also be related to the systemic atherosclerotic process that immune cells can not eradicate cancer cells, effectively, due to the insufficient blood supply of the tissues (7).

As a conclusion, several toxic substances found in cigarette smoke get into the circulation by means of the respiratory tract, and cause a low-grade vascular endothelial inflammation all over the body including the gastrointestinal and urinary tracts. The low-grade vascular endothelial inflammation eventually terminates with an accelerated atherosclerosis and relative immunosuppression. The prolonged vascular endothelial inflammation, accelerated atherosclerosis, relative immunosuppression, and sympathetic nervous system activation may induce motility, absorption, and infectious problems in the gastrointestinal and urinary tracts which may terminate with urolithiasis in smokers.

References

1. Bihl G, Meyers A. Recurrent renal stone disease-advances in pathogenesis and clinical management. Lancet 2001; 358(9282): 651–656.
2. Helvaci MR, Kabay S, Gulcan E. A physiologic events' cascade, irritable bowel syndrome, may even terminate with urolithiasis. J Health Sci 2006; 52(4): 478-481.
3. Parks JH, Worcester EM, O'Connor RC, Coe FL. Urine stone risk factors in nephrolithiasis patients with and without bowel disease. Kidney Int 2003; 63(1): 255–265.
4. Worcester EM. Stones from bowel disease. Endocrinol Metab Clin North Am 2002; 31(4): 979–999.
5. Ito H, Kotake T, Masai M. In vitro degradation of oxalic acid by human feces. Int J Urol 1996; 3(3): 207-211.
6. Kodama T, Akakura K, Mikami K, Ito H. Detection and identification of oxalate-degrading bacteria in human feces. Int J Urol 2002; 9(7): 392-397.
7. Helvaci MR, Aydin Y, Gundogdu M. Smoking induced atherosclerosis in cancers. HealthMED 2012; 6(11): 3744-3749.
8. Fodor JG, Tzerovska R, Dorner T, Rieder A. Do we diagnose and treat coronary heart disease differently in men and women? Wien Med Wochenschr 2004; 154(17-18): 423-425.
9. Grunberg NE, Greenwood MR, Collins F, Epstein LH, Hatsukami D, Niaura R, et al. National working conference on smoking and body weight. Task Force 1: Mechanisms relevant to the relations between cigarette smoking and body weight. Health Psychol 1992; 11: 4-9.
10. Walker JF, Collins LC, Rowell PP, Goldsmith LJ, Moffatt RJ, Stamford BA. The effect of smoking on energy expenditure and plasma catecholamine and nicotine levels during light physical activity. Nicotine Tob Res 1999; 1(4): 365-370.
11. Hughes JR, Hatsukami DK. Effects of three doses of transdermal nicotine on post-cessation eating, hunger and weight. J Subst Abuse 1997; 9: 151-159.
12. Miyata G, Meguid MM, Varma M, Fetissov SO, Kim HJ. Nicotine alters the usual reciprocity between meal size and meal number in female rat. Physiol Behav 2001; 74(1-2): 169-176.
13. Laaksonen M, Rahkonen O, Prattala R. Smoking status and relative weight by educational level in Finland, 1978-1995. Prev Med 1998; 27(3): 431-437.
14. Froom P, Melamed S, Benbassat J. Smoking cessation and weight gain. J Fam Pract 1998; 46(6): 460-464.
15. Helvaci MR, Kaya H, Gundogdu M. Gender differences in coronary heart disease in Turkey. Pak J Med Sci 2012; 28(1): 40-44.
16. Helvaci MR, Aydin Y, Gundogdu M. Atherosclerotic effects of smoking and excess weight. J Obes Wt Loss Ther 2012; 2: 7.
17. Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998; 316(7137): 1043-1047.

18. Helvaci MR, Kaya H, Gundogdu M. Association of increased triglyceride levels in metabolic syndrome with coronary artery disease. Pak J Med Sci 2010; 26(3): 667-672.
19. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002; 106(25): 3143-3421.
20. Helvaci MR, Kaya H, Yalcin A, Kuvandik G. Prevalence of white coat hypertension in underweight and overweight subjects. Int Heart J 2007; 48(5): 605-613.
21. De Pergola G, Pannacciulli N. Coagulation and fibrinolysis abnormalities in obesity. J Endocrinol Invest 2002; 25(10): 899-904.
22. Ross R. Atherosclerosis: An inflammatory disease. N Engl J Med 1999; 340(2): 115-126.
23. Ridker PM. High-sensitivity C-reactive protein: Potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation 2001; 103(13): 1813-1818.
24. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA 1998; 279(18): 1477-1482.
25. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol 1999; 19(4): 972-978.
26. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. JAMA 1999; 282(22): 2131-2135.
27. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003; 348(17): 1625-1638.
28. Adams KF, Schatzkin A, Harris TB, Kipnis V, Mouw T, Ballard-Barbash R, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. N Engl J Med 2006; 355(8): 763-778.
29. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005; 365(9468): 1415-1428.
30. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004; 109(3): 433-438.
31. Tonkin AM. The metabolic syndrome(s)? Curr Atheroscler Rep 2004; 6(3): 165-166.
32. Haidar, Soeatmadji DW. Effects of high-carbohydrate and high fat diet on formation of foam cells and expression of TNF-alpha in Rattus novergicus. Acta Med Indones 2007; 39(3): 119-123.
33. Rudijanto A. The role of vascular smooth muscle cells on the pathogenesis of atherosclerosis. Acta Med Indones 2007; 39(2): 86-93.
34. Clark LT, El-Atat F. Metabolic Syndrome in African Americans: implications for preventing coronary heart disease. Clin Cardiol 2007; 30(4): 161-164.
35. Franklin SS, Barboza MG, Pio JR, Wong ND. Blood pressure categories, hypertensive subtypes, and the metabolic syndrome. J Hypertens 2006; 24(10): 2009-2016.