Irritable bowel syndrome and smoking

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Abstract

Background: We tried to understand whether or not there is a significant relationship between irritable bowel syndrome (IBS) and smoking.

Method: IBS is diagnosed according to Rome II criteria in the absence of red flag symptoms.

Results: One hundred and four patients with IBS and 104 controls were studied. Interestingly, 78.8% (82 patients) of IBS patients were female with a mean age of 51.2 ± 9.9 (29-70) years. Prevalence of smoking was significantly higher in cases with IBS (29.8% versus 11.5%, p<0.001). Similarly, prevalences of hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia were higher in cases with IBS but the difference was significant just for hypertriglyceridemia (26.9% versus 16.3%, p<0.01) probably due to the small sample size of the study. On the other hand, mean body mass index (BMI) and prevalences of hypertension (HT) and diabetes mellitus (DM) were all lower in cases with IBS but the difference was significant just for HT (10.5% versus 26.9%, p<0.001) probably due to the small sample size of the study, again.

Conclusion: Although IBS may have a complex mechanism with a higher prevalence in females, smoking may be one of the several causes of IBS by causing a vascular endothelial inflammation all over the body. The disseminated inflammation may be the cause of lower BMI and associated lower prevalences of HT and DM in the IBS cases. On the other hand, higher prevalences of hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia in cases with IBS may actually indicate their roles as acute phase reactants in smokers in the body.

Key words:
Irritable bowel syndrome, smoking, metabolic syndrome, hypertriglyceridemia, dyslipidemia

Please cite this article as: Helvaci M. et al. Irritable bowel syndrome and smoking. World Family Medicine. 2017; 15(10):7-11. DOI 10.5742/MEWFM.2017.93130

Introduction

One of most frequent applications to primary health centers and internal medicine and gastroenterology polyclinics are due to recurrent upper abdominal discomfort (1). Although gastroesophageal reflux disease, esophagitis, duodenal and/or gastric ulcers, erosive gastritis and/or duodenitis, celiac disease, chronic pancreatitis, and malignancies are found among possible causes, irritable bowel syndrome (IBS) and chronic gastritis are probably the most frequently diagnosed diseases, clinically. Flatulence, periods of diarrhea or constipation, repeated toilet visits due to urgent evacuation or early filling sensation, excessive straining, feeling of incomplete evacuation, frequency, urgency, reduced feeling of well-being, and eventually disturbed social life are often reported by IBS patients. Although many patients relate onset of symptoms to intake of food, and often incriminate specific food items, a meaningful dietary role is doubtful in IBS. According to literature, 10-20% of the general population have IBS, and it is more common among females for unexplained reasons (2). Psychological factors seem to precede onset or exacerbation of gut symptoms, and many potentially psychiatric disorders including anxiety, depression, or sleep disorders frequently coexist with IBS (3). For instance, thresholds for sensations of initial filling, evacuation, urgent evacuation, and utmost tolerance recorded via a rectal balloon significantly decreased by focusing the examiners' attention on gastrointestinal stimuli by reading pictures of malignant gastrointestinal disorders in IBS cases (4). So although IBS is described as a physical instead of a psychological disorder according to Rome II guidelines, psychological factors may be crucial for triggering of the physical changes in the body. IBS is actually defined as a brain-gut dysfunction according to the Rome II criteria, and it may have more complex mechanisms affecting various systems of the body with a low-grade inflammatory state (5). For example, it was detected in a previous study that IBS may even terminate with urolithiasis in a significant proportion of patients (6). Similarly, some authors studied the role of inflammation via colonic biopsies in 77 cases with IBS (7). Although 38 patients had normal histology, 31 patients demonstrated microscopic inflammation and eight patients fulfilled criteria for lymphocytic colitis. However, immunohistology revealed increased intraepithelial lymphocytes as well as increased CD3 and CD25 positive cells in lamina propria of the group with "normal" histology those indicate immune activation. These features were more evident in the microscopic inflammation group who additionally revealed increased neutrophils, mast cells, and natural killer cells. All of these immunopathological abnormalities were the most evident in the lymphocytic colitis group who also demonstrated HLA-DR staining in crypts and increased CD8 positive cells in the lamina propria (7). A direct link between the immunologic activation and IBS symptoms was provided by work of some other authors who demonstrated not only an increased incidence of mast cell degranulation in the colon but also a direct correlation between proximity of mast cells to neuronal elements and pain severity in IBS (8). In addition to these findings, there is some evidence for extension of the inflammatory process beyond mucosa. Some authors addressed this issue in ten patients with severe IBS by examining full-thickness jejunal biopsies obtained via laparoscopy (9). They detected a low-grade infiltration of lymphocytes in myenteric plexus of nine patients, four of whom had an associated increase in intraepithelial lymphocytes and six demonstrated evidence of neuronal degeneration. Nine patients had hypertrophy of longitudinal muscles and seven had abnormalities in number and size of interstitial cells of Cajal. The finding of intraepithelial lymphocytosis was consistent with the reports of Chadwick and colleagues in the colon (7) and Wahnschaffe and colleagues in the duodenum (10). On the other hand, smoking is well-known cause of vascular endothelial inflammation all over the body. We tried to understand whether or not there is a significant relationship between IBS and smoking.

Material and methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between March 2006 and February 2007. Consecutive patients with upper abdominal discomfort were included into the study. We did not take patients above the age of 70 years to avoid debility induced weight loss in elders. Their medical histories including smoking habit, hypertension (HT), diabetes mellitus (DM), dyslipidemia, and already used medications were learnt. A routine check up procedure including fasting plasma glucose (FPG), low density lipoprotein cholesterol (LDL-C), triglycerides, high density lipoprotein cholesterol (HDL-C), an abdominal ultrasonography, and a questionnaire for IBS was performed. IBS is diagnosed according to Rome II criteria in the absence of red flag symptoms such as pain and diarrhea that often awakens/interferes with sleep, weight loss, fever, and abnormal physical examination findings. Patients with devastating illnesses including type 1 DM, malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. Current daily smokers at least for the last six months and cases with a history of five pack-years were accepted as smokers. Body mass index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions since there is evidence that heavier individuals systematically underreport their weight (11). Weight in kilograms is divided by height in meters squared (12). Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already using antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 100 and 126 mg/dL, and diagnosis of cases with a 2-hour plasma glucose level of 200 mg/dL or greater is DM (12). Additionally, patients with dyslipidemia were detected, and we used the National Cholesterol Education Program Expert Panel's recommendations for defining dyslipidemic subgroups (12). Dyslipidemia is diagnosed when LDL-C is 160 mg/dL or greater and/or triglyceride is 200 mg/dL or greater and/or HDL-C is lower than 40 mg/dL. Office blood pressure (BP) was checked after 5 minutes of rest in seated position with a mercury sphygmomanometer

on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in normotensives in the office due to the risk of masked HT after a 10-minute education session about proper BP measurement techniques (13). The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of 5 minutes in the seated position before measurement. An additional 24-hour ambulatory blood pressure monitoring (ABP) was not required due to an equal efficacy of the method with HBP measurement to diagnose HT (14). Eventually, HT is defined as a BP of 135/85 mmHg or greater on HBP measurements (13). Eventually, all patients with IBS were put into the first, and age and sex-matched controls were put into the second groups. Mean BMI and prevalence of smoking, HT, DM, hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia were detected in each group and compared in between. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

One hundred and four patients with IBS and 104 controls were included into the study. Interestingly, 78.8% (82 patients) of the IBS patients were female with a mean age of 51.2 ± 9.9 (29-70) years (Table 1). Prevalence of smoking was significantly higher in cases with IBS (29.8% versus 11.5%, p<0.001). Similarly, prevalence of hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia were all higher in cases with IBS but the difference was significant just for hypertriglyceridemia (26.9% versus 16.3%, p<0.01) probably due to the small sample size of the study. On the other hand, mean BMI and prevalence of HT and DM were all lower in the IBS patients but the difference was significant just for HT (10.5% versus 26.9%, p<0.001) probably due to the small sample size of the study, again.

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), and stroke (15, 16). 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 the well-known strong atherosclerotic effects of smoking, some studies reported that smoking in humans and nicotine administration in animals are associated with a decreased BMI (17). Evidence revealed an increased energy expenditure during smoking both on rest and light physical activity (18), and nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (19). According to an animal study, nicotine may lengthen intermeal time and simultaneously decreases amount of meal eaten (20). Additionally, BMI seems to be the highest in former, the lowest in current and medium in never smokers (21). 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 (22). Similarly, although CAD was detected with similar prevalences in both genders in a previous study (23), prevalence of smoking and COPD were higher in male patients with CAD against the higher prevalences of BMI, white coat hypertension (WCH), LDL-C, triglyceride, HT, and DM in female patients with CAD as the other atherosclerotic risk factors. This result

Table 1: Comparison of cases with irritable bowel syndrome and controls

Variables	Cases with IBS*	*p*-value	Control cases
Number	104		104
Female ratio	***78.8% (82)***	Ns†	78.8% (82)
Mean age (year)	51.2 ± 9.9 (29-70)	Ns	51.2 ± 10.6 (27-70)
Mean BMI‡	29.3 ± 5.3 (19-48)	Ns	***30.2 ± 6.2 (21-52)***
Prevalence of smoking	***29.8% (31)***	***<0.001***	11.5% (12)
Prevalence of HT§	10.5% (11)	***<0.001***	***26.9% (28)***
Prevalence of DM‖	14.4% (15)	Ns	***20.1% (21)***
Prevalence of hyperbetalipoproteinemia	***11.5% (12)***	Ns	8.6% (9)
Prevalence of hypertriglyceridemia	***26.9% (28)***	***<0.01***	16.3% (17)
Prevalence of dyslipidemia	***32.6% (34)***	Ns	26.9% (28)

*Irritable bowel syndrome †Nonsignificant (p>0.05) ‡Body mass index §Hypertension ‖Diabetes mellitus

may indicate both the strong atherosclerotic and weight decreasing roles of smoking (24). 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 (25). In other words, smoking is more dangerous for women about 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 (16). 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 until clearence from the circulation. But due to the repeated smoking habit of individuals, the clearence 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 (19-21). After smoking cessation, normal appetite comes back with a prominent weight gain in the patients but the returned weights are their physiological or 'normal' weights, actually. 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 in another study (26).

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 some metabolic disorders and smoking and alcohol are researched under the title of metabolic syndrome in the literature (27, 28). The syndrome is characterized by a low-grade inflammatory process on vascular endothelium initiated in early years of life (29). The inflammatory process is accelerated by some factors including excess weight, smoking, alcohol, chronic infections and inflammations, and cancers (30, 31). Metabolic syndrome can be slowed down with appropriate nonpharmaceutical approaches including lifestyle changes, diet, and exercise in early years of life (32). The syndrome includes overweight, WCH, impaired fasting glucose, impaired glucose tolerance, hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, smoking, and alcohol for the development of irreversible consequences including obesity, HT, DM, COPD, cirrhosis, CRD, PAD, CAD, stroke, early aging, and premature death (23). 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 (33). 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 cannot eradicate cancer cells due to the insufficient blood supply, effectively (15).

As a conclusion, although IBS may have a complex mechanism with a higher prevalence in females, smoking may be one of the several causes of IBS by causing a vascular endothelial inflammation all over the body. The disseminated inflammation may be the cause of lower BMI and associated lower prevalence of HT and DM in the IBS cases. On the other hand, higher prevalence of hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia in cases with IBS may actually indicate their roles as acute phase reactants in smokers in the body.

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