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Family history of mental illness or alcohol abuse and the irritable bowel syndrome

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ABSTRACT

Objective: We have observed that many patients with IBS drink very little alcohol and postulated that this may reflect membership in families affected by alcoholism and mental illness. We aimed to evaluate whether a family history of substance or alcohol abuse, or psychiatric illness, is associated with IBS.
Methods: A valid GI questionnaire was mailed to a randomly selected population-based cohort to identify IBS and healthy controls. The electronic medical record was reviewed to record the subjects' self-reported personal and family health histories.
Results: A total of 2300 subjects responded (response rate 55%; IBS 13%, $n = 287$); 230 subjects with IBS and 318 controls were eligible. Family history of alcohol/substance abuse was reported by 33% of cases and 25% of controls (OR = 1.4, 95% CI = 1.0–2.1, $p = 0.06$). Family history of psychiatric illness was reported by 37% of cases and 22% of controls (OR = 2.0, 95% CI = 1.3–2.9, $p < 0.001$). In the absence of a personal history of alcohol use, a family history of alcohol/substance abuse was predictive of IBS status (OR adjusted for age and gender = 1.5, 95% CI = 1.0–2.3, $p = 0.05$). In the absence of a personal history of alcohol use, reporting both a family history of alcohol/substance abuse and anxiety/depression/mental illness was clearly predictive of IBS status (OR = 2.5, 95% CI = 1.4–4.5; $p < 0.005$). Substance abuse as a child was associated with an increased risk of IBS (OR = 2.3, 95% CI = 1.1–4.8; $p < 0.03$).
Conclusion: IBS is independently associated with a family history of psychiatric illness and may be linked to a family history of alcohol/substance abuse.

Introduction

Irritable bowel syndrome (IBS) affects 10% of U.S. adults [1] and is a cause of significant patient suffering and utilization of health care resources [2,3]. IBS runs in families [4], and twin studies [5] and prospective population-based studies [6,7] support familial aggregation. However, the role of nature versus nurture in explaining this association remains uncertain.

Alcohol use does not appear to be increased in IBS compared with controls [8] although not all studies agree [9]. However, alcohol abuse, like IBS, is known to often be a familial disorder. Family, twin, and adoption studies demonstrate that genes are responsible for 50% to 60% of population variance in alcohol abuse [10]. Twin studies also demonstrate that alcohol, marijuana, and other drug use and problem use patterns have a genetic component [11,12], although there are environmental factors that are also critically important [13]. As with IBS, the exact contribution of these individual components remains to be described.

Vaillant [14], in his classic 60 year Harvard University follow-up study of adolescent men with alcoholism, observed that those with a strong family history of alcoholism were more likely to become and remain abstinent, an apparent paradox. Other data suggest similar associations may apply in women too [15]. The epidemiologic and physiologic parallels between IBS and alcoholism prompt the question: Could these two diseases co-aggregate in the same families? We have observed in clinical practice that many patients with IBS drink little or no alcohol, which is consistent with the epidemiological data [6]. However, the literature does not describe the alcohol and substance use and problem use patterns of their family members. We hypothesized *a priori* that IBS is more likely to occur in abstinent members of families with alcohol abuse and mental illness. Our aim was to determine if a family history of alcohol/substance abuse or psychiatric illness is associated with IBS.

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Methods

This study utilized a nested case–control design. Subjects with IBS and controls were selected from a cohort of responders to a population-based symptom survey conducted as part of a longitudinal natural history study [16]. The research was approved by the Institutional Review Board of Mayo Clinic.

Subjects

With the approval of Mayo Clinic's Institutional Review Board, we used the Rochester project medical record linkage system to draw a series of true random samples, stratified by age and gender, of residents of Olmsted County between 1988 and 1993 [17,18]. The cohorts were mailed validated gastrointestinal symptom questionnaires. The results of these studies have been reported previously [19,20]. Initially, the complete (inpatient and outpatient) medical records of these randomly selected subjects were reviewed and subjects were excluded if they had significant illnesses which might cause gastrointestinal symptoms.

In 2003, a new study questionnaire (see below) and an explanatory letter were mailed to a random sample of subjects who had been mailed a prior survey [16]. Reminder letters were mailed at 2, 4 and 7 weeks. Subjects who indicated at any point that they did not wish to complete the survey were not contacted further. Otherwise, non-responders were contacted by telephone at 10 weeks to request their participation and verify their residence within the county. A total of 4196 eligible subjects were mailed a survey. Of these, 2300 (55%) completed the survey, 1025 refused, and 871 did not respond. A detailed investigation has confirmed non-response bias in this population is unlikely [21].

Questionnaire

The Talley Bowel Disease Questionnaire (BDQ) is a self-report instrument that measures symptoms experienced over the prior year [22]. The BDQ has adequate validity [22] and contains a valid measure of non-gastrointestinal somatic complaints, the Somatic Symptom Checklist (SSC) [23].

Nested Case–Control Study

The survey responses were used to identify cases and controls for this study. We identified all respondents who reported symptoms that met the Rome II criteria for IBS [24]. We then selected at random an age and gender frequency-matched control group of subjects without symptoms of IBS, but stratified by age and gender to approximate the age and gender distribution of the cases. To qualify as members of the control group, respondents could not have experienced abdominal pain more than 6 times in the past year and did not report more than one of the following symptoms: mucous in stools, bowel movement frequency less than three per week or more than three per day, feeling of incomplete evacuation after bowel movement, urgency, or bloating.

Chart review

All Mayo Clinic patients since 1996 have two health history forms on file. One form, the Current Visit Information form (CVI) records information regarding the patient's current health, and the second form, the Patient Family History (PFH), records the individual's past medical history as well as family health history. A copy of the form is provided in Appendix A. We examined the subjects' personal and family health history forms to assess individual histories of alcohol use, physical or sexual abuse, and psychological illness and histories of the same among family members. These forms provide data regarding personal history of anxiety, depression, or mental illness, personal treatment for alcohol or drug abuse, and family history of drug/alcohol abuse or anxiety, depression, or mental illness, including father, mother, brothers, sisters, sons, daughters, and grandparents. In addition, the person can rate their level of stress on a 1 to 5 scale with 5 being the highest.

Mayo Medical Center has converted to an electronic medical record (EMR). The reviewer (JRK), blinded to the subjects case–control status, assessed each patient's electronic medical history and excluded those patients that lacked the necessary PFH and CVI forms. Thus, patients seen exclusively at Olmsted Medical Center and never at the Mayo Medical Center were excluded. Other medical exclusion criteria were documented diagnoses of inflammatory bowel disease (IBD), cancer, or colonic surgery in the last year. Of the 666 charts identified for review, 73 (11%) lacked the necessary personal or family history forms, 21 (3.2%) had a history of systemic cancer noted in the EMR within the past year, 13 (2.0%) were missing all data from relevant areas of the form, 7(1.1%) carried a diagnosis of IBD, and 4 (0.6%) had colonic surgery within a year of review. In total, 118 (15.5%) patients were excluded from the study. The reviewer then entered the necessary information into an Excel spreadsheet that was later converted to a SAS® data set format for data analysis. The first five charts were double-extracted and reliability was 100%, so single extraction was used thereafter.

Definitions

The CVI and PFH contain self-report data. Personal history of alcohol use was defined as any positive response to any alcohol related questions. Personal history of alcohol/drug abuse was defined as any positive response to personal need to cut down on alcohol. Personal history of anxiety/depression/mental illness was defined as any history of anxiety, depression, mental illness, or suicide. Abuse was defined as any positive response to the single abuse question (physical, sexual, or emotional). Stress was defined as any stress level greater than 3 or reporting a stressful situation. Family history of alcohol/substance abuse was defined as a positive response to this question or alcohol or substance abuse endorsed for any individual in the family information portion of the PFH. Similarly, family history of anxiety/depression/mental illness was defined as a positive response to this question or a family history of depression, other mental illness, or suicide attempts among any family members as addressed on the PFH.

Statistical analysis

Logistic regression analyses were used to identify predictors of IBS adjusting for age and gender. In the initial analyses, patient history items were evaluated in univariate models and multiple predictor variable models. The items considered included alcohol/drug abuse (substance abuse), alcohol use, anxiety/depression/mental illness (mental illness), stress, and physical, sexual, and/or emotional abuse.

In addition, logistic regression analyses were used to evaluate the association between family history of alcohol/drug abuse and anxiety/depression/mental illness and IBS. The initial evaluation utilized any personal or family history of a disorder as the independent (predictor) variables. The disorders considered included anxiety/depression/mental illness and alcohol/substance abuse. A separate model was evaluated in which histories of a disorder in specific family members were considered as predictor variables (i.e., father, mother, grandparent, sibling, child, and either/or mother and father).

Finally logistic regression models were examined in which the patients' history and family history predictors were evaluated as candidate predictor variables. In one model, four categories of alcohol/substance abuse were created (i.e., neither [the reference group], only personal history, only family history, and both personal and family history). A second model evaluated these same four categories for anxiety/depression/mental illness. Finally, two separate models were examined, one model for negative personal use of alcohol/substance abuse and a second model for a positive history of alcohol/substance abuse. In each model, family history of alcohol/substance abuse and anxiety/depression/mental illness were assessed (neither [the