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Opinion paper

The effect of anxiety and depression on the risk of irritable bowel syndrome in migraine patients

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ABSTRACT

Bidirectional co-morbidity between migraine and depression has been observed. Mood disorders are associated with an increased risk of both migraine and irritable bowel syndrome (IBS). The aim of this study was to evaluate the risk of developing IBS in patients with migraine and to compare the risks between those with and without anxiety or depression.

This research used the data contained in the National Health Insurance Research Database (NHIRD). A total of 2859 subjects with migraine and 5718 age-, sex-, hypertension-, diabetes-, mood disorder-matched controls were identified. Both cohorts excluded subjects with pre-existing catastrophic illness and IBS diagnosed before the index visit or within 30 days after the index visit. All individuals of both cohorts were tracked until either having the diagnosis of IBS, loss of follow-up, or IBS free up to 7 years. During the 7-year follow-up period, 8.4% of patients with migraine and 5.4% of control cohort developed IBS. Migraine is associated with an increased risk of developing IBS (HR = 1.58, 95% CI: 1.33–1.87). When separating the cohort into those with mood disorder and without it, migraine is a significant risk factor of IBS in patients without mood disorders, but not in patients with co-existed mood disorders. The findings of this study suggest that migraine is a risk factor of future IBS development for those without comorbid anxiety or depression. However, migraine does not contribute significantly additional risk to IBS development in patients with comorbid anxiety or depression.

1. Introduction

Migraine is an intense headache with throbbing or pulsating characteristics. It is frequently associated with nausea, vomiting and/or light and sound hypersensitivity. Irritable bowel syndrome (IBS) is a gastrointestinal syndrome with the absence of an identified cause, characterized by chronic abdominal pain and altered bowel habits.

Migraine and IBS have neither detectable organic causes nor biologic disease markers, and are diagnosed using symptom based criteria developed by expert consensus, such as The International Classification of Headache Disorders 3 Beta for migraine and the Rome III diagnostic criteria for IBS [1,2]. Both migraine and IBS are chronic and recurrent pain disorders, affect mainly women and young patients [3,4], and are often associated with a list of somatic and psychiatric comorbidities, including anxiety or depression [3–6]. Apart from their clinical similarities, their coexistence has been observed in many clinical observation and epidemiological studies [3–5,7–9]. Previous studies have revealed an increased risk of migraine in IBS patients [4,5,10] and an increased risk of IBS in migraine patients as well [8]. However, to the best of our knowledge, few researches have focused on how mood disorder affects the risk of IBS in patients with migraine.

Therefore, the aim of this study was to evaluate the risk of developing IBS in migraine subjects using a nationwide database of Taiwan, by controlling for age, sex, hypertension, diabetes and mood disorders (anxiety and/or depression). In particular, this research investigated the interaction of anxiety and/or depression on the development of IBS in migraine patients.

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2. Methods

2.1. Data source

This research used the data contained in the National Health Insurance Research Database (NHIRD). In Taiwan, the National Health Insurance (NHI) program started in 1995, providing health care to all Taiwan residents. The coverage rate has reached more than 99% since 2010. The Bureau of National Health Insurance releases NHIRD for research purposes. Detailed information is available on the official website (http://nhird.nhri.org.tw/).

NHIRD contains a variable composition of data set including Longitudinal Health Insurance Database 2005 (LHID2005). These data contain all registration and medical claims for 1,000,000 randomly sampled individuals from all of the 25.68 million beneficiaries registered in 2005.

2.2. Study cohort

We assembled a migraine cohort aged from 20 to 80 and having at least 3 outpatient visits with the diagnosis of migraine defined by the International Classification of Diseases 9th Revision, Clinical Modification (ICD-9-CM: 346) during the recruiting period between 2000 and 2001 from LHID 2005. We defined the index visit as the first outpatient visit with migraine diagnosis. In addition, we enrolled a control cohort aged from 20 to 80 among the remaining subjects in the recruiting period. The index date of control subjects were the first outpatient visit in the recruiting period.

Next, we excluded subjects who had NHI defined catastrophic illness before the index visit. Other excluding criteria included those subjects having any IBS diagnosis before or within 30 days after the index visit of migraine diagnosis, and those who missed long-term follow-up within 30 days after the index visit.

Because comorbidities might influence the development of irritable bowel syndrome, we matched sex, age (±2 years), hypertension, type 2 diabetes, and mood disorders defined above for both cohorts. Therefore, the two cohorts had the same proportions of gender, hypertension, type 2 diabetes, and mood disorders (anxiety or/and depression). Institutional Review Board of Changhua Christian Hospital approved this research protocol.

2.3. Definition of mood disorders

We defined mood disorders consisted of anxiety (ICD-9-CM: 300.0), dysthymia (ICD-9-CM: 300.4), and episodic mood disorders (ICD-9-CM: 296). To decrease the possibility of miscoding, at least three outpatient visits with specific ICD-9-CM code are required for the diagnosis during the baseline period (1999–2001). We considered patients with at least three outpatients' diagnoses of any one of the following code, 300.0, 300.4, or 296, as having mood disorders. For simplification, we defined both dysthymia (ICD-9-CM: 300.4) and episodic mood disorders as depression. Furthermore, we categorized all subjects into four mood subgroups: "no mood disorder" (without either anxiety or depression), "anxiety", "depression" and "both anxiety and depression".

2.4. Study endpoint

All individuals of both cohorts were tracked until either having the diagnosis of IBS, loss of follow-up, or IBS free up to 7 years. The diagnosis of IBS was made by the three consensus of outpatient diagnosis with ICD-9-CM code 564.1. The date of the first diagnosis was as the endpoint date.

2.5. Statistical analyses

We used Pearson chi square tests to examine the differences in categorical data such as gender, and co-morbid medical disorders. Survival analysis was carried out with Kaplan-Meier method. Log-rank test was used to compare the survival difference between the two cohorts. A Cox proportional hazard regression model was used to analyze the risk of IBS in patients with migraine before and after adjusting for potential confounders. We considered the test is statistically significant if P value is <0.05. All statistical analyses were performed by Stata version 13.1 (StataCorp LP., College Station, Texas, USA) and statistical graphs were plotted with R version 3.2.0 [11,12].

3. Results

A total of 2859 subjects with migraine and 5718 age-, sex-, hypertension-, diabetes-, mood disorder (anxiety or/and depression) matched controls were identified. The mean age of migraine patients and the control cohort was 46.5 ± 14.2 and 46.1 ± 14.6 years, respectively. In both cohorts, 71.4% were female, 22.1% had hypertension, 6.4% had diabetes, and 24.4% had mood disorders, including anxiety (16.4% versus 16.5%), dysthymia (7.9% versus 6.0%) and episodic mood disorders (5.0% versus 4.6%).

During the 7-year follow-up period, 8.4% (239 of 2859) of patients with migraine and 5.4% (307 of 5718) of control cohort developed IBS. The annual incidence of migraine and control cohort was 1.19% and 0.77%, respectively, and the hazard ratio for IBS between the migraine and control cohorts was 1.58 (P < 0.001). The hazard ratio significantly increased with advancing age, diabetes, and mood disorders, but not affected by gender or hypertension (Table 1).

According to the result of Cox regression model, people with mood disorders had significant risk to develop IBS (adjusted HR: 2.67, P < 0.001). (Table 1) While analysis was stratified by different mood subgroup, the risk of IBS was highest in patients with "both anxiety and depression subgroup", followed by "anxiety subgroup", "depression subgroup", and finally "control group". (Fig. 1 and Table 2). However, the effects of migraine associated with developing IBS could not be demonstrated in "anxiety subgroup", "depression subgroup", and "both anxiety and depression subgroup" but only be observed in subgroup without mood disorders (HR: 1.97, P < 0.001).

4. Discussion

This population-based 7-year follow-up study demonstrated that migraine subjects were at risk to develop IBS with an adjusted HR of 1.58 and annular incidence of 1.19%. However, the risk increase of IBS for patients with migraine could only be observed in patients without anxiety or depression (HR: 1.97); for those with anxiety or depression, migraine did not significantly increase the risk of IBS. To our knowledge, this interesting interaction has not been explored in previous studies.

Table 1
The adjusted hazard ratio (HR) for IBS during the 7-year follow-up period.

	HR (95% CI)	P-value
Migraine (Yes/No)	1.58 (1.33–1.87)	<0.001
Sex (Female/Male)	0.96 (0.80–1.16)	0.742
Age	1.01 (1.01–1.02)	<0.001
Hypertension (Yes/No)	1.00 (0.82–1.23)	0.983
Type 2 DM (Yes/No)	1.43 (1.08–1.90)	0.012
Mood disorder (Yes/No)	2.67 (2.25–3.16)	<0.001