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Newly Diagnosed Bipolar Disorder and the Subsequent Risk of Erectile Dysfunction: A Nationwide Cohort Study

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ABSTRACT

Background: Although erectile dysfunction (ED) is a common problem in men with mental disorders, there are few reports in the literature on the relation between bipolar disorder (BD) and ED.

Aims: To establish the incidence rate of ED in men with BD and assess the risk of ED in patients with BD according to type of treatment offered or no active treatment with medication during the 1st year of onset.

Methods: We identified 5,150 men with newly diagnosed BD using Taiwan's National Health Insurance Research Database. 2 matched controls per case were selected using the propensity score and a greedy matching method to obtain a balanced control group. Multivariate Cox regression analysis was used to examine the independent risk factors for ED, including obesity and comorbidities. Hazard ratios (HRs) for ED risk were calculated for the different psychotropic therapy groups, including antidepressants, antipsychotics, and mood stabilizers.

Outcome: HRs for ED risk were calculated for the different psychotropic therapy groups, including antidepressants, antipsychotics, and mood stabilizers. Patients with BD had a significantly higher HR for an ED diagnosis than controls.

Results: Patients with BD had a higher HR for an ED diagnosis than controls. Although some psychotropic medications can increase the risk of ED, patients with BD not actively treated with medication still showed a higher risk of ED than controls.

Clinical Implications: Because ED might be more prevalent in patients with BD than in the general population, clinicians should assess erectile function when selecting appropriate treatment for patients with BD to minimize the risk of ED as an annoying side effect and improve treatment compliance.

Strengths and Limitations: This is the first large-scale population-based study to explore the association between BD and ED. A particular strength of this study is its nationwide, population-based study design, which afforded substantial statistical power for detecting subtle differences between the 2 cohorts, thereby minimizing selection bias. There are some limitations to the present study. (i) Data on other potential risk factors is lacking. (ii) Patient compliance and dose effect between psychotropic medication and ED could not be established. (iii) We could not assess the relation between ED and the severity and phases of BD.

Conclusion: This cohort study found a temporal association between BD and subsequent ED in a large national sample of men. Clinicians should consider the risk of ED when choosing treatment for patients with BD. **Hou P-H, Mao FC, Chang G-R, et al. Newly Diagnosed Bipolar Disorder and the Subsequent Risk of Erectile Dysfunction: A Nationwide Cohort Study. J Sex Med 2018;15:183–191.**

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INTRODUCTION

Bipolar disorder (BD) is a severe mental illness that is characterized by elated or euphoric or irritable mood and increased activity or energy levels (also known as mania). BD occurs worldwide, with a lifetime prevalence of approximately 0.6% for BD type I and 0.4% for BD type II, with slightly higher rates reported in developed countries.[1,2] BD is associated with significant functional impairment, a likelihood of high comorbidity, lower quality of life, and a higher rate of suicide.[3]

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for sexual activity. Although essentially a vascular disease, ED also can result from neurologic and psychological conditions. For instance, some studies have reported that ED is a common problem in men with mental disorders, such as major depression,[4] anxiety disorders,[5,6] and psychotic disorders.[7] However, although ED and BD share some comorbidities, few reports in the literature have investigated the relation between BD and ED. For example, the risk of diabetes mellitus (DM), a vascular disease associated with ED, is increased in patients with BD.[8] Substance abuse, which can increase the risk of ED, also is a risk factor for BD.[9,10] These comorbidities indicate that ED not only might be associated with BD but also might complicate the treatment of BD.

In clinical practice, mood stabilizers, antipsychotics, and antidepressants are the main treatments of BD. ED can occur as an adverse effect of these psychiatric medications. Lithium, which is considered key treatment for BD, has been reported to increase the risk of ED.[11–13] Anticonvulsants, such as carbamazepine and valproate, have endocrine side effects and can cause sexual dysfunctions, such as ED, diminished libido, and sperm abnormalities in men with epilepsy.[14–17] However, few studies have investigated sexual function in patients with BD treated with anticonvulsants. Antipsychotics, especially atypical antipsychotics, are recommended for the treatment of BD. Strong evidence has shown that conventional and atypical antipsychotics significantly impair sexual function.[18,19] Furthermore, numerous studies have found that sexual dysfunction can occur with the use of antidepressants, especially selective serotonin reuptake inhibitors (SSRIs).[20–22] This side effect is associated with a negative attitude toward therapy and noncompliance to treatment.[23] It is important to consider ED in the treatment of BD.

There are sparse data on the relation between ED and BD. A key purpose of the present study was to investigate the incidence rate of ED in patients with BD. Moreover, psychiatric medication treatment can increase the risk of ED in patients with BD. There are no previous studies in the literature comparing the risk of ED between patients with BD who were treated with mood stabilizers, antipsychotics, or antidepressants and those who did not receive such treatment. We evaluated the risk of ED in patients with BD who were treated with different classes of psychiatric medication and those without active treatment.

METHODS

Data Sources

This cohort study was based on a prospective analysis of administrative claims data extracted from Taiwan's National Health Insurance (NHI) program, which was initiated in 1995 and covers approximately 99% of the 23.74 million residents of Taiwan. Taiwan launched a single-payer NHI program on March 1, 1995. The National Health Research Institutes in Taiwan established the Longitudinal Health Insurance Database 2010 (LHID2010), which contains all original claims data and registration files of 1,000,000 individuals randomly sampled from the 2010 Registry for Beneficiaries (n = 23.72 million) of Taiwan's NHI program. This database contains administrative and health claims data, including comprehensive information on inpatient and ambulatory care and prescriptions dispensed. The longitudinal nature of the LHID permits the identification of a cohort based on diagnoses, health services, and drug usage to track medical history and to establish a prescription drug profile. In this study, diseases were identified and classified according to the diagnostic codes of the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM).

Selection of Study Groups and Control Group

We identified 32,087 patients from the LHID2010 who had been diagnosed with BD (ICD-9-CM codes 296.0, 296.1, 296.4, 296.5, 296.6, 296.7, 296.8, and 296.9) during ambulatory care and hospital care visits from January 1996 through December 2009 (Figure 1). In the registration dataset, the accuracy of diagnosis might be less reliable compared with the accuracy of diagnosis by structured interview in clinical trials. Some miscoding of diagnosis might be present in the registration dataset. Therefore, to increase the validity of diagnosis in the present study, we adopted the definition at least 2 outpatient visits or 1 inpatient care visit with a BD diagnosis made by board-certified psychiatrists to include participants from 1996 through 2009 (n = 23,883). These definitions have been adopted in previous studies.[24] The aim of this study was to estimate the incidence of ED in patients with BD. To focus on men with BD, women were excluded (n = 12,537). To make the estimation of time from BD diagnosis to ED onset more precise, we attempted to include only patients newly diagnosed with BD starting from 2000. Thus, we adopted a washout period of 4