Bidirectional association between Bell’s palsy and anxiety disorders: A nationwide population-based retrospective cohort study

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\textbf{ABSTRACT}

\textbf{Objective:} Bell’s palsy and anxiety disorders share numerous risk factors (e.g., immune response, ischemia, and psychological stress). However, there have been no studies on the bidirectional temporal association between the two illnesses. In this study, we used the Taiwan National Health Insurance Research Database (NHIRD) to test the bidirectional association between Bell’s palsy and anxiety disorders. We hypothesized that patients with Bell’s palsy would have an increased risk of subsequent anxiety disorders later in life and that, conversely, those with anxiety disorders would have an increased likelihood of developing Bell’s palsy later in life.

\textbf{Methods:} We conducted two retrospective cohort studies using Taiwan’s National Health Insurance Research Database (NHIRD). Study 1 included 8070 patients diagnosed with anxiety disorders and 32,280 controls without anxiety disorders who were matched with sex, age, and enrollment date to analyze the following risk of Bell’s palsy among both groups. Study 2 included 4980 patients with Bell’s palsy and 19,920 controls without Bell’s palsy who were matched with sex, age, and enrollment date to analyze the following risk of anxiety disorders among both groups. The patient records selected for the studies were dated between January 1, 2000, and December 31, 2009. All subjects were observed until their outcomes of interest, death or December 31, 2009.

\textbf{Results:} After adjustment for age, sex, comorbidities, urbanization, and income, the hazard ratio (HR) for patients with anxiety disorders to contract Bell’s palsy was 1.53 (95% CI, 1.21–1.94, \( P < .001 \)), and the HR for patients with Bell’s palsy to develop an anxiety disorder was 1.59 (95% CI, 1.23–2.06, \( P < .001 \)).

\textbf{Conclusion:} This study found a bidirectional temporal association between Bell’s palsy and anxiety disorders. After one of these conditions develops, the morbidity rate for the other significantly increases. Additional studies are required to determine whether these two conditions share the same pathogenic mechanisms, and whether successfully treating one will reduce the morbidity rate for the other.

\section{1. Introduction}

Bell’s palsy is an idiopathic, acute paralysis of facial nerves, usually affecting only one side of the face. Varying degrees of recovery are often observed within 6 months (Berg et al., 2009; Kim et al., 2008). The annual incidence rate of Bell’s palsy is 13.1–53.3 per 100,000 people and is the most commonly diagnosed form of single-sided facial paralysis (Brandenburg and Annegers, 1993; Monini et al., 2010; Morris et al., 2002). Bell’s palsy can occur in all age groups; however, the prevalence is lowest in children and gradually increases with age (Gilden, 2004). Bell’s palsy is observed equally in both sexes, although a higher prevalence has been noted in pregnant women in their third trimester (Holland and Weiner, 2004). Treatment for Bell’s palsy involves administration of steroids within 72 h of the onset of symptoms (Numituavaj et al., 2011); administration of antiviral drugs often has no effect on the prognosis (Quant et al., 2009). Most patients fully recover from Bell’s palsy. However, nearly 30% recover only partially, and such patients must endure a changed appearance and the
associated psychological stress, which may severely impact their economic and social functions (Quant et al., 2009). Patients who do not fully recover often receive electrotherapy, Botox injections, or plastic surgery (May et al., 1989). Moreover, Bell's palsy generally causes anxiety, and patients may require psychotherapy; therefore, follow-up treatment for Bell's palsy often includes psychological care and emotional support (Mooney, 2013). Studies have determined that the psychological distress patients endure following facial paralysis is three to five times greater than that experienced by the average population (Stuart and Byrne, 2004; Sugiuara et al., 2003). Pouwels et al. (2016) revealed that patients with facial paralysis were three times more likely to suffer from anxiety compared with a control group.

Anxiety disorders are a common chronic mental illness. The lifetime prevalence of all anxiety disorders lumped together ranges from 9.2% to 28.7% (Somers et al., 2006). The economic burden engendered by anxiety disorders is gradually being examined, and such disorders are often accompanied by unexplained somatic symptoms and various physical disorders (Arkian and Gorman, 2001; Lépine, 2002). Preexisting or concurrent physical illnesses notwithstanding, studies have found that a history of anxiety disorders can increase the risk of developing additional physical illnesses (Chen et al., 2009; Chou et al., 2012; Culpepper, 2009).

Although psychological stress is considered to exacerbate Bell's palsy (Huang et al., 2012), no study has tested whether anxiety disorders may increase its development. Studies on Bell's palsy have demonstrated that it may cause psychological stress (Cross et al., 2000; Kosins et al., 2007; Kuga et al., 1998; Siol et al., 2001). Other studies have investigated the potential decline in personal interactions (Macgregor, 1990) and social functions resulting from facial paralysis (VanSwearingen et al., 1998). In our study, we used the Taiwan National Health Insurance Research Database (NHIRD) to test the bidirectional association between Bell's palsy and anxiety disorders. We hypothesized that patients with Bell's palsy would have an increased risk of subsequent anxiety disorders later in life and that, conversely, those with anxiety disorders would have an increased likelihood of developing Bell's palsy later in life.

2. Materials and methods

2.1. Data sources

Instituted in 1995, the Taiwan National Health Insurance (NHI) program is a mandatory health insurance program that provides comprehensive medical care coverage including outpatient, inpatient, emergency, and traditional Chinese medicine services to almost 99% of Taiwan's residents (Wu et al., 2012). The NHIRD contains comprehensive information on clinical visits, including prescription details and diagnostic codes based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The NHIRD is managed by the National Health Research Institutes (NHRI), and confidentiality is maintained in accordance with the directives of the National Health Insurance Administration, Taiwan. This study used data from the Longitudinal Health Insurance Database 2005 (LHD2005), a data set from the NHIRD. The data were systematically and randomly sampled from the LHD2005, which comprises data on one million people. The NHRI reported that no significant difference exists in the average insured payroll-related amount, sex distribution, or age distribution between patients in the LHD2005 and those in the original NHIRD (Database). The NHIRD has been used extensively in many epidemiologic studies in Taiwan (Li et al., 2012; Shen et al., 2013; Wu et al., 2012).

2.2. Ethics statement

The Institutional Review Board of the Taipei Veterans General Hospital approved this study. Obtaining written consent from participants was unnecessary because the NHI data set comprises secondary data for research purposes. The Institutional Review Board of Taipei Veterans General Hospital issued a formal written waiver for the need for consent.

2.3. Study 1: anxiety disorder leading to Bell's palsy

Using the LHID2005 data, we conducted a retrospective cohort study involving patients (20 years and older) who were newly diagnosed with anxiety disorder between January 1, 2000, and December 31, 2004. Anxiety disorders were defined on the basis of ICD-9-CM codes 300.0, 300.2, 300.3, 308.3, and 309.81. To ensure diagnostic validity and patient homogeneity, we included only patients who had been diagnosed by psychiatrists and had at least two consensus diagnoses for anxiety disorder. We excluded patients who had been diagnosed with Bell's palsy (ICD-9-CM code 351.0) before enrollment. For each anxiety disorder patient included in the final cohort, we randomly selected four age-, sex-, and enrollment-date-matched control patients from the LHID2005 who had not been diagnosed with an anxiety disorder or Bell's palsy. All anxiety disorder and control patients were observed until (1) diagnosis with Bell's palsy, (2) death, or (3) December 31, 2009. The primary clinical outcome assessed was Bell's palsy.

2.4. Study 2: Bell's palsy leading to anxiety disorder

Patients (20 years and older) who were newly diagnosed with Bell's palsy between January 1, 2000, and December 31, 2004 were selected. To ensure diagnostic validity and patient homogeneity, we included only patients who had at least two consensus diagnoses for Bell's palsy. We excluded patients who had been diagnosed with an anxiety disorder before enrollment. For each Bell's palsy patient included in the final cohort, we randomly selected four age-, sex-, and enrollment-date-matched control patients from the LHID2005 who had not been diagnosed with Bell's palsy or an anxiety disorder. All Bell's palsy and control patients were observed until (1) diagnosis with an anxiety disorder by a psychiatrist, (2) death, or (3) December 31, 2009. The primary clinical outcome assessed was psychiatrist-diagnosed anxiety disorder.

We estimated the monthly income of each patient according to their insurance premium, which was calculated on the basis of the total income of beneficiaries. Monthly income was grouped into low ( < NT $20,000), medium ( > NT $20,000 but < NT $40,000), and high ( ≥ NT $40,000). Urbanization was divided into three groups: urban, suburban, and rural. Urbanization and income levels were used to represent socioeconomic status. Numerous comorbidities were identified on the date of enrollment: hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, congestive heart failure, cerebrovascular disease, and malignancy.

2.5. Statistical analyses

For intergroup comparisons, an independent Student t-test was used for continuous variables and Pearson's χ² test for nominal variables. In study 1, the incidence of newly diagnosed Bell's palsy in patients with and without anxiety disorder was calculated after the data were stratified according to sex and age (equal to or older than 60 or younger than 60). Additionally, the conditional Cox regression model was used to investigate the hazard ratio (HR), with a 95% CI of Bell's palsy between the two groups after adjustment for demographic data (age, sex, income, and urbanization) and medical comorbidities (hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, congestive heart failure, cerebrovascular disease, and malignancy). In study 2, the incidence of newly diagnosed anxiety disorders in patients with and without Bell's palsy was calculated after the data were stratified according to sex and age. The conditional Cox regression
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