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Research paper

Persistent depressive disorder has long-term negative impacts on depression, anxiety, and somatic symptoms at 10-year follow-up among patients with major depressive disorder

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ABSTRACT

Objective: The study aimed to investigate the impacts of persistent depressive disorder (PDD) and pharmacotherapy on depression, anxiety, and somatic symptoms among patients with major depressive disorder (MDD) over a ten-year period.

Methods: 290 outpatients with MDD were enrolled, including 117 with PDD, at baseline. Subjects were followed-up at six-month, two-year, and 10-year points. MDD and dysthymic disorder were diagnosed using the Structured Clinical Interview for DSM-IV-TR. The Hamilton Depression Rating Scale, the Hospital Anxiety and Depression Scale, and the Depression and Somatic Symptoms Scale were used. Generalized Estimating Equation models were used to investigate the impacts.

Results: MDD patients with PDD had greater severities of depression, anxiety, and somatic symptoms at the three follow-up points as compared with those without; however, these results were of statistical significance only in patients without pharmacotherapy. MDD patients with PDD had a longer duration of pharmacotherapy and a lower remission rate as compared with those without. After controlling for depression and anxiety at baseline, PDD was independently associated with more severe depression, anxiety, and somatic symptoms.

Limitation: At the ten-year follow-up, approximately half of the subjects were lost to follow-up; this, in addition to the unequal follow-up intervals, might have caused bias.

Conclusions: Among the patients, PDD continued to have negative impacts on depression, anxiety, and somatic symptoms over the subsequent ten years. Differences in symptomatology between the patients with and without PDD were statistically insignificant when pharmacotherapy was utilized; however, pharmacotherapy did not fully compensate for the negative impacts of PDD.

1. Introduction

There are several types of chronic depression, including dysthymic disorder, major depressive disorder (MDD) superimposed on antecedent dysthymia (double depression), chronic major depression, and recurrent major depression with incomplete remission during episodes (Klein, 2010). In the DSM-V, persistent depressive disorder (PDD) includes these types of chronic depression (American Psychiatric Association, 2013). Chronic depression has a negative impact on the prognosis of depression and increases the burden of depression, such as increased psychiatric comorbidities and suicide attempts (Hölzel et al., 2011; Klein and Kotov, 2016; Kriston et al., 2010), resistance to treatments (Cuijpers et al., 2017), residual impairment in social function (Hellerstein et al., 2017), and increased usage of health care services (Kriston et al., 2010).

Approximately twenty percent of patients with a major depressive episode develop a chronic course (Hölzel et al., 2011). As chronic depression is common and has multiple negative impacts among patients with MDD (Hölzel et al., 2011; Torpey and Klein, 2008), understanding the long-term impact of chronic depression is important among patients with MDD. Although previous studies have investigated the risk factors, treatment, and prognosis of chronic depression (Agosti, 2014; Hellerstein et al., 2017; Hölzel et al., 2011; Kriston et al., 2010), few studies have investigated the impact and course of chronic depression over a ten-year period. Klein et al. published a series of studies that reported outcomes and course trajectories of chronic depression at the 10-year follow-up point (Klein et al., 2006,2008; Klein and Kotov, 2016). These studies focused on patients with dysthymic disorder

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(dysthymic disorder with or without superimposed MDD vs. non-chronic MDD), and found that dysthymic disorder resulted in a significantly slower improvement of depression and a greater severity of depression at the follow-up points in comparison with non-chronic MDD (Klein et al., 2006).

Although previous studies have compared the long-term course of dysthymic disorder with that of non-chronic depression (Klein et al., 2006; Klein and Kotov, 2016), several issues are worthy of further exploration, as follows. 1) One review article reported that antidepressants were effective for the acute treatment of chronic depression (von Wolff et al., 2013); however, another study reported that treatment was generally not associated with the outcome of chronic depression (Klein et al., 2006). Therefore, the role of pharmacotherapy in patients with chronic depression is controversial. 2) The outcome with regards to anxiety and somatic symptoms has been neglected; in fact, anxiety and somatic symptoms are important components of depression and have negative impacts on the prognosis of depression (Agosti, 2014; Fuller-Thomson et al., 2014; Hung et al., 2010). 3) It is unknown whether the negative impacts of chronic depression on patients with MDD are similar to those in patients with dysthymic disorder over a long-term follow-up period.

To our knowledge, no study has investigated the impacts of chronic depression on depression, anxiety, and somatic symptoms at the 10-year follow-up point among patients with MDD. Investigation of this issue is important, because understanding the role of pharmacotherapy and the long-term impacts of chronic depression on the three dimensions might improve prevention and treatment of depression at the initial stage, and encourage physicians to consider the three dimensions simultaneously in the treatment of MDD.

Therefore, this study aimed to investigate the impacts of chronic depression and pharmacotherapy on depression, anxiety, and somatic symptoms among patients with MDD over a ten-year period. We hypothesized that the negative impacts of chronic depression on the three dimensions would persist over the ten-year period and that pharmacotherapy might partially compensate for the negative impacts of chronic depression on the three dimensions.

2. Methods

2.1. Subjects

The study enrolled subjects from outpatient clinics of the psychiatric department of Chang Gung Memorial Hospital at Linkou, a medical center in northern Taiwan. From January 2004 to August 2007 (at baseline), consecutive outpatients (aged 18 − 65 years) were considered eligible subjects if they met the following criteria: 1) fulfilled the criteria for MDD and were experiencing a current major depressive episode (MDE) based on the DSM-IV-TR (American Psychiatric Association, 2000); and 2) had not taken antidepressants or other psychotropic medications in the past four weeks. The Structured Clinical Interview for DSM-IV-text revision (TR) Axis I Disorders was used to confirm the diagnoses of MDD, MDE, dysthymic disorder, and anxiety disorders (First et al., 2002). To prevent depressive symptoms from being confounded, three exclusion criteria were used: 1) a history of substance abuse or dependence without full remission in the previous four weeks; 2) psychotic symptoms, catatonic features, or severe psychomotor retardation; and 3) chronic medical diseases such as diabetes mellitus, hypertension, and other diseases. Moreover, the longitudinal course of depression at baseline was clarified by certified psychiatrists, and classified into three types: chronic depression including persistent MDE for more than 2 years; current MDE superimposed on antecedent dysthymic disorder; and current MDE with previous intermittent MDE without full remission for more than two years. The three types are categorized as persistent depressive disorder (PDD) in the DSM-V (American Psychiatric Association, 2013). In the following text, PDD replaces chronic depression.

At baseline, 290 participants were enrolled. The participants were followed-up at three time points (six months, two years, and ten years). In statistical analysis, baseline, six-month, two-year, and 10-year follow-up points were considered as the first, second, third, and fourth visits. The 10-year follow-up program was executed from August 2014 to December 2016. The program was approved by the Institutional Review Board of the Chang Gung Memorial Hospital. Written informed consent was acquired from all participants according to the guidelines regulated in the Declaration of Helsinki.

2.2. Psychometric scales for the evaluation of depression, anxiety, and somatic symptoms

The severities of depression and anxiety were evaluated using the 17-item Hamilton Depression Rating Scale (HAMD) (Hamilton, 1967) and the 7-item anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) (Zigmond and Snaith, 1983), respectively. The 10-item somatic subscale (SS) of the Depression and Somatic Symptoms Scale was used for the evaluation of somatic symptoms (Chou et al., 2017; Hung et al., 2012; Tse et al., 2017). The 10-item SS, which evaluates somatic symptoms in the past week, is composed of five pain and five non-pain symptoms. The SS is of good internal consistency reliability (Cronbach's alpha = 0.88) (Hung et al., 2006) and is highly-correlated with the physical subscale of the Short Form 36 (Hung et al., 2009). The reliability and validity of the SS and HADS-A have been established (Hung et al., 2010,2012). The 17-item HAMD was evaluated by investigators. The HADS-A and SS were self-administered scales. The scores ranged from 0–52, 0–30, and 0–21 for the HAMD, SS, and HADS-A, respectively. A higher score represented a greater symptom severity. Full remission of depression was defined as a 17-item HAMD score ≤ 7 (Moller, 2008).

2.3. Procedures

After enrollment at baseline, the HAMD was administered by a psychiatrist, and the HADS-A and SS were completed. The subjects were followed-up at six months, two years, and ten years after enrollment. At follow-up, the HAMD was evaluated by the same psychiatrist, and the HADS-A and SS were administered.

In order to understand the longitudinal symptoms of depression, at the 10-year follow-up point, participants were requested to grossly estimate the percentages of time during which they suffered from the following depressive symptoms over the past 10 years: depressed mood, anxiety, diminished motivation, anhedonia, insomnia, decreased appetite, fatigue, poor memory, indecisiveness, and feelings of guilt.

At the follow-up points, psychiatric pharmacotherapy was not controlled. Subjects were free to intermittently accept or quit pharmacotherapy as they chose over the 10-year period. Pharmacotherapy was identified as an important factor related to outcomes. Subjects who were not receiving pharmacotherapy at the index month of the follow-up point were categorized as the “without pharmacotherapy (in the index month) group”. Conversely, subjects who were receiving pharmacotherapy at the index month of the follow-up point were categorized as the “with pharmacotherapy group”. At the ten-year follow-up point, the total duration of psychiatric pharmacotherapy, both in our hospital and other hospitals, over the past 10 years was recorded.

At the two-year and 10-year follow-up points, patients were requested to report any suicidal attempts over the past two and 10 years, respectively.

2.4. Statistical methods

SPSS for Windows 20.0 was used for statistical analyses. The Chi-square test, Mann-Whitney U test, independent *t* test, Spearman's correlation, and Pearson's correlation were used in appropriate situations. Bonferroni correction was used to control the type I error rate resulting