Open Journal of Psychiatry, 2013, 3, 191-194 **OJPsych**
http://dx.doi.org/10.4236/ojpsych.2013.31A015 Published Online February 2013 (http://www.scirp.org/journal/ojpsych/)

Rate of social anxiety disorder, its comorbidity with depression and paroxetine effects in outpatients in Japan*

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Received 27 November 2012; revised 28 December 2012; accepted 7 January 2013

ABSTRACT

The prevalence of persons with social anxiety disorder (SAD) in Japan remains unknown. This study examined 293 patients with age between 20 and 60 at first visit on the outpatient clinic of psychiatry by the section of social phobia of M.I.N.I. and DSM-IV. After that, 10 patients with both SAD out of 16 patients (trial recruited) completed 12 weeks of treatment with paroxetine. Among 63 patients with 4 points and 40 patients with 3 points on the M.I.N.I., 21 patients (33%) and 16 patients (40%) were diagnosed as SAD on DSM-IV criteria, respectively. Together, 37 patients (12.6%) were diagnosed as SAD out of the 293 outpatients. Among 37 patients with SAD, 23 patients (62%) had comorbid depression. As for 10 patients after treatment with paroxetine, 8 patients improved from the point of recovery of depression (HAM-D scores below 10), whereas only 4 patients improved from the point of recovery of social phobia (L-SAS scores below 30). Three points as well as 4 points on the M.I.N.I. is meaningful for the diagnosis of SAD. For a while, paroxetine exerted less beneficial effects on SAD rather than on depression.

Keywords: Social Anxiety Disorder; Depression; Paroxetine; Comorbidity

1. INTRODUCTION

Social Anxiety Disorder (SAD) is characterized by social phobia, the fear of being observed or evaluated by others [1]. The patients often avoid situations that cause intense stress, resulting in a reduced quality of life [2-4].

A previous study reported that the comorbidity of social phobia with major depression is 70% and that social phobia usually predates the mood disorder [5]. Another study reported that 35% of patients with social phobia had experienced at least one major depressive episode [6]. Recent studies reported that social phobia is one of the clinical factors in treatment-resistant depression [7] or subsequent onset of depression [8,9]. The existence of comorbid social phobia predicted the long-term bad outcome of major depressive disorder [10]. Furthermore, depression was found to be the robust predictor of treatmement-seeking SAD [11,12].

Pharmacotherapy is reported to be effective in the treatment of SAD, as reviewed by elsewhere [5,13]. Selective serotonin reuptake inhibitors (SSRI), including citalopram, sertraline, fluvoxamine and paroxetine, are known to be effective as well as benzodiazepines at the first-line pharmacologic treatment for SAD.

The purpose of this study was to examine the prevalence of SAD, its relationship with depression, and the clinical sensitivity of the Mini-International Neuropsychiatric Interview (M.I.N.I.) to SAD [14] at a first visit of patients to an outpatient clinic of psychiatry in Japan. Furthermore, we challenged the treatment with paroxetine to patients with both SAD and depression to examine pharmacological difference in response.

2. METHODS

2.1. Subjects

All patients were recruited from the outpatient psychiatry clinic of Teikyo University Chiba Medical Center from August 2010 to July 2011 (N = 293). The age range was from 20 to 60 years. Patients who demonstrated one or more of the following conditions were excluded from the present study: a history of central nervous system disease, substance abuse, schizophrenia, epilepsy, dementia or mental retardation. The ethics committee of Teikyo University Chiba Medical Center approved the study. Written informed consent was obtained from all participants after the procedures had been fully explained.

2.2. Clinical Assessment

At the first visit, patients were evaluated using the section on social phobia of the Mini-International Neuropsychiatric Interview (M.I.N.I.) [14]. The patients giving

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three or four affirmative answers to the four questions were evaluated by the Liebowitz Social Anxiety Scale (L-SAS) [15]. L-SAS examines two dimensions, fear/anxiety and avoidance. We used the Japanese version, the reliability and validity of which has been confirmed [16]. Patients were diagnosed according to the Diagnostic and Statistical Manual and Mental Disorders, Fourth edition Text Revision, (DSM-IV) by senior-level psychiatrists. When a patient reported a depressive state, the patient's score on the 21-item Hamilton Rating Scale for Depression (HAM-D) was determined.

2.3. Paroxetine Treatment

Sixteen patients with both SAD and depression were recruited into the present study. Patients received paroxetine for 12 weeks. Doses were gradually increased form 10 to 40 mg/day for the first 6 weeks and maintained 40 mg/day for the last 6 weeks. Ten patients completed the treatment with paroxetine (62.5%). Six patients were dropouts without any clear reasons (37.5%).

2.4. Statistical Analysis

For statistical evaluation, one-way repeated measures analysis of variance (ANOVA) was performed to assess the overall differences between variables. Differences were considered to be significant when p values were less than 0.05.

3. RESULTS

Of 293 patients, 63 patients scored 4 points and 40 patients scored 3 points on the social phobia section of the M.I.N.I. Among them, 21 of 63 patients (33%) with 4 points and 16 patients of 40 patients (40%) with 3 points on the M.I.N.I were diagnosed with SAD on DSM-IV. Thus, 37 patients with SAD (12.6%) were found among 293 outpatients between the ages of 20 and 60. Among the 37 patients with SAD, 23 patients (62%) suffered from depression on DSM-IV.

Sixteen patients with both SAD and depression were recruited into the present study. Ten patients (62.5%) completed 12 weeks of treatment with paroxetine. The scores on the HAM-D were significantly decreased in proportion to treatment time (**Figure 1(a)**). Based on a 50% reduction of HAM-D scores, seven patients reached criteria, but three patients did not. Based on recovery from depression (HAM-D scores below 10), eight patients improved, one patient did not reach criteria, and one patient did not change.

The L-SAS scores decreased slightly without statistical significance (**Figure 1(b)**). From the viewpoint of recovery from SAD (L-SAS scores below 30), four patients improved, one patient did not reach criteria, and five patients did not change. Thus, the effects on SAD of

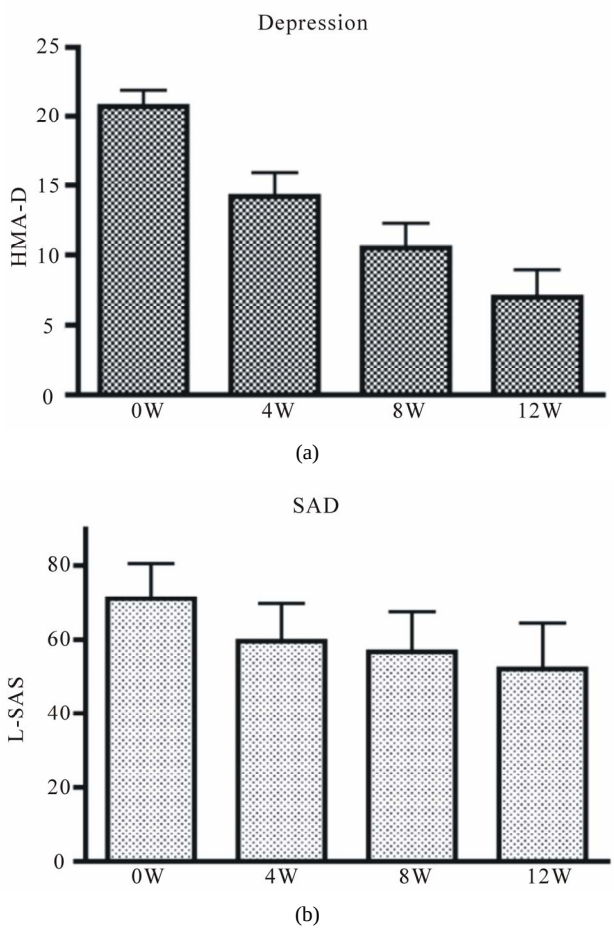

Figure 1. Paroxetine exerted more effective antidepressant effects on HAM-D than anti-SAD effects on L-SAS. (a) F (3.27) = 5.153, P = 0.0004; (b) F (3.27) = 1.778, P = 0.1650.

paroxetine were less strong than its effects on depression. We did not find any difference between two dimensions, fear/anxiety and avoidance, in L-SAS scores of the patients with good outcomes (data not shown).

4. DISCUSSION

The present study reveals epidemiologic data about social affective disorder (SAD) in patients at a psychiatric outpatient clinic in Japan. The prevalence of SAD from 20- to 60-year-old patients, excluding those with central nervous system disease, substance abuse, schizophrenia, epilepsy, dementia or mental retardation at the outpatient clinic is 12%.

Of the 293 patients, 63 patients scored 4 points and 40 patients scored 3 points on the section of social phobia on the M.I.N.I. Among them, 21 of 63 patients (33%) with 4 points on the M.I.N.I. and 16 of 40 patients (40%) with 3 points on the M.I.N.I. were diagnosed as SAD on DSM-IV. This result indicates that the M.I.N.I. score does not need full marks, but is diagnostic even at 3 points.

The comorbidity of major depression (n = 23) in the patients with SAD (n = 37) was 62 % in the present study. This is in a good agreement with a previous study (70%) by Van Ameringen *et al*. [5]. Interestingly, a recent study reported that social phobia was strongly associated with the subsequent onset of major depressive disorder [8]. These results indicate that psychiatrists should consider the high rate of already-onset of both SAD and depression when they see patients at their first visit on the outpatient clinic of psychiatry.

Ten of 16 patients (62.5%) completed the concurrent treatment study with paroxetine. This rate was similar to the previous report (around 60% for completion of the study) [17,18]. The high rate of dropout might be due to adverse reactions such as nausea, abnormal ejaculation, somnolence, and dizziness occurring at 15% [19]. There may exist unknown reasons for the dropout, which are important for poor clinical outcomes. A previous study showed that the rate of discontinuation of paroxetine study in social phobia was 20% [20]. The precise reasons for the dropout remains to be elucidated.

Paroxetine showed broader effectiveness for the treatment of depression than for SAD (**Figure 1**). The recovery rate of depression was 80%, whereas that of SAD was 40% according to the respective scores (HAM-D scores blow 10 and L-SAS scores below 30). This indicates that symptoms of SAD are not necessarily parallel with those of depression. Previous studies reported that the recovery rate of social phobia by paroxetine were 50% - 70% [20-22]. This percentage is better than the present result. It seems that symptoms of depression are more responsive than those of SAD to the treatment with paroxetine in the Japanese patients with both SAD and depression.

In support of this, SAD and depression are different from the biological perspective of cortisol response to d-fenfluramine administration. Patients with SAD had an augmented cortisol response to d-fenfluramine compared to healthy volunteers [23], while depressed patients had a response to d-fenfluramine that was similar to control subjects [24]. This pathology of the hypothalamic-pituitary-adrenal axis could be reflected in the different effects of paroxetine on SAD and depression seen in the present study, although this is speculation.

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