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Escitalopram versus paroxetine for social anxiety disorder: An analysis of efficacy for different symptom dimensions

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Abstract

Background: A previous factor analysis of pooled data demonstrated that the Liebowitz Social Anxiety Scale (LSAS) can be divided into six subscales. This paper examines data from a fixed-dose trial of escitalopram versus paroxetine, in order to determine the differential effects of these agents on symptom dimensions in social anxiety disorder (SAD). *Methods:* Data from a 24-week randomised, placebo-controlled, comparative study of fixed doses of escitalopram (5 mg, 10 mg, 20 mg) versus paroxetine (20 mg) in SAD were examined. The six factors identified in a previous factor analysis of baseline data from escitalopram studies on the primary efficacy scale, the LSAS, were used to compute subscale scores. These were analysed using analysis of covariance (ANCOVA), and standardised effect sizes were calculated. *Results:* The combined escitalopram data and the paroxetine data both demonstrated significant superiority to placebo on each of the 6 LSAS factors at week 24 (OC analysis). Escitalopram doses of 5 mg, 10 mg, and 20 mg were generally more effective than placebo for each of the factors. Escitalopram 20 mg was significantly more effective than paroxetine 20 mg on 5 of the 6 symptom dimensions. *Conclusion:* Factor analysis of the LSAS allows for useful secondary analyses that support and extend the primary efficacy analysis of this instrument. The analysis here indicates that different escitalopram doses are effective across the various symptom dimensions of SAD.

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1. Introduction

Social anxiety disorder (SAD) is increasingly viewed as a prevalent, chronic, disabling, and costly medical disorder (Magee et al., 1996; Schneier et al., 1994; Dupont et al., 1996; Mogotsi et al., 2000). When untreated, SAD is frequently complicated by the subsequent onset of comorbid disorders such as depression and substance use, and patients with such comorbidity are particularly impaired (Kessler et al., 1999). The fact that SAD continues to be underdiagnosed and undertreated further contributes to the economic costs associated with this condition (Davidson et al., 1993).

There is increased understanding of the psychobiology of SAD (Stein et al., 2002b), and effective pharmacotherapies and psychotherapies for this disorder are now available (Blanco et al., 2003; Ballenger et al., 1998; van der Linden et al., 2000). Expert consensus guidelines have advised that selective serotonin reuptake inhibitors (SSRIs) are a first-line pharmacotherapy of choice in view of their effectiveness and tolerability (Ballenger et al., 1998; Bandelow et al., 2002), and in randomised placebo-controlled trials of these agents, 60% or more of SAD patients in the medication arm are responders.

Additional progress in understanding and managing social anxiety disorder (SAD) may well depend on a deeper knowledge of the heterogeneity of this condition. There is evidence, for example, that the generalized form of SAD is more severe, and more familial than the non-generalized type (Schneier et al., 2002; Heimberg et al., 1993). There has also been some discussion of the potential clinical importance of different symptom dimensions within SAD; for example the Liebowitz Social Anxiety Scale (LSAS), the most frequently used outcome measure in SAD medication trials, differentiates between fear and avoidance symptoms.

Factor analyses of the LSAS have demonstrated that the main SAD symptom dimensions are not in fact social fear and avoidance, but rather include dimensions such as social interaction, speaking in public, eating and drinking in public, and assertiveness (Safren et al., 1999; Oakman et al., 2003; Perugi et al., 2001). An exploratory factor analysis of the LSAS by our group yielded six underlying dimensions; and we documented distinctive associations between these symptom dimensions and different areas of disability (Stein et al., 2004).

Our original exploratory factor analysis of the LSAS scale was based on baseline data from three randomised placebo-controlled clinical trials in SAD with escitalopram (Lader et al., 2004; Kasper et al., 2005; Montgomery et al., 2003). We reported that there was no association between these symptom dimensions and the short-term (week 12) response to escitalopram in comparison to placebo in two of these trials (Lader et al., 2004; Kasper et al., 2005) (the remaining trial was a relapse prevention study). In the current paper, we focus in more detail on data from the randomised-controlled trial of SAD, in which escitalopram, paroxetine, and placebo were compared over the medium-term (24 weeks) (Lader et al., 2004), addressing the response to individual doses of escitalopram, and to paroxetine and placebo of different SAD symptom dimensions.

2. Methods

2.1. Clinical trial

The escitalopram versus paroxetine SAD trial has been presented in more detail elsewhere (Lader et al., 2004). Successfully screened patients entered a 1-week, single-blind, placebo lead-in period before being randomly assigned to 24 weeks of double-blind treatment with escitalopram (5, 10, or 20 mg/day), paroxetine (20 mg/day) or matched placebo capsules. Paroxetine 20 mg is the manufacturer's recommended effective dose for the treatment of SAD, and previous data comparing paroxetine 20 mg, 40 mg and 60 mg/day demonstrate that there was no further significant benefit from the higher doses (Liebowitz et al., 2002).

Enrolled patients were 18–65 years of age, with a primary diagnosis of generalized SAD according to DSM-IV criteria, a total score of at least 70 on the LSAS, demonstrable fear and avoidance traits in at least four social situations, and a score of $\geq$5 on one or more of the Sheehan Disability Scale (SDS) subscales. Patients were excluded if they had another Axis I disorder designated the primary diagnosis within the previous 6 months, if they had moderate to severe depressive symptoms [defined as a MADRS (Montgomery-Åsberg Depression rating scale) total score $\geq$18], or if any of a range of comorbid psychiatric or general medical disorders were present.

The primary efficacy parameter was the LSAS, which was assessed at baseline and at regular intervals up to 24 weeks of treatment. The LSAS provides an overall measure of social anxiety from the total score and four subscales: performance fear, social fear, performance avoidance, and social avoidance. There are 24 items, and each is rated in terms of both fear and avoidance on a 0–3 scale.

2.2. Statistical analyses

In a previous factor analysis based on baseline data from 1197 subjects, six dimensions underlying the 24 LSAS items were identified. On the basis of their component items, these were labelled as follows: factor 1—social interaction (5, 10, 11, 12, 19, 21), factor 2—eating and drinking in public (3, 4), factor 3—speaking in public (2, 6, 14, 15, 16, 20), factor 4—assertiveness (1, 13, 18, 22, 24), factor 5—observation fear (8, 9, 17), and factor 6—partying (7, 23) (Stein et al., 2004).

Six symptom subscales were created by adding LSAS scores of items corresponding to these six factors. Each of the six subscale scores were analysed separately for the effect of escitalopram compared with placebo at week 24, using an ANCOVA with treatment and centre as factors, and baseline subscale score as covariate. In addition, the six subscale scores were analysed separately for the effect of escitalopram 20 mg compared with paroxetine 20 mg at week 24, again using an ANCOVA with treatment and centre as factors, and baseline subscale as covariate. To determine the magnitudes of the outcomes, standardised effect sizes were calculated as estimated differences divided by the standard deviations. Withdrawal rates in all treatment groups ranged from 26.6% to 33.5%, with most withdrawals in the first 12 weeks of the study; because of comparable patient withdrawal rates in the different treatment arms, the main analyses in this paper were based on observed cases (OC). Analyses using the last observation carried forward (LOCF) were also carried out.

3. Results

The data for the main analysis consisted of 839 randomised patients, evenly distributed between the five treatment