

Comment

Drug Treatment of Social Anxiety Disorder

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INTRODUCTION

This commentary reviews the current literature with respect to the pharmacological treatment of social anxiety disorder. The relative benefits of antidepressants and other psychotropic medication will be considered in respect of the reported efficacy of those medications. For the most part this will focus on randomized, controlled trials that have explored these medications in social anxiety disorder, either compared with other drugs or compared with placebo. The term social anxiety disorder is used interchangeably with social phobia.

Social anxiety disorder is diagnosed [1,2] when the patient shows a marked and persistent fear of at least one social situation whereby that patient perceives that they will be scrutinized by others, leading to humiliation. They need to recognize that this fear is excessive or unreasonable. However, significant distress must be reported by the endurance or avoidance of that situation. The condition must not be secondary to any other psychiatric condition or related to the fear of a comorbid medical condition.

Psychological treatment of social phobia appears to be most successfully restricted to cognitive therapy and exposure [3]. However, the remit of this paper focuses on pharmacological treatments.

MONOAMINE OXIDASE INHIBITORS

Monoamine oxidase inhibitors (MAOI) are not generally suitable for first-line treatment because of side effects and dietary restrictions. Nevertheless, a number of studies have been conducted examining the efficacy of tranylcypromine [4] and phenelzine [5–7], where the latter was found to be significantly more efficacious than placebo. The side effect profile is less problematic with reversible MAOIs such as moclobemide and brofaromine, but these are not considered as effective as the earlier compounds [3]. Some studies suggest that moclobemide is more effective than placebo [7,8], but this is generally at higher doses, where the risk of increased side effects akin to irreversible MAOIs is greater, although moclobemide may be an option when all others have failed [9]. Other studies of moclobemide show less positive outcomes, with similar efficacy to placebo [10,11]. A more recent study found that moclobemide performed equally as well as citalopram in treating social phobia [12].

Some studies provide support for the use of brofaromine, production of which is currently under review. For instance, patients showed significantly better Hamilton Anxiety Scale response on brofaromine than placebo [13]. This efficacy, compared with placebo, is confirmed elsewhere [14]. In another study, follow-up responses on Clinical Global Impression (CGI) global

improvement scales were at least 'much improved' in significantly more brofaromine patients than in those taking placebo [8].

TRICYCLIC ANTIDEPRESSANTS

The few studies that have examined tricyclic antidepressants (TCA) in the treatment of social phobia provide less than encouraging data. There is some evidence that clomipramine may have partial efficacy [15–17], but the findings are limited since the studies focused on general anxiety profiles and were poorly controlled. Imipramine has shown only moderate superiority over placebo in an 8-week open study with 15 patients [18].

SELECTIVE SEROTONIN REUPTAKE INHIBITORS

Selective serotonin reuptake inhibitors (SSRI) are used more commonly than other drugs to treat social phobia. The first published work to demonstrate this focused on fluvoxamine [19], whereby 30 patients with a DSM-III-R diagnosis of social anxiety received either fluvoxamine (150 mg) or placebo for 12 weeks. Response on the Liebowitz Social Anxiety Scale (LSAS) was significantly better for the treatment group than for placebo, although no difference was found between the groups on avoidance measures. A more recent study [20] demonstrated superiority of fluvoxamine over placebo in 92 patients on all social phobia ratings.

Paroxetine has received the most attention in social phobia research. Efficacy in large double-blind studies is well reported [21,22]. Indeed paroxetine is the only SSRI to be licensed in several countries for social anxiety disorder [23]. The double-blind studies represented three investigations conducted in North America [21] and South Africa and Europe [22]. The North American patients ($n=187$) received 10–50 mg of paroxetine or placebo over 12 weeks. Significantly more patients in the treatment group than in the placebo group were at least much improved (53.0% versus 23.9%). In the European/South African study ($n=290$), patients

were also randomized to a 12-week trial of paroxetine or placebo. Significantly more patients in the treatment group compared with the placebo group showed improvement in social anxiety symptoms and avoidance. These improvements were reflected in improved work and social functioning.

Fluoxetine has received less attention. Initial case histories [24,25] and open studies [26] suggest that fluoxetine is effective in treating social anxiety disorder, but placebo-controlled studies are scarce. One such recent study produced less than favourable findings [27]. In a 14-week double-blind trial, 60 patients were randomized to fluoxetine or placebo. No significant differences were found between the groups in respect of LSAS ratings, although the authors did note a high placebo response. Clearly further trials are warranted.

The efficacy of sertraline in the treatment of social anxiety has been investigated more thoroughly. In a small ($n=12$), flexible-dose study, sertraline was associated with significant improvement compared with placebo [28]. More recently, in a 20-week, double-blind trial, 204 Canadian patients were randomized to sertraline or placebo [29]. Significantly more patients in the treatment group demonstrated improvement in CGI at the end of treatment than those receiving placebo (53% versus 29%). Improvements in the Marks Fear Questionnaire and Brief Social Phobia Scale (BSPS) were also better for sertraline patients compared with placebo. Sertraline was as well tolerated as placebo (76% versus 78%). Sertraline has also been found to be efficacious in combination with exposure therapy [30], which was significantly better than either treatment alone.

There have been no randomized, controlled trials of citalopram, although the earlier reported study [12] showed citalopram to be as effective as moclobemide in treating social anxiety disorder. Citalopram (40 mg) in combination with psychoeducation counselling (performed on 12 children/adolescents, aged 8–17 years, with generalized social anxiety disorder) demonstrated significant improvements post-treatment [31], but there was no control group or placebo. Escitalopram is currently being examined with

regard to its efficacy in social anxiety disorder. At the Collegium Internationale Neuro-Psychopharmacologicum 2002 Congress, Montreal, Canada, a study was reported in which 358 patients with a primary diagnosis of social anxiety disorder were randomized to escitalopram (10 mg) or placebo over 12 weeks [32]. Overall LSAS scores improved significantly for the treatment group compared with placebo. Significant improvement in CGI, LSAS avoidance and fear/anxiety, and Sheehan Disability Scale were also noted for escitalopram, which was well tolerated in this patient population. However, this is yet to be published in a full report.

NEWER ANTIDEPRESSANTS

Only venlafaxine has received any attention in this context, and data are limited. One small study ($n=17$) showed that just half of the patients receiving venlafaxine demonstrated clinically relevant improvement [33]. In an open-treatment study of 12 patients with avoidant personality disorder (which is related to social phobia), who had failed to respond to SSRIs, LSAS scores were found to decrease significantly for patients receiving 112.5 mg–187.5 mg of venlafaxine [34]. Work is ongoing comparing venlafaxine with paroxetine, but is not yet published.

Trials are being conducted examining the efficacy of mirtazapine in the treatment of social anxiety disorder, but no randomized, controlled trials have been published yet. However, a pilot study of 14 patients receiving 30 mg mirtazapine for 12 weeks demonstrated that 41.7% of completers (five of 12) were shown to be responders on CGI Improvement (scores of 1 or 2) and LSAS (reduction of 40% or more); overall LSAS scores, plus anxiety and avoidance subscores, were significantly reduced [35].

BENZODIAZEPINES AND ANXIOLYTICS

Data are limited on the efficacy of benzodiazepines in the treatment of social anxiety disorder. These anxiolytics, as a rule, have been found

to be useful in the treatment of generalized anxiety disorder and panic disorder [36], but randomized, controlled trials in social phobia are restricted to two studies [5,37]. In the first study [5], 65 patients received alprazolam or placebo over 12 weeks. There was only modest efficacy of alprazolam over placebo in terms of response rates (38% versus 20%). In the second study [37], 75 patients were randomized to clonazepam or placebo over 10 weeks. Significantly more patients in the treatment group showed better CGI improvement than those receiving placebo (78% versus 20%). There are limitations to the use of benzodiazepines, owing to the risk of sedation. Furthermore, they show little effect in depression, which is a frequent comorbid condition with social phobia. This class of treatment might best be suited to those who have failed all other approaches.

BETA-BLOCKERS

Despite the use of beta-blockers to treat performance anxiety, there is no evidence to support their use in social anxiety disorder. Three placebo-controlled trials of atenolol confirm poor response [6,38,39].

GABAPENTIN AND PREGABALIN

Although more generally used as an anticonvulsant, gabapentin has been shown to have benefit in the treatment of social anxiety disorder [40]. Sixty-nine patients were randomized to gabapentin or placebo. While only 39 patients completed the study, there was significant improvement for treatment patients over placebo in respect of LSAS, Fear Questionnaire, BSRS, and CGI. However, the poor completion outcome was reflected by withdrawals due to adverse effects of gabapentin, including nausea, dizziness, somnolence, insomnia, nervousness, and facial oedema. Furthermore, there has been one unconfirmed report that suggests gabapentin may be involved in cholestasis [41].

Pregabalin has been found to be effective in treating generalized social phobia [42], but only

in higher doses. More data are needed about efficacy and tolerability before these findings can be generalized.

CONCLUSIONS

Current evidence suggests that SSRIs are recommended as the first-line treatment of social anxiety

disorder. Benzodiazepines can be used in the first week of treatment while waiting for SSRIs to become effective, although generally they should be used only in treatment-resistant patients. MAOIs should be reserved as second- or third-line treatment. Other treatments appear to present inconsistent outcomes. It should be noted that even with SSRIs the published studies focus on trial data that may bear little resemblance to real life clinical practice.

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