The Psychopharmacology of Social Phobia: An Update for 2001

Michael Van Ameringen, MD, FRCPC
Co-Director, Anxiety Disorders Clinic, McMaster University Medical Centre, Hamilton, Ontario; Assistant Professor, Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Ontario.

Although social phobia or social anxiety disorder has been found to be the third most common psychiatric illness in the general population (1), research into evaluating effective pharmacologic treatments has lagged significantly behind that for other common psychiatric disorders. The late start in psychopharmacological research for social phobia has been related to the inability of clinicians to see it as a distinct disorder. Social phobia is often lumped with agoraphobia and other phobias. Many consider social phobia to be either a normal personality trait or extreme shyness, while others consider it as an aspect of a personality disorder. Social phobia has, until recently, been viewed as medication-nonresponsive and not particularly prevalent or impairing. In 1985, social phobia was referred to as the “neglected anxiety disorder” (2). Since then, there has been a progressive increase in interest in the disorder, first by researchers, then by clinicians, and, finally, by the pharmaceutical industry and granting agencies.

Although cognitive-behavioural treatment for social phobia can be very effective, it is, unfortunately, unavailable to many patients, except for those in large urban areas or academic centres, because of a lack of trained therapists and costs. As a result, pharmacotherapy is often the most practical treatment option for patients with social phobia. The general aim of medication treatment is to relieve pathological anxiety by reducing physiological arousal, reducing anticipatory anxiety, diminishing catastrophic cognitions, and alleviating avoidance behaviours. Reduction of these symptoms often leads to an improvement in social and occupational functioning.

Various drug classes have been evaluated in placebo-controlled trials for the treatment of social phobia, including the monoamine oxidase inhibitors (MAOIs), the reversible inhibitors of monoamine oxidase A (RIMAs), the high potency benzodiazepines, and the selective serotonin reuptake inhibitors (SSRIs). The use of other agents, including beta blockers, buspirone, ondansetron, and mood stabilizers will also be discussed.

The MAOI phenelzine was the first medication to show efficacy in placebo-controlled trials of social phobia. Two controlled trials showed phenelzine to be better than placebo in doses from 45 to 90 mg daily (3,4). Although the MAOIs (in particular phenelzine) were once considered the gold-standard drug treatment for social phobia, the associated dietary restrictions and risk of significant life-threatening events, such as hypertensive crisis, have resulted in these agents being employed as a third-line treatment, particularly for use in treatment-resistant social phobia.

The RIMA moclobemide generated a lot of interest and excitement when it first came on the market and was actively studied in social phobia. Moclobemide initially showed some promising results when compared with phenelzine and placebo in a single-site study (5); several subsequent controlled studies, however, revealed little difference in efficacy between moclobemide and placebo (6–8). In spite of our great hopes for the RIMAs in social phobia, they have shown little, if any, efficacy, consigning them to be used as a fourth-line agent (9).

There has been 1 controlled study of the use of the high potency benzodiazepine, clonazepam, in the treatment of social phobia (10). It showed significant improvement with clonazepam treatment compared with placebo. Another benzodiazepine, alprazolam, was found to have limited efficacy (3). Our enthusiasm for the potential efficacy of these agents is somewhat tempered by our knowledge of their significant abuse potential by the target population (11). Given the limited and somewhat inconsistent data on benzodiazepines, the high rate of comorbidity of social phobia with substance abuse or dependency and depression, as well as the lack of efficacy of benzodiazepines in the treatment of depression, they should not be considered as first-line agents.

The SSRIs are the most-studied drug group in social phobia. Large controlled trials with sertraline, fluvoxamine, and paroxetine have all shown significant efficacy with a good drug–placebo difference (12–19). The SSRIs are thought to be safe and generally well tolerated, and they
cover the broad spectrum of comorbidity commonly seen in individuals seeking treatment for social phobia. Results from placebo-controlled trials support the emerging trend of clinicians to use SSRIs as the first-line pharmacologic treatment option for generalized social phobia.

Various other agents have also been studied in placebo-controlled trials of social phobia, including ondansetron, a serotonin receptor antagonist marketed as an antiemetic. This agent was found to be more effective than placebo in one study but nevertheless showed only a small effect size (20). The anticonvulsant gabapentin has also been shown to be better than placebo in one controlled trial (21), as has the yet-to-be-released medication pregabalin (22).

Some promising agents that have shown efficacy in open trials are currently being studied in placebo-controlled trials, including nefazodone (23–25) and venlafaxine (26–29).

Medications that do not work in social phobia include the tricyclic antidepressants (30) and the nonbenzodiazepine anxiolytic buspirone (31,32), which was shown to be ineffective in two controlled trials. The beta blockers have been primarily used by musicians for the treatment of performance anxiety. Many of these individuals do not meet criteria for social phobia. In the two controlled studies where beta blockers have been evaluated in social phobia, they have been found to be no more effective than placebo. It is possible, however, that certain individuals will benefit from the use of beta blockers over an extended period of time, whereas other individuals may benefit from their intermittent use, taken in advance of a specific performance situation. Controlled studies of propanolol and atenolol, however, have failed to demonstrate efficacy in social phobia (33,34).

The goals of pharmacotherapy are to target a multitude of symptom domains, including anticipatory anxiety, socially mediated panic attacks, cognitive misperceptions, avoidance behaviour, and comorbid conditions. Data from controlled trials strongly support using an SSRI as the first-line drug treatment. The starting dose should be similar to those that have been used in the treatment of depression (sertraline 50 mg daily, paroxetine 20 mg daily, and fluvoxamine 50 mg daily) (35). The dose of the medication should be increased to obtain a response. Often, some initial treatment response is seen by 8 weeks. People with social phobia generally require a medication trial of of 10 to 12 weeks at maximal doses; this should be attempted before a medication is considered as a failure. It often takes many months to consolidate a full treatment response and achieve a full remission. If the treatment is effective, it is recommended that it be continued for at least a year, and then very gradually tapered off. There are few data to guide treatment recommendations for SSRI-nonresponders. One study showed the potential benefits of augmentation with buspirone (36). The most common augmentation strategy is to add cognitive-behavioural treatment. Nonresponders may also benefit from switching to another SSRI or to another drug class, such as venlafaxine or nefazodone or an MAO inhibitor (phenelzine, tranylcypromine).

Although many individuals suffering from social phobia obtain a good response to pharmacotherapy, they do not achieve a full remission and require additional treatment, often in the form of cognitive-behavioural treatment.

Although we have made significant gains in the pharmacotherapy of social phobia, we require more research into treatment resistance, the use of these agents in pediatric populations, and the comparative efficacy of different drug classes, as well as an improved capability to predict response to treatment.

References

References


