

FEATURE ARTICLE

Pharmacological Treatment of Social Anxiety Disorder

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Editor's Note

In this article, Drs. Carmona, Raza, and Blanco review the fast-growing field of the pharmacological treatment of social anxiety disorder (SAD), also known as social phobia. SAD has become increasingly recognized over the past decades since its inclusion in the DSM diagnostic system. It is a common condition that carries a heavy burden of disability because the onset of disability is usually in the mid and late teens and, thus, it interferes with educational and social development. Thus, individuals with SAD do not fulfill their potential, and they may fail to develop stable relationships.

It is important that psychiatrists campaign to persuade the general public and politicians, particularly those controlling health care delivery, that SAD is *not* just medicalized shyness. It is a serious condition with the disabilities noted above.

The authors deal comprehensively with a range of treatments that have been proven to show some efficacy in SAD. In particular, they highlight evidence for the effectiveness of the selective serotonin reuptake inhibitors. This has been shown for various compounds, including paroxetine, sertraline, fluvoxamine, and, most recently, escitalopram. The use of drug therapy provides a window of opportunity for other measures, particularly nonpharmacological measures, to become effective. Discontinuation of a medication should be followed by successful control of

the phobic symptoms. Other medications shown to be effective in SAD include the benzodiazepines, the monoamine oxidase inhibitors (MAOIs), and the reversible MAOIs. The area in most urgent need of further research is guidelines development for the combination and temporal patterns of use for the various drug and nondrug treatments.

Introduction

Until a few years ago, the symptoms of social anxiety disorder (SAD), also known as social phobia, were frequently overlooked or seen as normal personality traits equivalent to shyness. SAD was first formally recognized as a mental disorder in the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III).¹ **The central feature of *social anxiety disorder* (SAD) according to the DSM, is a persistent, irrational fear accompanied by a compelling desire to avoid situations in which one might act in a humiliating or embarrassing way while under the scrutiny of others. Individuals with SAD fear they will do or say something that will embarrass or humiliate them in front of others. As a consequence, they often avoid situations in which they may be exposed to the judgment of others or endure those situations with intense distress. SAD often has an onset in childhood and a persistent course. The fourth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) diagnostic criteria for SAD require that the person *recognize the fear as excessive or unreasonable.***²

SAD may involve the fear of speaking or eating in public, writing in front of others, urinating in public lavatories, or saying foolish things in social situations. In the feared situation, individuals with SAD tend to be self-conscious and self-critical and often experience physical symptoms of anxiety, such as blushing, palpitations, sweating, or trembling.

SAD can be classified as generalized and nongeneralized. *Generalized SAD* refers to a subtype in which significant social anxiety occurs in most social situations, including performance and interpersonal situations. In contrast, individuals with *nongeneralized SAD* experience significant social anxiety in one or 2 types of social situations.

SAD has a 12-month prevalence of 4% to 6% and a lifetime prevalence of 7% to 13%. It is now clear that SAD is a prevalent and disabling disorder that can hinder the professional and emotional life of the patient. It is associated with important disability and diminished quality of life.¹

There is now substantial evidence that SAD is quite responsive to pharmacological treatment. Furthermore, **preliminary data suggest that pharmacological treatment may have an earlier onset of action and more potent short-term effects than cognitive behavioral treatment.** This article reviews the literature on the pharmacological treatment of individuals with SAD and offers some practical guidelines for its implementation.

Studies of Effectiveness of Various Psychopharmacologic Agents in SAD

Selective Serotonin-Reuptake Inhibitors (SSRIs):

At present, SSRIs probably represent the first-line treatment for SAD, based on their efficacy, tolerability, and safety. There is more evidence of the efficacy of the SSRI *paroxetine* (Paxil) for SAD than any other medication. Four published placebo-controlled studies have shown paroxetine to be a safe and efficacious treatment for this disorder.⁴⁻⁷ **Response rates for paroxetine in those studies have ranged from 55% to 70%, with response rates for placebo being generally about half the rate for paroxetine.**^{4,5} In all of the studies, a “responder” was defined as an individual who was rated as “much” or “very much” improved based on the *Clinical Global Impression Scale* (CGI) score.

Paroxetine was generally well tolerated, as demonstrated by the relatively low dropout rates and low incidence of adverse effects in these studies. **The most frequent central nervous system (CNS) adverse effects of paroxetine in clinical practice include headache, somnolence, insomnia, and asthenia. Common gastrointestinal adverse effects include nausea, dry mouth, and constipation. Sexual dysfunction is also a common adverse effect of paroxetine and can include delayed ejaculation in men and delayed orgasm or anorgasmia in women, as well as decreased libido in both sexes.**

There is also growing evidence of the efficacy of *sertraline* (Zoloft) for the treatment of SAD. In a small, preliminary crossover study in 12 patients, a statistically significant difference between sertraline and placebo in terms of Liebowitz Social Anxiety Scale (LSAS) score was found in 8. These findings were confirmed recently by a larger, placebo-controlled, parallel-group study by Van Amerigen and colleagues.⁷ 204 patients randomized to sertraline or placebo, with “responder” defined as an individual with a CGI score of “much” or “very much” improved by the end of the study.

Finally, *fluvoxamine* (Luvox) **has also shown efficacy in SAD in 2 relatively small, single-center, placebo-controlled studies, with effect sizes—a statistical measure of efficacy that does not depend on sample size—similar to those of paroxetine and sertraline.** To date, however, there have been no published controlled studies of *fluoxetine* (Prozac) *citalopram* (Celexa), or escitalopram (Lexapro) for the treatment for SAD, although published open trials have suggested their efficacy for this disorder.¹⁰⁻¹³

No published studies have compared different SSRIs with one another for the treatment of SAD. Because all SSRIs had similar effect sizes in the published studies and there is no demonstrated efficacy differential for SSRIs when used to treat other disorders, **it is likely that they have similar efficacy in SAD. Therefore, safety profile of the medication and response to prior treatment should be important considerations in the choice of medication.** However, in the absence of a clear advan-

tage to using one SSRI over another, it appears reasonable to select as the first choice the medications for which more evidence of safety and efficacy is available.

SSRIs should be considered the first-line pharmacological treatment for SAD. Although they have not been directly compared with other medications, **the results from several meta-analyses¹⁴⁻¹⁶ suggest that the SSRIs are probably as effective as monoamine oxidase inhibitors (MAOIs) and benzodiazepines, but with a more favorable safety profile. At the present time, there is no research documenting how long patients need to be on SSRIs. However, anecdotal evidence suggests that earlier discontinuation is associated with higher rates of relapse compared to late discontinuation.**

Benzodiazepines:

There is also evidence of the efficacy of benzodiazepines in the treatment of SAD. *Clonazepam* (Klonopin), *bromazepam* (Lexotan), and *alprazolam* (Xanax) **are the only benzodiazepines that have been studied in placebo-controlled trials.**

In one study, 75 patients were randomized to *clonazepam* or placebo.^{17,18} **The mean dose of clonazepam was 2.4 mg/day (range: 0.5–3.0 mg). At the end of the treatment, 78% of the patients treated with clonazepam were classified as responders, defined by CGI score, compared with 20% in the placebo group.**

Versiani and colleagues conducted a double-blind, placebo-controlled trial with *bromazepam* in 60 patients with SAD.¹⁹ **At the end of the study, bromazepam was statistically superior to placebo in all outcome measures, including the LSAS and the CGI.**

The only placebo-controlled study that included alprazolam failed to show the superiority of this medication over placebo.²⁰ It is possible that alprazolam may be less efficacious than other benzodiazepines in the treatment of SAD; however, it is also possible that the exposure instructions given to all participants in this study and the stringent definition of "response" used by the authors may have masked its superiority to placebo. In addition to these placebo-controlled studies, a number of open trials have suggested that benzodiazepines are efficacious in the treatment of individuals with SAD.^{21,22}

The most common adverse effects of benzodiazepines are those related to their CNS activity. **Although sedation is a common adverse effect during the first days of treatment, most patients develop a tolerance to the sedation within several days.** Another less frequent adverse effect of benzodiazepines is **ataxia, which is particularly important in elderly people, who are at higher risk for overdose because of a reduced metabolic rate associated with aging and for whom falling is particularly dangerous.** In addition, there are concerns about the potential for *abuse and dependence* with this group of medications, especially in individuals with a history of SAD.

In summary, the results from several open trials and placebo-controlled studies have suggested that benzodiazepines are efficacious in treating patients with SAD. **In addition, benzodiazepines, used every day, can help improve symptoms**

of other anxiety disorders such as *panic disorder* or *generalized anxiety disorder*, which are frequently comorbid with SAD. This gain must be balanced with the risk of sedation and other adverse CNS effects that could interfere in the quality of performance.

Irreversible, Nonselective MAOIs—Phenelzine (Nardil) and Tranylcypromine (Parnate):

Until recently, based on its efficacy and the number of published controlled trials, *phenelzine* (Nardil) was considered the gold standard for SAD therapy; however, due to the availability of other medications with similar efficacy and more favorable safety profiles, **phenelzine can no longer be considered a first-line treatment for most patients with SAD.**

Phenelzine

Evidence of the efficacy of phenelzine in treating patients with SAD emerged from 2 different sources. **Four studies of mixed populations showed *phenelzine* to be more effective than placebo in patients with a diversity of phobias, including SAD.**^{23–26} Although the studies had important methodological limitations, they provided some indication for MAOIs.

The second line of evidence came from studies of phenelzine for atypical depression. Two 1980 studies showed phenelzine to be more effective than tricyclic antidepressants in improving *interpersonal hypersensitivity*, a distinctive symptom of atypical depression. Because interpersonal hypersensitivity is probably a core feature of SAD, it was suggested that MAOIs might be useful in its treatment.

Phenelzine is the one of the best-studied treatments for SAD, although there have been more studies conducted with selective SSRIs than with MAOIs.

The most recent study compared phenelzine, placebo, an educational supportive group, and group cognitive behavioral therapy (CBGT).²⁷ **At the end of the 3-month acute phase, CBGT and phenelzine were significantly superior to the other 2 control treatments in terms of range of response, and did not differ from each other. On dimensional ratings, however, phenelzine was superior to CBGT on a number of measures. This result is important because it confirms previous findings from the Gelernter study suggesting that phenelzine might be more efficacious than psychotherapy, at least in short-term treatment.**²⁰

Recent meta-analyses have suggested that phenelzine efficacy may be similar to that of SSRIs and benzodiazepines in the treatment of patients with SAD.^{14–16} The availability of safer medications that have similar or greater efficacy suggests that **MAOIs should be reserved for cases in which other treatments have failed.**

Tranylcypromine (Parnate)

Tranylcypromine, another MAOI, has been studied much less than phenylzine. **Two studies by Versiani and colleagues suggest that it is also efficacious in the**

treatment of patients with SAD.^{28,29} However, the lack of controlled studies limits the strength of this evidence. Frequent adverse effects of MAOIs are sleep disturbances (insomnia, daytime drowsiness), hypotension, and disinhibition. The main disadvantage of nonreversible MAOIs (including phenelzine, of course) is the risk for a hypertensive crisis when dietary and related precautions are not strictly followed. To avoid a *tyramine crisis*, the patient should be instructed to avoid foods with a substantial tyramine content, such as aged cheese or pickled fish. Although a hypertensive crisis is a potentially more dangerous adverse effect, hypotension is a more common adverse cardiovascular effect. Use of elastic stockings or increased salt consumption is usually enough to treat hypotension. If postural hypotension becomes a problem, mineralocorticoids may be given while monitoring serum potassium concentrations to avoid hypokalemia. ***Patients should be instructed to inform their other doctors, including dentists, that they are taking a MAOI to minimize the risk for undesired drug interactions.***

Phenelzine appears to be effective in approximately two thirds of patients with SAD. The standard starting dose of 15 mg/day can be increased to 30 mg/day after 3 days. If it is well tolerated, it can be increased to 45 mg/day during the second week of treatment and 60 mg/day during the third or fourth week. The maximum recommended dose is 75 to 90 mg/day, unless the appearance of side effects precludes the use of those doses.

Tranylcypromine therapy can begin with 10 mg/day and increase to 60 mg/day. The usual dose is between 40 and 60 mg/day.

MAOIs must be tapered off gradually for safety, and dietary precautions should be continued for 2 weeks after discontinuation. As with the SSRIs, there is little information on how long these medications should be taken to prevent relapse. This is an area of important and ongoing research.

Reversible Inhibitors of Monoamine Oxidase A: Moclobemide (Aurorix) and Brofaromine (Conosar)

The safety profile of irreversible MAOIs, especially the risk for a hypertensive crisis when dietary restrictions are not followed, has stimulated an interest in the study of reversible inhibitors of MAOI-A (RIMAs). Clinical experience has shown that dietary restrictions are unnecessary for drugs in this group; unfortunately, they seem to be less effective than phenelzine.

Moclobemide was the first RIMA to be developed. **Four placebo-controlled studies have been published, with mixed results.** In the initial study, Versiani and colleagues found significant differences between moclobemide and placebo (in the range of the differences found in the phenelzine and SSRI studies),³⁰ but later studies have found either nonsignificant differences³¹ or effect sizes of limited clinical significance.^{32,33} **The only adverse effect noted to be greater in patients taking moclobemide compared with those taking placebo was nausea. All of this suggests that moclobemide, although probably better tolerated than phenelzine, is less effective in the treatment of patients with SAD.**

Although it is also a RIMA, **brofaromine** (Conosar) differs from moclobemide by having serotonin reuptake properties as well. There are 3 published studies of brofaromine in patients with SAD,³⁴⁻³⁶ all of which have shown brofaromine to be an efficacious treatment. Unfortunately, the development of brofaromine was stopped by the manufacturer due to reasons unrelated to its safety or efficacy in SAD, and it is not available for treatment. However, the effect size of brofaromine in the published trials is similar to that of the MAOIs and SSRIs, suggesting that its clinical development may have been stopped prematurely.

Although RIMAs are generally well tolerated, they are either of limited clinical efficacy or are not available. Therefore, the available evidence does not suggest a prominent role for this group of medications in the majority of patients with SAD.

Other Medications

β-Adrenergic Blockers

A number of open and placebo-controlled trials have failed to show the efficacy of β-blockers in the treatment of patients with SAD. However, it is important to note that most patients in those studies had generalized SAD. In contrast, anecdotal evidence suggests that β-blockers are effective for performance anxiety. *β-blockers have the advantage over benzodiazepines of rarely impairing concentration or coordination.* β-blockers are generally well tolerated. Adverse effects associated with β-blockers include hypotension, bradycardia, exacerbation of asthma or diabetes, and sexual dysfunction. *The use of β-blockers is generally contraindicated in athletes because they can impede physical performance.* Although doses need to be individualized for each patient, a 10- to 40-mg dose of *propranolol* (Inderal) or equivalent medication taken 45 to 60 minutes before the performance is sufficient for most patients.

Gabapentin (Neurontin)

Pande and colleagues conducted a 14-week, placebo-controlled trial of gabapentin in 69 patients meeting the DSM-IV criteria for SAD.³⁷ Response rates were 32% in the gabapentin group and 14% in the placebo group, based on CGI scores. Sixty-two percent of responders were taking gabapentin 3600 mg/day, the highest allowed dose in the trial, suggesting that high doses of gabapentin may be needed to achieve a response in patients with SAD. Adverse effects of this drug tend to be mild and transient; the most frequent are sedation, dizziness, and ataxia.

Venlafaxine (Effexor)

Venlafaxine selectively inhibits the reuptake of both serotonin and norepinephrine. An 8-week open trial of venlafaxine in patients with DSM-III-R criteria for

SAD³⁸ using doses of 75 to 300 mg/day, 50% of the patients who completed the study were considered responders according to CGI scores. **There was a high incidence of adverse effects, such as nausea, decreased libido, erectile dysfunction, and urinary difficulty. This trial seems to indicate that venlafaxine may not be as useful as phenelzine or SSRIs in the treatment of patients with SAD.** However, the new, extended-release formulation of venlafaxine appears to have a much better tolerability profile. A better assessment can be made when the results of ongoing trials are published.

Buspirone (BuSpar)

The efficacy of SSRIs in the treatment of patients with SAD stimulated an interest in the study of other drugs with properties that might be effective in this disorder. **Although the results from 2 open trials have suggested that buspirone could be effective for patients with SAD,^{39,40} these results were not confirmed by 2 controlled-placebo studies.^{41,42} Buspirone and its metabolites are excreted primarily by the kidneys. Therefore, it should be used with caution in patients with hepatic dysfunction and impaired renal function.** Although systematic evidence is lacking, buspirone may be a useful adjuvant in partial responders to SSRIs. *The combined use of MAOIs and buspirone is not recommended because of the potential for a hypertensive crisis.*

Tricyclic Antidepressants

In the only controlled study of these medications,⁴³ Emmanuel and colleagues treated 41 patients with imipramine (Tofranil) or placebo for 8 weeks and found no statistically significant difference. Similarly, Simpson and colleagues,⁴⁴ reporting a series of 15 patients treated with imipramine at a mean dose of 176.4 mg/day found only 20% of the patients to be improved at the end of the treatment period. Two other researchers found similar results,^{45,46} which suggests that **tricyclic antidepressants are not efficacious in the treatment of patients with SAD.**

Maintenance Treatment

In contrast with the wealth of literature on the acute treatment of patients with SAD, much less is known about the long-term management of this condition. This is particularly important, given the chronic course of this disorder and the need for predictors of relapse. **In the original study by Liebowitz and colleagues,^{47,48} patients who were considered to be responders to phenelzine in the acute phase were offered 8 additional weeks of treatment. The extended phase of the trial did not result in further gains; however, when half the patients were switched to double-blind placebo, one third of those patients relapsed. Similarly, in the Versiani³⁰ study a 50% loss of treatment gains was reported within 2 months after discontinuation of phenelzine in responders after 1 month of treatment under double-blind conditions.**

Liebowitz and colleagues^{47,48} compared the durability of response with *phenelzine* and CBGT in patients who had responded acutely to those treatments. **Relapse rates during maintenance did not differ from those observed between treatments; however, patients treated with phenelzine showed a statistically significant higher rate of relapse during 6 months without treatment.** Gelernter²⁰ found no loss of acute treatment benefits in phenelzine patients 2 months after interrupting treatment. Because these patients were given exposure instructions, these findings suggest that phenelzine and CBT may be complementary treatment approaches.

The only long-term data available for *paroxetine* are from an 11-week open trial followed by a 12-week, double-blind, placebo-controlled trial to evaluate relapse rates.⁴⁹ Relapse rates during the discontinuation phase were 13% for the group that continued paroxetine therapy versus 63% in the group that was switched to placebo. Walker and colleagues studied prevention of relapse in generalized social phobia in a 24-week trial in responders to 20 weeks of *sertraline* treatment.⁵⁰ **Relapse rates were 4% for patients who continued on sertraline versus 36% for patients who were switched to placebo.** Finally, van Vliet reported the findings of a study of *fluvoxamine* in 16 patients, 14 of whom chose to enter an additional 12-week continuation phase.⁵¹ The authors did not include a discontinuation phase in their design, however, making it impossible to compare relapsed rates for *fluvoxamine* with the rates of other SSRIs.

It appears that further gains are possible for some patients who continue drug therapy after the acute treatment phase, although the optimal length of treatment is unknown at the present time. A high proportion of patients tends to relapse when medication is discontinued. At present, there are no known predictors of relapse. Similarly, whether longer periods of treatment can decrease the risk of relapse is unknown.

Combination Therapy:

Although an increasing number of medications have been evaluated and have demonstrated efficacy for the treatment of patients with SAD, it has been increasingly acknowledged that psychosocial treatments can play an important role in the overall management of these patients. Cognitive behavioral therapy (CBT) is the most thoroughly studied nonpharmacological approach to SAD. Its efficacy has been shown in many investigations.⁵²⁻⁵⁴ **A recent meta-analysis and limited data from published studies suggest that the acute efficacy of CBT may be slightly lower than that of pharmacotherapy.¹⁵ However, limited data from a study by Liebowitz and colleagues suggest that the effects of CBT may last longer than pharmacological treatments after discontinuation.^{47,48}**

Although the concurrent use of medication and psychotherapy is common in clinical practice, few studies have examined the efficacy of this approach in the

treatment of patients with SAD. **Only 2 studies have provided data on combination therapy using medication and psychotherapy and, as was the case for drug-CBT comparisons, neither study examined medications that proved superior to placebo.^{55,56} In contrast, preliminary data from the Heimberg study indicate that the efficacy of the combination of CBGT and phenelzine may be superior to that of either approach alone.²⁷**

These results suggest that further studies on the efficacy of combination therapy during the acute treatment phase in patients with SAD are sorely needed. In addition, it will be important to determine whether sequential treatment (medication before or after nonpharmacologic therapy) will induce further improvement in partial responders or help prevent relapse in full responders.

Choice of Treatment:

The previous review has shown that a series of medications can be useful in the treatment of patients with SAD. It appears reasonable to offer a trial of medication to any individual with SAD, *provided there are no contraindications, such as pregnancy*. **The choice of pharmacological agent for a specific case depends on the diagnostic subtype of SAD, the presence of comorbidity, and patient preference.**

Cases of nongeneralized SAD, in which feared performance situations arise only occasionally and predictably, can be treated initially with β -blockers on an as-needed basis. In these situations, a β -blocker such as *propranolol* (Indural) or *atenolol* (Tenormin) can be taken 45 to 60 minutes before a specific performance situation. If these medications are not effective or are contraindicated, benzodiazepines can be used. Unfortunately, the benzodiazepine dose needed for these cases may cause sedation.

In cases of generalized or nongeneralized SAD with frequent unexpected performance situations, SSRIs, benzodiazepines (if tolerated at the needed doses), or MAOIs may be effective. SSRIs, due to their favorable safety profile and efficacy, are the treatment of choice for most patients, with benzodiazepines a second choice and MAOIs a second or third choice.

Little is known about predictors of response or treatment of nonresponders. Stein and colleagues combined data from 3 placebo-controlled, multicenter trials of paroxetine in patients with SAD to identify predictors of response.⁵⁷ **In paroxetine-treated patients, a substantial number of nonresponders at week 8 (46/166; 27.7%) had become responders by week 12. The only statistically significant predictor of treatment response was duration of treatment.** In contrast, demographic, physiologic, clinical, and trial variables did not predict responder status at the end of 12 weeks. **Based on the results of this study, it appears that an optimal trial of medication may have to continue beyond 8 weeks, in contrast to what is generally advocated for the treatment of a major depressive disorder.** Additional prospective work is needed to continue to search for predictors of response and to identify optimal strategies for treatment-resistant SAD.

Combining medications that have shown efficacy in patients with SAD is probably a reasonable strategy. However, data supporting the superiority of one combination of medications over others or even the efficacy of such combinations are lacking. When combining medications, it is important to keep in mind the risk for hypotension when MAOIs and β -blockers are given together. *MAOIs and SSRIs should never be combined due to the risk for serotonergic syndrome.*

Treatment of Children and Adolescents:

Although SAD often begins during childhood, little is known about pharmacotherapy appropriate for this age group. In an early study, Simeon and Ferguson treated a group of children with avoidance and anxiety disorders with open-label *alprazolam* (Xanax).⁵⁸ Child- and parent-rated anxiety symptoms decreased for both diagnostic groups, while cognitive functioning improved with treatment. However, these data could not be confirmed later in a placebo-controlled study by Simeon and colleagues.⁵⁹

Fairbanks and colleagues treated a group of children with mixed anxiety disorders that had not responded to psychotherapy.⁶⁰ Treatment with *fluoxetine* (Prozac) started with a dose of 5 mg/day that was increased by 5 to 10 mg/day each week for 6 to 9 weeks until improvement occurred or a maximum of 40 mg/day (for children under 12 years of age) or 80 mg/day (for children older than 12 years) was reached. Of the 10 children with SAD, 8 obtained a rating of very much improved based on CGI scores.

Most recently, Pine and colleagues studied 128 children aged 6 to 17 years who met criteria for social anxiety, separation anxiety disorder, or generalized anxiety disorder and had received psychological treatment for 3 weeks without improvement.⁶¹ Children were randomly assigned to *fluvoxamine* (Luvox) up to 300 mg/day or placebo for 8 weeks and were evaluated with rating scales designed to assess the degree of anxiety and impairment. The scores on the Pediatric Anxiety Rating Scale indicated that the children in both groups had high pretreatment levels of anxiety.

Children in the *fluvoxamine* group (n=63) had a mean decrease of 9.7 (SD = 6.9) points in symptoms of anxiety on the Pediatric Anxiety Rating Scale, compared with a decrease of 3.1 (SD = 4.8) points among children in the placebo group (n=65). According to CGI scores, 48 (76%) children in the fluvoxamine group responded to the treatment, as indicated by a score of < 4, compared with 19 (29%) children in the placebo group. Five children (8%) in the fluvoxamine group discontinued treatment because of adverse events, compared with 1 child (2%) in the placebo group. **The results of this trial suggest that fluvoxamine may be an effective treatment for children and adolescents with anxiety disorders, including SAD.**

Overall, these studies suggest that treatment with SSRIs (and maybe with other medications) may be highly efficacious in the reduction of symptoms of

anxiety, particularly social anxiety, in children. Early treatment of SAD in children holds theoretical promise for reduction of long-term morbidity; however, further research is needed to confirm these promising initial results.

Conclusion

In the last 2 decades, a growing interest in the study of SAD and a corresponding growth in the number of pharmacological treatments available for this disorder has been seen. This progress has led to new questions for clinical research. At present, there is no information on potential predictors of response or how long a medication regimen should be maintained before considering alternative treatment strategies.

Similarly, **little is known about maintenance treatment and prevention of relapse. Many patients are reluctant or unable to continue long-term medical maintenance therapy because of side effects, including teratogenic effects, or fear of becoming addicted to the medication. It would be useful to have some idea of an individual's vulnerability to relapse when making decisions about continuing or discontinuing medication treatment.**

Finally, **the area of combined and sequential treatment has not received sufficient attention. Although data from clinical trials suggest that between one half and two thirds of patients treated with medication are classified as responders, a closer look reveals that only half of those patients are "full responders" (ie, symptom-free at the end of treatment). Thus, despite enormous progress in the pharmacological treatment of SAD, the majority of patients remain symptomatic after treatment. Further work is needed to improve the prognosis and quality of life of individuals suffering from this pervasive, silently disabling disorder.**

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