

Social Anxiety Disorder Assessment and Pharmacological Management

I. Figueira, R. Jacques

Institute of Psychiatry – Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

Corresponding author: Dr. Ivan Figueira, M.D., Associate Professor of Psychiatry, Rua Dona Mariana 82/1503 Bloco 1, Botafogo, Rio de Janeiro – RJ, ZIP code 22280-020, Brazil, ilvf@uol.com.br

Abstract

Social phobia is one of the most common disorders in the general population, with a lifetime prevalence of 11% to 15%, and is highly prevalent in primary care settings. Only 5% of social phobic patients seek treatment, despite numerous related complications when the disorder goes untreated. It is advisable, therefore, that clinicians be prepared to recognize and effectively manage patients with this anxiety disorder. We provide a brief review of the assessment, differential diagnosis and pharmacological treatment of social phobia. We based our suggestions for treatment on the results of randomized clinical trials found in the PUB-MED/MEDLINE database from 1966 to February of 2001 as well as on our clinical experience with social phobic patients. Of the three classes of drugs with established efficacy in the treatment of social phobia (irreversible MAOIs, SSRIs and benzodiazepines) the SSRIs are considered the treatment of choice because of their tolerability, side effect profile and safety. Two other classes of drugs are considered of controversial efficacy (reversible type-A MAOIs and beta-blockers), while several new drugs have shown positive initial results (gabapentin, venlafaxine and nefazodone). When SSRI treatment is ineffective, psychiatrists should not shy away from prescribing benzodiazepines or MAOIs if the risks of abuse/dependency (with benzodiazepines) or hypertensive crises (with MAOIs) are outweighed by the suffering and impairment associated with severe cases (German J Psychiatry 2002;5:40-48).

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Introduction

Social Phobia (also known as social anxiety disorder) is a marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The main feature of this disorder is the patient's fear that he or she will act in a way (or show anxiety symptoms) that will be humiliating or embarrassing (American Psychiatric Association, 1994). It is often associated with anticipatory anxiety, leading the patient to avoid situations in which there is the risk of social exposure.

Recent research indicates that social phobia is the most common anxiety disorder, and is the third most common mental disorder after depressive disorder and alcohol abuse/dependency (Kessler et al., 1994). The degree of disability and impairment in social phobic patients is considered to be as serious as that of other chronic conditions like major depressive disorder. This impairment is worsened by the cluster of associated comorbidities that is present in most patients (Davidson et al., 1993a). Despite these factors, social phobia is still not widely recognized by health professionals.

Prevalence

Social phobia is the most common anxiety disorder in the general population (lifetime prevalence, 13.3%; one-year prevalence, 7.9%) (Kessler et al., 1994). It is the third most common mental disorder after major depression and alcohol abuse/ dependency. Only recently was social phobia studied in primary care settings (Bisserbe et al., 1996). These studies have shown that, in spite of its prevalence among primary care patients (7%) (Stein et al., 1999b), social phobia is under-recognized by primary care physicians (Bisserbe et al., 1996).

Age and Gender Distribution

Epidemiological research indicates that in the general population women are more frequently affected by social phobia than men (2.5:1) (Kessler et al., 1994). However, in clinical samples the inverse is more often seen. Some have interpreted this as evidence that men feel more impairment in their social and occupational lives (probably due to greater social expectations and pressures on men's performance). The peak of onset occurs in adolescence, although onset of social phobia may occur anywhere between 5 and 35 years of age (Burke et al., 1990; Sandanger et al., 1999).

Clinical Findings

Once considered the "neglected anxiety disorder" (Liebowitz et al., 1985), social phobia is receiving growing interest, mainly due to the positive results of new therapeutic strategies. In turn, these therapeutic advances are stimulating further clinical-epidemiological research, thus refining the social phobia diagnosis.

According to DSM-IV diagnostic criteria for Social Phobia (American Psychiatric Association, 1994), this disorder is characterized mainly by a marked and persistent fear of social situations, with the person is exposed to scrutiny. This exposure almost invariably provokes anxiety, and the person recognizes that this anxiety is excessive or unreasonable. Patients often avoid social situations, or endure them with intense distress. At last, symptoms are not due to substance abuse, and are not better accounted for by a general medical condition or another mental disorder.

The situations that social phobic patients tend to avoid are: public speaking, performing in front of others (e.g., singing, playing an instrument, joining in games), eating, writing, or urinating in public. Apart from these performance situations, social phobic patients also tend to avoid social interactions (e.g., being introduced to strangers, deal-

ing with authorities, returning products in stores) (Liebowitz, 1999). The most common physical symptoms of social phobia are: blushing, hand tremor, sweating and tachycardia. These symptoms usually appear in mild form well in advance of the feared situation, intensifying as it approaches, and reaching a peak during the social interaction. This somatic discomfort often becomes a source of distraction and embarrassment, further increasing the patient's anxiety. This positive feedback loop lasts as long as the patient is in the feared situation (some patients report that symptoms may diminish a bit if the situation lasts a long time, but nevertheless persist throughout). This is in contrast to "normal" social anxiety, which usually diminishes once the social interaction begins (as the individual perceives that his performance is adequate).

Subtypes

While some social phobic patients seem to have troubles in only one or a few situations, there is a group of patients who manifest extreme anxiety in a broad spectrum of performance situations as well as social interactions. This latter group is denominated "generalized social phobia", while the former is referred to as "specific" or "circumscribed social phobia". Research shows that generalized social phobic patients, in comparison with circumscribed social phobic patients, experience higher impairment, have more comorbid conditions, have more family members similarly affected, and more commonly meet criteria for avoidant personality disorder (Stein et al., 2000).

Comorbidity

Around 80% of social phobic patients are affected with a comorbid disorder during their lifetime, suggesting that comorbidity is more the rule than the exception (Schneier et al., 1992). In a review of epidemiological research, anxiety disorders were the most common comorbidity of social phobia (in about 50% of patients), followed by mood disorders (41%) and substance use disorders (39%) (Merikangas et al., 1995).

Epidemiological analyses show that the rate of suicide attempts is higher among social phobic patients with comorbidities compared with "pure" social phobic patients: 16% versus 1% (Schneier et al., 1992). On the other hand, the presence of comorbidities has been shown to be crucial in a patient's decision to seek treatment: more than half of patients with comorbidities seek medical help, while only 20% of those without comorbidities do so.

Clinical research demonstrates a strong bi-directional association between alcohol abuse and social phobia: a high prevalence of alcohol-related complications among social phobic patients, as well as a high prevalence of social phobia among alcoholics (Lepine et al., 1998). Drinking alcohol

when faced with a social situation is common among social phobic patients, occurring primarily before dates, social meetings, parties and business lunches. It is widely held that the majority of these cases are attempts at self-medication (Abrams et al., 2001).

Differential Diagnosis

Normal Social Anxiety

Distinguishing between social phobia and normal social anxiety, or just plain shyness, is not always an easy task (Katschnig, 1996). When faced with a shy or socially anxious patient, two important questions to ask are: (1) "Does the patient avoid the phobic situation, or endure it only with intense anxiety?" and, (2) "To what extent has the shyness impaired the patient's job, family or personal life?". These two questions are based on the DSM-IV criteria, which require not only that "feared social or performance situations are avoided or else are endured with intense anxiety or distress", but also that this avoidance or distress "interferes significantly" with the patient's life. The key point here is that normal social anxiety or shyness is an inconvenience, whereas social phobia seriously affects the sufferer's quality of life.

Panic Disorder

Careful observation of the nature and onset patterns of anxiety suffered by a patient can help clinicians distinguish between social phobia and panic disorder (with or without agoraphobia).

First and foremost, a panic disorder patient suffers more from the fear of a panic attack itself than from the fear of a social situation where an attack might take place (Uhde et al., 1991). Conversely, although social phobics may suffer panic attacks in feared social situations, what they fear is not the panic attack itself but the idea of being the focus of others' attention.

Onset is different in the two disorders: the anxiety associated with social phobia begins gradually, whereas panic disorder-related attacks are often of abrupt onset. In addition, panic disorder attacks often occur spontaneously, with no clear triggering events, in social phobia this is not the case: the panic attack only occurs in conjunction with the feared social situation.

A further important distinction between panic and social phobic patients is their relationship to other people: while panic patients seek to relieve their anxiety in the company of others (believing that if they have a panic attack someone will help them), social phobic patients seek to relieve their anxiety by avoiding others (fearing their judgment or scrutiny) (Moutier et al., 1999).

Other Disorders

Social phobic patients retain their interest in social interaction, but feel impeded or prevented from taking part by fear related to their anxiety. Schizoid personality disorder differs from social phobia in that schizoid patients have no interest in social interaction (Herbert et al., 1992). Depressive patients also avoid social activities, but this is due more to their anhedonia (i.e., loss of pleasure) than to fear or anxiety (Moutier et al., 1999).

Course and Prognosis

Social phobia is a disorder with an early onset (usually between age 15 and 20 years) and a steady and insidious course. Patients often suffer from symptoms for many years without looking for medical help. The long duration of this disorder increases the risk of comorbidities, which may serve to mask social phobia itself (Sareen et al., 2000). Unfortunately, virtually no studies have followed patients into their late life, so we can draw few conclusions about the natural history of social phobia.

Social phobia is a disabling condition that frequently causes marked impairment in the patients' functional life and interpersonal relationships. Subjects tend to avoid social interactions, leisure activities and parties. It is common for patients whose illness begins at a young age to drop out of school.

Social phobia often limits one's potential for work and income: some patients avoid job interviews and/or have difficulties dealing with superiors, colleagues, or the public. Studies have shown levels of impairment in social phobia comparable to those of major depressive disorder and panic disorder (Wittchen et al., 1996).

Pharmacological Treatment

The purpose of this section is, aside from giving a brief review of the efficacy of pharmacological treatment in social phobia, to give some guidance based on our clinical experience with these patients. Clinicians must have in mind that drugs are not the only efficacious treatment studied. Others treatments, specially cognitive behavioral therapy have proven to be a good choice in social phobic patients, (Heimberg et al., 1994; Heimberg et al., 1998; Juster et al., 1996; Otto, 1999; Taylor, 1996). Nevertheless, this is out of the scope of this article, and this treatment review will be focused on pharmacological agents.

Based on randomized clinical trials, psychopharmacological agents may be classified in 3 different categories in terms of efficacy in the treatment of social phobia: (1) medications with established efficacy (irreversible MAOIs, benzodiazepi-

Table 1: Double-Blind Controlled Studies of Irreversible MAOIs in the Treatment of Social Phobia

Authors	Total N	Duration (weeks)	Treatment	Dose (mg/day)	Results* (%)
Gelernter et al., 1991	65	12	Alprazolam	4.2	38
			Phenelzine	55	69**
			Placebo	-	20
Liebowitz et al., 1992	74	8	Phenelzine	75.7	64**
			Atenolol	97.6	30
			Placebo	-	23
Versiani et al., 1992	78	16	Phenelzine	69.3	91**
			Moclobemide	582	82**
			Placebo	-	43
Heimberg et al., 1998	133	12	Phenelzine	59.6	77
			Placebo	-	41

* Percent improvement on the Clinical Global Impression Scale

** Statistically significant differences were found for the following medications: phenelzine vs placebo (Gelernter, 1991; Liebowitz, 1992; Versiani, 1992; Heimberg, 1998) and for moclobemide versus placebo (Versiani, 1992).

nes and SSRIs); (2) those whose efficacy has not been completely established (beta-blockers and Type-A MAOI); and (3) medications that have shown initial positive results (gabapentin, venlafaxine and nefazodone).

Treatment of social phobic patients, whether pharmacological, psychological or a combined approach, should strive to monitor and reduce the following clinical aspects of social phobia syndrome: (1) fear; (2) distorted beliefs (e.g., "I will tremble if I sign my name while others are watching me"); (3) anticipatory anxiety; (4) avoidance behaviors; and (5) autonomic symptoms. The reduction of these 5 psychopathological dimensions is associated with a concomitant improvement in both the functional impairment and quality of life.

Medications with Established Efficacy

Irreversible MAOIs

The irreversible MAOIs (tranylcypromine and phenelzine) were the first pharmacological agents to be utilized in social phobia and are considered the most effective drugs in the treatment of this disorder. Analyzing 4 clinical randomized trials (Table 1), we observe that the irreversible MAOIs showed efficacy in about 2/3 of social phobic patients. However, aside from a number of side effects, treatment with MAOIs runs the risk of precipitating hypertensive crises in patients that ingest tyramine-rich food or drink, or as a result of interactions with sympathicomimetic medications. For this reason, at present the irreversible MAOIs are recommended only in the most serious and incapacitating cases of social phobia, which have shown resistance to psychological and other pharmacological treatments. Other side effects associated with irreversible MAOIs include postural hypotension, sleep disturbances (initial insomnia and afternoon somnolence) and weight gain.

Benzodiazepines

Of 3 benzodiazepines studied, two have shown efficacy in double-blind placebo trials: clonazepam (Davidson et al., 1993b), and bromazepam (Versiani et al., 1997). Bromazepam has not been frequently used due, among other reasons, to its low potency per milligram. It is only effective in high doses and has a high rate of sedation. Clonazepam is the most studied benzodiazepine in the treatment of social phobia. Davidson et al (1993) treated 75 patients with a median dose of 2.4 mg/day of clonazepam. The response rate with clonazepam and placebo was 78% and 20%, respectively. Clonazepam was well tolerated and the only undesirable effects that differentiated it in relation to placebo were the persistence and frequency of unsteadiness and dizziness. A third double-blind placebo trial was conducted with the benzodiazepine alprazolam; however, the results are unconvincing due to several methodological flaws (e.g., only 12 patients received alprazolam during the trial). This study found a very low efficacy for alprazolam compared to placebo: 38% versus 20%.

In our clinical experience with social phobic patients, we typically introduce clonazepam by prescribing 0.5 mg at breakfast and 0.5 mg at lunch, increasing 0.5 mg/day every two weeks until reaching the median dose of 2 mg/day. We pay special attention to the development of disinhibition (when the patient very rapidly begins to behave in a markedly unrestrained manner) and irritability. Patients do not usually report the development of these treatment complications spontaneously (they typically lack insight into their own behavioral changes); for this reason, the possible development of these side effects should be actively monitored.

Of greater concern in using benzodiazepines in the treatment of social phobia is the risk of physical dependency and abuse. As generalized social phobia is a chronic disease, we usually prescribe benzodiazepines for at least one to two years, a factor that elevates the risk of dependency. It is a serious error to take patients off benzodiazepines too quickly, and patients must be advised not to abruptly stop benzodiazepine treatment due to the risk of withdrawal

Table 2: Double-Blind Controlled Studies of Benzodiazepines in the Treatment of Social Phobia

Authors	Total N	Duration (weeks)	Treatment	Dose (mg/day)	Results* (%)
Gelernter et al., 1991	65	12	Alprazolam	4.2	38**
			Phenelzine	55	69
			Placebo	-	20
Davidson et al., 1992	75	10	Clonazepam	2.4	78.3
			Placebo	-	20
Versiani et al., 1997	60	12	Bromazepam	21	Bromazepam > placebo
				-	

* Percent improvement on the Clinical Global Impression Scale

** All comparisons between the different drugs were statistically significant; alprazolam versus placebo was the only exception

reactions (which in rare cases can cause severe convulsions). Nonetheless, withdrawal and dependency can be avoided through careful management: in our experience, by taking the patient off benzodiazepine very slowly (e.g., reducing the dosage by 0.25 mg/month of clonazepam over a period of four to ten months) dependence effects can be avoided. The likelihood of abuse of benzodiazepines in social phobia, though widely feared, is in our experience minimal among most patients.

In sum, although there are risks of abuse and dependency in using benzodiazepines in social phobia, we think the potential benefits outweigh the risks, especially for more severe cases. However, there are many patients with severe social phobia who never had received a trial with benzodiazepines trial due to the fear of abuse or dependency. We believe that no patient with severe social phobia should be considered treatment-refractory without having received a trial of at least 4 mg/day of clonazepam for a period of three to four months.

Selective Serotonin Reuptake Inhibitors (SSRIs)

The SSRIs are considered the first choice medication in the treatment of social phobia. The major advantages of the SSRIs in comparison with the irreversible MAOIs and the benzodiazepines include a more acceptable side effect profile, lower safety risk, and easier posology. Although the irreversible MAOIs and benzodiazepines such as clonazepam, according to data from randomized trials, appear to be more efficacious than the SSRIs, the risks associated with them (hypertensive crisis for MAOIs and abuse or dependency for benzodiazepines) make them second or third choice medications. The SSRIs are usually very well tolerated in the short term. In the first two months patients most frequently complain of gastrointestinal disturbances

(e.g. nausea, diarrhea), sleep problems (insomnia or afternoon sleepiness), and occasionally headaches. In the medium and long term, complaints center on side effects related to sexual function, mainly ejaculatory retardation and delay or lack of orgasm. These unwanted sexual side effects of SSRIs are estimated to occur in 40-70% of patients (initial studies estimated 1 to 10%). Patients typically do not report information about sexual problems spontaneously, so clinicians should actively question their patients about such side effects.

Over time, other side effects have surfaced. It has been shown that weight gain is a problem in a significant subgroup of patients who took paroxetine during a medium period (onset after 3 to 6 months of treatment). The lesson to be learned is that SSRIs are relatively new psychopharmacological agents and we have not yet mapped out the undesirable side effects of long term usage.

We found 7 randomized clinical trials showing the efficacy of SSRIs in the treatment of social phobia (Allgulander, 1999; Baldwin et al., 1999; Katzelnick et al., 1995; Stein et al., 1999a; Stein et al., 1998; van Ameringen et al., 2001; Stein et al., 1998; van Vliet et al., 1994). The standard initial dose for fluoxetine, paroxetine and citalopram is 20 mg/day; for sertraline it is 50 mg/day and for fluvoxamine 100 mg/day. In our experience, a reasonable time frame for a therapeutic trial of SSRIs in social phobia is between eight and twelve weeks.

About 30% of patients with panic disorder associated with social phobia suffer a worsening of panic symptoms when treated with SSRIs; such patients should therefore be treated with lower initial doses of SSRIs. For fluoxetine, for example, we recommend an initial dose between 5 and 10 mg/day (this initial dose may be increased if given in combination with benzodiazepines).

Psychopharmacological agents with indeterminate efficacy

Beta-blockers have a long tradition of use in the treatment of non-generalized social phobia. Since the 70s they have been used to improve performance anxiety experienced by musicians, speakers, marksmen and students during exams. Beta-blockers are used in these populations to control the autonomic symptoms (trembling, tachycardia, sweating, etc.) activated by the performance situation. Even today speakers use beta-blockers for this reason. A study showed that approximately 1/3 of the cardiologists giving lecturers in a symposium used beta-blockers to control their performance anxiety (Gossard et al., 1984). However, beta-blockers appear to be non-efficacious in generalized social phobia. In a landmark study, Liebowitz et al (1990) found that there was no significant difference between atenolol and placebo, with atenolol showing inferior results to those of phenelzine (Liebowitz et al., 1990). Likewise, Turner et al. found atenolol not superior to placebo: 47% versus 44%, respectively (Turner et al., 1994). Thus, the contemporary consensus is that beta-blockers are not efficacious for the generalized subtype of social phobia.; however, the small sample size of both studies makes it difficult to draw conclusions about the efficacy of beta-blockers in the non-generalized subtype of social phobia. Interest in beta-blockers as a treatment for non-generalized social phobia remains, largely because they are widely prescribed in treating non-clinical performance anxiety. However, positive results with non-clinical samples cannot be generalized to social phobic patients, and further clinical research focusing on nongeneralized social phobic patients is warranted.

Reversible Inhibitors of Monoaminoxidase A (RIMA)

Since the irreversible MAOIs can provoke potentially lethal side effects (hypertensive crises), new pharmacological agents were developed to eliminate this risk. As a result, a new class of reversible and selective inhibitors of monoaminoxidase were created: the reversible inhibitors of monoaminoxidase A (RIMA). Several studies have shown that type-A MAOIs such as moclobemide are safe in terms of the risk of hypertensive crises in patients who consume foods rich in tyramine (Hilton et al., 1995). However, the effectiveness of moclobemide in the treatment of social phobia has disappointed researchers and clinicians. Despite initial promising results (Bisserbe et al., 1994; Versiani et al., 1992; International Multicenter Clinical Trial Group on Moclobemide in Social Phobia, 1997), later studies have been unable to confirm the efficacy of moclobemide in social phobia (Noyes et al., 1997; Schneier et al., 1998). Nevertheless, some social phobic patients may benefit from this medication, especially in doses above 600 mg/day (Montgomery, 1997). Another type-A MAOI, brofaromine, has also shown initial positive results in randomized clinical trials but was withdrawn from the market by the manufacturer.

Preliminary Studies with Positive Results

Three different psychopharmacological agents (gabapentin, venlafaxine and nefazodone) have shown initial positive results in the treatment of social phobic patients. Of these 3 agents, gabapentin (an anticonvulsant) has the most well-documented efficacy since it was evaluated in a randomized clinical trial (Pande et al., 1999), while the other two (the antidepressants venlafaxine and nefazodone) were evaluated in open clinical trials (Altamura et al., 1999; van Ameringen et al., 1999). Further randomized clinical trials should

Table 3: Double-Blind Controlled Studies of SSRIs in the Treatment of Social Phobia

Author	Total N	Duration (weeks)	Treatment	Dose (mg/day)	Results* (%)
van Vliet et al., 1994	30	12	Fluvoxamine	150	46**
			Placebo	-	7
Katzelnick et al., 1995	12	10 crossover	Sertraline	133.5	50
			Placebo	-	9
Stein et al., 1998	187	12 multicenter	Paroxetine	50	55
			Placebo	-	23.9
Stein et al., 1999	92	12 multicenter	Fluvoxamine	202	42.9
			Placebo	-	22.7
Baldwin et al., 1999	290	12 multicenter	Paroxetine	34.7	65.7
			Placebo	-	32.4
Allgulander et al., 1999	92	12	Paroxetine	20 a 50	70
			Placebo	-	8.3
van Ameringen et al., 2001	204	20 multicenter	Sertraline	146.7	53
			Placebo	-	29

* Percent improvement on the Clinical Global Impression Scale

** All comparisons between the different drugs were statistically significant.

be undertaken in order to better assess the effectiveness of these new pharmacological strategies.

Conclusions

Social phobia is a disorder that is common, chronic, of early onset, and is considered a risk factor for depression, drug or alcohol abuse and substance dependency disorders. Social phobic patients, when untreated, suffer from impairment in numerous areas of daily life: affective (difficulty in romantic relationships), vocational (quitting jobs; refusing promotions), and educational (dropping out of school or classes). Although initially considered an infrequent disorder, today social phobia is estimated to be the third most common mental disorder in the general population. Due to its high prevalence, marked functional impairment (mainly in the generalized subtype), and the existence of effective treatments (psychotherapeutic and psychopharmacological strategies), social phobia is more and more frequently being considered a problem worthy of the attention of public health authorities.

The pharmacological agents with established efficacy include the SSRIs, irreversible MAOIs and benzodiazepines. The role of beta-blockers remains controversial, with potential applications in the p.r.n treatment of performance situations in social phobia. Initial positive results were found with gabapentin, venlafaxine and nefazodone. Tricyclic antidepressants have shown no efficacy in social phobia (though SSRIs are considered the treatment of choice, psychiatrists should be familiar with the numerous other treatment options available). When SSRI treatment is ineffective, psychiatrists should not shy away from prescribing benzodiazepines or MAOIs if the risks of abuse or dependency (with benzodiazepine) or hypertensive crises (with MAOIs) are outweighed by the suffering and impairment associated with severe cases.

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