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LETTER TO THE EDITORS

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Double-blind placebo-controlled pilot study of paroxetine for specific phobia

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Abstract Drugs are not recognized as a standard treatment for specific phobia, despite its apparent similarities to other kinds of phobia. Reluctance on the part of patients and clinicians to see the disorder as more than normal anxiety may explain the apparent resistance to pharmacotherapy. Eleven patients fulfilling DSM-IV criteria for specific phobia were randomized to 4 weeks of double-blind treatment with placebo or paroxetine up to 20 mg/day. They were assessed weekly with the Fear Questionnaire and the Hamilton Rating Scale for Anxiety. Paroxetine showed significant superiority in reducing all measures (ANCOVA for reductions in phobia scores F=7.9, P=0.02). One out of six patients responded to placebo, compared to three out of five patients on paroxetine. This new therapeutic option (i.e. drug treatment) for specific phobia deserves further examination in a larger trial.

Key words Anxiety · Phobic disorder · Paroxetine · Pharmacology · Serotonin

Introduction

Specific phobia, the inappropriate or excessive fear of specific situations like closed spaces, thunder or animals, is one of the commonest psychiatric conditions in the community; lifetime and 1-month prevalences are, respectively, about 12% and 6% (Regier et al. 1988; Magee et al. 1996). However, it is one of the rarest disorders in the psychiatric clinic. Presumably this is because most sufferers perceive the condition as on a continuum with normal anxiety, and do not think of it as a medical disorder requiring psychiatric treatment. Psychiatrists and researchers may share this perception to some extent; for example, panic disorder, another anxiety disorder, is only one-fifth as common as specific phobia, but has been the focus of much more extensive research. However, severe specific phobia can be as disabling as social phobia (Magee et al. 1996).

Standard treatments for the more generalized social phobias and agoraphobia include pharmacotherapy, but hitherto only behavior therapy has been a recognized treatment for specific phobia (Kaplan et al. 1994). Not all patients are willing to invest the effort demanded by behavior therapy, and not all of those who receive it respond to it. We are not aware of a controlled trial of drug treatment for specific phobia, nor was one found on a search of Medline and Current Contents. Yet specific phobia shares many clinical features with other phobias (Marks 1970), especially social phobia, and is classed as one of the anxiety disorders. The disorders may also share certain pharmacological characteristics. Situational phobics have been shown to react to 35% carbon dioxide in a similar manner to patients with panic disorder (Verburg et al. 1994). Some authorities have suggested that more attention be paid to commonalities among all neuroses (Andrews et al. 1990).

Agoraphobia responds to many antidepressants, and social phobia responds to the monoamine oxidase inhibitor phenelzine (Liebowitz et al. 1992) and the serotonin-specific reuptake inhibitors (SSRIs) fluvoxamine (van Vliet et al. 1994), sertraline (Katzelnick et al. 1995) and paroxetine (Stein et al. 1998). We therefore performed a small double-blind placebo-controlled trial of paroxetine in specific phobia.

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Materials and methods

The study was performed at an anxiety disorders clinic at a university hospital. Because specific phobia is rarely seen in the psychiatric clinic, most patients were recruited by advertisement. Eleven patients fulfilling DSM-IV criteria for phobic disorder were recruited. Diagnosis was confirmed with the SCID (Spitzer et al. 1990). Other psychiatric diagnoses (elicited on interview or with the SCID) and significant medical illness constituted exclusion criteria. Subjects underwent a standard medical interview, examination and laboratory tests to exclude medical illness, drug use and pregnancy. All gave written, informed consent and the study was approved by the hospital Helsinki committee.

At week 0 (baseline), a psychiatrist completed the Fear Questionnaire (Marks and Matthews 1979) and the Hamilton Rating Scale for Anxiety (HAM-A) (Hamilton 1959). These assessments, and a side-effects checklist, were repeated after 1, 2, 3 and 4 weeks by a psychiatrist who, like the patients, was unaware of the treatment assignment.

Subjects were randomized consecutively with a table of random numbers to double-blind placebo (last digit odd number) or paroxetine (last digit even number) treatment. Treatment consisted of a single capsule prepared in the anxiety disorders clinic containing glucose or glucose plus 6.67 mg paroxetine per day, for the first week. In the second week the daily dose was raised to two capsules and in the third and fourth weeks it was three capsules, i.e. placebo or 20 mg paroxetine. Other psychoactive agents were not allowed. Compliance was assessed by enquiry and by pill count at each visit.

Results

Four patients were males and seven were females. Six patients received placebo and five received paroxetine. Mean±SD age was 53±13 years. Duration of illness was 10.9±14 years. Only one patient had been offered any previous medication (lorazepam 2 mg). At baseline global phobia score (0=absent, 10=most severe patient you have ever encountered) was 7.0±2, i.e. between moderate and severe. There was no difference at baseline between the two treatment groups; 6.4±2 in the placebo group versus 7.8±2 in the paroxetine group [$F(1,6)=1.6$, NS]. HAM-A baseline scores (range=0–56) were 8.5±4, i.e. very mild. No instruction concerning self-exposure was given. In practice, all but one patient in each treatment condition was exposed to his or her phobic stimulus during the study.

Table 1 shows the phobic situation of each patient, his or her treatment allocation, and global scores on the Fear Questionnaire and total HAM-A scores, both at baseline and after 4 weeks of treatment.

Paroxetine was significantly more effective than placebo in reducing phobia, even in this small sample; analysis of variance, with baseline measures as covariates (ANCOVA), of change in patients' global phobia scores [$F(1,8)=7.9$, $P=0.02$]. If patients with a reduction of 50% or more in their global phobia scores are considered responders (Mavissakalian and Perel 1992; Benjamin et al. 1995; Oehrberg et al. 1995; Davis et al. 1997; Lecrubier et al. 1997), then one out of six patients responded to placebo, compared to three out of five on paroxetine. Paroxetine's effect was seen in both fear scores and avoidance scores (range for each=0–10). Mean change from baseline to end of week 4 on placebo was 1.6±2 and on paroxetine 5.1±2 in fear scores; in avoidance scores it was 1.3±2 on placebo and 4.3±2 on paroxetine. General anxiety, as reflected on the HAM-A, was reduced 2.0±3 by placebo and 4.6±5 by paroxetine [ANCOVA $F(1,8)=12.3$, $P=0.008$]. One patient on placebo complained of mild fatigue; one patient on paroxetine complained of mild nausea, one of mild polyuria, and one of mild loss of appetite and headache, and of moderate fatigue. No patient failed to complete the protocol. The clinician guessed the treatment assignment correctly in eight cases (kappa=0.44, NS), and the patients did so in seven instances (kappa=0.28, NS). No instances of non-compliance were discovered; we did not employ laboratory testing.

Discussion

This pilot study confirmed our expectation, that the SSRI paroxetine would demonstrate efficacy against specific phobia. The clinical relevance of the effect was borne out by responders' statements such as, "This has changed my life." This apparent pharmacotherapeutic similarity to other phobias is consistent with the current classification of specific phobia within the family of anxiety disorders.

Table 1 Phobic situations, treatment allocation, and global phobia scores and HAM-A scores, at baseline and after 4 weeks of treatment in 11 patients with DSM-IV specific phobia

Patient no.	Phobia	Treatment	Global phobia score		HAM-A score	
			Baseline	Week 4	Baseline	Week 4
3	Storms	Placebo	7	7	9	9
5	Confined spaces	Placebo	7.5	6	9	11
6	Storms	Placebo	8	5	13	7
7	Darkness	Placebo	4	2	9	3
8	Flying	Placebo	4	3	10	7
11	Cats	placebo	8	8	9	8
1	Dogs	Active	9	6	3	1
2	Heights	Active	8	1	6	4
4	Driving	Active	8	1	7	2
9	Driving	Active	5	3	4	3
10	Confined spaces	Active	9	3	15	2

The numbers involved were very small, because of the difficulty of persuading patients with specific phobia to consider drug treatment. For this reason the phobias differed, albeit slightly, between treatment groups; both groups included one animal phobic and one claustrophobic patient, but the two patients afraid of storms were randomized to placebo treatment, and the two afraid of driving were randomized to paroxetine treatment. Our sample was probably atypical in its severity and possibly in its fairly advanced age. The severe condition of our patients may have played a role in inducing them to consider psychiatric treatment, and may perhaps also have made the demands of behavior therapy seem more unrealistic than they do to patients with milder phobias. Whether the results reported here would generalize to all phobic patients is unknown. It also remains to be seen whether the behavioral gains achieved with the help of pharmacotherapy will persist if and when the drug is discontinued.

In the meantime, the present result confirms theoretical speculations concerning similarity between specific and other phobias, and, if replicated in larger studies, suggests a new therapeutic option for these patients.

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