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Cognitive-Behavioral Group Therapy versus Phenelzine in Social Phobia: Long-Term Outcome

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Abstract

To evaluate the effects of maintenance treatment and durability of gains after treatment discontinuation, responders to either phenelzine (PZ) or cognitive-behavioral group therapy (CBGT) from an acute trial comparing these two treatments as well as pill placebo and a psychotherapy control (educational supportive group therapy) were enrolled into maintenance and treatment-free follow-up phases. Experimental design: Responders to an acute trial contrasting PZ and CBGT entered a six-

month maintenance phase. Patients who continued to respond through the maintenance phase entered a six-month treatment-free phase. Patients receiving pill placebo or educational supportive group therapy in the acute trial did not enter the long-term study. Principal observations: PZ patients entered maintenance more improved than CBGT patients, and nonrelapsing PZ patients maintained their superior gains throughout the study. Relapse during maintenance did not differ between treatments. However, PZ patients showed a trend toward greater relapse during treatment-free follow-up. There was a greater relapse among patients with generalized social phobia with phenelzine. Conclusions: PZ and cognitive-behavioral group therapy may differ in their long-term effects. The superiority seen with PZ on some measures in the acute study persisted in patients who maintained their gains over the course of maintenance and treatment-free follow-up. However, CBGT may lead to a greater likelihood of maintaining response after treatment has terminated. Replication with larger samples is needed, as is a study of the acute and long-term efficacy of combined PZ and CBGT.

Keywords: cognitive behavioral group therapy, phenelzine, maintenance, discontinuation, follow-up

Introduction

The treatment of social phobia has become a focus of research interest after years of substantial neglect. While a number of psychopharmacological and psychosocial treatments have recently been found useful in controlled trials, it is unclear how pharmacotherapy and psychosocial approaches compare in the treatment of social phobia.

A study comparing medication and cognitive behavior therapy in social phobia was designed and carried out. Phenelzine (PZ) and cognitive-behavioral group therapy (CBGT) were chosen as the reference pharmacological and psychosocial treatments because of their well-demonstrated efficacy in social phobia (Heimberg et al., 1990; Liebowitz et al., 1992; Versiani et al., 1992; Gelernter et al., 1991). Both pill placebo and psychosocial control treatment were also utilized. The study was conducted at two sites, one expert in pharmacotherapy of social phobia, the other expert in cognitive behavioral therapy, with all four treatments administered at both sites. The relative acute efficacy of the different treatments in the initial 12-week acute treatment phase and the effects of site of treatment (expert pharmacotherapy/expert cognitive behavior therapy) on outcome were described in detail in an earlier report (Heimberg et al., 1998).

To summarize, both PZ and CBGT showed efficacy in comparison to the two control treatments, with the two active treatments resulting in equivalent rates of response at week 12. However, the PZ group was associated with greater improvement on a number of dimensional measures. There was no interaction of sites with treatment.

Social phobia is a chronic condition (Reich et al., 1994). Therefore, evaluations of treatment outcome must consider the durability of gains after initial progress has been achieved. At the time this study began, we did not have sufficient sense of the durability of gains during maintenance therapy or following treatment discontinuation for either treatment approach, although preliminary data suggested CBGT's effect following discontinuation would be more durable (Heimberg et al., 1993a). In a previous study, Liebowitz et al. (1992) found that responders to PZ in an 8-week placebo-controlled trial showed moderate relapse during an 8-week maintenance phase and a subsequent 8-week double-blind placebo substitution. In a similarly designed trial, Versiani et al. (1992) found PZ effects to be stable

during maintenance but not durable following treatment discontinuation. Unlike other studies of PZ in social phobia, Gelernter et al. (1991) reported continued benefits two months after termination of 12 weeks of PZ treatment; however, this study combined medication with detailed self-exposure instructions. Previous trials suggested that responders to CBGT continued to show improvement 4–6 years later (Heimberg et al., 1993a). Other studies of behavioral treatment of social phobia also suggested maintenance of treatment gains after the end of treatment (Mattick and Peters, 1988; Mattick et al., 1989; Juster and Heimberg, 1995).

Since the comparative long-term effects of PZ and CBGT were of great interest, the study was designed to include maintenance and follow-up phases. Specifically, we wanted to learn how PZ and CBGT responders to acute treatment compared after 6 months of maintenance treatment and 6 months after treatment discontinuation. Based on previous data, we expected the benefits derived from CBGT would be more durable than those derived from PZ following treatment discontinuation. To examine this rigorously, the maintenance and treatment-free follow-up periods were longer than those of prior medication trials in social phobia.

We also had several secondary goals. Phenomenological (Heimberg et al., 1993b), psychobiological (Levin et al., 1993), and acute treatment (Liebowitz et al., 1992; Hope et al., 1995; Brown et al., 1995) data suggest a difference between nongeneralized and generalized social phobia. However, no prior investigation has compared these subtypes in terms of their long-term treatment outcomes. Also, while prior investigation of social phobia have included both pharmacological and psychosocial treatments (Gelernter et al., 1991; Turner et al., 1994; Falloon et al., 1981; Clark and Agras, 1991; Otto et al., in press), no prior study involved collaborating clinics of differing treatment expertise, which allows examination of the interaction of site and treatment. Single-site short-term studies comparing cognitive behavior therapy and antidepressant medication in panic disorder suggest that both site and the investigator's theoretical orientation can affect outcome. For example, in panic disorder, cognitive behavioral treatment was superior to imipramine when compared at a psychotherapy-oriented center (Clark et al., 1994), while fluvoxamine was superior to cognitive behavioral treatment in a study conducted by a more psychopharmacologically oriented investigator (Black et al., 1993). While our acute phase data (Heimberg et al., 1998) did not suggest any site by treatment interactions, we still considered it important to examine this issue in a long-term trial.

Materials and Methods

The design of the acute study is described in the earlier report (Heimberg et al., 1998). Informed consent was obtained from subjects after the nature of the procedures was explained. After 12 weeks, patients in both control groups and nonresponders to CBGT and PZ were removed from the study, while CBGT and PZ responders were eligible to continue for 6 months maintenance treatment and 6 months treatment-free follow-up. Response was defined by a rating of 1 (markedly improved) or 2 (moderately improved) on the Social Phobic Disorders Change Scale (SPDC) (Liebowitz et al., 1992). Patients receiving a rating of 3 (minimally improved) or higher were classified as nonresponders. In the first 6 months,

PZ patients were maintained on medication, while contact with the physician was scheduled monthly. Medication could be adjusted up or down depending on clinical state and side effects, but could not exceed a maximum of 90 mg/day. CBGT patients met monthly for 2½-hour group sessions. Homework was actively devised by therapists and patients in CBGT sessions, assigned weekly, and reviewed in subsequent sessions. CBGT was individualized to work with specific thoughts and situations for each individual, although applied in a standardized format. Patients who continued to respond at the end of the maintenance phase then entered follow-up. During this six-month phase, no treatment was administered, other than to taper PZ over the first month.

Major assessments were conducted bimonthly but on an a priori basis, three assessments were selected for analysis: after 2 (M2) and 6 (M6) months of maintenance treatment and the end of follow-up at month 12 (M12). Patients whose change rating (SPDC) increased to 3 more at a major assessment were considered relapsers. Independent assessors (IAs) remained blind to treatment by coaching patients not to mention any details of their treatment and by avoiding inquiry into possible medication side effects.

The IA administered the following measures: (a) Liebowitz Social Anxiety Scale (LSAS) (Liebowitz, 1987; Heimberg et al., 1999), (b) Social Phobic Disorders Severity and Change Scales (SPDSC) (Liebowitz et al., 1992); and (c) the Clinician's Severity Rating Scale from the Anxiety Disorders Interview Schedule–Revised (ADIS-R) (DiNardo et al., 1993). Self-report measure included the Social Avoidance and Distress Scale (SADS) (Watson and Friend, 1969), the Fear of Negative Evaluation Scale (FNE) (Watson and Friend, 1969), the Fear Questionnaire (FQ) self-rating of severity of main fear and social phobia subscale (Marks and Matthews, 1979), the Social Interaction Anxiety Scale (SIAS) (Heimberg et al., 1992; Mattick and Clarke, 1998), and the Social Phobia Scale (SPS) (Heimberg et al., 1992; Mattick and Clarke, 1998). Theoretical and practical details concerning the IA administered and self-rating measures are included with the acute study findings (Heimberg et al., 1998).

Data Analyses

Categorical analyses utilized the chi-square statistic and Fisher's Exact Test. Relapse rates were calculated two ways. One included all patients who entered each phase in the denominator, similar to an intent-to-treat analysis. The other excluded dropouts from the relapse analyses. The analyses including all patients produce lower rates than those excluding some patients because of the larger denominator; the two estimates can be viewed as bracketing the true relapse rates.

2 (treatment) × 2 (entered vs. not entered the maintenance phase) × 2 (time of assessment: prior to treatment versus the end of acute treatment) repeated measures analyses of variance (ANOVAs) examined differences between eligible patients who entered the maintenance phase and those that did not. For these who entered maintenance, t-tests were used to compare groups by treatment on demographic and pretreatment measures. Within the same sample, analyses of covariance (ANCOVAs) were used to compare treatment groups on ratings obtained at the end of the acute phase (week 12) with corresponding pretreatment scores as covariates. For responders who completed each phase (M6, M12), ANCOVAs of IA and self-report measures, with pretreatment scores as covariates, were conducted for each of the following assessments: end of the acute phase (week 12), M2, M6, and M12 (for

patients completing M12). The assumption of homogeneity of regression in the ANCOVAs was evaluated for every dependent measure. Where it was not tenable, the Johnson-Neyman technique was performed to examine how the covariate interacted with treatment. Treatment *x* subtype (generalized, nongeneralized) × time of assessment repeated measures ANOVAs were conducted on the M6 and M12 completer samples to examine the interaction of subtype and treatment.

All statistical tests were two-tailed. Probability values of $P = .05$ or less were considered significant. For the repeated measures ANOVAs, when the assumption of sphericity was not tenable, the Huynh-Feldt adjustment of degrees of freedom was applied. For all ANOVAs and ANCOVAs which included two group (PZ, CBGT) comparisons at different time points, there were no corrections applied.

Results

Maintenance Phase

Sample

20/31 PZ and 21/36 CBGT patients were considered responders after 12 weeks of treatment and eligible to enter maintenance. Six PZ and 7 CBGT patients declined to enter maintenance due to: no perceived need for further treatment (PZ 2, CBGT 2), insufficient improvement (PZ 1, CBGT 2), events unrelated to treatment (PZ 1, CBGT 1), side effects (PZ 1), and unknown reasons (PZ 1, CBGT 2). The 3 patients who felt they had made insufficient improvement did not differ by inspection from the other patients who declined maintenance.

To examine for possible selectivity among patients who entered maintenance, we compared acute responders who entered maintenance ($n = 28$) and those who declined ($n = 13$) on demographic and clinical measures. There were no significant demographic differences. Patients who entered maintenance had lower scores on one self-rated measure, the FQ social phobia subscale, prior to acute treatment (entered maintenance FQ-SO 17.81 (6.08) vs. not entered 23.91 [7.25], $t = 2.65$, $df = 36$, $P = .01$) but there were no differences at the end of the acute phase.

There were no differences between the 14 PZ responders and the 14 CBGT responders who entered maintenance on age, gender distribution, employment, education, marital status, or subtype of social phobia (see Table 1). PZ and CBGT patients who entered maintenance were similar at the start of the acute study, but PZ patients improved more with acute treatment and thus entered the maintenance study in a less symptomatic state (see Table 2). Specifically, prior to acute treatment, PZ and CBGT patients differed only on the self-rated SADS, PZ patients having higher scores (PZ 21.29 [4.01] vs. CBGT 15.21 [10.13], $t = 2.09$, $df = 26$, $P = .05$). At the end of the acute phase, however, PZ patients were significantly more improved than CBGT who entered maintenance on 6 IA measures (4 LSAS subscales, SPDSC overall severity, and ADIS-R phobic severity) as well as on the SADS. This pattern is similar to the outcome for the whole acute study sample (Heimberg et al., 1998].

Table 1. Maintenance phase demographic characteristics phenelzine (n = 14) and CBGT (n = 14)

	Phenelzine	CBGT
Age (SD)	31.07 (8.59)	37.71 (10.53)
Gender (male/female)	7/7	8/6
Marital status (married/never married)	9/5	4/9*
Employment (employed/unemployed)	13/1	12/2
Education College graduate/some college/high school or less	6/6/2	10/1/3
Subtype (Generalized/nongeneralized)	10/4	7/7

*Missing data for 1 patient.

Table 2. Analysis of covariance (ANCOVA) for testing adjusted mean differences between phenelzine (PZ, N = 14) and cognitive behavioral group therapy (CBGT, N = 14) among maintenance phase entrants after the acute treatment phase (with pretreatment measures as the covariates)*

	Post test (week 12)			
	Adjusted mean		ANCOVA	
Measure	PZ	CBGT	*F*	*P*
Independent assessor				
LSAS social fear	4.68	9.79	11.94	0.002
LSAS performance fear	6.32	11.80	10.74	0.003
LSAS social avoidance	3.22	6.75	6.76	0.02
LSAS performance avoidance	3.57	8.23	7.24	0.01
Overall severity	2.33	3.46	8.69	0.007
ADIS-R clinician severity rating	2.06	2.95	4.63	0.04
Self-Rating				
Social avoidance and distress scale	3.81	15.47	24.94	0.0001
Fear of negative evaluation scale	14.92	20.21	3.78	0.06
Fear questionnaire social phobia	8.50	12.81	2.38	0.14
Fear questionnaire self-rating	5.01	5.63	0.33	0.57
Social interaction anxiety scale	21.92	31.17	3.47	0.08
Social phobia scale	21.71	18.83	0.12	0.37

*LSAS, Liebowitz Social Anxiety Scale; ADIS-R, Anxiety Disorder Interview Schedule–Revised

Outcome

Relapse and dropout rates did not differ between treatments during this phase. This was true for relapse whether all patients who entered maintenance were included or whether dropouts were excluded (Table 3). For PZ, 1 patient was classified as a relapser at M2 and 2 others at M6. One PZ responder dropped at M2, claiming no need to continue medication. For CBGT, one patient was classified as a relapser at M2, another at M6. One CBGT responder dropped at M2 to pursue another treatment option.

To examine PZ and CBGT maintenance phase responders, we compared them at the end of acute treatment, at M2 and M6, with pretreatment scores as covariates (Table 4). In summary, the overall pattern emerging after acute treatment continued during maintenance. PZ patients were less symptomatic than CBGT patient entering the maintenance

phase as a result of their greater gains during acute treatment. PZ patients who did not relapse or drop out continued to be less symptomatic than CBGT patients who did not relapse or drop out over the 6-month maintenance period.

Table 3. Relapse rates by treatment within phase and combined

	All patients	
	Phenelzine	CBGT
Maintenance	3/14 (21%)	2/14 (14%)
Follow-up	3/10 (30%)	0/11*
Combined phases	6/14 (43%)	2/14 (14%)
	Completers	
	Phenelzine	CBGT
Maintenance	3/13 (23%)	2/13 (15%)
Follow-up	3/9 (33%)	0/10*
Combined phases	6/12 (50%)	2/12 (17%)

* *Phenelzine vs. CBGT (Fishers* P = *.09)*

Treatment-Free Follow-up Phase

Sample

10/14 PZ and 11/14 CBGT patients were eligible to enter treatment-free follow-up. These treatments groups were compared on demographic and acute baseline clinical measures. There were no significant differences.

Outcome

While dropout rates did not differ between treatments during this phase, there was a trend for greater relapse with PZ (Fisher's Exact 3.42, $df = 1$, $P = .09$) (Table 3). For PZ, 2 patients relapsed during the first 2 months of treatment free follow-up, and a third did so between months 4 and 6 of this phase. One other PZ patient dropped after the end of maintenance for unknown reasons. For CBGT, while one patient dropped during the first two months of follow-up, no patients relapsed during this phase.

We compared M12 PZ and CBGT responders at M6 and M12 with acute baseline scores as covariates (see Table 5). To summarize, PZ patients entering treatment-free follow-up were less ill than were CBGT patients because of previous gains made in the study. PZ nonrelapsers continued to be more improved than CBGT nonrelapsers, although all did well.

To gain a clinical perspective, CBGT nonrelapsers progressed from an overall severity of 4.75 (closer to markedly than moderately ill) at baseline to approximately 2.9 (slightly less than mildly ill) at M12. With PZ, nonrelapsers' mean severity changed from a baseline mean of 4.5 (moderately to markedly ill) to a M12 mean of 1.5 (normal to borderline ill).

Table 4. Analysis of covariance (ANCOVA) for testing adjusted mean differences between phenelzine (PZ, *N* = 10) and cognitive behavioral group therapy (CBGT, *N* = 11) maintenance phase responders after the acute phase, month 2 and month 6 with pretreatment measurements as the covariate*

	Posttest				Month 2				Month 6			
	Adjusted mean		ANCOVA		Adjusted mean		ANCOVA		Adjusted mean		ANCOVA	
Measure	PZ	CBGT	*F*	*P*	PZ	CBGT	*F*	*P*	PZ	CBGT	*F*	*P*
Independent Assessor												
LSAS social fear	4.02	10.28	13.24	0.002	2.93	8.57	8.57	0.009	3.74	9.36	7.29	0.02
LSAS performance fear	5.48	13.12	16.71	0.001	4.33	11.48	16.41	0.001	4.44	11.66	11.49	0.003
LSAS social avoidance	2.55	6.25	6.84	0.02	2.07	6.13	7.98	0.01	2.76	6.74	5.89	0.03
LSAS performance avoidance	3.00	8.80	7.79	0.01	1.95	8.25	18.15	0.001	3.03	8.17	6.74	0.02
Overall severity	2.07	3.48	12.22	0.003	1.43	3.37	26.40	0.0001	1.71	3.39	14.46	0.001
ADIS-R clinician severity rating	1.80	3.08	7.37	0.01	1.34	3.06	19.82	0.0001	1.34	2.96	15.78	0.001
Self-Rating												
Social avoidance and distress scale	1.95	15.39	26.49	0.0001	4.43	15.23	11.84	0.004	0.97	9.28	6.90	0.02
Fear of negative evaluation scale	9.98	20.64	7.70	0.01	10.87	17.27	2.33	0.15	10.31	13.20	0.35	0.56
Fear questionnaire social phobia	6.47	12.23	3.31	0.09	9.20	11.33	0.54	0.48	5.25	11.38	3.42	0.09
Fear questionnaire self-rating	4.31	5.62	1.03	0.32	2.73	4.66	2.15	0.17	2.01	4.76	7.73	0.02
Social interaction anxiety scale	15.35	30.33	8.27	0.01	20.86	32.14	4.36	0.06	22.29	21.83	0.00	0.95
Social phobia scale	24.23	18.24	0.27	0.61	23.18	18.80	0.82	0.38	19.34	18.14	0.04	0.84

* LSAS, Liebowitz Social Anxiety Scale; ADIS-R, Anxiety Disorder Interview Schedule-Revised.

Table 5. Analysis of covariance (ANCOVA) for testing adjusted mean differences between phenelzine (PZ, *N* = 6) and cognitive behavioral group therapy (CBGT, *N* = 10) month 12 responders with pretreatment measures as covariates*

	Month 6				Month 12			
	Adjusted mean		ANCOVA		Adjusted mean		ANCOVA	
Measure	PZ	CBGT	*F*	*P*	PZ	CBGT	*F*	*P*
Independent Assessor								
LSAS social fear	5.09	8.02	1.46	0.25	3.06	8.61	2.87	0.11
LSAS performance fear	5.56	11.44	4.50	0.06	4.47	10.62	4.76	0.05
LSAS social avoidance	3.47	6.76	2.59	0.13	0.43	7.97	8.52	0.01
LSAS performance avoidance	2.96	8.60	4.83	0.05	2.43	7.87	4.49	0.05
Overall severity	1.94	3.23	5.35	0.04	1.60	2.61	3.17	0.11
ADIS-R clinician severity rating	1.70	2.86	7.50	0.02	1.36	2.37	3.78	0.07
Self-Rating								
Social avoidance and distress scale	0.25	8.50	8.02	0.02	2.55	10.48	3.34	0.11
Fear of negative evaluation scale	10.35	12.28	0.15	0.71	6.19	18.36	5.59	0.04
Fear questionnaire social phobia	3.56	11.07	4.28	0.07	4.77	12.09	3.47	0.11
Fear questionnaire self-rating	1.75	4.88	13.06	0.005	2.50	5.33	5.97	0.04
Social interaction anxiety scale	23.40	21.03	0.08	0.78	13.41	25.41	2.76	0.14
Social phobia scale	14.95	18.83	0.28	0.61	9.45	17.21	2.32	0.16

*LSAS, Liebowitz Social Anxiety Scale; ADIS-R, Anxiety Disorder Interview Schedule-Revised.

Subtype of Social Phobia

Seventeen generalized and 11 nongeneralized social phobic patients entered the maintenance phase. There was a difference in relapse within the generalized subtype as a function of treatment. During the study, among the generalized patients, 5/10 (50%) on PZ compared to 0/7 (0%) treated with CBGT relapsed (Fisher's Exact 4.72, $df = 1$, $P = .04$). With dropouts excluded, relapse rates for PZ (5/8, 62%) and CBGT (0/5, 0%) among the generalized patients showed a trend difference (Fisher's Exact 4.75, $df = 1$, $P = .08$). There was no difference in relapse by treatment among the nongeneralized social phobic patients. Dropout rates did not differ between treatment groups within either subtype.

To analyze the interaction of subtype of social phobia and treatment, we conducted treatment × subtype × time of assessment (pretreatment, post-acute treatment, M6, M12) repeated measures ANOVA for all patients completing the follow-up phase as responders. Since patients with generalized social phobia have been shown on multiple occasions to be more severely affected than patients with nongeneralized social phobia, we feared that covariance procedures would artifactually reduce the apparent impact of subtype. Therefore, these analyses were conducted without covarying pretreatment scores.

There were no Treatment by Subtype interactions. However, there were significant subtype by time of assessment interactions on 4 IA measures. Pairwise comparisons showed significant differences on the LSAS subscales at pretreatment, while after acute treatment, at month 6 and month 12, the subtypes did not differ (see Figs. 1 and 2 for representative measures). The findings suggest a convergence of the two subtypes in these successfully treated patients, occurring mostly over the course of acute treatment.

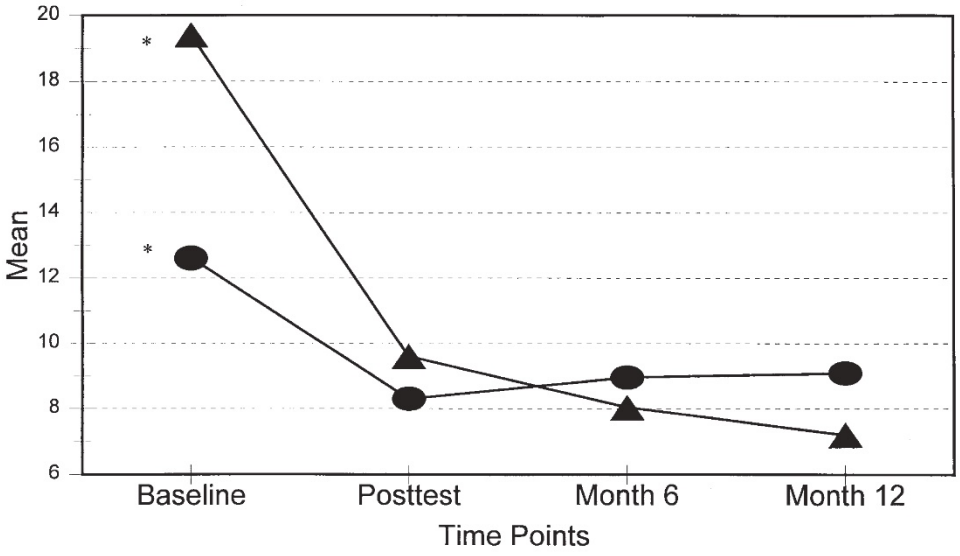

Figure 1. Observed means of LSAS performance fear for completers in generalized (GEN) and nongeneralized (NGEN) subtypes at baseline, posttest, month 6, and month 12. * $F = 6.16$; $df = 1, 11$; $P = .03$. ● NGEN, ▲ GEN.

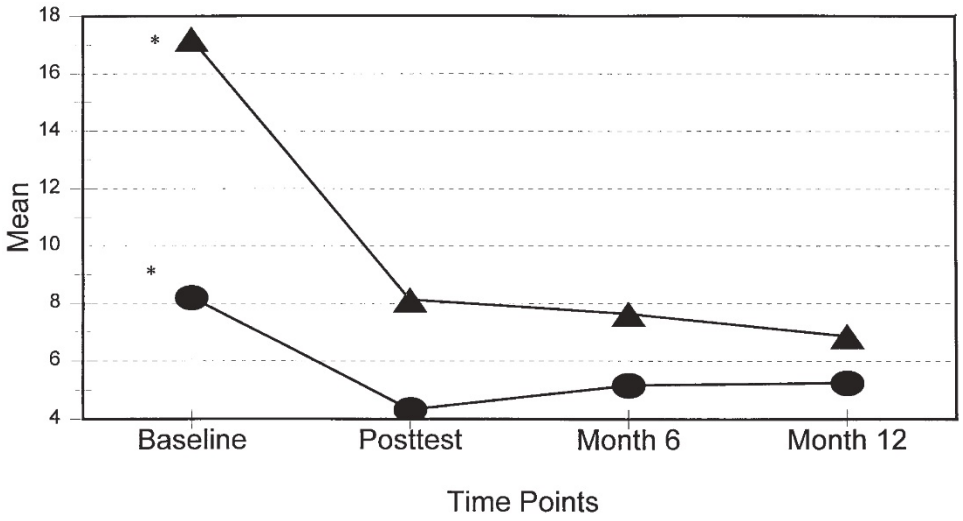

Figure 2. Observed means of LSAS social fear for completers in generalized (GEN) and nongeneralized (NGEN) subtypes at baseline, posttest, month 6, and month 12. * $F = 6.95$; $df = 1, 11$; $P = .023$. ● NGEN, ▲ GEN.

Site of Treatment

Sixteen of 20 (80%) eligible patients from Albany entered maintenance vs. 12/21 (57%) from New York City. There were no differences in enrollment rates, treatment assignment, subtype, sex, marital status, education or employment status. However, patients at New York (mean age 29.33, SD 7.45) were significantly younger than patients at Albany (mean age 38.19, SD 10.21) ($t = 2.54$, $df = 26$, $P = .02$). There were no pretreatment differences on clinical measures between sites except New York patients rated themselves higher on the SADS (NY 21.67 (5.52) vs. Albany 15.69 (9.02), $t = 2.02$, $df = 26$, $P = .05$). At the end of acute treatment, however, New York patients were more improved on 4 IA measures (2 subscales of the LSAS: LSAS-performance avoidance (adjusted mean: Albany 7.54 vs. New York 3.52) $F = 4.65$, $df = 1$, $P = .04$, LSAS performance fear (adjusted mean: Albany 10.92 vs. New York 6.31) $F = 6.28$, $df = 1$, $P = .02$) and 2 overall severity measures (SPDS-severity (adjusted mean: Albany 3.24 vs. New York 2.36) $F = 4.56$, $df = 1$, $P = .04$, ADIS-R-severity (adjusted mean: Albany 2.97 vs. New York 1.91) $F = 7.12$, $df = 1$, $P = .01$).

During maintenance and treatment-free follow-up, relapse and dropout rates did not differ by site. Combining both phases, with all patients included, relapse rates did not differ by site, but dropout rates were higher in New York (NY 4/12 (33%) vs. Albany 0/16, chi-square = 3.80, $df = 1$, $P = .02$). There was no significant relationship of age to relapse or dropout, and the sites still differed in dropout controlling for age.

Other Possible Predictors of Long-Term Outcome

Fifteen men and 13 women entered the maintenance study. There were no baseline demographic differences. Women had higher scores on one IA measure and one self-rated measure prior to acute treatment (IA LSAS–social fear: women 17.85 (5.15) vs. men 11.53 (6.45),

$t = 2.83$, $df = 26$, $P = .009$, self-rated SIAS: women 49.83 (11.24) vs. men 36.20 (15.57), $t = 2.54$, $df = 25$, $P = .02$) and one self-rated measure at the end of acute treatment (FQ: adjusted means) females 3.75 vs. males 2.71, $F = 4.35$, $df = 1$, $P = .05$). During the long-term study as a whole, with all patients included, women relapsed (7/13, 54%) at a higher rate than men (1/15, 7%) (chi-square = 6.24, $df = 1$, $P = .01$). Dropout rates did not differ by sex. There were no treatment by sex interactions or main effects of sex among patients completing either maintenance or follow-up as responders.

During the maintenance phase, PZ dosage did not appear to influence relapse, although small samples sizes limit the strength of the conclusions. The PZ relapser at M2 was on 30 mg/day, while the 2 at M6 were on 60 and 75 mg/day, respectively. Attempts were made to raise dosage above 30 mg/day for the M2 relapser, but a higher dose was not tolerated. Mean dose for nonrelapsers was 54.5 mg (12.3)/day vs. 56.7 mg (25.2)/day for relapsers, which did not differ. There was also no statistical difference in the M6 mean doses of PZ patients who, during treatment-free follow-up, subsequently relapsed (47.5 mg (21.7)/day) vs. those who did not (61.2 mg (12.0)/day), although doses in the range of 60 mg/day would be considered more adequate than doses in the 45 mg/day range. PZ patients did not experience any serious adverse effects during the maintenance phase.

Clinical measures for relapsers and nonrelapsers were compared prior to and at the end of acute treatment. Few significant differences emerged and are not considered meaningful in light of the multiple comparisons conducted.

Discussion

To summarize the findings, PZ patients were more improved upon entering the maintenance phase of the study, and among nonrelapsing completers, more improved when finishing it. There was a trend for greater relapse with PZ during treatment-free follow-up. Among those who did not relapse or drop out, however, PZ patients were more improved when finishing this phase. There was also greater relapse for PZ than CBGT among patients with generalized social phobia. Among nonrelapsing patients, the subtypes converged in symptom severity. With regard to site, patients at the New York site were somewhat more improved going into the maintenance phase, independent of treatment condition. However, the New York site suffered greater dropout than the Albany site. Finally female patients relapsed at a higher rate than did male patients during the long-term study.

PZ vs. CBGT

The maintenance and treatment-free follow-up phases of the study provide a valuable perspective. The significant clinical gains attained in the acute phase were maintained by most patients during maintenance treatment, and the treatment groups did not differ in this respect. PZ relapse during maintenance (3/14, 21%) was similar to that seen in a prior study in which 3/16 (19%) PZ patients relapsed during an 8-week maintenance phase after responding to acute treatment (Liebowitz et al., 1992).

During treatment-free follow-up PZ patients continued to relapse, whereas CBGT patients did not. The trend toward greater relapse following PZ vs. CBGT discontinuation, if

confirmed in future trials, may, in part, be related to the coping skills explicitly provided by CBGT. Does that mean CBGT had better long-term effects than PZ in this long-term study? CBGT treated patients may have less chance of relapse; however, PZ-treated nonrelapsers maintained greater gains. A cost-benefit comparison between PZ and CBGT does not produce a clear-cut winner or loser. Consideration must be given to patient preference, provider availability, and individual gains and adverse reactions to treatment. One clear negative for PZ is its potential risk in terms of hypertensive reactions. However, selective serotonin reuptake inhibitors (SSRIs) appear to have efficacy close to that of PZ without the same risk (Stein et al., 1998; VanVliet et al., 1994).

The Influence of Subtype

The greater tendency for PZ patients to relapse in the long-term study was especially evident among patients who met criteria for the generalized subtype of social phobia, where, with all patients included, there was a 50% relapse rate in the PZ group and none in the CBGT group. This was not seen among the nongeneralized patients, but sample size limited this analysis. Our estimates of relapse rates are imprecise because of the small samples.

The convergence of subtypes over the course of successful treatment has not, to our knowledge, been previously reported. In our acute study, patients with generalized social phobia continued to demonstrate greater impairment on dimensional measures than patients with nongeneralized social phobia. That this was not the case after acute treatment for the subset of patients completing our long-term study may be due to several factors. First, long-term study completers are a select subgroup who may have had a particularly favorable treatment response. Secondly, there may be a floor effect beyond which patients do not progress. The issue is confounded to some degree, however, by our having two active treatments. While no significant subtype by treatment interactions were noted, it is possible that PZ and CBGT differ in their efficacy for particular subtypes, but we lacked the sample sizes and the statistical power to detect this.

PZ Relapse vs. Nonrelapse

Our data, along with the results of prior studies (Liebowitz et al., 1992; Versiani et al., 1992; Gelernter et al., 1991), suggest that some social phobics can discontinue PZ after a period of acute and maintenance treatment without relapsing. While confirmation with larger samples and longer follow-up is needed, this is very promising for a chronic disorder such as social phobia. For this observation to be most useful, however, we must be able to identify which social phobic patients can stop medication after 4–9 months without relapsing.

To identify predictors of nonrelapse after medication discontinuation, we compared PZ relapsers and nonrelapsers on a variety of measures, including pretreatment demographic and clinical ratings, clinical rating prior to relapse, medication dosages, etc. Our analyses to date have not clarified the issue. One hypothesis is that patients undergoing greater cognitive change during PZ treatment might be less relapse prone after treatment discontinuation. This will be examined in subsequent studies. We sought but could not find features that characterized durable CBGT responders, with the goal of seeing if these characteristics

were more prevalent in PZ nonrelapsers than relapsers. A recent study has found a positive association of compliance with homework assignments and acute CBGT outcome (Leung and Heimberg, 1996), but we did not examine this.

Combining PZ and CBGT

Gelernter et al. (1991) reported no loss of PZ's effectiveness after 2 months of untreated follow-up. Unlike the present study, or Liebowitz et al. (1992) and Versiani et al. (1992), PZ was combined with detailed self-exposure instructions during the acute treatment period. If systematic self-exposure instructions increased durability of gains over the 2 months following medication discontinuation, then combining PZ and CBGT, which includes both systematic self-exposure instructions and a number of cognitive and behavioral coping strategies, should further increase the durability of gains following PZ discontinuation. Our findings of greater symptom reduction with PZ but greater long-term retention of gains with CBGT also suggest a possible synergy if the two treatments were to be combined.

Other Influences on Attrition

We are uncertain how to explain the finding of the higher dropout rate at the New York site. The procedures and treatment practices of the two sites with regard to the maintenance and follow-up phases of the study were intended to be identical. There were several site differences, however, that could account for differences in dropout rates. By virtue of being in a larger metropolitan area, the New York site was harder for some patients to reach and had to compete with other activities, which could enhance dropout. The Albany site was also a smaller research facility engaged in fewer studies, which could mitigate dropout. New York patients entered the maintenance phase more improved than Albany patients on some measures and may have been tempted to leave treatment prematurely because of their improved feeling. The New York site maintenance sample was also younger than the Albany sample, but age differences did not account for difference in attrition. Fortunately, we did not have any treatment by site interactions with regard to relapse. The finding of greater relapse among female patients was unexpected, and we have no ready explanation for this.

Methodological Limitations

Certain methodological limitations are important to note. Our relatively small sample sizes in maintenance and discontinuation limit the precision of our estimates, our statistical power, and our ability to identify predictors of specific outcomes. We also did not apply correction factors to reduce the possibility of type I error.

In addition, this study does not inform us about maintenance periods longer than 6 months or total treatment longer than 9 months. The study was also not designed to delineate the optimal maintenance length before treatment discontinuation. On the basis of our data, one might question the utility of any PZ maintenance treatment, since PZ patients showed fairly similar relapse rates during maintenance and follow-up. However, our maintenance and follow-up periods cannot be compared because of the different amounts of treatment patients had going into each. A study comparing maintenance to follow-up without treatment would have to use a common starting point. Suggesting that continued PZ

maintenance is helpful, Versiani et al. (1992) found much greater relapse in PZ patients switched to placebo on a double-blind basis after 16 weeks than those who continued on PZ.

Longer intensive treatment with CBGT may be associated with greater acute and long-term improvement. The effects of longer intensive and total treatment on outcome during and after maintenance are being examined in a study now underway, as are the effects of combining PZ and CBGT. The study now underway also has a 12-month follow-up phase, in contrast to 6 months for the study reported here.

Our criteria for entrance into maintenance and discontinuation were somewhat arbitrary, e.g., marked or moderate improvement after 12 weeks of acute treatment. One could argue that patients are ready for maintenance and/or discontinuation only when they are markedly improved, e.g., a change score of 1. Alternatively, a study could enter patients into maintenance or discontinuation when each patient's gains are individually optimized or maximized, as in clinical practice. One might also argue that if patients achieving minimally improved status after acute treatment were allowed to enter the maintenance phase, those who had received CBGT might be more likely to show further gains than those treated with PZ.

In this era we are still confined to looking for predictors and mechanisms of improvement in clinical terms. In the not too distant future, clinical trials in social phobia will also include pathophysiological studies before and after treatment that should help to identify psychobiological predictors and mechanisms of change.

Methodological Strengths

This study had a number of methodological strengths and innovations which justify confidence in the findings. It had a longer medication maintenance phase than any previous social phobia study. It was the first CBGT maintenance study in social phobia. Maintenance regimens of CBGT are relatively unstudied in anxiety disorder patients. The study also had a longer treatment-free follow-up than previously included in medication trials in social phobia. There are longer CBGT follow-ups (Heimberg et al., 1993a), but they were naturalistic and did not monitor intervening treatment as closely as did our study. We had good retention of patients who entered maintenance, with little attrition other than relapse. Our use of pharmacologic and attention-placebo controls offered excellent calibration for both active treatments in the acute phase. Most importantly, our two-site design combining expertise in cognitive-behavioral and psychopharmacological treatments helped ensure state of the art application of treatment, rigorous testing of allegiance effects in treatment, ability to see how nonexpert sites perform with specific treatments, and acceptance of findings as credible by broad clinical and research constituencies.

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