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A pilot study of clonazepam versus psychodynamic group therapy plus clonazepam in the treatment of generalized social anxiety disorder

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Abstract

Background—Both Psychodynamic Group Therapy (PGT) and clonazepam are used as treatment strategies in reducing symptoms of generalized social anxiety disorder (GSAD). However, many individuals remain symptomatic after treatment with PGT or clonazepam.

Method—Fifty-eight adult outpatients with a diagnosis of GSAD according to DSM-IV were randomized to 12 weeks PGT plus clonazepam or clonazepam. The Clinical Global Impression-Improvement (CGI-I) Scale was the primary efficacy measure. Secondary efficacy measures included the Liebowitz Social Anxiety Scale (LSAS) total score, the World Health Organization Instrument to Assess Quality of Life-Bref (WHOQOL-Bref) Scale and the Beck Depression Inventory (BDI).

Results—CGI-I data from 57 patients (intent-to-treat population) showed that patients who received PGT plus clonazepam presented significantly greater improvement than those who received clonazepam ($p=0.033$). There were no significant differences between the two groups in the secondary efficacy measures.

Conclusion/Discussion—Our study suggests that the combination of PGT with clonazepam may be a promising strategy for the treatment of GSAD, regarding gains in the global functioning.

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However the present study failed to detect more specific changes in social anxiety symptomatology between the two groups.

Keywords

Anxiety disorders; Social anxiety disorder; Social phobia; Psychodynamic therapy; Treatment; Anxiolytics

1. Introduction

Treatment strategies for Social Anxiety Disorder (SAD) have focused on psychotherapy and pharmacotherapy [49,51]. Controlled trials and meta-analyses suggest similar benefits from both psychological, mainly cognitive-behavioral therapy (CBT), and pharmacological [25,27,60] in the short-term treatment of SAD.

Monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, noradrenergic agents and the high-potency benzodiazepines, clonazepam and bromazepam have demonstrated efficacy for SAD [7,48].

To date, most clinical trials of psychotherapy have used CBT [16,17,28,50] and IPT [40,41] as the experimental intervention. Very little empirical work has been conducted using other psychotherapy approaches [1,20,36,37,41]. More systematic research using therapy modalities other than CBT is needed in GSAD because many patients achieve only partial decrease in symptoms or experience recurrence of symptoms in long-term follow-up [16,41].

Most of what is known about psychoanalytic treatment for GSAD comes from case reports or uncontrolled studies [21,31,35,55]. Although psychodynamic psychotherapy has been shown in other disorders [8,34,43,45,59], there is only one published study suggesting its efficacy in GSAD [33]. In a recent study thirty patients were randomized to PGT or to a control group for 12 weeks in order to evaluate the efficacy of PGT. The control group consisted of an educational supportive psychotherapy group previously used by Heimberg et al. [27] to examine the efficacy of group CBT. At the end of the study, patients randomized to PGT were rated as more improved than controls in one of the efficacy measures, with an effect size for the interaction term in the ANOVA of 0.1 (Partial Eta Squared; $p=0.036$), considered a medium effect size, suggesting that PGT may be a possible alternative to CBT or IPT for patients with GSAD [33].

Despite the efficacy of both psychotherapy and medication, only two thirds of patients who receive these treatments are considered responders, only half of those are considered remitters and most patients remain symptomatic after the initial treatment [28,38,46]. However, in contrast with the vast literature in the treatment of major depressive disorder (MDD), to date, only a few studies have focused on how to augment treatment response on GSAD. The present study was designed to compare the efficacy of PGT plus clonazepam *versus* clonazepam in the treatment of GSAD. We chose clonazepam based on the promising results of prior studies [14,29,46,52,57], as well as relapse prevention effects with long-term clonazepam treatment in SAD [9].

2. Method

2.1. Study design

This was a randomized, 12-week study of PGT plus clonazepam versus clonazepam in 58 adult outpatients of the Anxiety Program of Hospital de Clínicas de Porto Alegre (HCPA), Brazil, who met the DSM-IV [2] criteria for GSAD as determined by the Mini International Neuropsychiatric Interview (M.I.N.I.) –Portuguese Version 5.0 [3]. The study was approved by the Institutional Review Board (IRB) of HCPA. All subjects provided written informed consent prior to their enrollment in the study.

2.2. Prestudy procedures

The trial was conducted between March 2005 and November 2005. Participants were recruited from clinical referrals and media advertisements. Patients referred to the study were assessed by two psychiatrists with expertise in SAD to determine eligibility and willingness to participate. The assessment included a psychiatric history and the MINI [3]. Eligible subjects were randomly assigned to receive PGT plus clonazepam or clonazepam alone using a list of random numbers provided by a statistician not otherwise involved in the clinical trial. Randomization was stratified by symptoms severity using a cut off score of 82 in the LSAS total score [39], as suggested by prior studies [44]. After randomization, patients were scheduled for the pretreatment (i.e., baseline) assessment.

2.3. Patient sample

Inclusion criteria—Outpatients, 18–65 years old, who met DSM-IV criteria for primary diagnosis of GSAD for at least 2 years, and had a baseline LSAS of at least 55, with fear and/or avoidance in 4 social situations (at least 2 involving interpersonal interactions).

Exclusion criteria—A history of failure to respond to 2 mg of clonazepam taken for at least 12 weeks, hypersensitivity to benzodiazepines, prior or current psychotherapy for SAD (regardless of response). Current comorbid anxiety disorders whose symptoms were more severe than those of SAD, a depressive episode (BDI ≥ 30), or suicide risk, in the previous 6 months, bipolar disorder or substance use disorder (except nicotine dependence). Mental retardation or any neurological disease, use of psychotropic medications (including hypnotics) in the 4 weeks prior to the study, and women breastfeeding, pregnant or unwilling or unable to take adequate contraceptive precautions.

2.4. Treatments

Clonazepam treatment—Pharmacologic treatment consisted of individual 20-minute visits in weeks 1, 2, 4, 6, 8 and 10. Patient adherence to the medication regimen was measured by pill count.

No systematic psychotherapeutic interventions (cognitive, behavioral or interpersonal) were delivered during the visits. Clonazepam regimen was started at an initial dose of 0.5 mg taken twice a day in the first week. The dose could be increased to up to 1.0 mg taken twice a day in weeks 2–12 to maximize response. Dose reduction was allowed if necessary to improve tolerability (0.5 mg/day and 1 mg/day were considered minimum doses in week 1

and in weeks 2–12 respectively). At the end of the treatment period clonazepam was gradually discontinued using a fixed-dose taper of 0.25 mg/day every 2 weeks. Therefore, 16 weeks were required to taper off patients receiving the maximum dose of 2.0 mg/day. Safety assessments were based on reports of adverse events (possible adverse effects were monitored).

PGT and clonazepam treatment—The PGT intervention consisted of 12 weekly 90-minute group sessions using a treatment manual (available from Dr. Knijnik upon request) developed for a previous randomized trial of PGT versus educational supportive psychotherapy group [33]. The number of patients varied from 8 to 10 patients (mean 9) per group. Three groups, led by the first author (D.Z.K.), were conducted to achieve the sample size needed for the study.

The psychotherapeutic technique used in PGT was derived from Malan's [42] focused, short-term psychoanalytic psychotherapy, based on the hypothesis that recurrent and unconscious internal conflicts are connected to the symptoms of SAD.

The conceptual justification for the use of a group psychodynamic treatment for GSAD is the idea that the symptoms and behaviors of individuals reflect the unconscious processes [23] that defend against their repressed wishes, fantasies, and impulses [53]. As with other psychological symptoms, from a psychodynamic point of view, SAD is a symptom of a conflict. Individuals with SAD are conflicted about the wish to exhibit their sexual or aggressive urges. Social anxiety can be both an expression of the conflict and a punishment for the patient's wishes. Avoidance of social situations contributes to avoidance of the conscious experience of these wishes.

Clinical work suggests that certain internal object relationships are characteristic of individuals with SAD. Specifically, these patients have internalized representations of parents, caretakers, or siblings, who shame, criticize, ridicule, humiliate, abandon, and embarrass them. These perceptions are established early in life and later repeatedly projected onto persons in the environment who are then avoided, for fear of criticism and rejection. It is a tendency of punishing themselves for their angry feelings and fantasies towards parents or other meaningful people in their lives [24,61].

Its two phases help deliver PGT in a manner consistent with its conceptualization: *Phase I* includes two individual evaluation interviews with the group therapist to obtain a psychiatric and developmental history and to conceptualize each patient's focus. *Phase II* comprises 12 group sessions, divided into sessions 1–3 (address group formation, ensuring patients' agreement to focus exclusively on the treatment of GSAD and focus formulation), sessions 4–10 (the possible connection between symptoms and conflicts is investigated and interpreted as appropriate) and session 11–12 (discuss issues related to treatment termination).

In the group setting each patient's conflicts were discussed as the transference developed. Also, among the other group members, internal resources could be potentiated and therefore treated as follows: the therapist was very active during each session, encouraging patients to

talk, pointing out similarities among them and offering interpretations to each of them, as well as encouraging the others to reflect on similarities they could identify on their own social situations. In each session, some patients were more prone than others to speak about their life situations, but a balance was obtained to ensure that all patients had an opportunity to explain their suffering.

Brief Case Description—M, 25 years old, has developed a severe fear of interacting with colleagues at college. During early adolescence he was responsible for taking care of his 86-year-old grandfather. He never fully understood his mother's expectations from him because she always complained he did not take proper care of his grandfather. It was understood that each time he had to face a social situation he unconsciously lived it as if he was obliged to answer something to his mother who would criticize and humiliate him.

Patients in the combined treatment received PGT and clonazepam simultaneously, according to the procedures described above.

2.5. Efficacy measures

The Clinical Global Impression - Improvement subscale (CGI-I) [26] is a 7-point clinician-rated scale to assess treatment response, ranging from 1 ("very much improved") to 7 ("very much worse"). It was a structured interview to assess exclusively social anxiety symptoms. The CGI-I was completed by the blind independent evaluator (C.U.M.) previously trained in rating of the CGI scales in SAD patients. Before each assessment patients were reminded not to discuss their treatment in order to maintain its blind condition.

The LSAS [39] is a 24-item scale designed to assess both social interaction and performance-related anxiety in both severity of fear and anxiety and frequency of avoidance. A recent study [9] comparing the LSAS clinician-rated version (LSAS-CR) to its self-rated version (LSAS-SR) found that LSAS-SR is comparable to LSAS-CR and it is reliable. In the present study the LSAS-SR was administered with instructions read to the patients prior to the administration of the scale [4,10,22].

The World Health Organization Instrument to Assess Quality of Life-Bref (WHOQOL-Bref) [18] is a 26-item instrument that measures quality of life in four domains: physical, psychological, social relationship and environment. Two additional questions assess General Quality of Life.

The Beck Depression Inventory (BDI) [6] is a 21-item self-report measure that assesses the presence and severity of depressive symptoms.

2.6. Efficacy evaluation

The primary efficacy measure was mean change from baseline of CGI-I total score, which was assessed at weeks 2, 4, 6, 8, 10 and 12.

The CGI was chosen as primary outcome measure to be consistent with prior studies that had investigated the efficacy of clonazepam in the treatment of SAD [9,12–15,46]. The

continuous measure was chosen instead of the cut-offs because it increases power to detect differences between groups.

Secondary efficacy measures included the proportion of responders (defined as CGI-I = 2, “much” or “very much improved”, based only on social anxiety symptoms) and the percentage of patients in full remission according to two different definitions: a) LSAS total score ≤ 30; b) CGI-I score of 1 [49]. Additionally, mean change from baseline to endpoint of LSAS-SR total score and BDI were assessed at weeks 1, 6 and 12 and WHOQOL-Bref was assessed at weeks 1 and 12.

2.7. Treatment adherence

Fidelity to the manual was monitored through detailed written transcription of all sessions with the therapist (D.Z.K.) receiving weekly supervision on a once a week basis by the last author (C.L.E.), a training and supervising analyst of the International Psychoanalytic Association, with over 5 years of experience providing PGT. Adherence to the manual was measured by two independent raters, in order to evaluate if the therapist followed properly the manual within its three phases.

Additionally to the adherence to the manual, the degree of the psychoanalytical concept was also evaluated. To assess the adherence to psychoanalytical concept of PGT developed by D.Z.K, two independent raters evaluated the sessions through the written transcriptions and provided blind ratings using a structured instrument called Instrument for Evaluation of Psychoanalytical Psychotherapy Sessions – Group version (IEPPS-G) [11] found to be reliable between raters and capable of distinguishing PGT from another form of therapy.

The IEPPS-G was developed in our center to evaluate the psychoanalytical basis of therapeutic sessions. It is a 6-item instrument 5-point Likert scale, ranging from 6 to 30, with higher scores representing a higher psychoanalytical construct. The instrument evaluates therapist neutrality, therapeutic interventions, quality of the interpretations, timing of interpretations, transference, counter-transference and the atmosphere of the session. A cutoff point of 17 has been suggested to identify and classify the group sessions as being psychoanalytical [11].

2.8. Statistical analysis

Kolmogorov-Smirnov test and Levene’s test were used to evaluate normality of distribution and homogeneity of variances, respectively, prior to any statistical testing. Independent samples *t*-tests were used to examine differences in demographic and baseline characteristics between groups. Mann-Whitney Test was used to examine variables that did not follow a normal distribution. Categorical data were compared using Chi-square test and Fisher’s Exact test. Linear Mixed Models [56] were used to examine changes over time in the two treatment groups in CGI-I, LSAS-SR, WHOQOL-Bref, BDI and to evaluate the role of possible confounding factors.

The kappa coefficient was used to evaluate the agreement between the two independent evaluators regarding PGT treatment adherence to IEPPS-G.

Results are considered significant at the $\alpha=0.05$ level (two-tailed). All analyses were conducted using the SPSS 14.

3. Results

A diagram of the patient flow in the study is presented in Figure 1. No statistically significant differences between groups were detected with regard to demographic characteristics or mean baseline rating scale scores (Table 1). There were no significant differences in the proportion of patients who completed the study in each treatment group: 28 (96.6%) in the PGT and clonazepam group and 24 (82.1%) in the clonazepam group (Fisher's Exact p -value=0.102). Neither MDD nor Panic Disorder as comorbidities was associated with treatment outcome (data not shown).

Regarding treatment adherence, both independent raters agreed that the therapist followed properly the manual within its three distinct phases. They also rated IEPPS-G higher than 17 (evaluator A: 29 points; evaluator B: 25 points; Kappa=100%) showing a high psychoanalytical concept present across the sessions.

3.1. Efficacy outcomes

Consistent with our hypotheses, we found that the PGT plus clonazepam group showed significantly greater improvement than the clonazepam group ($F=2.47$, $df=5$, $p=0.033$) in the CGI-I (Table 2). Also consistent with our hypotheses, there were no differences in the BDI between the groups. In contrast, we failed to find significant differences in the LSAS-SR and in the domains of WHOQOL-Bref (Table 3).

Using a CGI-I of 1 or 2 as the criterion for response, the difference in the response rate of PGT plus clonazepam versus clonazepam approached significance (79.3% vs. 53.6%, respectively; Fisher's Exact p -value=0.052). However, there were no significant difference between remission rate in PGT plus clonazepam and clonazepam treatment groups based on the LSAS total scores (10.3% vs. 3.6%; Fisher's Exact p -value=.611) or on the CGI-I score of 1 (31% vs. 25%; $p=.770$).

3.2. Drug dosage

Mean dosage over the study period was calculated by dividing the total number of milligrams taken during the study by the number of treatment days. The mean dose for the PGT plus clonazepam group was 1.29 ± 0.35 mg/d. ($t=1.849$, $df=55$, $p=0.07$). The mean dose for the clonazepam group was 1.48 ± 0.41 mg/d. The mean dose for the PGT plus clonazepam group at week-12 was 1.51 ± 0.525 mg/d. The mean dose for the clonazepam group at week-12 was 1.67 ± 0.53 mg/d ($t=1.1$, $df=55$, $p=0.3$).

3.3. Safety

There were no unexpected or serious adverse events. Adverse events were reported by a similar proportion of individuals in both treatment groups: 28 (96.6%) in the PGT plus clonazepam treatment group and 23 (82.1%) in the clonazepam treatment group (Fisher's Exact $p=.102$). Only one adverse event, decreased libido, was less evident in the combined treatment group ($p=0.012$). Most of the adverse events were mild in severity.

4. Discussion

This study is the first to compare combined medication and PGT versus medication alone in the treatment of GSAD. Our findings suggest that PGT plus clonazepam may be a promising strategy for the treatment of GSAD, regarding gains in the global functioning as measured by the CGI-I. However there were no differences in the other outcome measures evaluated.

Our results are the first to provide some preliminary support for an augmentation strategy to medication treatment for GSAD. To date, only one other published study has examined this question. Davidson et al. [16] conducted a randomized trial (N=295) to examine improvement in response rates with the addition of fluoxetine to CBT and found that, addition of fluoxetine resulted in less than 3% incremental improvement of the combined treatment group over the CBT group, suggesting that combined treatment did not yield any further advantage over CBT alone.

Our study adds to a growing literature suggesting possible benefit of combined treatment over monotherapy for anxiety disorders, for example, in a treatment trial for panic disorder comparing CBT, imipramine and their combination, Barlow et al. [5] found combined treatment superior to either monotherapy. Similar findings have been suggested by some authors for the treatment of chronic MDD [30,32]. On the other hand, a recent study [19] found no benefit of adding clomipramine to CBT in the treatment of obsessive-compulsive disorder, reinforcing the hypothesis of combined treatments not being systematically superior to monotherapy.

On other measures in our study, both groups similarly improved in specific symptomatic domains as measured by the LSAS, in the psychological domain and in the general measure of quality of life as measured by the WHOQOL-Bref. However, we did not detect statistically significant differences between the treatment groups. Failure to detect differences in general quality of life appears to be related to limited power, although no differences were detected between groups in any domain of WHOQOL-Bref, even in the social relationship domain. The reasons for the discrepancy between clinician-rated scales (CGI) and self-rated scales (LSAS-SR) are less clear and may represent differences in response perception between clinicians and patients, a finding previously documented in depression [30,32,54] or it may be accounted for the fact that the addition of PGT to clonazepam was more effective in decreasing the global functioning but not the SAD symptoms considered alone. Furthermore, although the LSAS-SR has good psychometric properties to assess severity of SAD cross-sectionally, it may be less sensitive to change than other outcome measures [10]. Future augmentation studies should compare the sensitivity to change of the LSAS-CR versus the LSAS-SR.

The mean maximum dose of clonazepam in our study was 1.35 mg/day in both groups, lower than the mean maximum dose of clonazepam in two prior studies. However, there were no differences in medication dose between groups. This dose (0.5–2.0 mg/day) was chosen to prevent adverse effects (e.g. daytime sleepiness, cognitive disturbances) that are more common with higher doses and may interfere with patient functioning [14,58]. Consistent with this intent, clonazepam was well tolerated. We are aware of the fact that by

limiting clonazepam dose we provided only an attenuated form of clonazepam treatment. Consistent with this, response to clonazepam was smaller than that reported in prior studies using higher doses.

Our study has some limitations. First, our study had a relatively small sample size, limiting our power to detect significant results in certain measures. Second, this sample was composed of treatment-seeking patients who had GSAD with some restrictions at the enrollment phase (e.g., no severe depressive symptoms) and therefore our results may not be generalized to all patients with GSAD. Third, our study lasted only 12 weeks, a relatively short treatment period for a condition as chronic as GSAD. It is possible that longer periods of psychotherapy may be needed to obtain the full benefit of PGT for GSAD [47]. Also, due to its pilot nature, the study did not include a CBT arm, precluding a direct comparison of this treatment. There is a potential bias from the potentially single-blind assessment. Furthermore, it is possible that the relatively superiority of PGT could be due to nonspecific effects such as increased attention, or a natural process of exposure inherent to any group therapy.

Despite these limitations, our study suggests that the addition of PGT may be a promising augmentation strategy to clonazepam with some gains in the global functioning of patients with GSAD.

Future studies should investigate the effect of longer treatment periods, examine the efficacy of combining PGT with different medications, and compare PGT versus CBT as a strategy for the treatment of GSAD.

5. Conclusion

This study provides empirical information of a relatively understudied and novel approach that has possible benefits regarding the global functioning of those suffering from GSAD.

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Fig. 1.

Flowchart Diagram

Abbreviations: CNZ, Clonazepam; PGT, Psychodynamic Group Therapy; ITT, Intent to treat analysis.

Table 1

Demographic and Baseline Characteristics of the Intent-To-Treat Population of Patients Receiving Clonazepam or Clonazepam plus Psychodynamic Group Therapy in Generalized Social Anxiety Disorder

Characteristic	CNZ (n=28)	CNZ+PGT (n=29)	Statistic	p-value
Mean age	32.4 ± 9.3	34.3 ± 11.1	$t_{df=55} = -0.676$	.502 ^b
Male sex	12 (42.9)	10 (34.5)		.592 ^a
Level of education, yr	12.7 ± 4.0	13.1 ± 3.3	$t_{df=55} = -0.401$	.690 ^b
Marital status			$\chi^2_{df=2} = 0.265$	.876 ^c
Married	10 (35.7)	9 (31)		
Single	16 (57.1)	17 (58.6)		
Widow/Divorced/Separated	2 (7.2)	3 (10.3)		
<i>Psychiatric Comorbidity*</i>				
Any other psychiatric disorder	23 (82.1)	22 (75.9)		.747 ^a
Major depressive disorder	12 (42.9)	6 (20.7)		.092 ^a
Panic disorder	11 (39.3)	5 (17.2)		.082 ^a
Agoraphobia	18 (64.3)	13 (44.8)		.186 ^a
Generalized anxiety disorder	13 (46.4)	14 (48.3)		>.999 ^a
<i>Social anxiety disorder Characteristics</i>				
Duration of social anxiety disorder, years	16 (9.25 to 24)	18 (13.5 to 31)	$z = -1.126^e$	.260 ^d
CGI-S	5.86±0.93	5.97±0.9	$t_{df=55} = -0.445$	.658 ^b
LSAS-SR	91.1±22.6	92±24.7	$t_{df=55} = -0.142$	.888 ^b
BDI	15.4±7.1	13.7±9.1	$t_{df=55} = 0.751$	.456 ^b
<i>WHOQOL-Bref Domains</i>				
Physical	56.4±14.6	59.8±16.4	$t_{df=55} = -0.83$	.410 ^b
Psychological	46.0±13.1	52.7±16.2	$t_{df=55} = -1.73$	.090 ^b
Social Relationship	47.0±20.9	47.4±19.6	$t_{df=55} = -0.07$	.942 ^b
Environmental	47.6±14.1	54.7±16.3	$t_{df=55} = -1.76$	.085 ^b
General Quality of Life	50.9±18.6	55.6±21.8	$t_{df=55} = -0.876$	.385 ^b

Note: Values represent count (percent), mean ± SD or median (inter-quartile range). **Statistic:**

^a Fisher's Exact test

^b Independent samples Student's *t*-test

^c Pearson Chi-square test

^d Mann-Whitney test

^e standardized score for the Mann-Whitney test.

Abbreviations: CNZ = Clonazepam, PGT = Psychodynamic Group Therapy, LSAS = Liebowitz Social Anxiety Scale (self-report version), CGI-S = Clinical Global Impression Scale – Severity of Illness, BDI = Beck Depression Inventory, WHOQOL-Bref = World Health Organization Instrument to Assess Quality of Life (bref version), df = degrees of freedom.

* Reported only for disorders present in at least 10% of each group.

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Linear Mixed Models of CGI-I comparing Clonazepam versus Clonazepam plus Psychodynamic Group Therapy in Generalized Social Anxiety Disorder

Table 2

Interventions	Assessment Week							Effect Size ^a		p-value ^b	
	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12		Time	Treatment	Time * Treatment	
CNZ	3.2±1.1	2.9±1.1	2.5±1.2	2.4±1.1	2.3±1.1	2.5±1.3		<.001	.389	.033	
CNZ+PGT	3.6±1.0	2.8±1.0	2.4±0.9	2.2±0.8	1.9±0.8	1.9±0.7					

Note: Values represented mean ± SD. Abbreviations: CNZ = Clonazepam, PGT = Psychodynamic Group Therapy. Statistic:

^aWeek-2 to Week12;

^bLinear Mixed Models

Table 3

Linear Mixed Models of Clonazepam or Clonazepam plus Psychodynamic Group Therapy in Generalized Social Anxiety Disorder

	Baseline			Week 6			Week 12			<i>p</i> -value ^a
	CNZ (<i>n</i> =29)	CNZ+PGT (<i>n</i> =28)	CNZ (<i>n</i> =29)	CNZ (<i>n</i> =29)	CNZ+PGT (<i>n</i> =28)	CNZ (<i>n</i> =29)	CNZ (<i>n</i> =29)	CNZ+PGT (<i>n</i> =28)	Time	Time * Treatment
Symptomatic scales										
LSAS	91.1±22.6	92±24.7	76.9±24.3	78.1±26.1	74.3±25.9	71.4±27.4	<.001	.965		.657
BDI	15.4±7.1	13.7±9.1	11.2±7.1	10±7.4	12.2±8.6	9.4±8.9	<.001	.298		.710
WHOQOL-Bref										
Quality of life domains										
Physical	56.4±14.6	59.8±16.4			60.8±14.9	62.7±16.2	.074	.462		.713
Psychological	46.0±13.1	52.7±16.2			51.0±15.7	57.5±17.2	.010	.081		.932
Social	47.0±20.9	47.4±19.6			49.1±22.5	52.9±21.5	.097	.687		.454
Relationship										
Environmental	47.6±14.1	54.7±16.3			47.9±13.8	56.3±16.6	.513	.047		.632
General Quality of Life	50.9±18.6	55.6±21.8			57.1±17.1	68.1±16.2	<.001	.083		.148

Note: Values represent mean ± SD. **Abbreviations:** CNZ = Clonazepam., PGT = Psychodynamic Group Therapy, LSAS = Liebowitz Social Anxiety Scale (self-report version), BDI = Beck Depression Inventory, WHOQOL-Bref = World Health Organization Instrument to Assess Quality of Life (bref version). **Statistics:**

^aLinear Mixed Models