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Treatment of Mixed Anxiety-Depression Disorder: Long-Term Outcome

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Abstract. The aim of this paper was to test the long-term contribution of cognitive-behavioural therapy to the treatment of mixed anxiety-depression disorder. Fifty-seven patients, selected according to DSM-IV diagnostic criteria, were assigned to: 1) cognitive-behavioural therapy; 2) combined therapy (drug and cognitive-behavioural therapy); or 3) a standard drug therapy control group. A multigroup experimental design with repeated measures of assessment (pretreatment, posttreatment, and 3-, 6- and 12 month follow-ups) was used. Most patients who were treated (71%) in experimental groups showed significant improvement at the 12-month follow-up, but there were no differences between the two therapeutic modes. No improvement was shown by the control-group participants at the 6-month follow-up. The results of the present trial do not support the beneficial effects of drug therapy by itself for this disorder. Finally, several topics that may contribute to future research in this field are discussed.

Keywords: Mixed anxiety-depression disorder, drug treatment, behavioural-cognitive therapy, combined treatment, long-term outcome.

Introduction

The psychopathological proposal for a mixed anxiety-depression disorder has already been incorporated (F41.2) into the ICD-10 and is also found in the DSM-IV appendix. There was a field trial that led to the derivation of the DSM-IV MAD criteria to include patients with a non-specific pattern of anxious and depressed symptoms (Zinbarg et al., 1994). However, in other studies (Barkow et al., 2004) the MAD disorder seems to lack stability in its course.

The prevalence rate of this disorder among patients in primary care centres ranges from 1–10%. MAD disorder is difficult to cure with the usual drug and psychological treatments. In fact, the problem becomes chronic and often appears somatized, so these people excessively depend on professional assistance (Angst, Merikangas and Preisig, 1997).

The scant work done on the mixed anxiety-depression disorder has focused on the joint use of antidepressive and anxiolytic drugs or the exclusive use of antidepressants (Carrasco,

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Díaz and Saiz, 2000). Psychological therapy used in MAD disorder is a combination of coping strategies used in anxiety disorders and in dysthymia, which seem to be strengthened if treatment has a group format (Echeburúa, Salaberria, Corral, Cenea and Berasategui, 2000; Moras, Telfer and Barlow, 1993).

The main aim of this research is to test the long-term clinical effectiveness of a cognitive-behavioural programme specifically designed for the MAD disorder and carried out in a naturalistic setting of a health care centre. Posttreatment and short follow-up results are described elsewhere (Echeburúa et al., 2000).

Method

Participants

The sample for this study consisted of patients who sought treatment at the Vitoria Mental Health Center (Spain) from February 1997 to December 1999. Preselected subjects were referred to the Centre with unspecific symptoms of anxiety and depression by GP doctors.

After screening the subjects who came to the therapeutic programme for MAD disorder (69 subjects), the sample was reduced to 57 subjects, according to DSM-IV diagnostic criteria. Excluded subjects (6) did not meet the criteria for admission and there were 6 patients who did not want to participate in the clinical trial (refusal rate of 10%). Regarding the most significant demographic characteristics of the sample, most patients were women (93%); the socioeconomic level was middle and lower class; the mean age was 40 years; and 47% of the sample were housewives.

Experimental design

A multigroup experimental design with independent measures in the treatment factor and with multiple and repeated measures of assessment (pre-treatment, posttreatment and 3-, 6- and 12-month follow-up) was used. Patients were randomly assigned to three groups. Thus the resulting modalities were the following: a) cognitive-behavioural group therapy without drug therapy ($n = 24$); b) combined group therapy (cognitive-behavioural and standard drug therapy) ($n = 22$); and c) control group with only standard drug therapy ($n = 11$). For ethical reasons only two measurements (pre-treatment and 6-month follow-up) were conducted in the control group.

Assessment measures

An individual semi-structured interview was held to achieve the diagnostic criteria of MAD disorder according to the appendix of DSM-IV. In this interview the patients describe the symptoms, the history of the disorder and the previous treatments, as well as the extent of the maladjustment to the daily life. The data on interrater reliability obtained with this interview in this study are satisfactory (kappa = .91).

In addition, two scales administered by the independent interviewers were used: Hamilton Anxiety Rating Scale (HARS) and Hamilton Depression Rating Scale (HDRS). The self-reports used were the State-Trait Anxiety Inventory (STAI), the Beck Depression Inventory (BDI), the Rosenberg Self-Esteem Scale and the Maladjustment Scale. These instruments are accurately described elsewhere (Echeburúa et al., 2000).

Therapeutic modalities

Cognitive-behavioural therapy. This treatment, without any kind of medication, consists of three components: a) psychoeducative explanations about the nature and the features of the disorder (1st session); b) techniques focused on the therapy of anxiety symptoms: training in relaxation and breathing and hygiene of sleep (2nd session); exposure to avoided behaviours, self-instructions and cognitive distraction (3rd and 4th sessions); and c) techniques focused to cope with depressive symptoms by engagement in hobbies and entertainment and by cognitive restructuring of negative thoughts (5th–8th sessions). Lastly, in order to become stronger and reinforce the therapeutic change, patients are trained in improvement of self-esteem (9th session) and in problem solving techniques (10th session). Sessions 11–12 are devoted to relapse prevention and to planning the next future. The general characteristics of the therapeutic procedure are as follows: group modality (4–6 patients); two clinical psychologists adequately trained and with 5 years of experience as therapists; and 12×2 hours weekly sessions.

Combined therapy (drug and cognitive-behavioural therapy). This treatment consists of two parts: a) in an individual way, a standard drug treatment (benzodiazepines and/or SSRI antidepressant drugs) prescribed by the psychiatrist of the mental health centre; and b) in a group way, the cognitive-behavioural therapy above described.

Standard drug therapy control group. Patients assigned to this group continued to be treated in an individual way with the standard drug treatment (treatment, as usual, depending on the psychiatrist's clinician choice), but without the cognitive-behavioural therapy. Patients in this group had been on the drugs for an average of 15 months.

Results

Rates of improvement

In this study, therapeutic success was defined by two raters as a clinically significant reduction of diagnostic criteria of MAD disorder according to the appendix of DSM-IV and a decrease of at least 30% in the scores obtained by the patient before treatment in STAI and BDI.

In the 12-month follow-up the rate of improvement (71%) in experimental groups was as good as in prior research (Echeburúa et al., 2000), where experimental groups performed better than the control group. One year later, the CBT group (79.2%, $n = 19$) did better than the combined group (61.9%, $n = 13$), but these differences are not statistically significant. The rates of deterioration were low and similar in both groups (7%).

Results of the measures of anxiety, depression, self-esteem and maladjustment

Between-group analysis. The means and standard deviations of all variables studied are reported in Table 1. Therapeutic change continued to be good, with an effect size similar to that obtained in the short-term outcome (Echeburúa et al., 2000). There were no differences between the two therapeutic modalities in the 12-month follow-up.

Within-group analysis. The within-group evolution is very similar in all variables in both experimental groups, with a marked improvement between pre- and posttreatment, which tends to level off between the post- and the 12-month follow-up (Table 2).

Table 1. Means (and standard deviations) and F and t values in anxiety, depression, self-esteem and maladjustment

	CBT (A) M (*SD*)	Combined (B) M (*SD*)	Control (C) M (*SD*)	*F*	*t*
Anxiety					
STAI (0–60)					
Pretreat.	36,45 (8,96)	35,72 (11,54)	35,36 (6,24)	0,25	
Posttreat.	22,70 (7,68)	26,54 (11,42)			−1,34
6 months	21,83 (1,51)	23,28 (1,69)	31,72 (2,60)	6,38** C>B,A	
12 months	20,50 (5,48)	23,52 (7,96)			−1,49
HARS (0–56)					
Pretreat.	17,87 (4,41)	17,81 (4,22)	14,81 (4,64)	2,11	
Posttreat.	7,87 (4,71)	9,81 (5,31)			−1,31
6 months	6,66 (1,00)	9,00 (1,38)	14,36 (1,25)	7,72** C>B,A	
12 months	6,04 (4,77)	8,57 (5,39)			−1,66
Depression					
HDRS (0–62)					
Pretreat.	14,91 (3,46)	16,31 (4,40)	16,45 (2,73)	1,04	
Posttreat	6,04 (3,91)	8,90 (4,85)			−2,21*
6 months	5,33 (0,82)	8,09 (1,16)	13,72 (1,36)	12,23*** C>B,A	
12 months	5,12 (4,68)	7,76 (4,87)			−1,78
BDI (0–63)					
Pretreat.	18,87 (7,96)	25 (6,91)	24,9 (6,99)	4,72* A<B,C	
Posttreat.	11,20 (5,31)	15,72 (8,37)			−2,20*
6 months	9,70 (0,95)	13,71 (1,55)	24,54 (0,87)	8,33***	
12 months	9,50 (5,16)	13,66 (8,15)			−2,07*
Self-esteem (10–40)					
Pretreat.	27,5 (6,38)	23,5 (3,32)	22,8 (2,08)	5,60**A>B,C	
Posttreat.	29,29 (4,49)	26,59 (4,58)			2,01*
6 months	30,41 (0,88)	27,38 (0,69)	24,52 (0,87)	13,66***	
12 months	31,41 (4,08)	27,19 (3,70)			3,61***
Maladjustment (6–36)					
Pretreat.	15,25 (4,91)	18,77 (6,56)	19,18 (5,56)	2,85	
Posttreat.	8,04 (6,80)	12,77 (6,74)			−2,36*
6 months	5,87 (0,92)	10,38 (1,44)	16,36 (2,05)	12,37*** C>B,A	
12 months	5,08 (4,46)	9,61 (6,60)			−2,72**

* $p < .05$; ** $p < .01$; *** $p < .001$.

Discussion

The interest of this study stems from the choice of a significant and rarely studied clinical disorder, from having been conducted in a naturalistic setting, from the coherence of the results obtained in different variables, and from the long-term follow-up (one year).

The majority of patients studied were women with chronic problems of anxiety and depression, marked by functional physical complaints, and usually with many previous drug treatments. Unlike other studies (Barkow et al., 2004) and according to the data of our prior

Table 2. Within-group comparisons (F and t values) in anxiety, depression, self-esteem and maladjustment

	CBT	Combined	Control
STAI	$F = 29,45^{***}$	$F = 6,11^{***}$	
	t	t	t
Pre-posttreat.	5,88***	3,08**	2,51*
Pre-6 months	6,07***	3,70***	
Post-6 months	0,49	1,50	
6–12 months	1,05	−1,07	
HARS	$F = 46,10^{***}$	$F = 35,65^{***}$	
	t	t	t
Pre-posttreat.	6,64***	6,46***	0,24
Pre-6 months	7,58***	6,27***	
Post-6 months	1,97	2,46*	
6–12 months	0,80	1,44	
BDI	$F = 21,13^{***}$	$F = 22,42^{***}$	
	t	t	t
Pre-posttreat.	4,12***	5,03***	1,98
Pre-6 months	5,66***	5,63***	
Post-6 months	1,48	1,67	
6–12 months	0,35	1,55	
HDRS	$F = 76,37^{***}$	$F = 31,05^{***}$	
	t	t	t
Pre-posttreat.	8,98***	6,74***	2,64*
Pre-6 months	9,87***	6,67***	
Post-6 months	1,97	1,52	
6–12 months	0,62	0,08	
Self-esteem	$F = 5,12^{**}$	$F = 8,64^{***}$	
	t	t	t
Pre-posttreat.	−1,13	−4,65***	−3,19*
Pre-6 months	−2,37*	−6,11***	
Post-6 months	−1,89	−0,58	
6–12 months	−1,32	−0,37	
Maladjustment	$F = 33,39^{***}$	$F = 21,41^{***}$	
	t	t	t
Pre-posttreat.	5,61***	5,17***	1,65
Pre-6 months	8,32***	5,49***	
Post-6 months	1,94	1,45	
6–12 months	1,02	1,57	

$^{*}p < .05$ $^{**}p < .01$ $^{***}p < .001$.

paper related to short-term outcome (Echeburúa et al., 2000), the disorder is stable and does not remit or shift to diagnoses other than depression or anxiety.

The improvement rate in both experimental groups was 71% in the 12-month follow-up. These results show the superiority of both ways with respect to the control group, in which there were no improvements between the pre-treatment assessment and the 6-month follow-up. The CBT group did better than the combined group (12-month improvement rate of 79.2% vs. 61.9%; STAI results; HARS results), but these differences were not significant, perhaps because our study may be statistically under-powered.

As in other anxiety disorders, such as GAD (Barlow, Allen and Choate, 2004), cognitive-behavioural therapy is an adequate treatment for this disorder. The addition of a drug treatment does not contribute anything of value but it may be of interest, at least in the initial phases, for those patients who refuse to give up medication or for those in which the discomfort of the symptoms (insomnia or severe depression) constitutes a hindrance to the involvement in an exclusively psychological treatment.

An important conclusion of this study refers to its cost-effectiveness (Bower et al., 2000). The possibility of implementing a brief intervention in a group format could lead to a considerable cost saving, especially in public Mental Health Centres, which are currently very often overwhelmed by the number of patients in search of treatment.

It is the first study that tests the long-term effectiveness of cognitive-behavioural treatment designed ad hoc for the MAD disorder and is compared with standard drug treatment in a naturalistic setting. External validity can be regarded as a strength of the study.

This is only an exploratory study. Further research should be concerned about the statistical power of the studies, take into account the control of non-specific treatment effects, and should explain not only whether or not this treatment is effective, but why it is effective. Future studies should have wider samples of patients in order to establish the most suitable profile for patients for each of the effective therapeutic modalities, to design motivational strategies to involve psychological treatments for patients refusing to give up medication, and to define more accurate criteria for a therapeutic improvement, as well as to design measures to study treatment fidelity in the CBT groups.

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