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Psychotherapy versus drug therapy in depression in outpatient care

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Depression in Europe has a prevalence rate of 3.9%. One of the main work loads in out-patient care comes from treatment of affective disorders. The objective of the present study is to compare the efficacy of psychotherapy versus drug therapy in the treatment of affective disorders. The systematic review carried out has found 6 randomized controlled trials with a pill-placebo control group. The conclusions obtained after re-analyzing each study point out to comparatively equal efficacy of the active treatments and placebo in mild depressions. On the other hand, no significant differences were observed in relationship to the psychotherapeutic treatment efficacy versus drug treatments in moderate and severe depressions, these out-performing placebo efficacy.

Key words:
Psychotherap. Drug therapy. Placebo. Affective disorders. Depression. Efficacy.

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Psicoterapia frente a farmacoterapia en depresión en atención ambulatoria

La depresión en Europa tiene una tasa de prevalencia del 3,9%. Una de las principales cargas de trabajo en atención ambulatoria deriva del tratamiento de los trastornos afectivos. El objetivo del presente estudio es comparar la eficacia de la psicoterapia frente a la farmacoterapia en el tratamiento de los trastornos afectivos. En la revisión sistemática llevada a cabo se han encontrado seis ensayos clínicos aleatorizados con un grupo control de píldora-placebo relevantes para nuestra investigación. Las conclusiones obtenidas en el reanálisis de los resultados de cada estudio apuntan a una eficacia comparativamente igual de los tratamientos activos y de placebo en depresiones leves. Por otro lado no se observan diferencias significativas en relación con la eficacia de los tratamientos psicoterapéuticos frente a los tratamientos farmacológicos en depresiones moderadas y graves. En estos casos los tratamientos activos son superiores a placebo.

Palabras clave:
Psicoterapia. Farmacoterapia. Placebo. Trastornos afectivos. Depresión. Eficacia.

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INTRODUCTION

A prevalence rate of 3.9% for depressive spectrum disorders was observed in the Paykel Study[1] (European Study of the Epidemiology of Mental Disorders [ESMeD]) between 2000-2002 with a sample of 21,425 persons.

One of the most important work loads in out-patient care comes from treatment of affective disorders. Prescription of new generation antidepressants has improved the treatment of these disorders. This is mainly due to the lower frequency in the appearance of adverse events and to the better safety in their management, but not due to their better efficacy. However, comparative efficacy with other therapeutic approaches (brief psychotherapies) has not been adequately evaluated.

Currently, the development and application of evidence based psychiatry is pursued in both the clinical practice as well as research. This means prescribing those treatments that have demonstrated efficacy and safety through randomized clinical trials and which, a posteriori, have been integrated into the clinical guidelines after having been reviewed and, if appropriate, meta-analyzed. The clinical guidelines gather the advances in relationship to the most effective and adequate treatments of a certain disorder. In the case of affective disorders, there are clinical guidelines having high quality methodology such as that of the National Institute Clinical Excellence or NICE[2] and those of the American Psychiatric Association or AP[3]. The importance of psychotherapy in the treatment of depression is manifested in these guidelines. In the NICE clinical guides, we have found statements such as «antidepressants are not recommended for the initial treatment of mild depression since the risk/benefit ratio is poor. In both mild depression and in moderate

depression, psychological treatments specifically focused on the depression (such as, for example, problem solving therapy, brief cognitive behavior psychotherapy and counseling) should be considered for 6 to 8 sessions during 10 or 12 weeks». In turn, the clinical guidelines of the APA state that «the choice of a psychotherapeutic treatment versus drug therapy in the acute phase is mediated both by clinical factors (such as symptom severity) and by other factors (preferences of the patients, cost-effectiveness analysis). The use of an effective psychotherapy should be considered as the only treatment in mild and moderate depression». These statements are recommendations that provide moderate clinical confidence and are based on reports and opinions of expert's committees or clinical experience of respected authorities. However, there are many clinical trials that compare the efficacy of drug therapy compared to psychotherapy and which, therefore, may provide first order scientific evidence.

There are several reviews regarding comparative efficacy of psychotherapy compared to drug therapy in the treatment of depression. The first narrative review in this area was that presented by Weissman[4]. It compares the psychotherapy versus drug therapy in the treatment of the depressed patients. Variable results were obtained between studies. Of the five studies found, one indicated the superiority of the efficacy of psychotherapy (cognitive therapy) compared to drug therapy (imipramine) in the treatment of depression. Another study found both interventions to be equally effective, while three others stressed the superiority of the efficacy of drug therapy compared to psychotherapy (interpersonal, group or therapy with couples) in the prevention of relapses or reduction of symptoms.

A total of 56 studies were included in a meta-analysis on the treatment of unipolar depression in adults[5]. Several types of psychotherapy were studied (behavioral therapy, social-interpersonal learning therapy, cognitive therapy, couple therapy and a combination of cognitive therapy, social learning and behavioral therapy) and drug therapy (the two most common ones were amitriptyline and imipramine). The comparison of drug therapy compared to psychotherapy indicates a better benefit of the latter. However, the low methodological quality of the works and the fact that the active treatment arms were studied separately compared to a control group make the results inconclusive.

DeRubeis[6] developed a mega-analysis in patients with severe depression. The data indicate the therapeutic equivalence of behavioral cognitive therapy and drug therapy. This study has been criticized because it generalizes the results to all antidepressants[7]. Another methodological criticism suggests the possibility of bias in the data due to the different measurements of the results used[8], and the main one refers to the inclusion of studies without a control-placebo group[9].

Another review included a sample of 883 patients with major depressive disorder[10]. The treatment lasted from 10 to 34 weeks. Analysis by intention to treat indicated that the antidepressants (tricyclic antidepressants and phenelzine) and psychotherapy (cognitive behavioral and interpersonal psychotherapy) were more effective than the control conditions, but that there were no differences between the active treatments. The percentages of remission for all the patients randomized and assigned to medication, psychotherapy or control conditions were 46.4 %, 46.3 % and 24.4 %, respectively. In addition, a significantly larger number of patients in the control situation (54.4 %) were lost to follow-up in each one of the active treatments with medication (37.1 %) or psychotherapy. However, this study has been cited, among other reasons, because it had included three studies that did not have a control group with the placebo pill[11].

The primary objective of this work is to compare efficacy of different antidepressants and different brief psychotherapies in the treatment of depression in out-patient care. To do so, a systematic review was made of the literature and all those studies that met our inclusion criteria were collected.

SEARCH STRATEGY

The electronic search strategy was designed and developed in collaboration with the Cochrane Iberoamerican Foundation. The search was conducted in the following databases: Medline (1964-2006), Embase (1974-2006), CINAHL (1982-2006), PsycINFO (1873-2006), The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2005, number 4) and LILACS (1982-2006). The search strategy was designed with the terms in free and descriptor text related with the intervention, its comparison (psychotherapy and antidepressants) and health problem of interest (depression). The search strategies in each electronic database may be requested to the first author.

INCLUSION CRITERIA

Randomized clinical trials with at least three treatment arms were included. One arm of brief psychotherapy (structured psychotherapy with an adequate design and that complied with the intervention protocol established and with a duration under 12 weeks), another arm of drug therapy (antidepressants of any drug family) and another arm of pill-placebo. Those studies that included another type of control treatment such as psychotherapy-placebo, waiting list or usual treatment were excluded. The studies should include a randomization of the patients to the different treatment arms and an evaluation of the results conducted by evaluators who were not clinical personnel and who were blinded to the patient's allotment to the treatment arms. The participants selected were adults (>18 years) diagnosed of affective disorder (major depression or dysthymia) in acute treatment. Those studies in which the patients had been diagnosed of psychotic depression, manic depressive

episodes or depression secondary to substance abuse and all those studies whose interventions were developed in patients with treatment refractory depression or in maintenance and/or relapse prevention phases were excluded from our analysis.

In relationship to the measurements of the results, those studies that had remission rates of depressive symptoms and that allowed for analysis of data by intention to treatment were included. The remission rate should be based on psychometric measurements for which there is a validated remission criterion, such as, for example, the Hamilton depression rating scale (HDRS), the Montgomery-Asberg scale, Beck depression inventory or global clinical impression scale.

DATA COLLECTION AND ANALYSIS

Two reviewers (IG and JB) independently evaluated the publications obtained, checking the title, summary or both. If there was any doubt on the relevance of the article, they obtained copies of them and evaluated them in depth in order to verify if the inclusion criteria were met or not.

An individual analysis was made of the remission data based on the data of the analysis by intention to treat of each one of the studies. The results of the studies were extracted in 2xK tables, K being the number of treatment arms in comparison. The statistical analyses of the size of effect were based on the odds ratio (OR) of each one of the treatment arms in regards to the pill-placebo control group. The significance tests were based on a general chi square test followed by specific analyses for the contrasts of interest in each one of the studies. All the analyses were performed with the Stata v.9 program.

RESULTS

Six studies that met the inclusion requirements previously proposed in the method's section were obtained.

As can be seen in table 1, the studies found show variability in regards to the diagnoses and severity of the depressive disorders. On the other hand, variability is also seen in regards to the antidepressants used, the most common being paroxetine, and in relationship to the different types of psychotherapies, the most common being problem solving therapy. Regarding treatment times, these ranged from 8 to 16 weeks. In relationship to remission criteria used, only 2 trials used the clinical criterion established of a score on the HDRS-17 ≤ 7[12,13]. Two other studies used the more restrictive criterion of a score on the HDRS-17 ≤ 6[14,15]. Another study used a laxer criterion of HDRS-17 ≤ 12[16]. Finally, one of the studies used the 21-item version and established a criterion of HDRS-21 ≤ 9[17].

Table 1 Summary of the characteristics of the studies included

Study	Elkin (1989)	Mynors-Wallis (1995)	Jarret (1999)	Williams (2000)	Barret (2001)	DeRubeis (2005)
N	239	91	108	415	239	240
Age range (years)	21-60	18-65	NI	60-93	18-59	27-52
Diagnosis	Major depressive disorder	Major depresion	Major depressive disorder with atypical traits	Dysthymia or minor depression	Dysthimia or minor depression	Major depressive depression
Scores in baseline (mean-SD)	HDRS-17 19.5 (4.4)	HDRS-17 19 (4,4)	HDRS-21 20.8 (6.7)	HDRS-17 13,4 (2,7)	HDRS-17 14.2 (3.3)	HDRS-17 23.4 (2.9)
Drug therapy	Imipramine	Amitriptyline	Fenelzine	Paroxetine	Paroxetine	Paroxetine
Psychoterhapy	CBT IPT	PST	CT	PST	PST	CT
Treatment time (weeks)	16	12	10	11	11	8
Remission criteria	HDRS-17 ≤ 6 BDI ≤ 9	HDRS-17 ≤ 7	HDRS-21 ≤ 9	HDRS-17 ≤ 7	HDRS-17 ≤ 6	HDRS-17 ≤ 12

NR: not reported; CBT: cognitivebehavioral therapy; CT: cognitive therapy; IPT: inter-personal therapy; PST: problem solving therapy; HDRS: Hamilton Depression Rating Scale; BDI: Beck Depression Inventory.

The Elkin et al. study[15] had adequate statistical power. Allotment of the patients to different treatment conditions was based on a randomized order generated by computer and stratified for each center. The drug therapy sessions were conducted by a double-blind therapist. The study had a sample of 239 patients, 70% of whom were women, with an age range between 21 and 60 years and diagnosed of major depressive disorder. Inclusion criteria to participate in the study were minimum education of eighth grade and sufficient ability to read and understand to fill out the self-applied forms; diagnostic criteria for a current episode of major depressive disorder; score on the HDRS of 17 items > 14. Exclusion criteria to participate in the study were additional specific psychiatric disorders; two or more schizotypal traits; background of schizophrenia; organic brain syndrome; mental retardation; concurrent treatment; presence of specific physical disease or other medical contraindications for the use of imipramine, and presence of a clinical condition inconsistent with participation in the research protocol (i.e., suicidal risk or need for immediate treatment). Duration of the clinical trial was 16 weeks. Clinical management was introduced into the drug treatment arm in order to improve compliance and to direct the ethical matters related with the use of placebo with depressed patients. Imipramine was administered in doses that ranged from 150-185 mg/d. Session duration was 45 to 60 minutes in the initial session and 20 to 30 minutes in the remaining sessions. There were two treatments in the psychotherapy arm. The first was cognitive behavioral therapy (CBT)[18], whose basic principles were to help the depressed patients correct their negative and distorted views about themselves, the world, the future and underlying disadaptive thoughts that favor these cognitions. The second treatment was interpersonal therapy (IPT)[19], whose objectives were to help the patients to identify and understand their interpersonal and conflicts problems better and to help them to develop more adaptive ways of relating with the others. The intervention duration was 50 minutes. The placebo group worked in the same way as the drug therapy arm. In relationship to the losses or drop-outs during the study, 77 patients ended it before completing the study (less than 15 weeks and/or 12 treatment sessions). There were 19 early terminations in the CBT group, 19 in the imipramine group and 25 in the placebo group. According to the authors, there is no evidence that each one of the psychotherapies was significantly less effective than the standard reference treatment. The data from our re-analysis (table 2) suggest that IPT and imipramine are significantly more effective than placebo, CBT being marginally non-significant. On the other hand, the therapeutic equivalence test of the three active treatments indicates that none of them seem to be superior to the other two.

Table 2 Study data of Elkin et al., 1989

Results	Placebo	ITP	CBT	Imipramine
Remission	13	26	21	24
No	49	35	38	33
Total	62	61	59	57
OR (95% CI)	1	2.8 (1.3 to 6.2)	2.1 (0.93 to 4.7)	2.7 (1.2 to 6.1)
P value		0.011	0.076	0.014
Adjusted P value		0.028	0.218	0.037

General χ^2 test (3 gl): 8.18; P: 0.042. IPT test = CBT = imipramine; χ^2 (2 gl): 0.75; P: 0.6859. ITP: interpersonal therapy; CBT: cogntive behavioral terapy.

The Mynors-Wallis et al. study[12] has adequate statistical power. The patients were randomized to the treatments using a system of stamped envelopes. The patients and therapists were blind to the placebo-pill treatments. A total sample of 91 patents was included, 77% of whom were women with an age range between 18 and 65 years and a diagnosis of major depression. Inclusion criteria were presence of depressed mood accompanied by at least four key symptoms of depression, such as appetite alterations, sleep difficulties, loss of energy, poor concentration, guilt, suicidal thinking, loss of interest or pleasure in daily life activities and psychomotor slow-down for at least two weeks as well as a score on the HDRS-17>13. Exclusion criteria were having another psychiatric alteration (other than anxiety) before the onset of the depression; receive any psychological or drug treatment at present; have psychotic symptoms at the present time; have serious suicidal attempts; have a background of schizophrenia; recent abuse of alcohol or drugs; physical problems that may exclude the capacity to take amitriptyline. Intervention duration was 12 weeks. The drug therapy group was administered amitriptyline, at a dosage of two capsules of 50 mg for two nights, followed by an increase of 25 mg every third night until reaching six capsules (150 mg). The duration of the interventions was 60 minutes the first session and the following ones were approximately 30 minutes. Problem solving therapy (PST) was performed in the psychotherapy arm. The therapist gave a simple explanation on the functioning of PST. After, the problems were identified and listed, the PST phases were demonstrated with one of the problems on the list and the other problems were treated in the same way in the following sessions. The placebo group had the same functioning as the drug therapy group. In relationship to losses or drop-outs, the patients discontinued the treatment because they were not improving (one in the problem solving group, one in the amitriptyline group and eigth in the placebo group) or due to adverse events (three in the amitriptyline group and two in the placebo group). Five patients were eliminated from the placebo group because they had not responded to the treatment. The conclusions of the authors were that PST was more effective than the placebo and as effective as amitriptyline in the treatment of major depression in primary care. Our analyses (table 3) suggest that PST is significantly better than the placebo

Table 3 Study data of Mynors-Wallis et al., 1995

Results	Placebo	PST	Amiltriptyllne
Remission	8	18	16
No	22	12	15
Total	30	30	31
OR (95% CI)	1	4.1 (1.4 to 12.3)	2.9 (1.0 to 8.6)
P value		0.011	0.049
Adjusted P value		0.017	0.089

General χ^2 test (2 gl): 7.27; P: 0,026. PST = amitriptyline; χ^2 (1 gl): 0.43; P: 0.5102. PST: problem solving therapy.

while drug treatment is marginally non-significant. The test of comparison of the two active treatments indicates their therapeutic equivalence.

In the Jarrett et al. study[17] the patients were randomized under the supervision of a statistician, who maintained the research staff blinded to the allotment (fenelzine or placebo) during the study. The evaluators were blinded to the allotment of the patients to treatments. The study had a sample of 108 patients, 73 of whom were women and 35 men with a diagnosis of major depressive disorder and atypical traits according to the DSM-III-R. In order to enter into the study, the patients had to meet the criteria for depression with atypical traits, including: *a)* maintain reactive mood, and *b)* show two or more of the following factors: *1)* appetite increase or weight gain; *2)* oversleeping; *3)* extreme heavy feeling or sensation of leaden paralysis in arms or legs while the patient is depressed, and *4)* long-standing pattern of sensitivity to interpersonal rejection and a HDRS-21 > 14 during the initial intervention. Exclusion criteria were presence of medical alteration or concurrent treatment that may cause depressive symptoms or require medication incompatible with the MAOI; refusal to be randomized or to maintain a tyramine free diet; have another primary comorbid psychiatric disorder; score of HDRS-21 < 14 before the randomization; be unable to fill out questionnaires; suicidal risk; have previously participated in an adequate trial of MAOI or cognitive therapy (CT). The trial duration was 10 weeks. In the drug therapy arm, there were aspects such as drug adjustment and symptom count, adverse events, blood pressure, weight, etc. The patients in both conditions (drug therapy and placebo) followed a tyramine low diet. The doses were increased gradually for 10 weeks to reach a therapeutic response to fenelzine of approximately 0.85 mg/kg or 1 mg/kg in patients who did not respond to lower doses. The psychotherapy arm was based on the Beck CT. Nine patients randomized to fenelzine did not complete the trial. Of these, the psychiatrist eliminated 3 whose depressive symptoms required an alternative treatment, and 6 more dropped out. Twenty-three patients randomized to the placebo arm did not complete the trial. The psychiatrist eliminated 4 because their symptoms needed an alterative treatment and 2 others who did not comply with the study procedures. The adverse events mentioned most by the fenelzine group were fatigue, sedation, insomnia, dry mouth, dyskinesia and appetite increase. More patients treated with fenelzine reported adverse events in comparison to the placebo group. According to the authors, CT and fenelzine are effective treatments for patients with major depressive disorder and atypical traits. The implication is that CT is as effective as MAOI in the treatment during the acute phase of patients with major depressive disorder and atypical traits, as our re-analysis indicates (table 4).

In the Williams et al. study[13] blocks and stratifications were created by sites and diagnosis. A computer generated random distribution table was created. The numbered envelopes contained the allotment codes. The evaluators who were blinded to the allotment of the patients and treatment and were not involved in the allotment or treatment processes scored the evaluation instruments. The sample was made up of 415 patients, 41% of whom were women, with age range between 60 and 93 years of age, a diagnosis of dysthymia or minor depression evaluated by the DSM-III-R and PRIME-MD, and the disease severity was moderate or severe. A total of 121 patients presented comorbid disorders of anxiety. Inclusion criteria mean the presence of three or four depressive symptoms during 4 weeks and score on the HDRS > 10. Exclusion criteria were presence of major depression, psychosis, schizophrenia, schizoaffective disorder, bipolar disorder, alcohol abuse or abuse of other substances during the previous 6 months, antisocial personality disorder, borderline personality disorder, serious risk of suicide, moderate or severe cognitive alteration (Folstein MMSE < 23), medical disease with a prognosis of at least 6 months of life, and patients currently under treatment (except 50 mg or less of amitriptyline or its equivalent). The clinical trial duration was 11 weeks. In the drug therapy arm, dose ma-

Table 4 Study data of Jarrett et al., 1999

Results	Placebo	PST	Fenelzine
Remission	10	21	21
No	26	15	15
Total	36	36	36
OR (95% CI)	1	3.6 (1.4 to 9.8)	3.6 (1.4 to 9.8)
P value		0.010	0.010
Adjusted P value		0.017	0.017

General χ^2 test (2 gl): 8.97; P: 0.011; CBT test = fenelzine; χ^2 (1 gl): 0; P: 1. PST: problem solving therapy.

nagement, symptoms evaluation, a review of the adverse events and general support were studied. The study began with one dose of paroxetine of 10 mg/d initially, going to 20 mg/d the second week, from the fourth week to the sixth one to 30 mg/d; from the sixth week to the eighth one 40 mg/d (for the patients who showed partial improvement or did not improve). In each session, the patients self-reported adherence to the treatment. The duration of the interventions was 15 minutes. In the psychotherapy arm, PST was used based on the cognitive-behavior principles. Three steps were followed principally: *a)* the symptoms of the patients were linked with their daily life problems; *b)* the problems were defined and clarified, and *c)* an attempt was made to solve the problems in a structured way. The intervention duration was one hour in the first session and 30 minutes in the following ones. In the placebo group, the management was the same as in the paroxetine group. In relationship to losses and drop-outs in the paroxetine group, 17 persons did not receive any treatment and 14 were eliminated. In the PLA group, 8 persons did not receive any treatment and 13 were eliminated. The conclusions of the authors were that PST cannot be recommended for elderly persons with minor depression or dysthymia. Drug therapy with SSRI was effective in the treatment of elderly subjects with minor depression or dysthymia. However, our re-analysis of the primary data of efficacy of the study (table 5) indicated that none of the active treatments in our sample studied were significantly superior to placebo.

The Barrett et al. study[14] is methodologically similar to the previous study, except the comparison by age of the patients included. The sample studied was 239 patients, 63,9% of whom were women and 36,1% men, with an age range between 18 and 59 years and diagnosed of dysthymia or minor depression, with mild to moderate severity. The comorbid anxiety disorders evaluated by the PRIME-MD at baseline were present in approximately 25% of the patients, but with non-significant differences among the three groups. The inclusion criteria were diagnosis of dysthymia or minor depression (three out of nine symptoms of the DSM-II-R for major depression; one of these had to be depressed mood or anhedonia, and had to be present for at least 4 weeks) and a HRDS-17 ≥ 10. The patients had to be under treatment in primary health care, to have a stable address, and it had to be possible to locate them by telephone. The exclusion criteria included diagnosis of major depression during the initial evaluation or during the 6 previous months; current use of antidepressants, with the exception of those patients who were taking 50 mg or less of amitriptyline, or an equivalent use for chronic pain, migraine or fibromyalgia if the patient was willing to discontinue this drug 2 weeks before repeating the evaluation and during the study; current use of Saint John's Wort; Phen-Fen dietary regime; or benzodiazepines were also excluding factors. In addition, if they were receiving any form of psychotherapy or counseling, had presence of any of the following psychiatric conditions: psychosis, schizophrenia or schizoaffective disorder, bipolar disorder; alcohol or substance abuse during the previous 6 months, antisocial personality disorder; borderline personality disorder, serious risk of suicide, moderate or severe cognitive disorder; end-stage medical disease and pregnancy were also reasons for exclusion. The duration of the trial was 11 weeks. The drug therapy analyzed included dose management, symptoms evaluation, review of adverse events and general support. Paroxetine was initiated with 10 mg/d and was increased the second week to 20 mg/d. Between the fourth and sixth week, the dose could be increased again to 30 mg/d and during the sixth and eighth week to 40 mg/d. Duration of the interventions was about 10 or 15 minutes. PST lasted one hour in the first visit and 30 minutes in the following visits. The placebo group was managed in the same way as that of paroxetine. In the paroxetine group, 6 patients discontinued treatment due to adverse events and 1 patient for medical disease; 23 patients with at least 1 visit discontinued treatment for other reasons. According to the authors, paroxetine and to a lesser degree PST improved remission of dysthymia more than the use of placebo and non-specific clinical management. The interventions were equally effective for minor depression, so that general clinical management is an appropriate treatment option. Our re-analysis grouping the categories of dysthymia and minor depression (table 6) indicates that none of the active treatments in the sample studied is superior to placebo.

Table 5 Study data of Williams et al., 2000

Results	Placebo	CBT	Paroxetine
Remisssion	53	54	52
No	87	84	85
Total	140	138	137
OR (95% CI)	1	1.1 (0.65 to 1.7)	1 (0.62 to 1.6)
P value		0.260	0.249
Adjusted P value		1	1

General χ^2 test (2 gl): 0.06; P: 0.971; CBT test = paroxetine; χ^2 (1 gl): 0.04; P: 0.8415. CBT: cogntive behavioral terapy.

In the DeRubeis et al. study[16] the patients and drug-therapist were blinded to the pill content. After 8 weeks of drug therapy, the double-blind condition was opened (except for the evaluator) and the pill-placebo arm disappeared for ethical requirements. The study had a sample of 240 patients, 59% of whom were women and 41% men, with an age range between 27 and 52 years and with moderate to severe severity of the disease. A total of 90% of the patients had chronic or recurrent depression. There was a comorbidity with anxiety disorders in 53% of the cases, posttraumatic stress disorder in 175, eating disorder in 17%, substance abuse or dependent; personality disorder 57%.

Table 6 Study data of Barrett et al., 2001

Results	Placebo	PST	Paroxetine
Remission	37	40	45
No	44	40	35
Total	81	80	80
OR (95% CI)	1	1.2 (0.64 to 2.27)	1.5 (0.82 to 2.8)
P value		0.583	0.181
Adjustable P value		1	0.359

General χ^2 test (2 gl): 1.82; P: 0.403; PST test = paroxetine; χ^2 (1 gl): 0.63; P: 0.4286. PST: problem solving therapy.

The inclusion criteria were major depressive disorder diagnosis in accordance with DSM-IV; age range between 18 and 70 years; speaking English; desire and capacity to give informed consent; HDRS-17 ≥ 20. Exclusion criteria were a background of bipolar disorder; substance abuse or dependence in which the need for treatment was evaluated; present or past psychosis; other disorder on axis I of DSM-IV in which the need for treatment was evaluated preferentially for depression; one of the three disorders excluded from axis II of DSM-IV considered as unadvisable for the treatment under investigation; suicide risk that required immediate hospitalization; medical condition that contraindicated the study medications; no response to an adequately designed trial of paroxetine in the previous year. The clinical trial duration was 16 weeks. The drug therapy was accompanied by: *a)* medical management: education on drugs, dose adjustment and discussion of adverse events, and *b)* clinical management: review of functioning of the patients in wider spheres of life; brief support by counseling, and giving limited advice. All the patients began with paroxetine 10-20 mg/d. This dose was increased by 10-20 mg based on tolerability, response and occurrence of adverse events, up to a maximum of 50 mg/d in the sixth week or until observation of significant reduction of symptoms. For the patients who did not meet the response criteria at 8 weeks, treatment was increased with lithium carbonate or desipramine. The initial sessions lasted 30 and 45 minutes. The following sessions lasted about 20 minutes. The cognitive therapy (CT) sessions lasted 50 minutes and were held weekly. The placebo group received the same management as the drug therapy group. A total of 13 patients were lost in the drug therapy arm, 9 patients in the CT arm and two in the placebo group. Eight patients in the drug therapy arm and 2 from the placebo group were eliminated due to adverse events. According to the authors themselves, the CT may be as effective as the medication for the initial treatment of moderate or severe depression, but this grade of effectiveness may depend on the high grade of experience of the therapist. Our secondary analyses indicate that the drug therapy arm is significantly better than the placebo while the CT is marginally non-significant, although both active arms of the treatment have a therapeutic equivalence (table 7).

DISCUSSION AND CONCLUSIONS

The analysis of the data obtained makes it possible to outline several conclusions and considerations in regards to comparative efficacy of psychotherapy versus drug therapy in out-patient care. If we analyze the data in regards to severity of depression, the results vary in a very suggestive way. Both the Barrett et al. study[14] and that of Williams et al.[13] present milder severity indexes since the diagnoses included in these studies are minor depression and dysthymia and present lower values of HDRS in the baseline. Based on our re-analyses, there are no significant differences in any of these studies among the three treatment arms (paroxetine, problem solving therapy and placebo). From this, we can deduce that the three interventions are equally effective in the treatment of depression and dysthymia and thus the clinical management may be a sufficient intervention for the treatment of this type of disorders. However, the authors had analyzed the subgroups based on the diagnoses and stratifications by centers so that their conclusions differ from ours and indicate that the three interventions have a comparable efficacy in the treatment of minor depression while the active arms are better than placebo only in the dysthymia group.

In relationship to the studies that work with more severe depressions[12,15-17], all of them conclude that there are no significant differences regarding efficacy of the psychotherapy arms (CBT, CT, ITP, PST) compared to drug therapy arms (tricyclic antidepressants, MAOI, and SSRI) in the treatment of major depression. Both psychotherapy and drug therapy are more effective than treatment with placebo. Our analyses solidly support the conclusions of the authors. We have found marginally non-significant values for the amitriptyline arm (adjusted value P 0.089) in the Mynors-Wallis study[12],

Table 7 Study data of DeRubei et al., 2005

Results	Placebo	CBT	Paroxetine
Remission	15	26	60
No	45	34	60
Total	60	60	120
OR (95% CI)	1	2.3 (1.1 to 5)	3.0 (1.5 to 6)
P value		0.036	0.002
Adjusted P value		0.067	0.002

General χ^2 test (2 gl): 10.31; P: 0.006. CBT test = paroxetine; χ^2 (1 gl): 0.71; P: 0.3991. CBT: cogntive behavioral terapy.

the CT arm in the Elkin study[15] (adjusted value P: 0,218) and CT arm in the DeRubeis study[16] (adjusted value P: 0,067). However, the general test for equality of active treatments in the three studies indicates that their difference is not statistically significant.

An analysis in relationship to the rates of losses and drop-outs of the studies reported by the authors themselves allows us to observe that the general calculation of drop-outs for the six studies due to adverse events was greater for the placebo and drug therapy groups compared to the psychotherapy arms.

The conclusions proposed herein raise a series of questions in regards to the treatment of the affective disorders in the out-patient setting. Is it necessary to treat mild depressions (minor depression and dysthymia) or is mere clinical management sufficient? Why don't we usually treat the moderate depression or even severe ones (major depressive disorder) with psychotherapy in the out-patient setting? Can psychotherapy assure a greater adherence to treatment than drug therapy and thus better middle and long term results?

In spite of the difficulty to offer conclusive answers to these questions, we invite the clinicians and investigators to continue to study in this area in order to obtain better cumulative evidence on the comparative efficacy of structured psychotherapies and drug treatments in the different settings of health care and regarding the different severity of the depressive disorders.

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