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REVIEW

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A systematic review of research findings on the efficacy of interpersonal therapy for depressive disorders

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Abstract *Objective* Interpersonal psychotherapy (IPT) is a time-limited psychotherapy for major depression. The aim of this study is to summarize findings from controlled trials of the efficacy of IPT in the treatment of depressive spectrum disorders (DSD) using a meta-analytic approach. *Methods* Studies of randomized clinical trials of IPT efficacy were located by searching all available data bases from 1974 to 2002. The searches employed the following MeSH categories: Depression/Depressive Disorder; Interpersonal therapy; Outcome/Adverse Effects/Efficacy; in the identified studies. The efficacy outcomes were: remission; clinical improvement; the difference in depressive symptoms between the two arms of the trial at endpoint, and no recurrence. Drop out rates were used as an index of treatment acceptability. *Results* Thirteen studies fulfilled inclusion criteria and four meta-analyses were performed. IPT was superior in efficacy to placebo in nine studies (Weight Mean Difference (WMD) – 3.57 [–5.9, –1.16]). The combination of IPT and medication did not show an adjunctive effect compared to medication alone for acute treatment (RR 0.78 [0.30, 2.04]), for maintenance treatment (RR 1.01 [0.81, 1.25]), or for prophylactic treatment (RR 0.70 [0.30, 1.65]). IPT was significantly better than CBT (WMD –2.16 [–4.16, –0.15]). *Conclusion* The efficacy of IPT proved to be superior to placebo, similar to medication and did not increase when combined with medication. Overall, IPT was more efficacious than CBT. Current evidence indicates that IPT is an efficacious psychotherapy for DSD and may be superior to some other manualized psychotherapies.

Key words meta-analysis · depression · interpersonal therapy · efficacy

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Introduction

Interpersonal Psychotherapy (IPT) was developed in the 1970's by Klerman et al. (Klerman 1984) as a time-limited, weekly outpatient treatment for major depressive disorder.

In the quarter century since its initial formulation, IPT has been applied and extended to a variety of other psychiatric diagnoses (dysthymic disorder, bulimia nervosa, recurrent depression, bipolar disorder, substance abuse, social phobia, panic disorder, body dysmorphic disorder, chronic somatization, and borderline personality disorder) (Klerman 1984; Weissman 2000). IPT deals with current, rather than previous interpersonal relationships, focusing on the patient's immediate social context. Moreover, it intervenes in symptom formation and the social dysfunction associated with depression, rather than addressing the enduring aspects of personality (Weissman 1998). The original IPT format had

three phases. The first one usually comprised one to three sessions and included the psychiatric diagnostic assessment. The therapist reviews symptoms, evaluates the patient as depressed, according to the standard criteria (APA 1994) and confers the sick role on the patient (Parson 1951). A review of the patient's current social functioning and close relationships, including the habitual patterns and expectations characterizing those relationships and how they influence the patient's mood, is accomplished. This review provides a framework for understanding the social and interpersonal context present at the onset of the depressive symptoms and defines the focus of treatment (Weissman 1998). Symptoms are then linked to the patient's situation in a formulation (Markowitz 1997) that comprises one (or more) of the following problem areas in the patient's life: a) grief; b) interpersonal role disputes; c) role transitions; or d) interpersonal deficits (Weissman 1998).

The second phase of treatment entails the development of specific strategies for the chosen interpersonal problem area. The last phase of IPT takes place during the concluding 12–16 weeks of treatment and it is aimed at giving support to the patient's renewed sense of independence and competence, by recognizing and consolidating therapeutic gains.

The efficacy of IPT as a treatment for depression and other disorders has been reviewed previously (Jarrett and Rush 1994; Klerman 1994). These reviews afforded some evidence that IPT is efficacious, as a single agent, in the treatment of Depressive Spectrum Disorders (DSD) (we included in this spectrum major depressive disorder, dysthymic disorder, and recurrent depression, and excluded bipolar disorder). Accordingly, IPT was recommended in the practice guidelines for depression of the American Psychiatric Association (Karasu 1993) and in those for Primary Care (Department of Health and Human Services 1993), as an efficacious treatment for DSD. The aim of the current study is to update prior reviews in the field and to investigate whether IPT is superior to other brief psychotherapies, and whether IPT exerts an adjunctive effect when combined with antidepressant medications, in the treatment of Depressive Spectrum Disorders.

Methods

The following databases were searched for the period 1974–2002 inclusive for RCTs comparing IPT with antidepressants, placebo or other psychotherapies: MEDLINE, EMBASE, LILACS, PsycINFO, The Cochrane Depression, Anxiety and Neurosis Group Database of Trials, The Cochrane Controlled Trials Register, and the SCISEARCH. The following medical subject heading (MeSH) categories were used: Interpersonal therapy; Outcome/Adverse Effects/Efficacy; Depression/Depressive Disorder. Studies representing: a) randomized controlled clinical trials; b) employing a standardized method of diagnosing depressive disorder; c) a clearly defined trial time duration, i. e. 12, 24 weeks, etc., were examined for possible inclusion in the study. The results of the electronic search were expanded with the bibliographic references in the selected articles and in recently published textbooks on IPT (Markowitz 1998; Weissman 2000), as well as through contacts with IPT research centers (Cornell University Medical College Medical School, Columbia University, University of Pittsburgh Medical Center).

All the RCTs comparing IPT with other treatments or placebo for patients with DSD, diagnosed according to standardized criteria, were eligible for inclusion in this review. To determine eligibility two reviewers analyzed the abstract of each reference identified by the search. Finally, the full articles were checked to evaluate if they fulfilled all inclusion criteria. The reviewers independently rated each study as regards eligibility. Their assessments were then compared and in cases of disagreement, the final judgment arrived at through consensus. Since the current study was completed, two IPT studies for depression appeared both supporting the efficacy of IPT (Spinelli and Endicott 2003), and a clinical trial performed in Uganda (Bolton, Bass et al. 2003). It was decided not to include these studies in the present review to keep this review restricted to the period originally established (from 1974 to 2002), and the inclusion of individual psychotherapy approach.

Studies varied widely as regards measures of treatment efficacy. The selected measures of treatment outcomes were grouped as follows: (a) the proportion of patients per treatment group with remission of depressive symptoms, defined as having no symptoms or a score below 8 points on the 17 item Hamilton depression rating scale (HAM-D); (b) proportion of patients per treatment group with clinical improvement of depressive symptoms, defined as having a 50 % or higher reduction of depressive symptoms; (c) the difference in mean depressive symptoms at endpoint; (d) the proportion of patients per treatment group, with no recurrence of a new depressive episode. In addition to efficacy, acceptability of treatment was also measured based on the (e) proportion of patients per treatment group that dropped out during the study.

Meta-analytical calculations were performed using the RevMan program (RevMan 2000), and the ratio of *events* (remission and dropouts) in the control group to that in the experimental was also estimated. Remission, clinical improvement and dropout rates were analyzed by calculating the *relative risk* (RR) with a confidence interval (CI) of 95 %, for each trial. The estimates of the RR for individual trials were then used to calculate the pooled *risk ratio* for all strata, employing a random effects model. A RR lower than 1 indicated that an event was more likely to occur in the IPT group than in the control group. All meta-analytical calculations were collected from intention-to-treat (ITT) data.

For the analysis of the differences in depressive symptoms at the endpoint, from an intent to treat analysis both the mean and the standard deviation of the depressive symptom scores for each trial were assessed and the weighted mean difference (WMD) within each stratum was examined. A WMD significantly lower than 0.0 indicates that IPT has superior efficacy to the control condition.

Results

Reports of 23 separate trials were retrieved for more detailed information (Klerman, Dimascio et al. 1974; DiMascio, Weissman et al. 1979; Weissman, Prusoff et al. 1979; Prusoff, Weissman et al. 1980; Elkin, Shea et al. 1989; Frank, Kupfer et al. 1990; Sotsky, Glass et al. 1991; Reynolds, Frank et al. 1992; Shapiro, Barkham et al. 1994; Hardy, Barkham et al. 1995; Markowitz, Klerman et al. 1995; Brown, Schulberg et al. 1996; Mossey, Knott et al. 1996; Reynolds, Frank et al. 1996; Schulberg, Block et al. 1996; Coulehan, Schulberg et al. 1997; Frank, Hlastala et al. 1997; Lave, Frank et al. 1998; Markowitz, Kocsis et al. 1998; Stewart, Garfinkel et al. 1998; Mufson, Weissman et al. 1999; Reynolds, Frank et al. 1999; Reynolds, Miller et al. 1999; Rossello and Bernal 1999; O'Hara, Stuart et al. 2000; Williams, Barrett et al. 2000; Mello, Myczcowisk et al. 2001; Zlotnick, Johnson et al. 2001; Browne, Steiner et al. 2002). Thirteen trials met the inclusion cri-

teria and are the subject of this review (Klerman, Dimascio et al. 1974; Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Frank, Kupfer et al. 1990; Mufson 1993; Brown, Schulberg et al. 1996; Markowitz, Kocsis et al. 1998; Reynolds, Frank et al. 1999; Reynolds, Miller et al. 1999; Rossello and Bernal 1999; O'Hara, Stuart et al. 2000; Mello, Myczcowisk et al. 2001; Browne, Steiner et al. 2002) (Table 1).

Among trials failing to meet inclusionary criteria, four did not employ IPT (Shapiro, Barkham et al. 1994; Mossey, Knott et al. 1996; Coulehan, Schulberg et al. 1997; Williams, Barrett et al. 2000). Two trials evaluated cost-effectiveness (Lave, Frank et al. 1998) and the impact of Cluster C personality disorder on treatment response (Hardy, Barkham et al. 1995), instead of remission, clinical improvement or dropout. One trial compared patients with bipolar disorder, which is a disorder outside the scope of this review (Frank, Hlastala et al. 1997). Other publications were excluded because they reported preliminary or post-hoc results or their findings appeared in other publications (DiMascio, Weissman et al. 1979; Prusoff, Weissman et al. 1980; Sotsky, Glass et al. 1991; Reynolds, Frank et al. 1992; Markowitz, Klerman et al. 1995; Brown, Schulberg et al. 1996; Reynolds, Frank et al. 1996; Stewart, Garfinkel et al. 1998; Reynolds, Miller et al. 1999).

The methodological quality of the 13 studies was evaluated by two independent raters using a version of the Jadad criteria adapted for psychotherapeutic RCTs (Jadad, Moore et al. 1996). The adaptation addressed issues regarding the nature of the randomization process, the blinding of raters, the presence of an intention to treat analysis (ITT), that is an analysis that included all randomized subjects, irrespective of whether they in fact received treatment. Scores on the adapted Jadad criteria range from 0 to 5 (with 5 being the best quality). Of

Table 1 Methodological characteristics of included studies

Study	Year	Groups	Duration (weeks)	N	Population	Outcome measures
Mello et al.	2001	Moclobemide X IPT plus moclobemide	48	35	Dysthymia	HDRS-D, MADRS, GAF, QOLQ
Browne et al.	2002	IPT X IPT plus Sertraline X sertraline	96	707	Dysthymia with/out MDD	MADRS, SAS, CES-D, VAS, pharmacoeconomics measures
O'Hara et al.	2000	IP X WL	12	120	MDD (postpartum)	HRSD, BDI, SAS, PPAQ, IDD
Roselló e Bernal	1999	CBT X IPT-A X WL	12	80	Major depressive episode, Dysthymia, Double depression	CDI, PHCSCS, SASCA, FEICS
Mufson et al.	1999	IPT-A X Clinical Monitoring	12	48	Major depression	HRSD; BDI; C-GAS; SAS-SR; SPSS-SR
Reynolds III et al.	1999	Nortriptyline + IPT X IPT + placebo X Nortriptyline alone + medication clinic X placebo + medication clinic	16	157	Major depression	HDRS; MMSE; BSI; GMS; ICG.
Reynolds III et al.	1999	Medication Clinic + nortriptyline X Medication Clinic + placebo X IPT-M + nortriptyline X IPT-M + placebo	150 maintenance	180	Recurrent major depression	HDRS; MMSE
Markowitz et al.	1998	IPT X CBT X SP x SP + imipramine	16	101	Mood disorder	HDRS; BDI; KS; CSPRS
Brown et al.	1996	Nortriptyline X IPT X usual Care	32	157	Major depression	HDRS; MOS
Frank et al.	1990	IPT-M alone X IPT-M + Imipramine X IPT-M + placebo X medication clinic visits + IMI X medication clinic visits + placebo	150 maintenance	128	Recurrent major depression	HDRS, RDS
Elkin et al.	1989	CBT X IPT X imipramine + medication clinic X placebo + medication clinic	16	240	Major depression	HDRS; GAS; BDI; HSCL-90
Weissman et al.	1979	Amitriptyline + IPT X Amitriptyline Alone X IPT alone X usual care	16	96	Major depression	RDS; HDRS
Klerman et al.	1974	{Amitriptyline X placebo X no pill} + IPT* {Amitriptyline X placebo X no pill} low interpersonal Contact	32	150	Neurotic depression (DSM-II)	HSC; HDRS, SAS

HDRS Hamilton Depression Rating Scale; *GAFS* Global Assessment of Functioning Scale; *QOLQ* Quality of Life Questionnaire; *BDI* Beck Depression Inventory; *C-GAS* Children's Global Assessment Scale; *SPSK-SR* Social Problem-Solving Skills revised self-report; *RDS* Raskin Depression Scale; *KS* Karnofsky Scale; *CSPRS* Collaborative Study Psychotherapy Rating Scale; *MOS* Medical Outcomes Study 36-item Short Form Health Survey; *DSIC* Duke Severity Illness Checklist; *MMSE* Mini Mental State; *BSI* Brief Symptom Inventory; *GMS* Grief Measurement Scale; *ICG* Inventory Complicated Grief; *GIR* Global Illness Rating; *SAS-SR* Social Adjustment Scale Self report; *MADRS* Montgomery Asberg Depression Rating Scale; *BHSI* Brown Health Services Utilization Inventory; *CDI* Children's Depression Inventory; *PHCSCS* Piers-Harris Children's Self-concept Scale; *SASCA* Social Adjustment Scale for Children and Adolescents; *FEICS* Family Emotional Involvement and Criticism Scale; *VAS* Visual analogue scale; *CES-D* Center for Epidemiologic Studies Depression Scale; *HSC* Hopkins Symptom Checklist; *IDD* Inventory to Diagnose Depression; *DAS* Dyadic Adjustment Scale; *PPAD* Postpartum Adjustment Questionnaire; *IPT* Interpersonal Therapy; *IPT-M* a maintenance form of IPT; *CBASP* Cognitive behavioral-analysis system of psychotherapy; *CBT* Cognitive Behavioral Therapy, *SP* Supportive Therapy, *WL* Wait List

* IPT at that time was called as high social contact intervention although had IPT format

the 13 studies that we reviewed and rated, 4 received a consensus score of 5, 5 studies, a consensus score of 4, 3 studies a consensus score of 3 and one study a consensus score of 2. The initial score of the two raters differed with regard to only 4 studies and in each instance they differed by only one point.

Three studies were multicenter trials (Klerman, Dimascio et al. 1974; Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989). Six studies compared IPT with tricyclic antidepressants (Klerman, Dimascio et al. 1974; Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Frank, Kupfer et al. 1990; Brown, Schulberg et al. 1996; Reynolds, Frank et al. 1999; Reynolds, Miller et al. 1999), and one with sertraline (Browne, Steiner et al. 2002). Six studies assessed the efficacy of combined therapy (IPT plus an antidepressant against antidepressant alone (Klerman, Dimascio et al. 1974; Weissman, Prusoff et al. 1979; Frank, Kupfer et al. 1990; Reynolds, Frank et al. 1999; Reynolds, Miller et al. 1999; Mello, Myczcowisk et al. 2001; Browne, Steiner et al. 2002). Antidepressant dosages were usually those recommended by the pharmacological guidelines (150 mg of imipramine or equivalent). Three studies compared IPT with cognitive behavior therapy (Elkin, Shea et al. 1989; Markowitz, Kocsis et al. 1998; Rossello and Bernal 1999), just one (Markowitz, Kocsis et al. 1998) trial also compared IPT with supportive therapy. Three studies compared IPT with a waiting list or clinical monitoring, considered a placebo (Mufson, Weissman et al. 1999; Rossello and Bernal 1999; O'Hara, Stuart et al. 2000). Seven trials compared IPT with medication placebo (Klerman, Dimascio et al. 1974; Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Frank, Kupfer et al. 1990; Reynolds, Frank et al. 1999; Reynolds, Miller et al. 1999). The trials recruited outpatients spontaneously seeking treatment for depression, or also included volunteers for the research, recruited through advertisements.

Two studies were limited to adolescents (Mufson, Weissman et al. 1999; Rossello and Bernal 1999), and two others included older patients (over 60 years old (Reynolds, Frank et al. 1999; Reynolds, Miller et al. 1999). Two studies included dysthymic patients (Mello, Myczcowisk et al. 2001; Browne, Steiner et al. 2002), but in one of these, patients had an associated major depression (Mello, Myczcowisk et al. 2001).

The patients were evaluated at treatment termination [12 weeks (Mufson, Weissman et al. 1999; Rossello and Bernal 1999; O'Hara, Stuart et al. 2000), 16 weeks (Elkin, Shea et al. 1989; Markowitz, Kocsis et al. 1998; Reynolds, Frank et al. 1999), and most of them at follow-up, which occurred a number of weeks after treatment termination (32 weeks (Klerman, Dimascio et al. 1974; Brown, Schulberg et al. 1996), 48 weeks (Mello, Myczcowisk et al. 2001), and 96 weeks (Browne, Steiner et al. 2002)]. The patients from the IPT-M (maintenance) were evaluated at trial termination, after 150 weeks of study (Frank, Kupfer et al. 1990; Reynolds, Frank et al. 1999). The results of the meta-analyses pertaining to studies involving acute treatment (less than 24 weeks), maintenance treatment (over or up to 24 weeks), and recurrence prophylaxis treatment are presented separately.

The combined relative risks and confidence intervals for total remission obtained by the four meta-analyses performed are given in Table 2 displays the results. The weighted mean differences in depressive symptoms at the end point are given in Table 3, and the combined relative risks for drop outs in both groups can be found in Table 4.

Meta-analysis 1. IPT alone versus Medication

Overall, nine studies were included in this comparison (Klerman, Dimascio et al. 1974; Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Frank, Kupfer et al. 1990;

Table 2 Meta-analysis of RCT of IPT: combined relative risks and confidence intervals for total remission

Type of comparison/type of treatment	Pooled RR	95 % CI
IPT versus medication		
Acute treatment (≤ 4 months)		
Total	1.11	0.83, 1.49
Maintenance treatment (> 6 months)		
Total	1.20	0.94, 1.52
Prophylaxis (no recurrence)		
Total	2.01	0.99, 4.05
IPT plus medication versus medication		
Acute treatment (< 4 months)		
Total	0.78	0.30, 2.04
Maintenance treatment (> 6 months)		
Total	1.01	0.81, 1.25
Prophylaxis (no recurrence)		
Total	0.70	0.30, 1.65
IPT versus placebo		
Acute treatment (≤ 4 months)		
Total	0.72	0.51, 1.02
Prophylaxis (no recurrence)*		
Total	0.76	0.61, 0.95
IPT versus CBT		
Acute Treatment (≤ 4 months)		
Total	0.82	0.63, 1.07

* $P < 0.05$
CI Confidence interval

Table 3 The meta-analysis of RCT of IPT: weight mean difference and confidence intervals in depressive symptoms at end point

Type of comparison/type of treatment	WMD	95 % Confidence Interval
IPT versus placebo		
Acute treatment (≤ 4 months)*		
Total	−3.57	−5.98, −1.16
IPT versus CBT		
Acute treatment (≤ 4 months)*		
Total	−2.16	−4.16, −0.15

* $P < 0.05$

Table 4 Meta-analysis of RCT of IPT: combined relative risks and confidence intervals for total dropouts

Type of comparison/type of treatment	Pooled RR	95 % CI
IPT versus medication		
Acute treatment (< 4 months)		
Total	0.92	0.69, 1.22
Maintenance (> 4 months)		
Total	0.54	0.27, 1.06
Prophylaxis (no recurrence)		
Total	0.58	0.19, 1.75
IPT versus placebo		
Acute treatment (< 4 months)*		
Total	0.59	0.36, 0.99
IPT plus medication versus medication		
Acute treatment (< 4 months)		
Total	0.67	0.35, 1.27
Maintenance (> 4 months)		
Total	0.97	0.73, 1.26
Prophylaxis (no recurrence)		
Total	0.60	0.26, 1.39
IPT versus CBT		
Acute treatment (< 4 months)		
Total	0.68	0.44, 1.03

* $P < 0.05$
CI Confidence Interval

Brown, Schulberg et al. 1996; Markowitz, Kocsis et al. 1998; Reynolds, Frank et al. 1999; Reynolds, Miller et al. 1999; Browne, Steiner et al. 2002) (947 patients, of whom 488 were randomized to IPT and 459, to medication). The remission of major depression was defined as being less than 8 in the Hamilton score, for all studies (Klerman, Dimascio et al. 1974; Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Frank, Kupfer et al. 1990; Brown, Schulberg et al. 1996; Markowitz, Kocsis et al. 1998; Reynolds, Frank et al. 1999; Browne, Steiner et al. 2002). For dysthymic patients, a Hamilton score of less than 4 was required (Mello, Myczcowisk et al. 2001). Three studies reported a difference in the depressive symptoms at the endpoint.

Acute treatment. In acute treatment (4 months or less) remission was reported in 5 trials (Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Brown, Schulberg et al. 1996; Markowitz, Kocsis et al. 1998; Reynolds, Frank et al. 1999). In general, this was more likely to occur with the patients on medication than in the IPT group (51 % versus 43.8 %). As there was no evidence of any heterogeneity in the trial results, with reference to remission following medication and IPT, it was possible to perform a pooled analysis, and no difference was found between groups (RR = 1.1; 95 % CI: 0.83, 1.49).

Maintenance treatment. Remission in maintenance treatment (6 months or more) was reported in three trials (Klerman, Dimascio et al. 1974; Brown, Schulberg et al. 1996; Browne, Steiner et al. 2002). In general, this was also more likely to occur with the patients on medication than in the IPT group (59.6 % versus 52.8 %), but the difference between the groups failed to reach statistical significance (RR = 1.20; 95 % CI: 0.94, 1.52).

Prophylactic treatment. No recurrence among persons on prophylactic treatment was reported in two trials (Frank, Kupfer et al. 1990; Reynolds, Frank et al. 1999). Recurrence was more common in the medication group (67.9 % versus 36.4), but this difference between groups was not statistically significant (RR = 2.01; 95 % CI: 0.99, 4.05).

Treatment acceptability. There was no difference in the acceptability of treatment, despite IPT group having fewer dropouts. Pooled data from five studies (Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Brown, Schulberg et al. 1996; Markowitz, Kocsis et al. 1998; Reynolds, Frank et al. 1999) showed that in acute treatment the overall dropout rates were 31.7 % for patients who were treated with IPT, as compared to the 33.3 % for those on medication (RR = 0.92, 95 % CI: 0.69, 1.22). In maintenance treatment, three studies (Klerman, Dimascio et al. 1974; Brown, Schulberg et al. 1996; Browne, Steiner et al. 2002) showed that the overall dropout rates were 16.6 % for the IPT patients and 28.6 % for the group on medication (RR = 0.54, 95 % CI: 0.27, 1.08). In prophylactic treatment two studies (Frank, Kupfer et al. 1990; Reynolds, Frank et al. 1999) showed that the overall dropout rates were 13 % for IPT and 23.2 % for medication (RR = 0.58, 95 % CI: 0.19, 1.75).

Meta-analysis 2: IPT plus medication (combined therapy) versus medication alone

There was no difference between the groups in relation to efficacy and acceptability in either acute or maintenance treatment.

Acute treatment. Remission was more likely to occur in the combination group (76.8 % versus 67.7 %, RR = 0.78; 95 % CI: 0.30, 2.04) after four months or less of therapy (Weissman, Prusoff et al. 1979; Reynolds, Miller et al. 1999; Mello, Myczcowisk et al. 2001).

Maintenance treatment. Rates were similar (60.5 and 60.8 %, RR = 1.01, 95 % CI: 0.81, 1.25) when duration of trials was higher than 6 months (Klerman, Dimascio et al. 1974; Mello, Myczcowisk et al. 2001; Browne, Steiner et al. 2002).

Prophylactic treatment. For prophylactic treatment the recurrence was less likely to occur on the combined treatment (78 % versus 67.9 %, RR = 0.70, 95 % CI: 0.30, 1.65), but this difference did not reach statistical significance (Frank, Kupfer et al. 1990; Reynolds, Frank et al. 1999).

Treatment acceptability. The dropout rate among persons in treatment was 23.2 % for the combined therapy, as compared to the 44.8 % for medication alone (RR = 0.67; 95 % CI: 0.35, 1.27). For maintenance, the dropout rates were similar, 28.1 % for those in combined treatment, and 28.7 % for those on medication alone (RR = 0.97; 95 % CI: 0.73, 1.28). Dropout rates among persons receiving prophylactic treatment were lower for combined treatment for those on medication alone (14 % versus 23.2 %), but this difference was not statistically significant (RR = 0.60, 95 % CI: 0.26, 1.39).

Meta-analysis 3: IPT versus placebo

Nine studies (Klerman, Dimascio et al. 1974; Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Frank, Kupfer et al. 1990; Mufson, Weissman et al. 1999; Reynolds, Frank et al. 1999; Reynolds, Miller et al. 1999; Rossello and Bernal 1999; O'Hara, Stuart et al. 2000) were included in this comparison (653 patients, of whom 337 were randomized to IPT and 316 to placebo).

Acute treatment. In acute treatment, remission was more likely to occur in patients on IPT than in the placebo group (68.1 % vs. 48.7 %), but again this finding did not achieve conventional levels of statistical significance (RR = 0.72, 95 % CI: 0.51, 1.02). When we looked at the difference in depressive symptoms at endpoint there was a statistically significant difference favoring IPT (WMD = –3.57; 95 % CI: –5.98, –1.16), as displayed in Table 3.

Prophylactic treatment. No recurrence in prophylactic treatment was reported in two trials (Frank, Kupfer et al. 1990; Reynolds, Frank et al. 1999). In general no recurrence was more common in the IPT group (36.4 % versus 15.4 %), a statistically significant difference favoring IPT (RR = 0.76; 95 % CI: 0.61, 0.95).

Treatment acceptability. Short-term dropout rates were reported in six trials (Weissman, Prusoff et al. 1979; Elkin, Shea et al. 1989; Mufson, Weissman et al. 1999; Reynolds, Miller et al. 1999; Rossello and Bernal 1999; O'Hara, Stuart et al. 2000). A total of 424 patients with 210 being randomized to IPT and 214 to placebo. The overall dropout rates were 19.2 % for IPT as compared to 37.7 % for those on the placebo (RR = 0.59, 95 % CI: 0.36, 0.99), a difference statistically significant. In prophylactic treatment the dropout rates were 13 % for IPT as compared to 5.8 % for those on placebo (Frank, Kupfer et al. 1990; Reynolds, Frank et al. 1999), a difference not statistically significant between treatments (RR = 2.22; 95 % CI: 2.22, 26.18).

Meta-analysis 4: IPT versus CBT

Three studies compared the efficacy of IPT with that of CBT. The studies comprised 204 patients, of whom 102 were randomly assigned to IPT and 102 to CBT (Elkin, Shea et al. 1989; Markowitz, Kocsis et al. 1998; Rossello and Bernal 1999).

Acute treatment. The remission rates were higher for the IPT (56.1 % versus 47.1 %), but the difference was not statistically significant (RR = 0.82; 95 % CI: 0.63, 1.07). However, when depressive symptoms were compared at the endpoint, there was a statistical significant difference favoring IPT (WMD = –2.16; 95 % CI –4.16, –0.15).

Treatment acceptability. The overall dropout rates were 26.6 % for IPT and 37.1 % CBT, but the difference was not statistically significant (RR = 0.68; 95 % CI: 0.44, 1.03).

Discussion

This review confirms and strengthens the findings from numerous individual trials documenting the efficacy and acceptability of IPT in the treatment of DSD. Limited sample sizes in some of these individual studies restricted their ability to find moderate differences in efficacy between interventions. This meta-analysis helps to remedy this problem by increasing the statistical power available for detecting clinically important differences in efficacy.

In this current view of RCT of treatment for DSD, IPT proved more effective than placebo, and also had greater acceptability as indexed by lower drop-out rates. By contrast, there were no differences between the efficacy and acceptability of IPT and medication. These latter results from the IPT and medication alone comparison are not surprising, but apart from efficacy, other issues such as cost, staff's previous experience and training and patient preferences should be considered when recommending a specific treatment. Browne et al. (Browne, Steiner et al. 2002) showed that after two years the combined therapy, despite not having better efficacy than medication alone, showed significantly better pharmacoeconomics results, suggesting that the combined therapy is more preferable when costs are considered.

Combined therapy (IPT plus antidepressant medication) and medication alone are similar as regards both efficacy and acceptability. This apparent absence of an adjunctive effect for IPT seems counter-intuitive and requires further study.

Another important finding is the greater efficacy (but not greater acceptability) of IPT compared to CBT. The authors consider this to be a result of the IPT format and its conceptual development based on compelling scientific evidence of a correlation between depression and social environment. Its brief format is directed towards patient's recognition of his or her depressive symptoms,

linking this to a current interpersonal problem. The therapy focuses on active changes in the patient to find a solution for the interpersonal problem, probably acting on some environmental (social) etiopathogenetical mechanisms of the depressive disorders, which may account for its greater efficacy. However, this finding of greater efficacy for IPT as compared with CBT is based on a relatively limited number of studies. It requires additional replication.

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