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Five-year follow-up of first-episode depression treated with psychodynamic psychotherapy or antidepressants

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ABSTRACT

Short-term psychodynamic psychotherapy (STPP) both combined with medication and alone has been shown to be effective in major depressive disorder (MDD). However, few studies compared STTP and pharmacotherapy in monotherapy during acute phase and there is lack of data concerning the prevention of recurrences. The aim of this retrospective study was to evaluate the clinical course of patients who achieved remission from their first life-time major depressive episode after treatment with antidepressant (AD) therapy or brief dynamic therapy (BDT), a specific type of STPP, examining the recurrence rates during a 5-year treatment-free period.

The analysis was conducted on 93 subjects (remitters to BDT $n = 46$; remitters to AD $n = 47$).

Treatment with BDT was associated with a significantly higher proportion of patients without depressive recurrences during the observation period. Among patients who were remitters to BDT, 71.7% did not experience depressive recurrences at the end of the observation period, compared to 46.8% of those treated with pharmacotherapy.

BDT may be more effective than AD pharmacotherapy in improving the long-term outcome of patients with a first major depressive episode; further studies comparing STPP and AD in terms of efficacy and cost-effectiveness are needed.

1. Introduction

There has been a vast increase in the number of studies that examined the efficacy of short-term psychodynamic psychotherapy (STPP) for depression, compared to controlled conditions and to other psychotherapies. The findings showed that STPP both combined with medication and alone can presently be considered effective in major depressive disorder (MDD) (De Maat et al., 2007a, b, 2008, 2009; Driessen et al., 2010, 2015). However, few studies have investigated the effectiveness of STPP versus pharmacotherapy in MDD: to our knowledge only 3 RCTs were performed and no significant differences were found between STPP and antidepressant (AD) medication (Salminen et al., 2008; Bressi et al., 2010; Barber et al., 2012). Moreover, there is still a lack of high-quality, rigorous, controlled trials concerning the efficacy of STPP in the long-term prevention of depressive recurrences.

The efficacy of brief dynamic therapy (BDT), a specific type of STPP derived from Malan's focused short-term psychoanalytic psychotherapy (Malan et al., 1976), has been extensively studied by our research group in recent years. With regards to the efficacy of BDT in monotherapy, we found it to be more effective than brief supportive psychotherapy (BSP) at 6-month follow-up, in patients with minor depressive disorders (Maina et al., 2005), and even more in patients with moderate depressive disorders (Rosso et al., 2013). Concerning the efficacy of adding BDT to AD therapy in the treatment of MDD, we found that supplemental BDT was significantly preferable to non-specific supportive intervention (BSP) (Maina et al., 2007). Furthermore, the efficacy of BDT in the long-term prevention, a naturalistic 48-month treatment-free follow-up BSP was performed on depressed patients responsive to combined treatment (BDT plus pharmacotherapy) or antidepressants alone: we found that subjects treated with combined therapy seem less likely to experience a recurrence in comparison with patients initially treated with pharmacotherapy alone (Maina et al., 2009).

To our knowledge there are no studies comparing monotherapy with STPP and pharmacotherapy in patients at the moment of their first major depressive episode with regards to prevention of recurrences in a long-term perspective.

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The aim of this study is to evaluate the rate of depressive recurrence after the first major depressive episode treated with AD medication or BDT.

2. Methods

2.1. Procedure and patients

The study consists of a 5-year treatment-free retrospective follow-up.

Data was obtained from medical records of individual patients, containing information about sociodemographic characteristics, clinical picture, treatment, individual psychiatric history, and family history of psychiatric disorders.

Subjects comprised of consecutive patients referred to Department of Neuroscience, University of Turin (Italy), from January 2000 to December 2012.

Patients with main diagnosis of MDD, single episode, according to DSM-IV (APA, 2000) were considered. For the purposes of the present study, we included only patients with mild to moderate severity of depressive symptoms, since they can be treated alternatively with medication or psychotherapy as suggested by the Practice Guidelines of the Treatment of Patients with Major Depressive Disorder (APA, 2010).

Furthermore, patients were selected according to the following inclusion criteria: (a) acute treatment with BDT or AD pharmacotherapy; (b) achievement of remission (remission was established by the clinicians, based on symptomatic remission and recovery of overall functioning); (c) discontinuation of any treatment (i.e. AD medication or BDT) after the end of the continuation phase.

Exclusion criteria were: (a) hypomanic/manic switch during acute treatment or during the observation period; (b) severe axis II psychopathology; (c) concurrent severe or unstable or active neurological or physical diseases; (d) concomitant substance and/or alcohol abuse or dependence; (e) pregnancy during the observation period; (f) lack of data.

Included patients were observed retrospectively for a period of 5 years; subjects who discontinued control visits after remission or during the follow-up period were contacted for updates on the clinical course.

2.2. Treatments

2.2.1. Pharmacotherapy

Patients were treated with first line agents for major depression (paroxetine, citalopram, escitalopram, fluoxetine, sertraline, mirtazapine, venlafaxine and duloxetine) according to the main international guidelines. All subjects received monotherapy AD treatment. Some patients had been prescribed benzodiazepines during the treatment period.

2.2.2. Brief dynamic therapy

The psychotherapeutic technique we apply in our Department as BDT derives from Malan's focused, short-term psychoanalytic psychotherapy (Malan et al., 1976). In the initial phase of BDT, the clinical picture is assessed and a primary problem area is defined as a focus. Symptoms, conflicts or crisis may represent primary problem areas. In the middle phase, the identified focus is addressed. In the terminal phase, the end of the treatment is explicitly discussed, progress is reviewed and gains are consolidated. Patients are told from the outset that their treatment will be time-limited and final session is previously established. BDT was provided by graduated therapists (4 clinical psychologists and 3 psychiatrists) who had completed a personal training in psychodynamic psychotherapy, with at least four years of experience in BDT and individually supervised by a senior therapist (not involved in the treatment of patients). Sessions were weekly, lasting 45 min, and the number of sessions ranged from 15 to 30.

2.3. Statistical analysis

Subjects' characteristics were summarized as means and SD for continuous variables and as frequencies and percentages for categorical variables.

The comparison between the 2 groups (patients treated with BDT versus patients treated with pharmacotherapy) was performed using χ^2 tests for categorical variables (sex ratio, marital and occupational status, rates of depressive recurrences) and t-tests for continuous variables (index age, educational level).

Survival curves were estimated using the Kaplan Meier method and compared using the log-rank test.

The results from every statistical comparison of the treatment groups were presented as 2-sides p values rounded to 3 decimal places. The criterion for statistical significance in all comparison was a p value < 0.05.

To define the sample size of the 2 groups, we used the formula for minimum sample size related to the expected incidence of depressive recurrences in a 5-year follow-up. Given a significance level of 0.05 and a statistical power of 90%, the size of each subgroup had to be at least 42 patients.

All statistical analyses were performed by SPSS software version 22.0.

3. Results

One hundred eighty-eight patients who achieved remission from their first major depressive episode after treatment with BDT or AD (90 remitters to BDT and 98 remitters to AD) were selected. Of those, 95 (50.5%) were excluded from the analysis for the following reasons: manic or hypomanic episode during the observation period ($n = 11$; 5.8%), any psychiatric treatment at the beginning of the follow-up period ($n = 26$: 13.8%), severe personality disorders ($n = 8$: 3.9%), concurrent substance and/or alcohol abuse or dependence ($n = 15$: 7.9%), concurrent severe physical diseases ($n = 3$: 1.6%), pregnancy during the observation period ($n = 5$: 2,6%) and lack of data and inability to establish contact ($n = 27$: 14.3%).

It is noteworthy that we found a statistically significant difference between remitters to BDT and remitters to AD in the rate of onset of manic or hypomanic episodes during the observation period (BDT 2.2% vs AD 9.2%: $p = 0.042$).

Ultimately, we completed this research using 93 subjects. The demographic and clinical characteristics of the patients (remitters to BDT $n = 46$; remitters to AD $n = 47$) at the beginning of the observation period are given in Table 1. There was no significant difference between the two groups.

AD medications are summarized in Table 2. Twelve patients (25.5%) treated with AD had been prescribed benzodiazepines during the acute phase.

We found that treatment with BDT was associated with a significantly higher proportion of patients without depressive recurrences during the observation period (Log Rank = 4.66; $p = 0.031$) (Fig. 1). Among patients who were remitters to BDT, 71.7% did not experience depressive recurrences at the end of the retrospective naturalistic 5-year follow-up period, compared to 46.8% of those treated with pharmacotherapy ($p = 0.020$).

4. Discussion

The aim of this retrospective study was to evaluate the clinical course of patients who achieved remission from first life-time major depressive episode after treatment with AD medication or BDT, examining the recurrence rates during a 5-year treatment-free period.

Reviews and meta-analyses have demonstrated that STPP can be considered as an efficacious treatment for depression (De Maat et al., 2007a,b, 2008, 2009; Driessen et al., 2010, 2015), but few studies

Table 1
Demographic and clinical characteristics of the sample (n = 93).

	Remitters to BDT (n = 46)	Remitters to AD (n = 47)	Analysis $\chi 2/t$	d.f.	p
Gender, N (%)					
Male	17 (37)	17 (36.2)	0.006	1	1.000
Female	29 (63)	30 (63.8)			
Age, years, mean (± s.d.)	46.24 (11.57)	43.26 (11.26)	1.58	1	0.211
Marital status, N (%)			0.16	1	1.000
Married	18 (39.1)	17 (36.2)			
Divorced	9 (19.6)	10 (21.3)			
Never married	17 (37)	18 (38.3)			
Widover/widow	2 (4.3)	2 (4.3)			
Working for pay, Yes, N (%)	28 (60.9)	28 (59.6)	0.016	1	1.000
Duration of depressive episode, weeks, mean (± s.d.)	22.2 (7.1)	23.1 (7.7)	0.35	1	0.552
Duration of the treatment, weeks, mean (± s.d.)	29.9 (2.1)	32 (7.4)	3.22	1	0.076
Follow-up visits, mean (± s.d.)	4.20 (1.78)	4.98 (2.17)	3.601	1	0.61
Psychiatric comorbidities, Yes, N (%)	9 (19.56)	7 (14.89)	0.005	1	1.000
Anxiety disorders	6 (13.04)	5 (10.63)			
Personality disorders	2 (4.34)	2 (4.25)			
Bulimia Nervosa	1 (2.17)	0 (0)			

Table 2
Antidepressant medications of patients treated with pharmacotherapy (n = 47).

Antidepressant medication	*N* (%)
Paroxetine	13 (27.65)
Citalopram	9 (19.14)
Escitalopram	8 (17.02)
Fluoxetine	5 (10.63)
Sertraline	4 (8.51)
Mirtazapine	1 (2.12)
Venlafaxine	5 (10.63)
Duloxetine	2 (4.25)

compared STPP and pharmacotherapy in monotherapy during the acute phase (Salminen et al., 2008; Bressi et al., 2010; Barber et al., 2012) and there is lack of data concerning the prevention of recurrences.

Our results showed significantly lower recurrence rates in the group of remitters to BDT in comparison with remitters to AD (28.3% vs 53.2%). Our data is consistent with studies that support long-term efficacy of STPP in MDD (Driessen et al., 2015) and suggest that STPP may be even superior to AD pharmacotherapy in improving the long-term outcome of MDD. The primary objective of BDT, which is to enhance the patient's insight into repetitive conflicts and trauma and to provide a corrective emotional experience, might be a specific therapeutic factor sustaining the patient's improvements not only during the treatment sessions, but also during the follow-up period (Maina et al., 2005, 2007, 2009).

An additional result we found was that rates of onset of hypomanic/manic episodes during the observation period were significantly higher in remitters to AD than in remitters to BDT (9.2% vs 2.2%). This finding is worthy of interest, as conversion to bipolar disorder (BD), together with non-remission and recurrence, is one of the crucial determinants of poor outcome in the treatment of MDD. Many studies recently tried to identify characteristics within patients suggesting a higher risk of conversion to BD. Ratheesh and colleagues performed a systematic review and meta-analysis of prospective transition from major depression to BD (2017), hypothesizing MDD to be a pre-onset stage for BD in some patients. Nearly a quarter of adults (22.5%) and adolescents with MDD followed up for a mean length of 12–18 years developed BD, with the greatest risk of transition being in the first 5 years. Predictive factors of bipolar transition in adults were family history of BD, earlier age of onset of depression and presence of psychotic symptoms. In view of our results, we hypothesize that BDT may represent a preferable treatment option compared to AD in patients with single mild-moderate major depressive episode, when predictors of BD can be identified.

The main limitation of this research is represented by the retrospective design of the study, particularly with regard to the clinical ascertainment of illness course and to the lack of some socio-demographic and clinical information in the medical records, such as family history of psychiatric disorders. Furthermore, limitations of this study include sampling from patients referred to specialist clinic and the relatively small sample size: a larger size would allow researchers to confirm these findings with stronger statistical power. Still, while we observe better outcomes in patients originally treated with BDT than in those treated with AD, we cannot determine if this represents a true treatment effect (BDT conveys more protection against recurrences) or a selection effect (BDT had been chosen for patients able to accept a

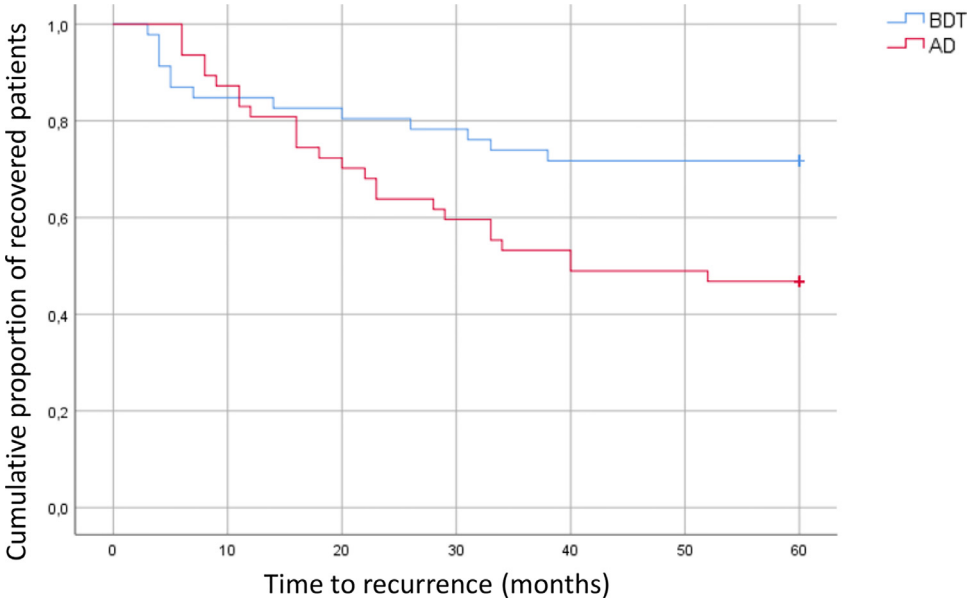

Fig. 1. Kaplan–Meier (BDT vs AD: Log Rank = 4.66; p = 0.031).

psychotherapeutic approach, with a focal problem and/or a recent precipitant life event). Another limitation concerns the heterogeneity in AD medication.

Instead, the homogeneity of the study sample (all selected patients were recovered from a single mild/moderate first major depressive episode in remission) can be considered a strength of the study in terms of generalizability and external validity. Long-term observational studies have found that the risk of recurrence in major depressive disorder increases with the number of previous episodes and decreases with the duration of recovery (Mueller et al., 1999; Solomon et al., 2000); other factors that may increase the risk of recurrence include the presence of residual symptoms despite a therapeutic response (Judd et al., 1999), and the persistence of psychosocial impairment (Solomon et al., 2004). The selection of unipolar single episode with complete remission to acute treatment limits all possible bias due to these factors. A further strength is represented by the follow-up duration (5 years).

Our data suggest that BDT may be more effective than AD pharmacotherapy in improving the long-term outcome of patients with a first major depressive episode. Prospective long-term outcome studies on larger samples comparing STPP and AD in terms of efficacy and cost-effectiveness are needed. Moreover, further research is necessary to evaluate whether subgroups of patients can be identified that might find STPP more beneficial and whether such characteristics can be used as a guide in selecting treatment for every patient.

Conflict of interest

Gianluca Rosso is /has been a speaker and/or has received research grants from Angelini, Janssen, Lundbeck, Otsuka.

Alessandro Cuomo is /has been a consultant and/or a speaker from Angelini, Janssen, Lundbeck, Otsuka.

Andrea Fagiolini is /has been a consultant and/or a speaker and/or has received research grants from Allergan, Angelini, Apsen, Boheringer Ingelheim, Doc Generici, FB-Health, Italfarmaco, Janssen, Lundbeck, Mylan, Otsuka, Pfizer, Recordati, Sonofi Aventis, Sunovion, Vifor.

Gabriele Di Salvo has been a speaker and has received research grants from Lundbeck.

Giuseppe Maina is/has been a consultant and/or a speaker and/or has received research grants from Angelini, Boheringer Ingelheim, FB-Health, Janssen, Lundbeck, Otsuka.

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