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Combined therapy with interpersonal psychotherapy adapted for borderline personality disorder: A two-years follow-up

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Highlights

- IPT- BPD plus drug was superior to single drug after 32 weeks trial.
- Difference persisted at 24 months follow-up for impulsivity and relationships.
- It also persisted for perception of psychological and social functioning.
- Differences concerning anxiety and affective instability were lost after 6 months.
- The most of benefits of combining IPT-BPD endured two years after termination.

1. Introduction

Borderline personality disorder (BPD) is a severe and complex mental disorder that encompasses pervasive dysfunctional patterns of experience and behavior. Patients with BPD are characterized by instability in affects and interpersonal relationships, impulsive behavioral dyscontrol, transient stress-related cognitive-perceptual symptoms and low level of identity integration (Gunderson, 2001; Skodol, 2005; Gabbard, 2014). A common feature of BPD subjects is the tendency to be poorly adherent to treatments and to discontinue the therapeutic program in early phases. Difficulties in obtaining patients' compliance and relatively high rates of drop-out may partially explain the paucity of studies that investigate long-term efficacy of therapeutic interventions in this mental disorder (Gunderson, 2001; Gunderson et al., 2005; Bender, 2005; Gabbard, 2014).

In accordance with the results of systematic reviews and treatment guidelines for the management of BPD, options to treat this disorder include both pharmacotherapy and psychotherapy (American Psychiatric Association, 2001; Oldham, 2005; NICE, 2009; NHMRC, 2012; Stoffers et al., 2012) and combination of them can be considered a valid approach in treating this clinical population (American Psychiatric Association, 2001; Oldham, 2005). Some authors suggested that psychotherapy may enhance pharmacotherapy effects, although it remains unclear how this treatments actually interact (Lieb et al., 2010). To date, psychotherapy models more extensively studied in BPD as single or combined treatment are: dialectical behavioral therapy (Linehan, 1993; Linehan et al., 1999, 2006; Verheul et al., 2003), followed by mentalisation-based treatment (Bateman and Fonagy, 1999, 2008), transference-focused psychotherapy (Clarkin et al., 2006), cognitive therapy (Davidson et al., 2006), schema-focused therapy (Kellogg and Young, 2006; Giesen-Bloo et al., 2006), and system training for emotional predictability and problem solving (STEPPS) (Blum et al., 2002). In recent years, interpersonal psychotherapy modified for BPD patients (IPT-BPD) was added to the other specific models of psychotherapy. IPT adapted for BPD was derived from the standard model of IPT for major depression initially developed by Klerman et al. (1984) and was designed by Markowitz (2005) to address the peculiar features of BPD and to deal with difficulties in interpersonal relationships experienced by these patients. The adaptation included noticeable changes in methods and techniques of IPT: a different conceptualization of the disorder was proposed (BPD was defined as a mood-inflected chronic illness similar to dysthymic disorder, but with sporadic outbursts of anger); length of treatment was prolonged (up to 34 IPT sessions over 8 months, with an acute phase of 18 IPT sessions to establish a therapeutic alliance and a continuation phase of 16 sessions to develop more adaptive interpersonal relationships); flexibility of setting was enhanced (a 10-minute telephone contact once a week

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was provided) to handle crises and minimize the risk of therapeutic ruptures.

Although several studies have established the efficacy of different psychotherapies of BPD at the end of short-term trials, only few investigations have evaluated the long-term effects of these treatments (Bateman and Fonagy, 2001, 2008; Fassbinder et al., 2007; McMain et al., 2012). In the majority of these studies the duration of follow-up has been shorter than one year (Linehan et al., 1993, 1999, 2006; van den Bosch et al., 2005).

In the case of IPT adapted to BPD no trials are available considering long-term follow-up either of single psychotherapy or combined therapy. Favourable data supporting the long-term efficacy of IPT derived from follow-up studies of IPT or therapy combining IPT and pharmacotherapy that were performed in other mental disorders, such as major depression of adolescents (Young et al., 2006, 2010; Jacobson and Mufson, 2012; Zhou et al., 2015) and adults (Schramm et al., 2008; Zobel et al., 2011; Toth et al., 2013; Lemmens et al., 2015), perinatal depression (Brandon et al., 2012; Reay et al., 2012), dysthymia (Browne et al., 2002), and eating disorders (Wilfley et al., 2002; Carter et al., 2011; Hilbert et al., 2012).

In a randomized controlled study (Bellino et al., 2010, 2015) we compared efficacy of combined therapy with IPT-BPD and fluoxetine (20–40 mg/day) versus single fluoxetine (20–40 mg/day) for 32 weeks in a group of BPD patients without concomitant psychiatric comorbidity and we analysed clinical predictors of response to combined therapy. At the end of the trial, combined therapy was found significantly superior to single fluoxetine in decreasing severity of three symptoms of BPD (disturbance of interpersonal relationships - $P=0.009$, affective instability - $P=0.02$, and impulsivity - $P=0.01$), anxiety (HARS - $P=0.006$), and two factors of subjective quality of life (subjective perception of psychological functioning - $P=0.003$-and social functioning - $P=0.008$).

In the present study we prospectively investigate whether the differences of efficacy of combined therapy with IPT-BPD and fluoxetine versus single fluoxetine registered at 32 weeks were maintained during a follow-up period of 2 years.

2. Methods

2.1. Procedure

The present study is the follow-up of a 32 weeks controlled trial, that was published in 2010 (Bellino et al., 2010). Methods concerning design, procedures, selection and randomization of patients, and evaluation tools in the short-term trial were described in detail in our previous article.

In the original study, 55 consecutive outpatients meeting DSM-IV-TR criteria for BPD were enrolled from subjects attending the Center for Personality Disorder of the Psychiatric Clinic, Department of Neurosciences, University of Turin, Italy, from January to December 2007. People with a lifetime diagnosis of delirium, dementia, amnestic disorder, or other cognitive disorders; schizophrenia or other psychotic disorders; bipolar disorder; and patients with a concomitant diagnoses of Axis I or II disorders were excluded. Patients of childbearing age were excluded if they were not using an aduate method of birth control, in accordance with the judgment of the clinician. Patients that received psychotropic drugs in the last 2 months and (or) psychotherapy in the last 6 months were also excluded. Diagnoses were made by an expert clinician and were confirmed using the Structured Clinical Interview for DSM-IV Axis I and II disorders (First et al., 1997a, 1997b). Written Informed consent was acquired from all subjects before their participation. Declaration of Helsinki guidelines were followed and the Ethical Committee approval was obtained.

2.2. Treatment

In the initial 32 weeks trial, patients were randomly allocated to two treatments: (1) 28 patients received fluoxetine (20–40 mg/day) plus clinical management; (2) 27 patients received fluoxetine (20–40 mg/day) plus IPT-BPD. Randomization was performed using the web program Research Randomizer version 3.0 (Urbaniak and Plous, Social Psychology Network, Wesleyan University, Middletown, CT). Pharmacotherapy and psychotherapy started at the same time. Psychotherapy was provided by two therapists who were not the psychiatrist prescribing medication and who had at least 5 years of experience practicing IPT. The two psychotherapists treated respectively 14 and 13 subjects. Therapists in both treatment arms were well experienced in the management of borderline personality disorder. Sessions of psychotherapy were supervised twice per month by a senior psychotherapist (S.B.) checking for the fidelity to manual. Thirty-four sessions of IPT-BPD were provided.

Forty-four patients who completed the 32 weeks trial (22 who received combined therapy and 22 who received single antidepressant) underwent 24 months of follow-up. All subjects received single pharmacotherapy with fluoxetine (20–40 mg/day) during the follow-up period.

2.3. Measurement

Clinical assessment was repeated at 6, 12, and 24 months of follow-up. This study used the same evaluation instruments as the original investigation: a semi-structured interview for clinical and demographical characteristics; the severity item of the Clinical Global Impression scale (CGI-S) (Guy, 1976); the Hamilton scales for depressive and anxious symptoms (HDRS, HARS) (Hamilton, 1959, 1960); the Social and Occupational Functioning Assessment Scale (SOFAS) (Goldman et al., 1992); the Satisfaction Profile (SAT-P) (Majani and Callegari, 1998); the Borderline Personality Disorder Severity Index (BPDSI) (Arntz et al., 2003). Some of these instruments (CGI-S, HDRS, HARS, SOFAS, and BPDSI) were administered by a single clinician with a long experience in rating scales, who was not the same clinician who made the diagnosis and was not involved in the treatment procedures. All these characteristics of the assessor were required in order to obtain a higher reliability and to avoid any interference between assessment and treatment.

The CGI is a clinician-rated scale for the global assessment of illness and consists of three different measures: severity of illness, global improvement, and efficacy index (comparison between patient's baseline condition and a ratio of current therapeutic benefit and severity of side effects). In this study, we considered the first scale: severity of illness. It is a 7-point scale that requires the clinician to rate the severity of illness at the time of assessment: (1) normal, (2), borderline mentally ill, (3) mildly ill, (4) moderately ill, (5) markedly ill, (6) severely ill, (7) extremely ill.

The HDRS is a clinician-rated scale that scores severity of 21 depressive symptoms in the last week. Items are variably scored 0–2, 0–3, or 0–4, with a total score ranging from 0 to 64. Higher scores indicate more severe symptoms of depression.

The HARS is a clinician-rated scale scoring severity of 14 symptoms of anxiety in the last week. Item are all scored 0–4, with a total score ranging from 0 to 56. Higher scores indicate more severe anxiety symptoms.

The SOFAS is a clinician-rated scale to measure a patient's impairment in social and occupational areas. It is independent of the psychiatric diagnosis and the severity of the patient's symptoms. The score is ranged between 0 and 100. Higher scores indicate a better functioning.

The SAT-P is a self-administered questionnaire that consist of