

Psychotherapeutic and Psychosocial Approaches in Bipolar Disorder: A Systematic Literature Review

Sibel ÇAKIR¹, Ayşegül ÖZERDEM²

Abstract

Objective: Aim of this systematic review was critical presentation of psychosocial approaches in bipolar disorders with regard to their fundamentals and impact on the clinical course and outcome of the illness.

Method: PubMed, Medline, PsycINFO and Turkish databases between 1980 and 2009 were searched by using keywords "bipolar disorder" and "psychotherapy", "psychosocial approaches", "psychological intervention". Randomized controlled trials, reviews and meta analysis were included.

Results: Fifty studies met the inclusion criteria where four types of interventions -psychoeducation, family focused, cognitive behavioral and interpersonal psychosocial rhythm therapy- were studied. Twenty two of 24 original research papers were randomized controlled trials, 23 were reviews and 3 were meta analysis. In almost all studies psychotherapeutic approach was applied as adjunctive to pharmacotherapy. Group psychoeducation was more effective in preventing manic relapses, whereas cognitive behavioral and family focused therapies showed efficacy in preventing depressive episodes. Additional benefits on such secondary outcomes as medication compliance, number and duration of hospitalizations, time to recurrence were reported. Effects on functionality and quality of life were assessed rarely, but reported to be beneficial. Cultural adaptation studies are scarce and needs exploration.

Conclusion: Psychosocial interventions adjunctive to pharmacotherapy in bipolar disorder seem to be effective in relapse prevention. Stage of illness where the therapy is initiated and the targeted episode for prevention varies between interventions. Future studies are needed to strengthen the place of psychosocial interventions in treatment guidelines and would contribute to narrow the gap between effectiveness of pharmacotherapy and functional improvement.

Key Words: Bipolar disorders, psychotherapy, psychoeducation, psychosocial approaches

INTRODUCTION

Recurrence rates in bipolar disorder remain high despite progress in its medical treatment and the fact that genetic and neurobiological fundamentals are better known. The long term remission rate is only 24% (Angst et al., 2005) and even with a good level of adherence to drug treatment, the 5-year relapse rate is 73% (Gitlin et al., 1995). Patients with bipolar disorder experience sub-syndromal symptoms during half of their life that cause significant social, academic and occupational dysfunction (Judd et al., 2002). Noncompliance with medical treat-

ment is a major problem in bipolar disorder and occurs in 42% of patients (Perlick et al., 2004). Symptoms reduce significantly with good compliance; however, similar improvement cannot be achieved in quality of life and functionality (Goldberg et al., 1995; Revicki et al., 2005). Recent medical treatments have been effective on symptom relief, but not sufficient enough in preventing relapses, reducing disease burden, or regaining functionality. Various psychotherapeutic interventions as adjunctive to pharmacotherapy seem to be beneficial in fulfilling some of the unmet needs in long term treatment mentioned above.

Received: 23.09.2009 - Accepted: 02.12.2009

¹MD, İstanbul U, İstanbul Medical School Psychiatry Department, Mood Disorders Unit, Çapa İstanbul, Turkey, ²Prof. Dokuz Eylül U, Faculty of Medicine, Psychiatry Department, İzmir, Turkey

Sibel Çakır MD., e-mail: drsibelcakir@yahoo.com

Stressful life events, conflicts within the family, social relationships, disruptions in the sleep-awake cycle, and drug noncompliance play an important role in relapses by precipitating the underlying biological factors (Hays et al., 1998). The stress-diathesis model constitutes an integrated biopsychosocial approach which focuses on the interaction of social, biological, and psychosocial factors in the etiopathogenesis of bipolar disorder. During last two decades therapy approaches based on the stress-diathesis model have reported improvement in the course of bipolar disorder. Despite different methods applied in each therapeutic intervention, the main and common goals have been extending remission time and preventing relapses. In contrast to historical psychodynamic approach which focused on coping with the illness related losses, gaining insight, and the psychological conflicts, modern approaches involve psychoeducation of the patients and their family members, improving treatment compliance, relapse prevention, rebalancing interpersonal relationships, and regulating the sleep-awake cycle (Swartz et al., 2006). Controlled trials evaluating the efficacy of psychosocial approaches used several different outcome criteria such as reduction in relapse rates (Colom et al., 2003a, 2003b; Lam et al., 2003, 2005; Scott et al., 2006), extending the time to relapse (Perry et al., 1999; Miklowitz et al., 2003, 2008), reduction in rate and duration of hospitalization (Cochran et al., 1984; Colom et al., 2003; Bauer et al., 2006), and improvement in quality of life and functionality (Perry et al., 1999; Bauer et al., 2006). Additionally, decrease in adjunctive medication requirement (Perry et al., 1999; Weiss et al., 2004) and suicide rates (Rucci et al., 2002) have been assessed. In earlier studies, psychosocial interventions were used only to increase awareness of illness and medication compliance in the patients (Peet and Harvey, 1991; Perry et al., 1999). In all of these trials, psychotherapeutic approach was investigated as adjunctive to pharmacotherapy. Psychotherapeutic interventions in bipolar disorder were found to have some effects on depressive symptoms (Swartz and Frank, 2001; Miklowitz et al., 2007) and reported positive results in maintenance treatment when used as adjunctive to pharmacotherapy (Perlis and Keck, 2005). Some psychosocial therapies were started immediately after acute mood episodes (Miklowitz et al., 2003; Miller et al., 2004; Simon et al., 2006). However no data up to date regarding use of psychotherapeutic approaches in acute manic episodes exist.

Efficacy of psychotherapy in bipolar disorder has not been studied until recently. This was mainly due to lack of well defined outcome goals and measurement tools. In the present paper, different psychotherapeutic

approaches that have been used in bipolar disorder are introduced and a critical review of data on the efficacy of these psychotherapeutic interventions is presented.

METHOD

PubMed, Medline, PsycINFO were searched for articles published between 1980 and 2009 using the keywords, bipolar disorder and psychotherapy, psychosocial approaches, and psychological intervention. In addition, we searched for Turkish articles using ULAKBİM Turkish Medical Series, Turkish Psychiatry Series, and the references sections of the articles. Articles that included individual or group therapies and at least 6 months of follow-up of adult patients with the diagnosis of bipolar disorder I and II were included in the review. Trials that included only geriatric or pediatric patients were excluded. Although clinical course determinants or measurement materials were not among the inclusion criteria of this review, the primary and secondary measurements of studies are examined and discussed.

RESULTS

Fifty publications met the inclusion criteria; 24 of these were original research papers, 23 were reviews, and 3 were meta-analyses. Among the 24 research papers, 22 were randomized controlled trials. One of the two uncontrolled studies included a series of psychodynamic group psychotherapy patients (Gonzalez and Prihoda, 2007) and the second was a study that investigated the effects of psychotherapeutic interventions as adjunctive to medication on suicide (Rucci et al., 2002). The types of psychotherapeutic approach used in each controlled trial are shown in Table 1. Further details of the trials are summarized in Table 2. Two of the randomized controlled trials were multi-center studies (Bauer et al., 2006; Scott et al., 2006).

A. Randomized controlled trials

The main psychotherapeutic interventions studied in randomized controlled trials in bipolar disorder are: psychoeducation, interpersonal and social rhythm therapy (IPSRT), family focused therapy (FFT) and cognitive behavioral therapy (CBT). Studies conducted using each method will be reviewed separately.

1. Psychoeducation

Basic goals of psychoeducation are improving treatment compliance, teaching illness management, early recognition of relapses, and development of effective

TABLE 1. Distribution of controlled studies according to therapy method

Therapy Method	Number of study	Studies
Psychoeducation	5	Clarkin et al., 1998; Perry et al., 1999; Colom et al. 2003; Bauer et al., 2006; Reinares et al., 2008
CBT	5	Cochran et al., 1984; Ball et al., 2006; Lam et al., 2003, 2005; Scott et al., 2006
FFT	6	Miklowitz et al., 2003, 2008; Rea et al., 2003; Miller et al., 2004, 2008; Solomon et al., 2008
IPSRT	2	Frank et al., 2005, 2008
CBT + individual psychoeducation	2	Zaretsky et al., 2007, 2008
Systematic care	1	Simon et al., 2005
Psychoeducation + CBT + FFT	1	Miklowitz et al., 2007
Total	22	

CBT: Cognitive Behavioral Therapy

FFT: Family Focused Therapy

IPSRT: Interpersonal Psychosocial Rhythm Therapy

strategies for coping with symptoms, decreasing the risk of suicide, improving quality of life and providing increase in social and occupational activities. Psychoeducation can be given to individuals (Perry et al., 1999) or in groups (Colom et al., 2003a, 2003b). Different study groups used varying number of sessions, ranging between 6 and 21. Practical and theoretical data are important to recognize the taking responsibility of the results of illnesses instead of feeling guilty because of the results and to form a good cooperation between patients and clinicians. Patients with bipolar disorder frequently tend to be in denial of the illness. Overcoming stigmatization and increasing awareness on early signs of relapse are the first steps of psychoeducation. Psychoeducation is fairly efficacious in overcoming medication noncompliance which usually causes negative feelings among clinicians. As it is difficult to distinguish prodromal symptoms from subsyndromal symptoms which tend to exist during euthymia, patients are trained to watch over their symptoms on regular basis for early recognition of a relapse. Obtaining information about the illness improves treatment compliance. Increased awareness of symptoms and disorder and better insight can lead to changes in impulsive behaviors and dysfunctional decision-making mechanisms. Application of psychoeducation to the euthymic patients is important, cause euthymic state prevents distractibility and maintains optimum learning.

In recent years group psychoeducation was investigated in well-designed randomized controlled trials which used similar efficacy criteria as in drug trials. The approach was found to be efficacious in reducing relapse rates, delaying relapses, prevention or decreasing the number of hospitalizations. The first psychoeduca-

tion trial in bipolar disorder was performed by Peet and Harvey (1991). It was reported that patients developed positive attitude towards lithium and became more adherent to the medication after being educated about the illness and its treatment; however, the effects of psychoeducation on clinical outcome was not reported. A randomized controlled trial (Perry et al., 1999) reported 30% decrease in relapse rates after 7-12 personal psychoeducation sessions. Time to first manic relapse was delayed; fewer hospitalizations, and better clinical course and social functionality were observed. The same study also showed that psychoeducation helped detecting early signs of mania, but not of depression. Another trial reported decrease in severity of maladaptive behaviors and in the number of hospitalizations after psychoeducation (Van Gent, 2000). The Life Goals Program is a well-structured multi-model group psychoeducation program for bipolar disorder (Bauer et al., 1998). In this program, the group that received psychoeducation had shorter manic episodes, showed better social adjustment, reported higher quality of life and treatment satisfaction (Bauer et al., 2006).

A double-blind randomized controlled trial with a reliable methodology was conducted as a part of the Barcelona Bipolar Disorder Project (Colom et al., 2003a). Once-a-week 90-minute group psychoeducation was given to groups of 8-12 euthymic patients over a 6-months period. A total number of 120 patients received 21 sessions of psychoeducation. All of them experienced fewer relapses into all types of mood episodes during the 2-year follow-up period. The number and duration of hospitalizations also decreased; however, the number of hospitalized patients did not change. Psychoeducation ad-

TABLE 2. Controlled Studies of Psychosocial Treatments in Bipolar disorders

Study	Cases(n, other features)	Controls	Therapy Method	Study Duration	Duration of follow-up	Main results	Seconder results
Cochran (1984)	28 BD I, II	Standard treatment	CBT	6 weeks sessions	6 months	Reduced hospitalization with CBT (14% vs. 57%)	
Clarkin et al. (1998)	33 BD I	Standard treatment	Spouse psychoeducation	11 months, 25 sessions	11 months	No change in relapses. Better functionality and drug compliance	
Perry et al. (1999)	69 BD I, II (in remission, 1 or more relapses in last 12 months)	Standard treatment	Individual psychoeducation	7-12 sessions	18 months	Delay in manic relapses with psychoeducation	Better occupational and social functionality
Colom et al. (2003a)	120 BD I and II (no comorbid diagnosis, in maintenance treatment at least 2 years and euthymic for 6 months)	Unstructured group support	Group psychoeducation	21 weeks	2 years	Fewer relapses in patients who had group psychoeducation	
Miklowitz et al. (2003)	101 BD I, (recently episodic and has hospitalization, partially stable)	Crisis Management (3 sessions)	FFT	9 months 21 sessions	2 years	Delayed relapses with FFT	Better drug compliance, communications with FFT. FFT is more efficacious in depression than mania
Rea et al. (2003)	53 BD I	Individual psychoeducation (21 sessions)	FFT	Recent manic episode, hospitalization, partially stable	2 years	Delayed time to relapses and hospitalizations with FFT	
Lam et al. (2003, 2005)	103 BD I. In fully remission or mild symptoms; 2 or more episodes in last 2 years)	Minimal psychiatric care	CBT	6 months, 12-18 individual sessions	30 months	Fewer relapses, less duration of hospitalization with CBT at 12. months; fewer depressive relapses at 30 months	Better social functions with CBT at 24 th months
Miller et al. (2004, 2008)	92 BD I (acute episode; 69/92 acute mania, 84/92 hospitalized)	Usual maintenance treatment	Single family therapy, multiple family therapy	12 single family sessions, or 6 multiple family sessions	Up to 28 months	No differences	Effectiveness of family therapy is higher in depression than mania
Frank et al. (2005)	175 BD I, (in depressive, mixed, or manic episode)	Individual clinic control	IPSRT	Weekly acute episode to remission, then biweekly, onthly, 2 years	2 years	Longer remission with IPSRT in maintenance that commenced at acute episode	
Ball et al. (2006)	52 BD I, II, In fully remission or mild symptoms; 1 or more episodes in last 18 months	Usual maintenance treatment	CBT	6 months, weekly 20 sessions	18 months	Delayed time to depressive relapses with CBT (p=0.06)	Less dysfunctional attitude, social disability at 6 months, no differences at 18 months ; no differences in compliance
Study	Cases(n, other features)	Controls	Therapy Method	Study Duration	Duration of follow-up	Main results	Seconder results

TABLE 2. Controlled Studies of Psychosocial Treatments in Bipolar disorders

Study	Cases(n, other features)	Controls	Therapy Method	Study Duration	Duration of follow-up	Main results	Secunder results
Scott et al. (2006)	253 BD I and II.various; 32% in episode)	Usual maintenance treatment	CBT	26 weeks, 22 sessions	18 months	No differences	CBT is more effective in patients with number of total episodes had less than 12
Simon et al. (2005)	441 BD I and II.	In maintenance treatment. At least 1 psychiatric follow up at last year. Mostly symptomatic.	Systematic care	5 weeks group sessions, then biweekly up to 2 years	2 years	Less probability of manic relapses in 24 moths. No change on depression.	More effective in patients started to treatment with loaded symptoms
STEP-BD (Miklowitz et al., 2007)	293 BD I and II (patients in acute depressive episode)	3 sessions short psychoeducation	IPSRT, FFT, CBT	9 months, 30 sessions	1 year	Patients with intensive treatment remained in remission 1.58 times more	General functionality, relation functions and life satisfaction is better with intensive therapy
Miklowitz et al. (2008)	58 BD I, II and not otherwise specified, have recent episode, partially stable	3 sessions short psychoeducation	Adolescents FFT	9 months 21 sessions	2 years	FFT is related to rapid improvement in depression	No differences in time to relapses across the groups. Less depressive days with FFT.
Zaretsky et al. (2007, 2008)	79 BD I and II (fully or partially stable)	Individual psychoeducation (7 sessions)	CBT +individual psychoeducation	Sessions long 20 weeks	1 year	No differences	Patients with CBT had less depressive days, had less dosage of antidepressant drugs
Frank et al. (2008)	175 BD I patients, after acute episode, 125 in maintenance	Intensive clinical follow up	IPSRT, in 4 stages	variables	total 2.5 years, 6 months acute, 2 years maintenance	Patients who had IPSRT in acute episode improved rapidly in occupational functions. No differences in maintenance. Females had more benefits and rapid improvement	
Reinares et al. (2008)	113 BD I, II. (euthymic for 3 moths, living with caregivers; no axis I comorbidity)	Standard treatment	Caregivers, multiple family treatment	3 months, 12 sessions, monthly group	15 months	Study group had fewer relapses (42% versus 66%)	Effective in hypomanic and manic relapses, no effectiveness in depressive relapses
Solomon et al.(2008)	92 BD I patients	Standard maintenance drug treatment	1. Individual family treatment, various sessions 2. Multiple family treatment.6 sessions	-Individual family therapies. Number of sessions various. - Multiple family groups.6 sessions	28 months	No differences in relapses. Multiple family groups is more effective for prevention hospitalizations	

BD : Bipolar disorder , IPSRT: interpersonal psychosocial rhythm therapy , FFT: family focused therapy , CBT: cognitive behavioral therapy

dresses such issues as what bipolar disorder is, what are the relapse rates, medications used in this disorder and their side effects, precipitating factors, the importance of drug compliance, how to handle symptoms, stress management, suicide risk, impact of pregnancy on the course of illness, social issues like stigmatization, being aware of early signs and the recognition of relapse, importance of avoiding alcohol-substance use, and ways of maintaining daily life. The same study group reported similar efficacy rates for psychoeducation in a small number of patients who already had good medication compliance and proposed that psychoeducation's effectiveness is not only related to improvement in medication compliance (Colom et al., 2003b). Psychoeducation is thought to show its effect through improving drug compliance, helping the patient organize his/her daily life, increasing patient's ability for early recognition of prodromal signs, changing misbeliefs about the illness and increasing awareness for the illness.

Educating the family members is as important as psychoeducation of the patients. Clarkin et al. (1998) applied psychoeducation to a small group of spouses of patients. Although the symptom severity of the study population did not differ compared to the control group, the study group presented better functionality and more frequent feelings of well-being than the control group. In another study, the Barcelona group had provided 12 psychoeducation sessions to the parents of patients and had reported decreased manic and hypomanic relapse rates and delay in time to relapse (Reinares, 2008); however, similar effects were not detected for depressive and mixed episodes. Management of illness by parents, improvement of family relations in this study is similar to ones in FFT. Considering the presence of close family relations and the tendency to stay in large families in our society, we suggest that family psychoeducation could become a useful tool for illness management in our country.

Group psychoeducation was found to prevent relapses in bipolar patients with comorbid personality disorder (Colom 2005). Although psychoeducation was thought to be effective in patients with personality disorder comorbidity and patients with poor prognostic course and treatment difficulties, in a recent study we detected limited attendance for psychoeducation among patients who had high number of total episodes and hospitalizations, poor drug adherence and prognosis (Çakır et al., 2009). We concluded that noncompliance to psychotherapy may be the mechanism for a less favorable psychotherapeutic outcome in patients with adverse course

of illness. Our finding may be indicative of the possible beneficial effect of placing psychoeducation as a part of treatment at early stages of illness.

2. Interpersonal and social rhythm therapy (IPSRT)

IPSRT was developed by Ellen Frank and her team (2000) to be used in bipolar disorder. It was based on interpersonal therapy, which was used as an intervention for depressive relapses by Klerman and Weissman (1984). The psycho-chronological theory intended to clarify mood disorders (Ehlers et al., 1988, 1994; Monk et al., 1990, 1994) and the disrupted life model concept for bipolar patients by Goodwin and Jamison (1990) had provided the inspiration for development of this therapy in relation of stressful life events. Psychological and chronobiological factors may induce relapses via perturbing the circadian rhythm. Combining the basic principles IPRST is proposed to regularize social rhythm and diminish relapses and mood symptoms. IPSRT uses also cognitive behavioral techniques to solve interpersonal problems in addition to psychoeducation. IPSRT is applied just after acute episode as four stages: In the first stage; the structure of the recent episodes and interpersonal relations of patients, basic problematic states are examined; social rhythm is defined and then regulated by psychoeducation. In the second stage the therapist and the patient are in collaboration for regulation of daily routines, diminishing interpersonal problems, solving problematic issues related to illness. In the third stage it is aimed that the patient would be more independent and competent on the pointed issues of IPSRT. In the last stage: patients are aimed improvement in functionality, independent living skills, and accomplishment of relapse prevention methods.

Early research using this technique was encouraging, however, regarding the results of such investigations; the effects on relapse time, interpersonal problems and drug compliance were not clear (Frank et al., 1999; 2000). A multimodal trial of the efficacy of IPSRT in acute and maintenance treatments has shown that, among patients who have experienced major depressive episodes, those in therapy tended to recover faster. IPSRT was also effective in preventing suicide but there was no decrease in relapse rates. Frank et al. (2005), in a randomized controlled trial, compared the effects of two psychosocial interventions, IPRST and intensive clinical management (ICM) for acute and maintenance states in two phases. It was found that, even though there was no difference in time to remission for symptoms of acute episodes, increased social rhythm stability, and decreased relapse

rates in the maintenance phase were detected in patients who received IPSRT. It was also shown that IPRST contributed to regaining the functionality of patients in a shorter time (Frank et al., 2008). This is a theoretically comprehensible model; however there are accoutrement difficulties such as experience, time and funds in the application.

3. Family focused therapy (FFT)

It was reported that high levels of expressed emotions in family and partners were related to relapses and poor prognosis (Miklowitz 1986; Simoneau 1998). The FFT model was developed by Goldstein and Miklowitz (1997) and comprises a psychoeducation-oriented technique. The attitudes of family members, partners, and caregivers enable the recognition of early signs, symptoms and facilitate development of coping strategies. This method aims for developing functionality by controlling emotions by means of dealing with highly expressed-emotions, the emotional responses and conflicts between patients and caregivers, improving interpersonal relations in the state of conflict, problem-solving and rehearsals of coping strategies. Therapy is initiated just after the acute phase and lasts 9 months, with a total of 21 sessions in 3 modules. The first module consists of psychoeducation. Later, in the second module the patients practice developing communication patterns. Finally, in the last module, problem solving techniques are used. Up to now, the efficacy of this therapy has been investigated in 6 randomized controlled trials. In the first trial (Rea et al., 2003) FFT and individual therapy, of the same duration, were compared at the end of the first year and there was no difference observed in relapse rates. However, by the end of the treatment, FFT participants showed a lower relapse rate and had longer survival times to relapse and hospitalization. In a larger series (Miklowitz et al., 2003) patients living in high expressed-emotion environments received crisis management or FFT as an adjunct to pharmacotherapy; by the end of the 2 year follow-up period, it was observed that the FFT group showed a lower relapse rate, better drug compliance, and had longer survival times to relapse. FFT was found to be more effective in the prevention of depressive relapses than manic relapses in this study. This was thought to be a result of improved relations between patients and relatives. Improvement in drug compliance seemed to be important in the prevention of manic episodes even though there was limited effectiveness observed. Some questions have still not been answered; which module of FFT is important in healing, or for which patients it is

required. It is anticipated to be more successful in families with high expressed emotion. Multi-family therapies were found, by Miller et al. (2004, 2008), to be more economical and effective with regard to depressive symptoms. In bipolar adolescents experiencing acute depressive episodes or having sub-threshold depressive symptoms; it was shown that they got over their depression in a shorter time and experienced fewer depressive days in a two- year period, compared to patients who had had brief exposure to psychoeducation, when FFT was given, (Miklowitz et al., 2008). Moreover FFT had had no effect on manic symptoms in this group. Solomon et al. compared families receiving individual psychotherapy as an adjunct to pharmacotherapy to families receiving group psychotherapy and to a control group that received pharmacotherapy alone. Although there was no difference between the three groups with regard to relapse rates and survival time to relapse in 28 months; lower hospitalization rates were detected in patients receiving family group psychotherapy. In this trial, in which patient number was limited, the efficacy of family group psychotherapy on hospitalization rates was obvious, whereas no effect on relapse rates was detected.

4. Cognitive behavioral therapy (CBT)

This model has been applied in various forms by different groups. It works on negative, automatic thoughts about illness and illness diaries. Cognitive therapies have been adapted to 20-25 session programs for bipolar patients. Several issues, such as psychoeducation, prevention of relapses, reforming dysfunctional thoughts and beliefs, improving drug compliance, stabilizing of social rhythm, stress management and recognizing and coping with mood swings are dealt with (Basco and Rush 1996; Lam 1999; Scott 2001).

A trial performed by Cochran et al. (1984) using several cognitive behavioral techniques and psychoeducation items, is the first randomized, controlled study in bipolar disorder. 6-session-CBT aiming improvement of medication adherence was applied to the patients in Lithium clinic and during 6 months follow up less hospitalization rates and better medical adherence among those patients were detected. The study had limitations, such as the small sample size of the study, investigating failure to investigate the survival time to relapse, and a failure to mention the types of relapse episodes. In a pilot study, which formed one of the first examples related to this therapy model (Scott and Garland 2001), patients who were administered 22 sessions of cognitive therapy, adjunctive to pharmacotherapy, showed im-

proved general functioning and a reduction in depressive symptoms with respect to the control group. Cognitive therapy has little effect on manic relapses however; relapse rates are lower than those of the control group regarding all episodes in a 1 year follow-up. In another randomized controlled trial (Lam et al., 2003) involving 12-20 individual cognitive therapy sessions during a 12-month follow-up, fewer patients had relapses and shorter episode durations were observed, fewer symptoms were verbalized in the mood diary and patients showed better drug compliance.

In a study consisting of the same sample (Lam et al., 2005) in a 30-month follow-up, it was detected that CBT did not prevent manic episodes, but depressive relapses were reduced. The therapy applied by Lam (1999) differed from the traditional cognitive therapy developed by Beck in some respects, in that it included psychoeducation constituents such as regulating night-day rhythms, avoiding factors that may precipitate illness episodes, recognizing and managing early symptoms, and preventing relapses. Ball et al., (2006) detected longer survival time to depressive relapses, better functionality and better patient control in patients receiving cognitive therapy lasting for a 6-month period, in a randomized controlled study. The disappearance of these differences after the 18th month revealed that additional supportive therapies are necessary.

Scott et al. (2006) standardized the CBT method and performed an 18-month multi-centered randomized controlled trial, but the results were not as positive as had been expected; CBT was not effective in the prevention of relapses for patients who had previously experienced several episodes; whereas it was effective in patients who had had less than 12 episodes. This result supports the idea that it is important to start psychosocial approaches at the early phases of the illness.

B. Meta-analysis studies

The results of 22 controlled studies that investigated the effectiveness of therapy models in maintenance mentioned above are summarized in table 2 as well as in the section where they are dealt with in detail. The main studies that included similar inclusion and outcome criteria were assessed in 3 meta-analyses, just one of them (Scott et al., 2007) used accurate meta-analytical techniques. The patients who received only pharmacological treatment were compared, in this study, in terms of relapse rates, with patients receiving therapy additional to pharmacological treatment. When 8 randomized

controlled studies were assessed meta-analytically, psychosocial therapies were observed to reduce relapse rates by 40%. However, they were most effective when initiated in euthymic patients and less effective in patients with high numbers of total episodes. In another meta-analysis, Beynon et al., (2008), found that CBT and psychoeducation were effective in euthymic patients, however FFT was no more or less effective than individual psychosocial therapy. Integrated group therapy (Weiss et al., 2000) or care management (Simon et al., 2006) were not found to be effective in the prevention of relapse. A meta-analysis (Justo et al., 2007) which investigated the efficacy of family attendance, assessing 7 randomized controlled studies, found that psychosocial therapy, given to a caregiver, spouse or family member, made no significant difference in relapse rates or symptom control, although the results were considered to be inconclusive due to the limited and complex nature of the data. The meta-analysis work and making efficacy comparison across the therapy types is hard as published studies had varied outcome criteria, non-standardized therapy models, different inclusion criteria and commencing periods. However some significant effectiveness of adjunctive psychosocial treatments in relapse prevention is a common conclusion of meta-analysis studies mentioned above.

C. Treatment guidelines and psychosocial approaches

Adjunctive psychoeducation in maintenance treatment has been incorporated into treatment guidelines (APA, 2002; Goodwin 2003; Calabrese 2004; Yatham et al., 2005, 2009). The American Psychiatric Association has indicated the benefits of psychotherapeutic approaches, according to the needs of patients and the skills of physicians (APA, 2002). The effectiveness of controlled studies was stated, in the updated guidelines, in 2005 (Miklowitz et al., 2003, Lam et al., 2003; Colom et al., 2003 a; b; Frank et al., 2005). Their conclusion was that psychosocial treatments as an adjunct to maintenance treatments that focused on the management of illness, compliance, early detection of symptoms, and problems relating to interpersonal relationships, are beneficial, whereas there were no information given concerning the benefits of supportive and psychodynamic-eclectic therapies (APA 2005). The Texas Medication Algorithm Project is an expert consensus guideline which emphasizes that psychoeducation and cognitive therapies are beneficial in light of evidence-based medicine and should be administered adjunctively to pharmacological treat-

ments. When patients are assessed clinically, the possible psychosocial approach is also recommended. This emphasizes the importance of psychotherapy and patient education during the implementation of optimum maintenance treatments (Suppes, 2005). The Canadian Network for Mood and Anxiety Treatments Guidelines state that psychoeducation is beneficial in relapse prevention in long term maintenance treatments, whereas CBT is controversial (Yatham et al., 2005). IPSRT was not beneficial at the first stage after an acute episode, but shows favorable results in 2-year follow-up studies. A study mentioned in the updated, 2009 version of this guide is important: Of 204 patients who received 6 sessions of psychoeducation or 20 sessions of CBT in an 18-month follow-up study, all showed a reduction in symptoms (Parikh et al., 2007). Both groups have significant benefits in terms of relapse prevention compared to the control group, but these two approaches did not differ in efficacy. The treatment-cost effectiveness of psychoeducation and CBT was also mentioned in the guidelines and psychoeducation was suggested first because of its lower costs. With regard to the remaining symptoms, other psychosocial methods were suggested. This practical approach seems to be both effective and feasible. The guidelines of the British National Institute for Health (NICE, 2006) for bipolar disorders report that psychosocial approaches had fairly positive effects in maintenance treatments. Psychoeducation and other psychosocial therapies were especially suggested in special populations, such as alcohol-substance abusers and sufferers from rapid cycling illnesses. Moreover, the benefits of structured therapies having psychoeducation components consisting of at least 16 sessions lasting over a 6-9 month period were pointed out to patients and families after the remission of an acute episode. A guideline which was prepared by the Turkish Psychiatric Association's Mood Disorders Working Group underlines therapeutic collaboration, important issues in therapeutic relations, long term goals and quality of life in the light of biopsychosocial models, rather than a particular psychosocial model. The guidelines deal with issues such as the Losses related to illness, effects on patients, families and social environments, treatments, compliance, concerns and appropriate managements for the emotional experience of stigma in the remission period (Vahip and Kocadere, 2003).

DISCUSSION and CONCLUSION

Even if pharmacological treatments are capable of alleviating the symptoms of bipolar disorder, this is not re-

flected in the patient's quality of life. Adjunctive psychotherapeutic approaches could narrow this gap, as their positive effects on relapse prevention, time to relapse, number of hospitalizations, and some secondary outcome measurements arising from the controlled studies assessed above have been demonstrated and evidence has been growing concerning their effectiveness. Moreover Lam et al. (2005) have established a significant reduction in service use and cost-efficacy ratios in patients who have had cognitive therapy. It is also known that psychotherapeutic approaches were effective in suicide prevention in patients suffering from bipolar disorders (Rucci 2002).

Although psychoeducation prevents manic and depressive episodes, reduces the number and duration of hospitalizations (Colom et al., 2003a) and improves social functionality (Bauer et al., 2006), prevention in depressive relapse was not confirmed by Perry et al. (1999). Discrepant results related to psychoeducation and depressive relapses should be investigated. Psychoeducation is suggested as the initial psychosocial method under the current guidelines (Yatham et al., 2009) due to its ease of application, absence of requirements for special experience, and reasonable cost-efficacy. It is also appropriate for the conditions prevailing in Turkey. The CBT, FFT, and IPSRT approaches require experienced therapists and have high costs. Evidence-based findings have showed that CBT and FFT were effective in depressive relapse prevention (Lam et al., 2005; Ball et al., 2006; Miller et al., 2004; 2008; Miklowitz 2008). CBT is more effective in patients with a lower number of episodes (Scott et al., 2006). FFT and CBT have more advantages compared to psychoeducation in achieving remission and depressive relapse prevention. However, the weak points of these methods are; low efficacy in manic prevention and low cost-effectiveness. Therefore the use of these methods for the large patient populations in our country seems to be unfeasible. There is no study that directly compared the efficacy of different therapy methods except for some data provided by indirect sub-analysis. Some therapies were able to be applied primarily in certain special populations. For instance CBT and FFT are beneficial for patients with sub-threshold depressive symptoms and patients with clinical course have predominant depressive episodes. FFT may be effective in families with high emotional expression and IPSPT for patients for whom relationship problems cause depressive symptoms or precipitate mood episodes. It is known that psychosocial stressors may trigger mood episodes (Hays et al., 1998). The presence of these fac-

tors in relapse episodes may help with the selection of therapy models. The combination model of Zaretsky et al. (2007; 2008) investigated the efficacy of CBT addition to individual psychoeducation when psychoeducation is not enough by itself. It has been determined that patients who were assigned 13 sessions of CBT in addition to psychoeducation, experienced fewer depressive days. Combinations of psychotherapy models will be much more prevalent treatment methods in the future and should be tested with selected patient groups.

Design and methodological variations among studies on psychosocial therapies cause difficulties in carrying out review and meta-analysis, comparing methods and with the follow-up of qualitative results. Some authors included patients at different stages of illness (Miklowitz et al., 2003; Miller et al., 2004, 2008; Frank et al., 2005; Bauer et al., 2006; Scott et al., 2006) whereas others included only euthymic patients (Colom et al., 2003a; Lam et al., 2003, 2005; Ball et al., 2006; Zaretsky et al., 2007, 2008). In conclusion it was found that CBT and psychoeducation are more effective in euthymic patients whereas FFT and IPSRT are more effective when commenced just after an acute episode (Beynon et al., 2008). Factors such as family structure and dynamics, socio-economic level, education, cultural features, environment, comorbid personality disorders, alcohol-substance use, stigma, superstition and support systems have not been evaluated in the research.

Other overlooked aspects of psychosocial therapy studies are functionality and quality of life, which have not been evaluated except for in a few studies (Perry et al., 1999; Bauer et al., 2006; Miklowitz et al., 2007), most of which are single-site studies (except Scott et al., 2006; Bauer et al., 2006; Miklowitz et al., 2007). Moreover the effects of mixing various standard pharmacological treatments across physicians and clinics, suicide and adverse events were ignored. The inclusion of relapse rates and hospitalizations, as outcome criteria seems to be a positive step towards the development of a standardized methodology; however ignorance of issues such as quality of life, functionality, some qualitative factors and others, are drawbacks. Because; even the patients who had been applied these therapies experiences relapses, it might be less severe, last in shorter time and achieve remission faster. Nevertheless improvement in the symptoms of patients may not be functional, moreover there might be bipolar patients that have relapses but who have rapidly improved in functionality. Ignorance of cognitive deficits, rehabilitation and regaining occupational functionality are the other deficits of psychoso-

cial therapies. Usually, the previous therapy experiences of investigators may cause positive prejudice and biases. Mean follow-up periods of studies vary between 6 months and 2 years. Bipolar disorder is a chronic illness, therefore longer follow-up periods would bring better data to evaluate efficacy in maintenance.

The cultural validity of the psychosocial therapy model should be investigated across cultures with various social roles (Bernal, 2006). Models of psychosocial approach were usually developed in western cultures and there is a lack of knowledge when they are implemented in different cultures. Even though it does not have a systematic validity, a study (Özdemir et al., 2009) that investigated the effectiveness of FFT, demonstrated the beneficial results on clinical course and might be incorporated without any change. Cultural validity studies are also needed for other psychotherapies. There is no national data related to systematic psychotherapies for bipolar disorder. The lack of experienced therapists, undocumented practical applications without any research, failure to transfer experience to following generations and the absence of culture-specific therapy models are other weaknesses.

Although they are called by different names, all psychotherapeutic approaches work on shared psychoeducational components that are; recognition of illness, improvement in awareness and compliance, regulation of social rhythms, recognition and management of internal and external stressors that may trigger relapses. The differences in therapeutic methods are created by the proportion of these components. Improvement of illness knowledge and compliance and the early recognition of prodromal symptoms seem to be effective in the prevention of manic episodes, whereas the regulation of diurnal rhythms like sleep, improvement in communications within the family and changing dysfunctional habits are important for the prevention of depressive relapses. Which of these therapy methods are effective in which patient groups have not been studied directly. Therefore matching patients to the appropriate therapy method according to clinical and cultural features may improve the effectiveness of psychosocial approaches. Colom et al. (2003a) found that the relapse rate of bipolar patients with good compliance in a 2-year period, who attended psychoeducation sessions, was 60% and 92% in control patients who had not attended these sessions. Even though there is a statistical difference, a 60% relapse rate in patients with good compliance and who have attended psychoeducation, demonstrates that the success of a combination of pharmacological and psychotherapeutic methods is still constrained. Nevertheless in patients at a certain remis-

sion stage, the benefits of psychotherapeutic approaches on clinical course are doubtless. The psychotherapies, which have been involved in guidelines and their combinations with pharmacologic treatments, are an obligation rather than an option (Calabrese 2004; Goodwin 2003; Yatham et al., 2009). The implementation of psychosocial approaches before the occurrence of biological, social and psychological disabilities would be an aid to both pharmacological treatment and quality of life. Even patients who are difficult to treat, with rapid cycling illness, alcohol-substance abuse and treatment resistance seem to be appropriate targets; it has not known how motivation and

the tendency of these patients for therapeutic alliance are appropriate and which therapy method would be more beneficial yet. Although there is growing evidence-based data regarding the benefits of psychosocial treatments, it has remained uncertain which type of therapy should be appropriate for which patient group, when they should start and in which duration. Nevertheless psychosocial treatments that would be selected appropriately with clinical course, morbidity, social environment, family, cultural features, experience and opportunity of treatment centers greatly contribute to the treatment of bipolar disorder, which is a chronic and relapsing illness.

REFERENCES

- Angst J, Gamma A, Neuenschwander M et al. (2005) Prevalence of mental disorders in the Zurich Cohort Study: a twenty year prospective study. *Epidemiol Psychiatr Soc.* 14:68-76.
- APA (2002). [http:// www.psychiatryonline.com/pracGuide/pracGuideTopic_8.aspx](http://www.psychiatryonline.com/pracGuide/pracGuideTopic_8.aspx)
- APA (2005). <http://www.psychiatryonline.com/content.aspx?aid=148430>
- Ball JR, Mitchell PB, Corry JC et al. (2006) A randomized controlled trial of cognitive therapy for bipolar disorder: focus on long-term change. *J Clin Psychiatry*, 67:277-86.
- Basco and Rush (1996) *Cognitive-Behavioral Therapy for Bipolar Disorder*. Guilford Press .
- Bauer MS, McBride L (1996) *Structured group psychotherapy for bipolar disorder: the Life Goals Program*. New York, NY: Springer Publishing Co.
- Bauer MS, McBride L, Chase C et al. (1998) Manual-based group psychotherapy for bipolar disorder: a feasibility study. *J Clin Psychiatry*, 59:449-55.
- Bauer MS, McBride L, Williford WO et al. (2006) Cooperative Studies Program 430 Study Team: Collaborative care for bipolar disorder, II: impact on clinical outcome, function, and costs. *Psychiatr Serv*, 57:937-45.
- Bernal, G. (2006). Intervention development and cultural adaptation research with diverse families. *Family Process*, 45: 143-51.
- Beynon S, Soares-Weiser K, Woolacott N et al. (2008) Psychosocial interventions for the prevention of relapse in bipolar disorder: systematic review of controlled trials. *Br J Psychiatry*, 192:5-11.
- Calabrese JR, Kasper S, Johnson G et al. (2004) International Consensus Group on Bipolar I Depression Treatment Guidelines. *J Clin Psychiatry*, 65:571-9.
- Clarkin JF, Carpenter D, Hull J et al. (1998) Effects of psychoeducational intervention for married patients with bipolar disorder and their spouses. *Psychiatr Serv*, 49:531-3.
- Cochran SD (1984) Preventing medical noncompliance in the outpatient treatment of bipolar affective disorders. *J Consult Clin Psychol*, 52:873-8.
- Colom F, Vieta E, Martinez-Aran A et al. (2003a) A randomized trial on the efficacy of group psychoeducation in the prophylaxis of recurrences in bipolar patients whose disease is in remission. *Arch Gen Psychiatry*, 60: 402-7.
- Colom F, Vieta E, Reinares M et al. (2003b) Psychoeducation efficacy in bipolar disorders: beyond compliance enhancement. *J Clin Psychiatry*, 64: 1101-5.
- Colom F, Vieta E, Tacchi MJ et al. (2005) Identifying and improving non-adherence in bipolar disorders. *Bipolar Disord*, 7:24-31.
- Cakir S, Bensusan R, Akca ZK et al. (2009) Does a psychoeducational approach reach targeted patients with bipolar disorder? *J Affect Disord*. 119: 190-3.
- Ehlers CL, Frank E, Kupfer DJ (1988) Social zeitgebers and biological rhythms: a unified approach to understanding the etiology of depression. *Arch Gen Psychiatry*, 45: 948-952.
- Ehlers CL, Kupfer DJ, Frank E et al. (1994) Biological rhythms and depression: the role of zeitgebers and zeitstörers. *Depression*, 1:285-93.
- Frank E, Swartz HA, Mallinger AG (1999) Adjunctive psychotherapy for bipolar disorder: effects of changing treatment modality. *J Abnorm Psychol*, 108:579-87.
- Frank E, Swartz HA, Kupfer DJ (2000) Interpersonal and social rhythm therapy: managing the chaos of bipolar disorder. *Biol Psychiatry*, 48:593-604.
- Frank E, Kupfer DJ, Thase ME et al. (2005) Two-year outcomes for interpersonal and social rhythm therapy in individuals with bipolar I disorder. *Arch Gen Psychiatry*, 62:996-1004.
- Frank E, Soreca I, Swartz HA et al. (2008) The role of interpersonal and social rhythm therapy in improving occupational functioning in patients with bipolar I disorder. *Am J Psychiatry*, 165(12): 1559-65.
- Gitlin, M.J., Swendsen, J., Heller, T et al. (1995) Relapse and impairment in bipolar disorder. *American Journal of Psychiatry* 152, 1635-1640.
- Goldberg JF, Harrow M, Grossman LS (1995) Course and outcome in bipolar affective disorder: a longitudinal follow-up study. *Am J Psychiatry*. 152:379-84.
- Goldstein MJ ve Miklowitz DJ (1997) *Bipolar disorder: A family focused treatment approach*, NY Guilford Press
- Gonzalez JM, Prihoda TJ (2007). A case study of psychodynamic group psychotherapy for bipolar disorder. *Am J Psychother*, 61:405-22.
- Goodwin F, Jamison K (1990): *Manic-Depressive Illness*. New York: Oxford University Press.
- Goodwin GM, Young AH (2003). The British Association for Psychopharmacology guidelines for treatment of bipolar disorder: a summary. *J Psychopharmacol*, 17(4 Suppl): 3-6.
- Harvey NS, Peet M (1991) Lithium maintenance: effects of personality and attitude on health information acquisition and compliance. *Br J Psychiatry*, 158: 200-4.
- Hays JC, Krishnan KR, George LK et al. (1998) Age of first onset of bipolar disorder: demographic, family history, and psychosocial correlates. *Depress Anxiety*, 7(2): 76-82.
- Judd LL, Akiskal HS, Schettler PJ et al. (2002) The long-term natural history of the weekly symptomatic status of bipolar I disorder. *Archives of General Psychiatry*, 59: 530- 537.
- Justo LJ, Soares BG, Calil HM (2007) Family interventions for bipolar disorder. *Cochrane Database Syst Rev*, 17(4): CD005167.
- Klerman GL, Weissman MM, Rounsaville BJ et al. (1984) *Interpersonal Psychotherapy of Depression*. New York, NY: Basic Books Inc.
- Lam DH, Jones S, Hayward P et al. (1999) Cognitive Therapy for

Bipolar Disorder: A Therapist's Guide to Concepts, Methods and Practice. New York, John Wiley & Sons.

Lam DH, Watkins ER, Hayward P et al.(2003) A randomized controlled study of cognitive therapy for relapse prevention for bipolar affective disorder: outcome of the first year. *Arch Gen Psychiatry*, 60:145–52.

Lam DH, Hayward P, Watkins ER et al.(2005) Relapse prevention in patients with bipolar disorder: cognitive therapy outcome after 2 years. *Am J Psychiatry*, 162: 324–9.

Miklowitz DJ, Goldstein MJ, Nuechterlein KH et al. (1986) Expressed emotion, affective style, lithium compliance, and relapse in recent onset mania. *Psychopharmacol Bull*, 22(3).

Miklowitz D, Goldstein MJ (1997) *Bipolar Disorder: A Family-Focused Treatment Approach*. New York: Guilford.

Miklowitz DJ, Simoneau TL, George EL et al. (2000) Family-focused treatment of bipolar disorder: 1-year effects of a psychoeducational program in conjunction with pharmacotherapy. *Biol Psychiatry*, 48: 582–92.

Miklowitz DJ, George EL, Richards JA et al. (2003) A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder. *Arch Gen Psychiatry*, 60: 904–12.

Miklowitz DJ, Otto MW, Frank E et al.(2007) Intensive psychosocial intervention enhances functioning in patients with bipolar depression: results from a 9-month randomized controlled trial. *Am J Psychiatry*, 164:1340–1347.

Miklowitz DJ (2008). Adjunctive psychotherapy for bipolar disorder: state of the evidence. *Am J Psychiatry*, 165(11): 1408-19.

Miller IW, Solomon DA, Ryan CE et al. (2004) Keitner GI. Does adjunctive family therapy enhance recovery from bipolar I mood episodes? *J Affect Disord*, 82:431–6.

Miller IW, Keitner GI, Ryan CE et al. (2008) Family treatment for bipolar disorder: family impairment by treatment interactions. *J Clin Psychiatry*, 69:732–40.

Monk TH, Flaherty JF, Frank E et al. (1990) The Social Rhythm Metric (SRM): an instrument to quantify the daily rhythms of life. *J Nerv Ment Dis*, 178:120-6.

Monk TH, Petrie SR, Hayes AJ et al. (1994) Regularity of daily life in relation to personality, age, gender, sleep quality and circadian rhythms. *J Sleep Res*, 3:196-205.

NICE clinical guideline on bipolar disorder: <http://www.nice.org.uk/guidance/CG38>

Ozerdem A, Oguz M, Miklowitz D et al. (2009) Family focused treatment for patients with bipolar disorder in Turkey: a case series. *Fam Process*. 48: 417-28.

Parikh S, Zaretsky A, Beaulieu S et al. (2007) Psycho-education versus cognitive behavioural therapy for bipolar disorder: A multi-site national RCT [Abstract NR322]. New Research Abstracts, Annual Meeting of the American Psychiatric Association. Washington D.C.: American Psychiatric Association.

Peet M, Harvey NS (1991) Lithium maintenance: 1. A standard education program for patients. *Br J Psychiatry*, 158: 197–200.

Perlick DA, Rosenheck RA, Clarkin JF et al.(2004). Impact of family burden and affective response on clinical outcome among patients with bipolar disorder. *Psychiatr Serv*, 55: 1029-35.

Perlis RH, Keck PE (2005) The Texas implementation of medication algorithms update for treatment of bipolar I disorder. *J Clin Psychiatry*, 66(7):818-20.

Perry A, Tarrier N, Morriss R et al.(1999) Randomised controlled trial of efficacy of teaching patients with bipolar disorder to identify early symptoms of relapse and obtain treatment. *BMJ*, 318:149–53.

Rea MM, Tompson M, Miklowitz DJ et al.(2003) Family focused treatment vs individual treatment for bipolar disorder: results of a randomized clinical trial. *J Consult Clin Psychol*, 71:482–92.

Reinares M, Colom F, Sánchez-Moreno J et al. (2008) Impact of caregiver group psychoeducation on the course and outcome of bipolar patients in remission: a randomized controlled trial. *Bipolar Disord*, 10:511–9.

Revicki DA, Matza LS, Flood E et al. (2005) Bipolar disorder and health-related quality of life : review of burden of disease and clinical trials. *Pharmacoeconomics*, 23: 583-94.

Rucci P, Frank E, Kostelnik B et al. (2002) Suicide attempts in patients with bipolar I disorder during an acute and maintenance clinical trial. *Am J Psychiatry*, 159:1160–4.

Scott J, Garland A, Moorhead S (2001) A pilot study of cognitive therapy in bipolar disorders. *Psychol Med*, 31: 459–67.

Scott J, Paykel E, Morriss R et al. (2006) Cognitive-behavioural therapy for severe and recurrent bipolar disorders. Randomised controlled trial. *Br J Psychiatry*, 188: 313–20.

Scott J, Colom F, Vieta E (2007). A meta-analysis of relapse rates with adjunctive psychological therapies compared to usual psychiatric treatment for bipolar disorders. *Int J Neuropsychopharmacol*, 10(1):123-9.

Simon GE, Ludman EJ, Unützer J et al. (2005) Randomized trial of a population-based care program for people with bipolar disorder. *Psychol Med*, 35:13-24.

Simon GE, Ludman EJ, Bauer MS et al. (2006) Long-term effectiveness and cost of a systematic care program for bipolar disorder. *Arch Gen Psychiatry*, 63(5): 500-8.

Simoneau TL, Miklowitz DJ, Saleem R (1998) Expressed emotion and interactional patterns in the families of bipolar patients. *J Abnorm Psychol*, 107(3): 497-507.

Solomon DA, Keitner GI, Ryan CE et al. (2008) Preventing recurrence of bipolar I mood episodes and hospitalizations: family psychotherapy plus pharmacotherapy versus pharmacotherapy alone. *Bipolar Disord*, 10:798-805.

Suppes T, Dennehy EB, Hirschfeld RM et al. (2005) Texas Consensus Conference Panel on Medication Treatment of Bipolar Disorder. The Texas implementation of medication algorithms: update to the algorithms for treatment of bipolar I disorder. *J Clin Psychiatry*, 66(7):870-86.

Swartz HA, Frank E (2001) Psychotherapy for bipolar depression: a phase-specific treatment strategy?. *Bipolar Disord*, 3(1):11-22.

Swartz et al. (2006). *American Psychiatric Publishing. Textbook of mood disorders*. Chapter 25.

Vahip I and Kocadere M (2003) İki Uçlu Duygudurum Bozuklukları Sağaltım Kılavuzu. Türkiye Psikiyatri Derneği Yayınları.

Van Gent EM (2000) Follow-up study of 3 years group therapy with lithium treatment. *Encephale*, 26:76–9.

Weiss RD, Griffin ML, Greenfield SF et al. (2000) Group therapy for patients with bipolar disorder and substance dependence: results of a pilot study. *J Clin Psychiatry*, 61: 361–7.

Weiss RD, Kolodziej M, Griffin ML et al. (2004) Substance use and perceived symptom improvement among patients with bipolar disorder and substance dependence. *J Affect Disord*, 79: 279-83.

Weissman M, Markowitz J, Klerman G (2000) *A Comprehensive Guide to Interpersonal Psychotherapy*. New York, NY: Basic Books Inc;

Yatham LN, Kennedy SH, O'Donovan C et al. (2005) Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines for the management of patients with bipolar disorder: consensus and controversies. *Bipolar Disord*, 7(Suppl 3):5-69.

Yatham LN, Kennedy SH, Schaffer A et al. (2009) Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: update 2009. *Bipolar Disord*, 11: 225-55.

Zaretsky AE, Rizvi S, Parikh SV (2007) How well do psychosocial interventions work in bipolar disorder? *Can J Psychiatry*, 52:14–21.

Zaretsky A, Lancee W, Miller C et al (2008) Is cognitive-behavioural therapy more effective than psychoeducation in bipolar disorder? *Can J Psychiatry* 2008; 53: 441–8.