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Bipolar Disorder and Suicide

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1. Introduction

Bipolar disorder (BD) is a chronic psychiatric disorder characterized by remissions and exacerbations of mood disturbances. BD is associated with increased mortality due to the adverse outcomes of medical disorders, accidents and complications of commonly comorbid substance use disorders /Ahrens et al., 1995/. By far, however, the major source of early mortality is a high risk of suicide /Kessler et al., 2005; Tondo et al., 2005/. Suicide behaviour and particularly, committed suicide are among the most tragic events in human life causing a serious changes among relatives and friends as well as imposing a great economic problem for the whole society /Rihmer & Kiss, 2004/. Approximately about one million deaths from suicide are recorded every year and a world-wide number of suicide attempts is estimated to be 10 – 15 millions per annum /Wassermann, 2000/. Reviewing 17 follow-up studies on committed suicide in patients with primary affective disorders, Guze & Robins /1970/ found that about 15% of formerly hospitalized depressed patients would die by suicide. Goodwin & Jamison /1990/ also concluded that 19% of depressed patients (mainly inpatients) died by suicide /Rihmer, 2006/. In their metaanalysis of studies on suicide risk in psychiatric disorders, Harris & Barraclough /1997/ analyzed separately the risk of suicide in unipolar major depression and in BD. They found that the risk of suicide was about 20-fold for patients with index diagnosis of unipolar major depression and the same figure for BD was 15. However, these three studies /Goodwin & Jamison, 1990; Guze & Robins, 1970; Harris & Barraclough, 1997/ cannot provide a precise estimation of separate suicide risk in unipolar and bipolar disorder, that is they overestimate the risk for unipolar depression and underestimate it for BD.

Bipolar disorder is associated with a high frequency of both completed suicides and suicide attempts. Twenty-five percent to 60% of all bipolar patients will have attempted suicide at least once in their lifetime, and 18.9% of deaths among bipolar patients are due to suicide, but with accurate treatment we can prevent suicide risk in 50% of patients /Goodwin & Jamison, 1990/.

2. Epidemiology

2.1 Suicide risk

In the general populations of developed countries, recent rates of completed suicide averaged $0.015 \pm 0.007\%$ annually /Tondo et al., 2005/. Risks associated with major

affective disorders, including BD, are much greater /Baldessarini et al., 2006/. Suicide rates among patients diagnosed with BD (mostly BD-I), as well as in severe forms of recurrent major depressive disorder, are not only much higher than in the general population but also substantially greater than in association with other psychiatric, substance use, or general medical disorders /Ahrens et al., 1995/. In BD, this risk is annually 0,9% or 30-60 times above the general population rate of 0.015% annually. Suicide accounts for 15% to 20% of deaths among BD patients /Tondo et al., 2005/. In addition, BD is associated with 2-3-fold excess of mortality due to common, stress-sensitive general medical disorders /Hawton et al., 1998/. Suicide risk factors can be classified hierarchically /Rihmer & Kiss, 2004, table 1/.

<div><div>1. Primary (psychiatric-medical) suicide risk: major psychiatric illness (depression, schizophrenia, substance use disorders)/ comorbid anxiety an/or personality disorders, serious medical illness, feeling of hopelessness and insomnia, concomitant anxiety; previous suicide attempts; communication of wish to die/ suicide intent (direct or indirect; suicide among family members (biological and/or social “inheritance”); disregulated serotonergic system, low total serum cholesterol, abnormal dexamethasone suppression test during depression – competence: health-care</div><div>2. Secondary (psycho-social): childhood negative life-events (separation, parental loss, etc.); isolation, living alone (divorce, separation, widowhood, etc.); lost of job, unemployment; severe acute negative life-events (loss of close relative or friend, recent unemployment, etc.) – competence: community leaders, teachers, psychologists, religious and civil organizations, health-care</div><div>3. Tertiary (demographic) suicide risk: male gender; adolescent and young males, old age (both genders); vulnerable intervals (spring/early summer, pre-menstrual period, etc.); minority groups (relatives of suicide victims of disasters, bisexuality, same-sex orientation, etc.) – competence: ?</div></div>
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Table 1. Hierarchical classification of suicide risk

Suicide attempts are very common, in about a third to a half of these individuals /Scott, 2005/. In the general population, the attempts: suicide ratio ranges between 20:1 and 40:1, with some uncertainty owing to unreliability and probable under-reporting of suicide attempts /Baldessarini et al., 2006; Hawton et al., 1998/. The risk of suicide attempts among BD patients averages 3, 9% annually or nearly 3-time higher than the rate of completed suicides. The suicide ratio may indicate relatively high lethality of suicide attempts in BD, presumably reflecting both level of intent to die and the lethality of methods used.

Recent results showed that about 50% of unipolar depressions were found to be bipolar depressions after careful and skillful probing for past hypomania or mania as well as focusing on not only mood but also overactivity /Benazzi & Akiskal, 2003a; Ghaemi et al., 2000/. Unfortunately, the risk of suicide is particularly high in bipolar patients during the first few years of illness, whereas diagnosis and establishing a sustained program of long-term, mood-stabilizing treatment is typically delayed by 5-10 years from illness-onset /Baldessarini et al., 2006/. Such delays often are longer in women and in bipolar II

disorder than in men and in bipolar I disorder /Baethge et al., 2003/. This delay underscores the need for much earlier diagnosis and treatment especially in juveniles, since delay of treatment may increase suicidal risk /Faedda et al., 1995/. Suicide rates in bipolar patients are also characterized by high lethality of suicide attempts: one death out of three attempts, compared to one completed suicide out of 30 attempts in the general population /Aubry et al., 2007/.

Analyzing the clinical characteristics of 230 inpatients with recurrent major depression, Bulik et al. /1990/ found that bipolar II diagnosis was significantly more frequent among the 67 patients who attempted suicide (19%) than in the 163 patients who did not attempt suicide (9%). Dunner et al. /1976/ reported that 3% of the 73 unipolar, 6% of the 68 bipolar I and 18% of the 22 bipolar II patients died by suicide during their 1-9 year follow-up study. Considering all the above, the findings strongly suggest that bipolar II patients might be overrepresented among suicide victims. The two published reports where the prevalence of bipolar II, bipolar I and unipolar depression have been analyzed separately among the suicide victims show that among the 125 consecutive suicide victims with primary major depression at the time of suicide, 44% had bipolar II depression, 2% had bipolar I depression and 54% had first episode or recurrent unipolar depression /Rihmer et al.1995, Rihmer et al. 1990/. Because the lifetime prevalence rates of DSM-III/IV bipolar II illness in the population are relatively low compared with unipolar major depression (2-5% and 15-17% respectively) /Angst, 1998/, these results suggest that bipolar II disorder imparts a particularly high risk of committed suicide among the three different subgroups of major mood disorders. /Rihmer, 2006/.

2.2 Risk factors

In the general population and in unipolar MDD patients, suicide rates are several times higher in men, but in BD patients, the risk is much more similar among men and women /Baldessarini et al., 2006/. Other risk factors for suicide generally, including in BD, in addition to current depression, include white ethnicity, being unmarried, previous severe depression or suicide attempts, current feelings of hopelessness and active abuse of alcohol or illicit drugs, and perhaps limited access to support or clinical services /Tondo et al., 2006/. Stress factors also can contribute to suicidal risk, including deaths, divorce, separations and other major losses, scandals or imprisonment, social isolation.

Interpretation of analyses of risk factors associated with suicide is limited by not knowing of potential suicides that may have been prevented by timely assessment and effective interventions. Although screening of BD patients for the risk factors just summarized has uncertain power to predict specific risk and timing in individuals, their consideration is an important component of clinical assessment of suicidal risk /Jacobs, 2003/. Such clinical unpredictability can be especially challenging with BD patients, given sometimes rapid shifts in mood (lability), strong reactivity to losses, frustrations, or other stressors, impulsivity, disinhibiting effects of commonly abused central depressants, including alcohol, comorbid anxiety disorders, and potential adverse effects of excessive use of antidepressants /Ghaemi et al., 2004/. The most powerful and clinically explorable suicide risk factors in BD are listed in Table 2.

1. Family history of suicide in first degree relatives
2. Past history – previous suicide attempts: high lethality / violent > low lethality / nonviolent
3. Diagnostic subtype: bipolar II > bipolar I (> unipolar); hypomania, mania
4. Clinical features: severe depression, hopelessness, guilt, agitation, thinking of death, suicide intention, etc.; comorbid anxiety disorder, substance use disorder, personality disorder, serious medical illness; mixed states (dysphoric mania, depressive mixed states); aggressive personality features
5. Psychosocial stressors – negative life events: adverse life events (death of close persons, unemployment, marital breakdown, etc.).

Table 2. Suicide risk factors in bipolar disorders

2.2.1 Family history

Family history of suicide is a significant risk factor for suicide behaviour, particularly in persons with BD. If a patient has a family member who suffers from affective disorders or alcoholism, or had one who committed suicide, very careful clinical attention should be given. Inquiries should be made into the patient’s history of affective disorders or alcoholism /Takahashi, 1993/. Bipolar patients with positive family history of suicide in first-degree relatives were found to be significantly more likely to attempt suicide (38%) than those without (14%) / Roy, 1983/ and it has been reported that 0,9% of unipolar depressives, 1,8% of bipolar I and 2,9% of bipolar II patients had a family history of committed suicide /Dunner et al., 1976/. Another study has found a 6,5-fold higher rate of suicide committed among the first-degree relatives of 129 bipolar II (3,9%) than that of the 188 bipolar I (0.6%) patients /Tondo et al., 1998/. Investigating the family history of suicide in first degree relatives among 85 inpatients with DSM-III-R major depression (28 bipolar II, 57 unipolar), Rihmer /2006/ finds that the rate of persons with positive family history of completed suicide was significantly higher in bipolar II than in unipolar patients (21% vs 9%).

2.2.2 Past history – Prior suicide attempt

It is well documented that attempted suicide (particularly in the case of affective disorder) is among the most powerful predictor of committed suicide /Cheng et al., 2000; Wassermann, 2000/. Up to 55% of suicide victims with BD have had at least one previous suicide attempt and every fifth patient with BD dies by suicide /López et al., 2001/. As shown above, with regard to the specific subtypes, it is particularly bipolar II patients that are at the highest suicide risk /Vieta et al., 1997; Mořovský, 2009/. The clinician must not neglect to ask whether the patient has attempted suicide in the past. One out of 10 who have attempted suicide will make another attempt and will die by suicide /Stengel, 1964/. Lay people often insist, “Those who say that they will kill themselves will never do so,” which is a commonly believed myth. As stated before, Japan’s suicide rate is 17, 8 per 100 000 among the general population; therefore, among those who have attempted suicide once, the rate is 540 times higher. Some researchers have pointed out that a history of attempted suicide is the most reliable risk factor for suicide. Any form of suicide attempt should be taken seriously.

Detailed information should be collected about any suicide attempt. Was the attempt carried out in a place that would make discovery difficult? Was the detailed plan for suicide premeditated? Were any warning signs conveyed to friends or acquaintances? Did the person write a suicide note? If the person has attempted suicide by violent methods, such as firearms or hanging, the subsequent suicide risk should be considered higher than with nonviolent methods. Persons who have recently experienced another's suicide have a higher suicide rate. Especially, those who fulfill other risk factors, experience other suicides directly or indirectly through the mass media, and identify themselves with other suicides tend to become suicidal suddenly. The danger of so-called suicide cluster is great, particularly among adolescents / Takahashi, 1993/.

2.2.3 Diagnostic subtype

Analyzing the specific diagnostic subtypes of 69 consecutive (nonviolent) suicide attempters with current DSM-IV major depression in Budapest, Hungary, it has been found that 45 (65%) had unipolar major depression, 19 (28%) had bipolar II depression and 5 (7%) had bipolar I depression /Balász et al., 2003/. Considering the fact that the lifetime prevalence rates of DSM-III-R unipolar major depression, bipolar II and bipolar I disorder in the general population of Hungary are 15, 1%, 2, 0% and 1, 5% respectively /Szádóczy et al., 1998/, this study suggests that bipolar II patients are relatively overrepresented not only among depressed suicide victims but also among depressed suicide attempters. Bipolar patients with comorbid anxiety, personality and substance-use disorders are also at an increased risk of attempted or completed suicide /Chen & Dilsaver, 1996; Vieta et al., 1997/. One of the major sources of the highest suicide risk in bipolar II patients may be the very high rate of comorbid anxiety disorders /Akiskal, 1981; Brieger, 2000/ and depressive mixed states, frequently called "agitated depression" /Benazzi & Akiskal, 2003b/.

2.2.4 Clinical features

Major depressives with history of suicide attempts or committed suicide have a more severe symptomatology in general /López et al., 2001/, are more frequently agitated /Fawcett, 1997/, report more hopelessness, self-blame and guilt /Bulik et al., 1990; Oquendo et al., 2000/ and experience more commonly marital isolation (being single, separated or divorced) and/or loss event than non suicidal depressives /Bulik et al., 1990; Cheng et al., 2000/. It is also well documented that major depressives as well as bipolar patients with comorbid anxiety disorders /Fawcett, 1997; Hawton & van Heeringen, 2000/, substance use disorders /Cheng et al., 2000; Hawton & van Heeringen, 2000/, personality disorders /Cheng et al., 2000; Hawton & van Heeringen, 2000/ or serious medical illness /Cheng et al., 2000; Hawton & van Heeringen, 2000/, are also at an increased risk of attempted or committed suicide. One of the major sources of the highest suicide risk in bipolar II patients may be the very high rate of comorbid anxiety disorders /Akiskal, 1981/ and substance use disorders /Rihmer et al., 2001/. In a study aimed at identifying clinical predictors of suicide attempts in subjects with BD, Dalton et al. /2003/ studied 336 subjects with a diagnosis of bipolar I, bipolar II, or schizoaffective disorder (bipolar type) and examined predictors of suicide in attempters and nonattempters. They found that the lifetime rate of suicide attempts for the entire sample was 26.7%. Bipolar subjects with comorbid substance-use disorder had a 39.5% lifetime rate of attempted suicide, compared with a 23.8% lifetime rate

for those without substance-use disorder. The researchers concluded that lifetime comorbid substance-use disorder was associated with a higher rate of suicide attempts in patients with BD.

Leverich et al. /2003/ at the Stanley Foundation Bipolar Network asserted that "to the extent that bipolar illness puts teenagers and young adults at risk for the accumulation of comorbidities, it seems appropriate to pay attention to these and other factors associated with suicide attempts so that some of these elements might be prevented or ameliorated". In an investigation of the association between suicide attempts and the predictive factors previously described in the literature, researchers followed 169 patients identified with bipolar I disorder /Purifacion et al., 2001/. More than one third (56) of the patients had a history of 1 or more suicide attempts. The rate of suicide attempts was much higher in patients with onset of bipolar disorder at or before the age of 25 years than in patients with onset after age 25 (25% vs 10%, respectively). Other factors related to suicide were drug abuse, family history of affective disorders, and severe depressive episodes. The patients who abused drugs had a history of more suicide attempts than those who did not.

2.2.5 Psychosocial stressors – Negative life events

Various life stresses include financial loss, loss of position, physical illness and trauma, death of a relative, and lawsuit, unemployment, major financial problems as well as adverse recent life event (including recent loss of a loved person) have been shown to be a risk factor for attempted and completed suicide/Cheng et al., 2000; Hawton & van Heeringen, 2000/. More than half of completed suicides in both bipolar I and unipolar affective disorders are associated with recent negative life events, but the stressors are commonly dependent on the victim's own behaviour, particularly in the case of bipolar I disorder /Isometsä et al., 1995/. It might be the consequence of the fact that hypomanic or manic periods easily can result in aggressive behaviour, financial extravagance, episodic promiscuity, generating interpersonal conflicts and marital breakdown /Akiskal, 1981; Goodwin & Jamison, 1990/. Loss of a family member or friend is often followed by grief-reaction, that later can develop into complicated grief /Horowitz et al., 1997/ and into major depression. Lack of social support system is also an important risk factor. People who are single, divorced, separated, or recently left by significant others show a threefold higher suicide rate than those who are married /Takahashi, 1993/. Those who are excluded from a group in society are also reported to have a higher suicide rate. In a study of 32,000 bipolar patients' records /Simon et al., 2007/ the highest risk factor for suicide was being male and having a comorbid anxiety disorder, compared with being young and having a substance-use disorder, which predicted attempts but not necessarily suicide.

3. Specific situations – The high suicide risk

Because specific subtypes of major affective disorder (unipolar, bipolar II and bipolar I) differ from both clinical and research perspective, it is logical to assume that each subgroup might have its own different suicide risk. Current mood states are critical determinants of suicidal risk in BD, particularly depressive and dysphoric-irritable mixed states, which together account for at least three-quarters of suicides in BD, whereas suicide is infrequent in mania and rare in hypomania /Baldessarini et al., 2006; Jacobs, 2003/.

3.1 Mixed states

Mixed episode is a complex syndrome which is difficult to diagnose, has the most prolonged duration of bipolar episodes and more frequent psychotic profile than pure mania with high suicidality and poor response to drugs. Mixed state mania has been well known since Kraepelin in classification systems with criteria that include both a manic and major depressive episode nearly every day for at least a one-week period /Oral, 2005/.

With its relatively high incidence rates, bipolar disorder constitutes a considerable health problem not only for the individual patient and his/her family but also for the economy. Individual patients are in danger of suicidal acts, especially in the depressive phase and with mixed mania which, in its mild form, i. e., with less depressive features, is also known as "dysphoric mania". In studies of this affective mixed state by Strakowski et al. /1996/ 26% or even 55% in another study, of the patients were judged to be in acute danger of suicide. About 25-50% of all bipolar patients make at least one attempt at suicide in the course of their illness. In this respect, women are affected more frequently than men. During the ten-year observation period of a Scottish study, the suicide rate in patients with BD was 23fold higher than that of the general population; the most of the suicides occurred relatively early in the illness, namely between the second and fifth year after diagnosis. A particular, additional risk factor was living alone or in separation; also most suicide victims came from the lower social classes. This has not inconsiderable social- political implications against the background that divorces among bipolar patients are three times more frequent than in the general population and that the manifestation of BD is not coupled to any particular social class. On the contrary, on average families of bipolar patients have higher educational and income levels than the families of unipolar depressive patients /Walden & Grunze, 2004/.

The importance of depressive mixed states in predicting suicide is supported in long-term naturalistic follow-up study of moderately to severely ill affective disorder patients (80% of them were inpatients at the index episode) they found that 39% of those who later committed suicide (n=36) as well as 220% of the nonsuicidal comparison subjects (n=373) were in mixed or cycling depressive episode at intake /Maser et al., 2002/.

Among bipolar patients, however, it is not the depressive episode that is the only risk period for suicide. In contrast to classical (i. e. euphoric) mania, where suicidal tendency is extremely rare, suicidal thoughts and attempts are relatively common in dysphoric (mixed) mania or hypomania /Strakowski et al., 1996/.

3.2 Short depressive episode

The so-called recurrent brief depression consists of recurring, short depressive episodes (as rule not longer than two weeks). Frequently 8 or more episodes can occur in 1 year. These short depressions are generally difficult to treat with usual mood stabilizers or antidepressants. The average duration of an episode amounts to 3 days. About 5% of the population is assumed to suffer from these short-lasting depressions. Above all, the irregular rhythm and the unpredictability of the depressions are a serious problem for the afflicted subjects. Accordingly, the danger of suicide is particularly high in this group. It is assumed that this is a separate clinical entity and that the recurrent brief depression does not belong directly to the bipolar spectrum /Walden & Grunze, 2004/.

3.3 Postpartum psychosis

Postpartum psychosis (PPP) is a medical emergency that occurs in 1-4 of every 1000 postpartum women. Though rare, this is the condition that makes for horrifying national headlines: There is a risk of infanticide in 4% of these cases. There is also a significant risk of maternal suicide.

3.3.1 Recognition of PPP

Prompt recognition and treatment of this disorder are paramount. Symptoms of PPP begin 3 to 14 days after delivery 75% of the time. Another 10% of cases will have occurred by one month after delivery. Early symptoms can mimic postpartum blues or postpartum depression, with sleep disturbance, depression, hypomania or fatigue. Rapidly, the symptoms of agitation, hyperactivity, insomnia, confusion, hallucinations, delusions, volatile mood shifts, bizarre behaviour and panic develop. PPP has a strong genetic component. There is controversy over whether it is a distinct entity or a bipolar episode. If the latter, is the bipolar episode genetically prompted by childbirth, simply occurring as a response to stress, or coincidentally occurring after delivery? Whatever the case, if a woman is affected with BD and has a family history of a relative who had PPP, she has a 75% chance of incurring PPP herself. If she is affected with bipolar but has no family history of PPP, her chance of PPP falls to 30%. A large population study in 1987 found that women with BD were hospitalized more often for PPP than were women who had a history of schizophrenia or depression. The identified risk factors included being unmarried, having a first baby, undergoing a caesarean delivery, and infant death.

3.3.2 Treatment of PPP

Treatment of postpartum psychosis begins with hospitalization. Even with the use of medication, hospitalization can be lengthy. Therefore, ECT, which often results in more rapid symptom remission, can be useful, because there's less time lost for the mother-infant bonding process. In some cases, ECT and medication will be prescribed. ECT is safe, rapidly effective, widely recognized treatment for a medical emergency /Finn, 2007/.

A women who is affected by bipolar disorder at the age of 25 years (which corresponds to the average age): has her life expectancy reduced by the 9 years; loses 12 years of normal, healthy life, an also loses 14 years of normal professional and family life /Walden & Grunze, 2000/.

3.4 Suicide in bipolar children and teens

3.4.1 Symptoms and factors of suicidal behaviour

Suicide is the most severe complication of BD /not only in children and teens/. Death wishes or suicidal thoughts are commonly seen in a young person with BD, particularly when he or she is depressed or is in an episode of mania (especially during a mixed or psychotic state). In fact, high school students with BD have more suicidal thoughts (44%) and poorer functioning ((74,9%) than youth with major depression (22,2% and 83,6%) (without mania or hypomania) or healthy teens (1,2% and 87,5%) /Lewinsohn et al., 1995/. Depressed children may see themselves, their surroundings, and their future negatively.

Some describes depression as “wearing dark glasses” a state in which everything is seen pessimistically. A depressed person may feel hopeless and wish to be dead. A child with a mood disorder may experience a negative event(s) such as abuse; a fight with a friend; the death of the friend, relative or pet; or exposure to violence. This negative event may cause this child’s mood to worsen, and he or she may become very hopeless. If the child does not have the skills to cope with the stress and/or does not have support, he or she may consider suicide as solution for the problem. If the person who is considering suicide becomes desperate and has an available method, like a gun or drugs at home, he or she may use the gun, overdose, or try to commit suicide with other methods. The use of alcohol and drugs; the presence of impulsivity, ADHD, or conduct disorders; or a family history of suicidal behaviours in a depressed person increases the risk of suicide. On the other hand, good coping skills, support, spirituality, consideration of others’ reactions to suicide, and no access to a method of suicide diminishes the risk for suicide.

3.4.2 Recognizing and management of suicidal behaviour

Suicidal ideation includes thoughts about wishing to kill one-self, making plans of when, where and how to carry out the suicide and thoughts about the impact of one’s suicide on others. Suicidal attempts involve any behaviour that is intended to end the person’s life. Suicide attempts are much less common than suicidal ideations. The most common method used to attempt suicide in the United States is by overdosing with over-the-counter or prescribed medications. Other common methods include superficial cutting of the arms or neck, but the method used depends on the availability of the method, opportunity and local customs. Suicidal attempts are more frequent in children and adolescents with psychiatric disorders, especially depression and BD, but it can occur in youth with other psychiatric disorders. Also, it can happen after a stressful situation even if the child does not have psychiatric problems. It is more common in Caucasian males but it has been steadily increasing in African-American males. Approximately 90% of teens who commit suicide have a psychiatric disorder, including BD, major depression, conduct problems and abuse of alcohol and illicit drugs. Suicide is more common in those youth who have tried to attempt suicide, have a family history of mood disorders or suicide and in those who have experienced stressful life situations such as physical and sexual abuse /Shaffer & Pfeffer, 2001/. Even mild suicidal attempts may be indications that the child is at serious risk for committing suicide. It appears that suicidal attempts and completions are more frequent in bipolar disordered youth than in other psychiatric disorders. In a study of high school students /Lewinsohn et al., 1995/, 40% of bipolar teens had at least one suicide attempt in comparison with 20% in teens with unipolar depression and 1% in youth without any psychiatric disorder.

Steve Edwards and colleagues published a simple and straight-forward guide for general medical practitioners to better recognize and respond to suicidal behaviour in youth /Edwards & Pfaff, 1996/. Their core concepts have been developed over many years of clinical practice with young people and have been utilized previously in a wide range of medical and allied health settings. Edwards and colleagues recommend the 4R’s principles – a “ticket of entry” for parents and others wanting to help an emotionally distressed youth by recognizing and responding to suicidal behaviours. The 4R’s include: A/ Recognizing of signs, B/ Raising the issue, C/ Realizing the risks, D/ Responding.

- a. The following signs or symptoms should alert parents (teachers and other relatives) that their children may be at risk to develop suicidal thoughts or attempts: persistent symptoms of depression, BD, conduct problems, anxiety disorders, abuse of illicit drugs or alcohol, psychosis (hallucinations or delusions), borderline personality disorder, past or present attempts of suicide, recurrent suicidal ideation, male sex and older than 14 years old. The risk of suicide further increases if in addition to one or more of the above noted signs your child has or more of the following problems: psychological, social or academic problems: poor school performance, employment problems, few or no friends, legal problems, frequent conflict with others (friends, family, teachers), poor coping and problem-solving skills, family or environmental stressors: physical or sexual abuse, neglect, interpersonal loss (girl-or boyfriend, death in the family), rejection by others, family history of mood disorders or suicide, exposure to stress and conflicts in his/her neighborhood/school, exposure to media (e. g. television, radio or newspapers) glorifying suicide, physical health: poor physical health (chronic illness, AIDS, cancer), availability of method (e. g. guns at home, pills).
- b. Some “myths” regarding suicide that you should know: Talking about suicide give the child ideas about suicide.
Not talking about suicide or minimizing the talk about the ideas of suicide will distract the child and he or she forgets about it.
Children or adolescents who talk about suicide are manipulating or seeking attention.
It is important show children that our main goal is to help and protect them.
- c. The lack of hope or “no light at the end of the tunnel” indicates that the child is thinking that there is no way out of his troubles and he or she may be seriously considering committing suicide. Youth that cannot cope with stressful situations and cannot find solutions for their problems may become more hopeless when confronted with a stressful situation and try to commit suicide. In contrast, certain protective factors such as religious beliefs, caring about the effect of suicide on his/her parents, siblings and friends, and having a strong support system may delay or stop the suicidal behaviour. Finally, having an available method (e. g., guns, pills) increases the risk that a person who is thinking about suicide will use the method. Additionally, the suicide risk is greatest for bipolar patients: during a depressive or mixed episode, while transitioning from the manic/hypomanic state to the depressive state, immediately following psychiatric hospitalization, particularly if the admission to the hospital was due to suicidal ideation or attempt /Birmaher, 2004/.
- d. It is important to carefully monitor child. If child was hospitalized due to suicidal behaviours, after his or her discharge from the hospital it is important to have prompt follow-ups because most suicide attempts occur during the first months after discharge from the hospital. The treatment of suicide includes psychosocial therapy and medications depending on the underlying psychiatric disorder and the circumstances around the suicidal attempt. Specific studies to have shown that cognitive-behavioural therapy (CBT), interpersonal psychotherapy (IPT) and psychodynamic psychotherapy are ball options for the management of a suicidal youth but further studies are necessary /Brent et al., 1997/. Studies on the efficacy of lithium for suicide in children and adolescents are needed. Importantly, lithium (and other medications) should not be self-administered by suicidal youth because it is very dangerous in case of an overdose.

The use of medications that may increase disinhibition or impulsivity, such as the benzodiazepines, should be prescribed with caution because they may increase the risk for suicide and are dangerous in the case of an overdose. It is important to mention that in cases where a child has committed suicide, his or her relatives, friends and teachers may benefit from psychotherapy to facilitate grieving, reduce guilt and depression, and decrease the effects of guilt. Having the traumatic experience of a significant other committing suicide is often helped through psychotherapy. Moreover, the psychosocial interventions may minimize the risk of imitative or copycat suicides /Shaffer & Pfeffer, 2001/.

4. Treatment

Since suicide is a multicausal human behaviour with many biological, psychological and cultural components, its prevention should also be complex, even in the case of bipolar disorder which is the "most biological" illness in the field of psychiatry and which requires long-term pharmacotherapy in the majority of the cases. Since bipolar disorders usually show a peak onset between 15 and 25 years of age, but there is 8-10 years of delay in correct diagnosis /Akiskal, 2002; Ghaemi et al., 2000; Goodwin & Jamison, 1990/, early detection of bipolarity, the nature of the disorder, including the soft manifestations as well, is the first step in suicide prevention. Misdiagnosis of bipolar depression as unipolar depression results in treatment with antidepressants alone, and this can have negative effects on the course of the illness, because of inducing mixed depressive episodes, hypomanic or manic switches, rapid cycling and therefore increasing the chance of suicidal behaviour /Rihmer, 2006; Benazzi & Akiskal, 2003/.

Effective acute and long-term treatment has a strong protection against suicide and probably against other complications (secondary substance-abuse disorders, marital instability, loss of job, cardiovascular mortality, etc.) /Rihmer, 2006/. Intensive treatment including pharmacotherapy, psychotherapy, especially cognitive-behavioural therapy and electroconvulsive therapy should be conducted.

Schwartz & Thase /2011/ examined all randomized trials evaluating the use of pharmacotherapy in the treatment of acute bipolar II depression. Studies with mixed samples of bipolar I and II or bipolar II and unipolar depression were examined as well. Twenty-one randomized trials were identified and reviewed. Therapeutic agents were rated according to the quality of evidence supporting their efficacy as treatments for bipolar II depression. Ninety percent of relevant trials were published after 2005. Quetiapine was judged as having compelling evidence supporting its efficacy. Lithium, antidepressants, and pramipexole were judged as having preliminary support for efficacy. Lamotrigine was considered to have mixed support. Although progress has been made, further research on bipolar II depression is warranted.

4.1 Psychopharmacological therapy

While successful acute pharmacotherapy of depressive or mixed episodes can only prevent the risk of suicide connected with a given episode, it is adequate prophylactic therapy that can provide long-term results in patients with BD.

4.1.1 Lithium

Long-term treatment with lithium provides more consistent and compelling evidence of reduced suicidal risk than any other treatment. The efficacy of lithium in the treatment of manic states and in prevention of recurrences of bipolar patients is well documented /Goodwin & Jamison, 1990; Maj et al., 2000; Bowden, 2002/, and recent data indicate that combination of lithium (and other mood-stabilizers) with antidepressants reduces the chance of hypomanic or manic switching when bipolar depression is treated with antidepressants only (Henry et al., 2001). However, about 50% of bipolar patients do not show satisfactory prophylactic response to lithium. The identification of certain factors predicting a good response versus a partial or non-response to lithium treatment has been made possible by the data that has emerged from research protocols as well as from clinical practice /Bowden, 1998; Swann et al., 1999/. These predictors include a good response to lithium a previous treatment for a manic state, a 'pure' (that is to say, euphoric) manic episode, only a small number of episodes previous to the current episode, absence of rapid cycling, absence of psychotic characteristics, no substance abuse, a manic episode that is for the most part moderate, positive family history of bipolar illness, early onset, mania-depression interval type of course predicts a good prophylactic response, while higher frequency of episodes, depression-mania interval type of course, dysphoric mania, rapid cycling, comorbid substance-use disorders, late onset of manic episodes and mania secondary to a somatic problem; indicate partial or non-response /Aubry et al., 2007; Rihmer, 2006; Bowden, 2002; Maj et al., 2000/. Tondo et al /1997/ concluded that the risk of suicide is seven times higher in patients who are not taking lithium than in those who are. Even emphasizing that the patients were not assigned to the two groups in a random manner in these studies and differences can be observed in the severity of the disorder and/or the compliance of the patients in the two groups, the results are still impressive. In another study, Tondo et al. /1998/ evaluated the risk of suicide before, during and after lithium treatment in 310 bipolar patients. Again the authors demonstrated that the risk of suicide was about 6,5 times lower when a lithium maintenance treatment was administered /review in Baldessarini et al., 2002/. In a meta-analysis of 32 randomized trials comparing lithium, placebo and other active treatments, Cipriani et al. /2005/ found that patients who received lithium were less likely to die by suicide. However, this conclusion has been challenged because one study giving a strong argument for a protective effect of lithium was misunderstood /Connemann, 2006/. Kessing et al. /2005/ reported the results of a nationwide survey in Denmark including about 13 000 patients who purchased at least one the rate of suicide decreased with the number of prescriptions of lithium. Although this study adds to prior evidence that continued lithium treatment is associated with reduced suicide risk, this risk is still considerably higher (about 10 fold) than the rate for the general population. To date, it remains difficult to determine when lithium's preventative effect on suicide takes effect, but it has been reported that this effect was already noticeable in the months following the start of lithium treatment /Dunner, 2004/. Some studies /Kessing et al., 2005; Baldessarini et al., 2006/ include cases of recurrent major depression or schizoaffective disorders as well as a majority of bipolar disorder patients and so are represent manic depressive disorders broadly. There is a nearly four-fold lower relative risk of suicide attempts, and over nine-fold lower risk of suicides, during lithium treatment, and the attempt rate with lithium is only twice that estimated for the international general population, whereas the suicide rates remains 10-times above the general population risk.

Of some importance, the ratio of attempts to suicides, a proposed index of lethality (of intent or means) of suicidal behaviour, is low in manic depressive disorders patients without lithium treatment, and 2,5-times higher with lithium treatment, suggesting decreased lethality with lithium treatment. Moreover, risk increases soon after stopping lithium, especially abruptly /Baldessarini et al., 2006/.

We found the presence of suicidal thoughts and attempts in inpatients with BD (DSM-IV) and assessed changes of treatment with lithium over the period of time /Breznoščáková et al., 2009/. It was retrospective survey of 125 in-patient's file hospitalized at the 1st Dept. of Psychiatry, University of P. J. Šafárik, Košice (1997 - 2007) with typical limitations for restrospective case survey. The average age was 31 years at all, but during first hospitalization 24 years /Tab. 3/. The first episode was depressive in 62% of patiens and average number of episodes was 7, 6 /Tab. 4/. It was trend of decrease in use of lithium over the time (68% vs 84% in men, 29% vs 60% in women).

N=125	men	women	together
Average age during last hospitalization in years	35,4	26,2	30,8
First hospitalization - average age	25,2	23,3	24,1

Table 3. Average age and the 1st hospitalization

	men	women	together
Average number of episodes	8,8	6,7	7,6
The number of depressive episodes	5,0	3,3	4,1
The number of manic episodes	3,3	1,9	2,6
The number of mixed episodes	0,5	1,5	1,0

Table 4. The number of episodes

The average dose of lithium in men was 1, 7g and serum lithium concentration: 0, 65 mmol/l; in women average dose of lithium: 1, 3g and serum lithium concentration: 0, 7 mmol/l /Fig. 1/. During depressive episode given average dose of lithium was 1, 29 g and average serum lithium concentration was 0, 98 mmol/l in men. During depressive episode was given average dose of lithium 0, 57g and average serum lithium concentration was 0, 64 mmol/l in women/Fig. 2/. Average dose of lithium was 1, 37g and average serum lithium concentration was 0, 48 mmol/l during manic episode in men. Any woman had been treatment of lithium during manic episode, what can be possible to explain only hypothetically that there was preferred treatment with atypical antipsychotics for better and faster onset of effect or for higher risk of side effects.

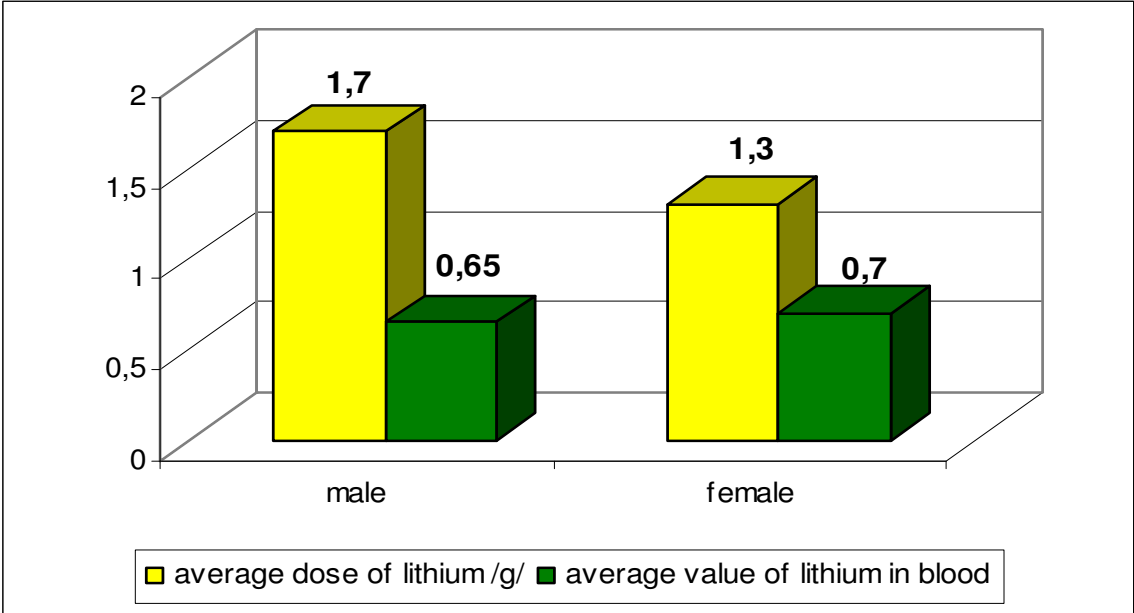


Fig. 1. Dose of lithium/ day(g) and serum lithium concentrations(mmol/l)

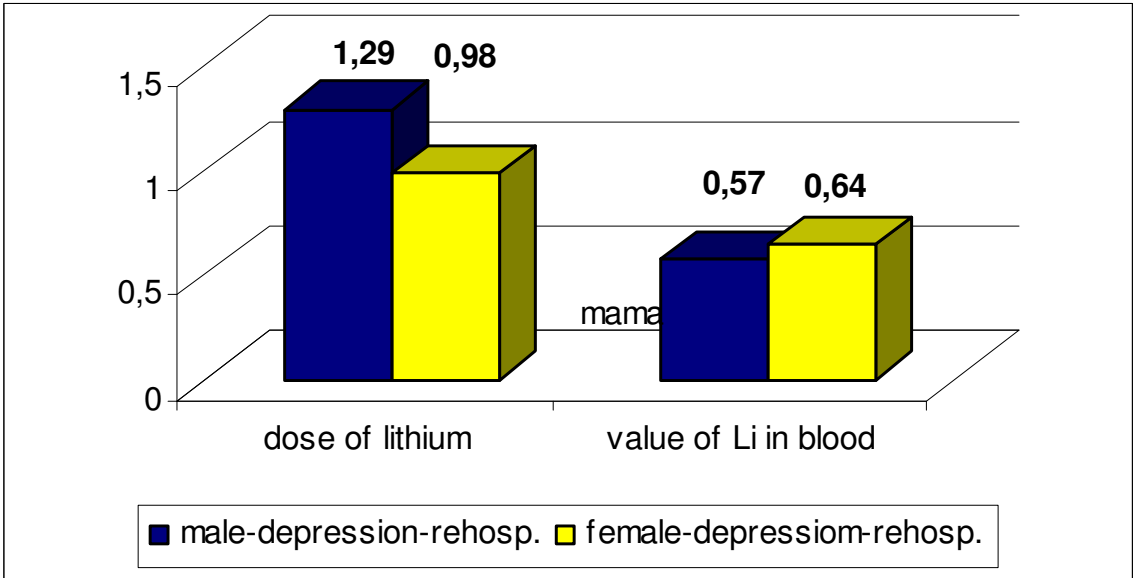


Fig. 2. Dose of Li/Li concentration - depressive episode

The occur of suicidal thoughts was frequent during depressive episode (in 50% of women and 18% of men).

During this time suicidal thoughts occurred in 22 men at all and suicidal attempts in 5 men (the same patient could have suicidal thoughts and attempts, too). We found suicidal thoughts in 62 women and suicidal attempts in 14 women /Fig. 3/. Suicidal thoughts occurred in 24 women without treatment of lithium /from 34/. On the other hand we found higher occur of suicidal thoughts in men with treatment of lithium /19 from 34/. In 20 men /60%/ and in 40 women /79%/ without treatment of lithium were occurred suicidal attempts /Fig. 4/.

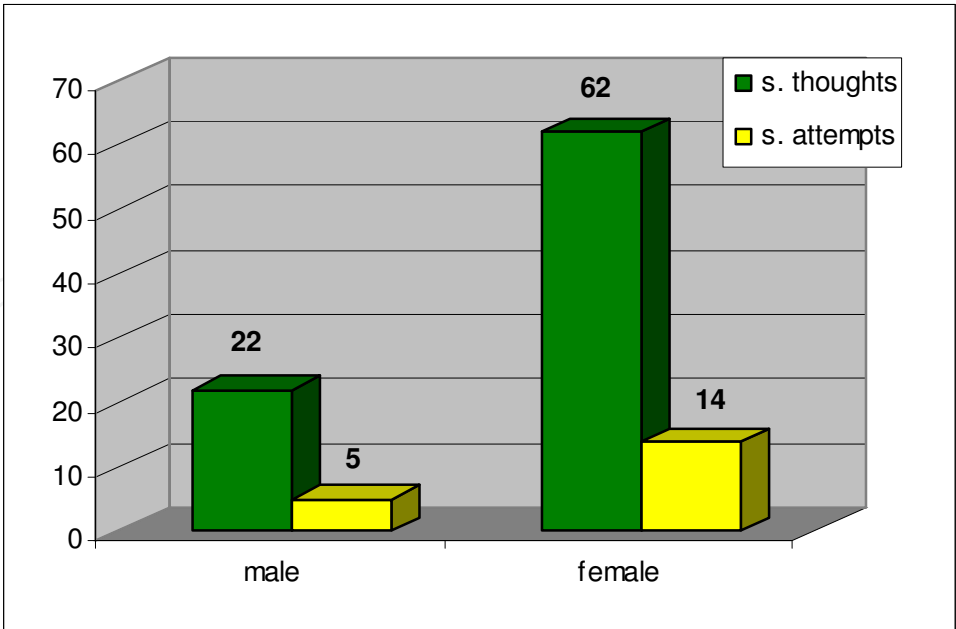


Fig. 3. Frequency of suicidal thoughts and attempts (N=125)

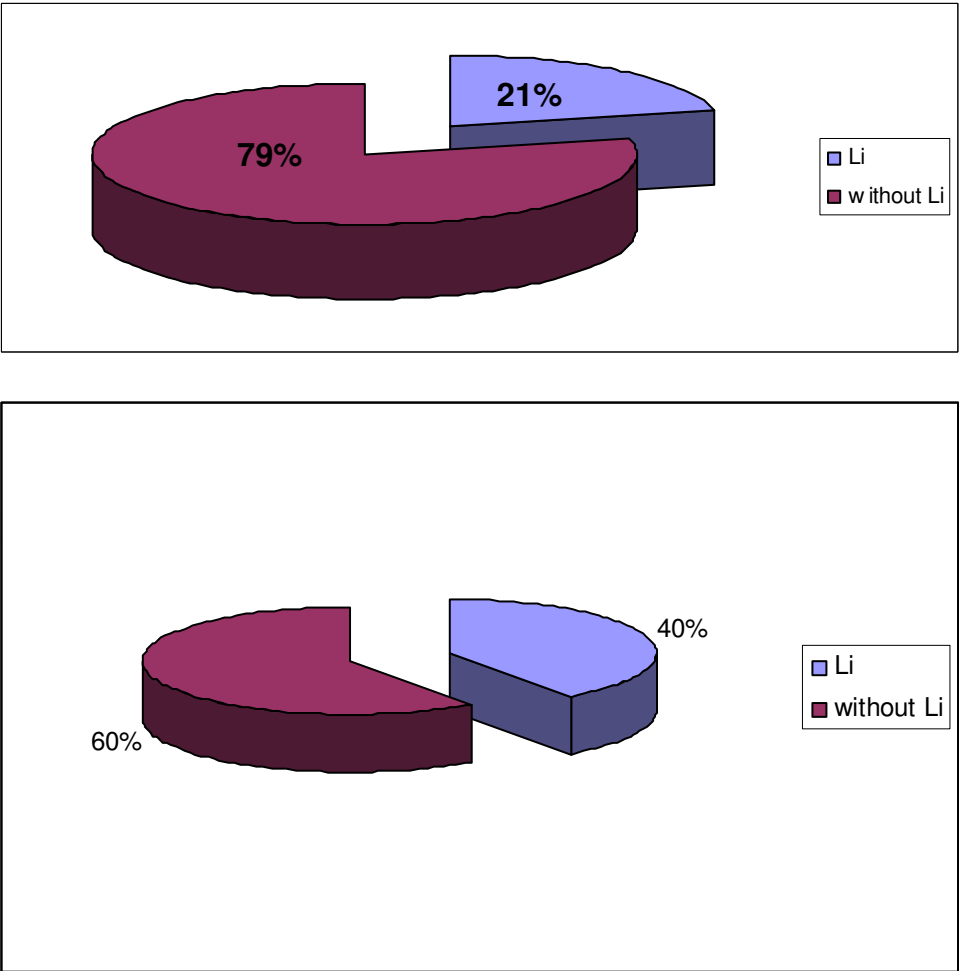


Fig. 4. Suicidal attempts and treatment /men and women/

We can conclude that higher frequency of episodes BD was in men than in women (9 versus 7). The men were taking higher doses of lithium at all /1, 7 versus 1, 3g/ and had lower serum lithium concentrations /0, 65 mmol/l against 0, 7 mmol/l/ as women. We attended trend of decreasing of treatment of lithium in women (29% versus 60%) and men, too (68% versus 84%), what is possible to explain of increasing of use of atypical antipsychotics in role of new mood stabilizers. In 74% of women and 54 % of men are occurred suicidal thoughts, more frequent during depressive episode. Three times more suicidal thoughts and attempts were in women than in men with BD. We found 1, 5 times higher occur of suicidal thoughts in women with BD without treatment of lithium. One of the most important assignments is fourfold higher occur of suicidal attempts in women without treatment of lithium than in with treatment with lithium.

To summarize, even if the suicide rate in bipolar patients treated with lithium remains higher than in the general population, lithium' s preventative effect on suicide is widely acknowledged /Aubry et al., 2007/.

4.1.2 Other anticonvulsants

Unfortunately, vey few data are available on the antisuicide effects of other anticonvulsants in BD. A few years ago, Goodwin et al. /2003/ published a retrospective study based on the follow-up of more than 20 000 patients treated for BD. They showed that the risk of fatal suicide was 2, 7 times higher in patients treated with valproate than in patients treated with lithium. In a randomized, open-label, perspective, 2, 5-year follow-up study Thies-Flechtner et al. /1996/ investigated the number of suicide events in 175 bipolar, 110 schizoaffective and 93 recurrent depressive patients. The patients were randomly assigned to lithium, carbamazepine or amitriptyline. There were 14 very serious suicide events (9 completed suicides and 5 serious attempts) during the study and 7 out of the 14 suicide acts were among bipolar patients. Most of the 14 suicide acts happened in the carbamazepine group (4 suicides and 5 attempts), and none of the 14 suicidal patients were taking lithium. Most anticonvulsants remain largely unexamined for possible beneficial effects on suicidal behaviour. Nevertheless, there is some evidence that other anticonvulsants may be less effective than lithium against suicidal behaviour /Baldessarini et al., 2006/.

4.1.3 Antipsychotics

Clozapine is the first treatment to receive FDA approval for reducing risk of suicidal behaviours, though only for schizophrenia patients, and without clear evidence of reduced risk of completed suicides /Hennen & Baldessarini, 2005/. This time, ability of antipsychotics to limit risks of suicidal behaviour remains untested.

4.1.4 Antidepressants and electroconvulsive therapy

Suicidal behaviour is particularly strongly associated with acute depressive illness and antidepressants have been proved effective, at least in the short-term treatment of acute, non-psychotic, nonbipolar major depressive disorder of moderate severity /Baldessarini & Tarazzi, 2005/. Adverse behavioural responses to antidepressant treatment in mood disorder patients, including insomnia, restlessness, irritability, and agitation, may well increase risk of aggressive-impulsive acts, perhaps including suicidal behaviour, in some adults and children, and particularly in depressive or mixed phases of BD /Fawcett J, 1997/.

The indication for electroconvulsive therapy (ECT) may exist, besides for refractoriness to drug treatment, also for pregnancy which places restrictions on drug treatment and for patients at high risk for suicide in whom a rapid improvement is required, such as, e. g. in mixed mania. In these cases the early use of ECT can be considered, as well as for severe and, especially, psychotic manias and depressions /Walden & Grunze, 2004/. Nevertheless, effectiveness of ECT for sustained suicide prevention has not been proved, and requires further study, including in BD patients, specifically /Jacobs, 2003/.

4.2 Psychosocial interventions

Rucci et al. /2002/ investigated the lifetime rates of suicide attempts among 175 bipolar I patients during a 2-year period of intensive pharmacotherapy (lithium, valproate, carbamazepine), and one of two adjunctive psychosocial interventions (psychotherapy specific to bipolar disorder or nonspecific intensive clinical management). They found that the patients experienced threefold reduction during maintenance. There was no significant difference regarding suicide attempts between the two subgroups with different psychosocial interventions. It has been reported that successful episode-preventive medication with mood stabilizers in bipolar patients, counteracted dysfunctional cognitions (including lowered self-esteem), and adjunctive cognitive therapy could help to optimize the long-term course of bipolar illness /Wolf & Müller-Oerlinghausen, 2002/. Psychotherapeutic techniques based on problem-solving, rehearsal, and cognitive or behavioural methods may limit suicidal risk in relatively mildly ill depressed patients. It is highly encouraged to make a so-called "emergency plan" for patients, especially with BD /Breznošćáková et al., 2008/.

5. Conclusion

Leverich et al /2003/ referred to bipolar disorder as "the most complex, highly comorbid, and potentially lethal illness among the major psychiatric disorders and far higher than in general population". They concluded that without the healthcare support required to deal with the illness, its associated morbidity and suicidality will continue to have devastating effects on large numbers of individuals and their families. Suicidal acts are likely to occur early in BD illness, and in association with severe depressive or mixed states /Baldessarini et al., 2006/. Acute, serious negative life events can precipitate suicide behaviour in depressed patients especially, who are particularly vulnerable for suicide behaviour. Evidence of long-term effectiveness of treatments against mortality risks in BD is limited, with the notable exception of lithium prophylaxis, which clearly reduces risk of death from suicide and may also limit risk of death from natural causes /Ahrens et al., 1995; Cipriani et al., 2005/. As for suicide prevention, the main target should not only be persons who are acutely suicidal, but all depressive (and other psychiatric) patients. Their treatment should start as early as possible in order to prevent the progression of the illness and the development of suicidal thoughts and behaviour /Rihmer & Kiss, 2004/.

We are, of course, unable to prevent all suicides. However, our present pharmacological and psychosocial interventions are effective enough to minimize the chance of suicide in patients with BD that represents the highest risk of self-inflicted death /Rihmer, 2006/.

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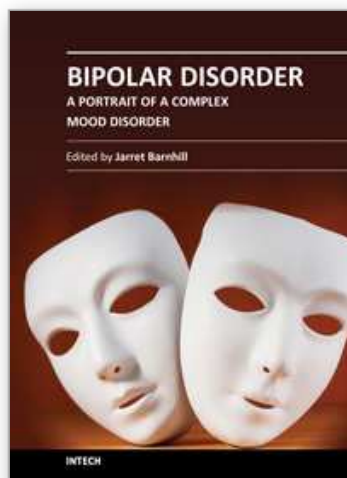
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Bipolar Disorder: Portrait of a Complex Mood Disorder is a step towards integrating many diverse perspectives on BD. As we shall see, such diversity makes it difficult to clearly define the boundaries of BD. It is helpful to view BD from this perspective, as a final common pathway arises from multiple frames of reference. The integration of epigenetics, molecular pharmacology, and neurophysiology is essential. One solution involves using this diverse data to search for endophenotypes to aid researchers, even though most clinicians prefer broader groupings of symptoms and clinical variables. Our challenge is to consolidate this new information with existing clinical practice in a usable fashion. This need for convergent thinkers who can integrate the findings in this book remains a critical need. This book is a small step in that direction and hopefully guides researchers and clinicians towards a new synthesis of basic neurosciences and clinical psychiatry

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