Bipolar disorder
Diagnosis and management  Module 182: October 2012

BIPOLAR DISORDER HAS A PREVALENCE RATE of 1-2% and is associated with considerable morbidity. A careful history and mental state examination should usually establish the diagnosis of a classical manic episode. However, it is important to obtain a collateral history from a reliable informant (e.g., a spouse) as some patients may be able to ‘contain’ their symptoms in a 10-minute consultation and it can be difficult to obtain an accurate history of the manic phase.

While the manic phase of bipolar disorder is the most florid element of the condition, the bulk of the morbidity associated with bipolar disorder is associated with the depressive phase of the illness. It is estimated that one-third of patients with bipolar disorder are misdiagnosed with unipolar depression. One reason for this is that patients with bipolar disorder in the depressive state seek treatment two to three times more often than when in the manic state.

In addition to the core symptom of low mood, the symptoms of depression generally can be remembered by the mnemonic SIG E CAPS: Suicidal feelings, decreased Interest, Guilt, low Energy, poor Concentration, Anorexia (loss of appetite), loss of Pleasure, and Sleep disturbance.

Symptoms, signs and diagnosis
The ICD-10 Classification of Mental and Behavioural Disorders1 and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)2 largely agree on a set of operational criteria of a manic episode. Symptoms need to endure for a minimum of a one-week period, but a shorter duration is sufficient in more marked cases that require hospitalisation.

Psychosis, requiring hospitalisation, reflects more serious manic illness and is seen in type 1 bipolar disorder. Approximately 40% of patients with type 1 bipolar disorder develop psychotic features during the manic phase. (The emergence of psychotic symptoms after the mania resolves would be more consistent with a diagnosis of the related condition schizoaffective disorder).

Type 2 bipolar disorder is the more common form of the condition, and it occurs when depressive spells alternate with hypomanic episodes. Type 2 bipolar disorder is associated with more depressive episodes than seen in type 1.

Both classification systems recognise elevated mood and/or irritability as the core feature of a manic episode. Patients usually describe a state of feeling ‘high’ or ‘hyper’. It is important to recall that depressive symptoms and mood liability may occur in the context of a manic or hypomanic episode, with an elated patient appearing depressed or tearful on occasions. Mixed states can occur, whereby patients simultaneously experience symptoms of both mania and depression. Not uncommonly, manic mood symptoms are associated with inflated self-esteem, grandiosity and over-optimism.

Somatic/biological symptoms of mania are often seen and are useful in differentiating mania from its differential diagnoses, e.g., personality disorder. The biological symptoms include a characteristic combination of lack of sleep and increased energy. Other somatic symptoms of mania include increased libido, lack of concentration and distractibility.

Effects of mania
The activating effects of mania on thought and speech are also common and include flight of ideas and increased talkativeness, sometimes to the degree of pressure of talk. Manic patients may report subjective feelings of thoughts racing or ‘speeding up’. As outlined above, thoughts may get distorted with grandiose themes and over-optimistic plans. Not uncommonly, this may evolve into full-blown grandiose delusions which may carry religious themes. Because of their perceived special importance, patients may also experience persecutory delusions. The presence of psychotic symptoms in mania signifies both higher level of severity and increased risk.

A variety of perceptual abnormalities may occur during manic episodes. These include hallucinations, with or without the above described psychotic symptoms. As early as the prodrome phase of mania, many patients describe sharpening of senses with colours appearing brighter than usual and voices being more clear. This phenomenon can be used as an early identifier of impending manic relapse in patients with established diagnosis of bipolar affective disorder. Of note, the most reliable indicators of impending relapse of mania are insomnia and excessive feelings of wellbeing.

The DSM-IV describes the phenomenon of ‘increased
goal-directed behaviour” during manic episodes. This can take the form of excessive house cleaning or excessive studying in a manic college student. Manic patients tend to normalise such activities, and a good clinical judgement is needed to establish the inappropriateness of these activities. The timing these activities are performed at, e.g. 3am, is a good discriminator. Increased goal-directed behaviours can easily be missed for obsessional rituals. Commonly, manic patients lose appreciation of normal social boundaries. In a behavioural sense, this presents as overfamiliarity or even disinhibition in severe cases.

**Hypomania**

Hypomania can simply be defined as a less severe form of mania, but sharing most of the symptoms outlined above. The presence of psychotic symptoms automatically rules out hypomania and qualifies for diagnosis of a manic episode. For a diagnosis of hypomania, a minimum four days duration of symptoms is needed compared with that of a week in mania. However, the most reliable measure to differentiate mania from hypomania is the effect of symptoms on occupational and social functions of the patient. By definition, a manic episode should be severe enough to impair normal functions of the individual while a hypomanic patient may still compensate for such functions.

**Risks associated with mania and hypomania**

Manic symptoms can pose a risk of harm to patients and others. A primary care physician should make it routine to screen manic or hypomanic patients for such risks, as they could have significant impact on the management plan. This may include psychiatric admission or detention under the Mental Health Act.

Commonly highlighted risks in patients with mania and hypomania include the risk of reckless driving. Other risks include risks of financial and sexual exploitation, risk of violence and risk of alcohol and substance misuse. Poor engagement with treatment and risk of absconding from psychiatric hospitals is common.

Manic patients are also at increased risk of suicide. A careful assessment for suicidal feelings or thoughts or impulses should be regarded as an important part of assessment of both depressed and manic or hypomanic patients presenting to primary care centres.

**Differential diagnosis**

As shown in Table 1, there are a number of features that may help differentiate bipolar depression from unipolar depression. The depressive episodes seen in bipolar disorder tend to be prolonged and treatment-resistant in nature. Bipolar depression is often long-lasting and non-responsive to conventional antidepressant therapy. Bipolar depression is also relatively less responsive to psychotherapy. There may be a history of treatment with antidepressants, giving rise to activation or even hypomanic-like spells.

Bradyphrenia and bradykinesia (slowness of thinking and movement) are commonly observed in bipolar depression, as is hypersomnia. Psychosis is also more characteristic of bipolar depression. Psychotic features commonly include brief second-person auditory hallucinations (often in the form of a critical or derogatory voice talking to the patient) or mood-congruent delusions (which can include themes of guilt or physical illness).

Early-onset of depression tends to be seen in bipolar depression, especially in women. One study has shown that one-third of women with bipolar disorder experience their first depression within a year of the onset of puberty, and generally depression tends to develop before 25 years of age. A positive family history of bipolar disorder is also often noted. Bipolar disorder often runs in families. A thorough family history is a key diagnostic step.

While misdiagnosing unipolar depression instead of bipolar is common, equally, there are many conditions that can be mistaken for bipolar disorder. Schizophrenia, emotionally unstable/borderline personality, anxiety-related conditions, and attention deficit hyperactivity disorder (ADHD) are possible differential diagnoses.

While bipolar patients usually achieve a relative recovery between episodes, in schizophrenia there is a poorer inter-episode recovery. Detailed history, including collateral information, may be helpful in revealing disorganised behaviour, withdrawal and gradual overall functional decline that is commonly seen in the prodromal phase of schizophrenia.

During psychosis, the presence of first rank symptoms, more bizarre delusions, often mood incongruent, may point towards schizophrenia. Negative symptoms, such as apathy and decreased motivation and poverty of thought, are usually more persistent and not just seen in acute episodes. Both affective and psychotic symptoms are equally prominent in an episode of schizoaffective disorder. Psychotic symptoms in bipolar disorder usually subside when the patient’s mood improves and returns to normal.

Drug-induced mania is not clinically distinguishable from endogenous mania, but history and drug screening will show drug use. The most common drugs causing mania include amphetamines, cocaine and ecstasy. Iatrogenic mania can arise in the context of treatment with many medications, the most common being steroids and levodopa.

Patients with a diagnosis of emotionally unstable personality disorder tend to complain of intense but brief (commonly observed to be hours) mood swings. Mood changes are often precipitated by external or internal factors and they usually last for the shorter time duration of hours or days, but not weeks. Patients describe anxious, irritable, angry, often empty mood; they have difficulties in regulating their own emotions in the particular situational
context. They rarely experience risky behaviour associated with disinhibition on account of mood elevation. Nevertheless, emotionally unstable patients display risky impulsive behaviour, usually chronic and recurrent suicidal ideations and self-harm tendencies not necessarily associated with mood changes.

Patients with bipolar disorder have high rates of anxiety, and this can be the presenting complaint. Bipolar patients, especially during the phase of depression, may experience various worries which are usually not as excessive, generalised and persistent as in generalised anxiety disorder. Although patients with a primary anxiety disorder can be kept awake by unpleasant worries, often ruminative in pattern, there is no reduced desire for sleep. Patients with obsessive-compulsive disorder can be involved in excessive cleaning or related activity, lasting sometimes for hours; however, this is typically ego-dystonic activity, whereas in bipolar disorder overactivity is usually less goal-directive and not associated with the unpleasant, intrusive urge to do things over and over.

ADHD is characterised by inattention, hyperactivity and impulsivity with a poor sense of danger. Features of this condition are usually noticed by relatives from early childhood. Hyperactivity is a more consistent feature whereas in bipolar disorder, patients usually become episodically overactive due to hypomania. Patients with hypomania may appear as impulsive or distracted due to a short attention span, but there is no pressure of speech or flight of ideas evident. These patients typically do not experience grandiosity, sexual disinhibition or reckless overspending.

Elderly patients presenting with the first episode of mania require detailed physical/neurological evaluation to rule out any organic brain lesion (usually located in the right hemisphere). Various medical conditions imitate mood disorders. In particular, hyperthyroidism may create a picture of hypomania or agitation depressed, whereas hypothyroidism may present as depression. Secondary mania can also be triggered by a range of medical conditions such as dementia, Parkinson’s disease, multiple sclerosis, cancer or cerebral lupus.

Compliance and treatment
Throughout medicine generally, compliance is a challenging issue for both patients and doctors. A useful but sobering statistic is the compliance rule of thirds – one-third of patients comply with treatment, one-third comply with some aspects of treatment some of the time, and one-third of patients don’t comply at all. The overall point prevalence of compliance generally in medicine is around 55%.

In bipolar disorder, compliance is a particular problem during the manic phase. During depression, patients tend to show good insight and high compliance, but this diminishes markedly during mania. Furthermore, patients can be reluctant to give up the pleasurable feelings that can be associated with the early phases of mania. The increased energy, euphoria, and heightened self-esteem are often recalled favourably while unpleasant features are minimised.

The following factors are associated with poorer compliance: manic phase, a past history of non-compliance, complicated treatment regimens, and problems with side-effects.

Limited compliance is associated with poorer outcomes and is the single biggest cause of relapse in bipolar illness. Interestingly, complying poorly with lithium (a not uncommon occurrence, whereby patients frequently stop and then re-start the medication) leads to a poorer outcome than if the medication is not used at all. While studies employing talk therapies such as cognitive behavioural therapy and interpersonal therapy for bipolar disorder have yielded disappointing results overall, psychoeducation has been shown to be effective, particularly in aiding patient compliance.

In this regard, GPs can take several steps:
• Adopt an active role during patient reviews, with an open but focused approach towards examining and promoting compliance.
• Introduce a review of compliance by acknowledging that compliance is difficult; doing this encourages the patient to speak more freely and frankly about their own compliance.
• Ask about missed doses and thoughts of stopping medications.
• Check patient knowledge of medications and each medicine’s indication, as self-knowledge helps foster self-reliance.
• Review the rationale for treatment, as this helps bolster adherence. Side-effects often lead to abandoning medications, and should be reviewed. Mood diaries help strengthen patient perception of the beneficial effects of medications.

Drug treatments
Regarding treatments, the mood stabiliser lithium remains the gold standard for bipolar disorder. Lithium is effective in approximately 60% of cases. It is less effective where organic brain damage is present (eg. epilepsy, learning disability, head injury); in rapid-cycling bipolar disorder; where substance abuse is prominent; or where the usual pattern of illness (mania followed by depression) is reversed, ie. where depression precedes mania.

In the population generally, renal function declines by 1% per annum after the age of 40. With lithium therapy, this rate of decline is accelerated, and a minority of patients develop significant renal function impairment. Thus regular renal function testing is mandatory, as is measurement of thyroid function.

Sodium valproate is also widely used as a mood stabiliser. It is particularly teratogenic and care is needed around this. Side-effects can include weight gain, ataxia, sedation, alopecia, thrombocytopenia and pancreatitis.

The atypical antipsychotics, including aripiprazole, risperdone, quetiapine, and olanzapine, are useful agents for treating mania. Asenapine is the most recently licensed antipsychotic for treating mania here in Ireland. It is indicated for the treatment of moderate to severe manic episodes associated with bipolar 1 disorders.

The treatment of the depressive phase of the condition remains challenging pharmacologically. The first approach for bipolar depression is to optimise mood stabiliser...

Lamotrigine is used when the clinical course is one of predominantly recurrent depressions. Doses are typically 100mg to 200mg daily, and care needs to be taken with slow titration upwards to help avoid rashes and the potential for Stevens-Johnson syndrome.

Quetiapine is licensed for the treatment of acute bipolar depression (and is also used in treating unipolar depression). It is used at doses of 150mg to 300mg daily for this indication. Side-effects can include sedation, headache and postural hypotension, and may be helped by use of slow-release preparations.

Antidepressants are widely prescribed in bipolar disorder, despite their potential to induce a switch to mania and their limited efficacy for bipolar disorder. If prescribed, cautious use of low doses of serotonin-selective reuptake inhibitors is probably the best option.

Psychological approaches

Cognitive behavioural therapy (CBT) and interpersonal therapy, among other therapies, have undergone rigorous testing in clinical trials which have documented their effectiveness in treating unipolar depression. Results to date for trials of talk therapies for bipolar depression have been relatively disappointing generally. However, this therapy can be particularly helpful where comorbidity is evident, eg. anxiety, substance abuse, or personality difficulty.

Of note, psychoeducation has shown promise as a counselling method. The focus of this approach is to foster improved knowledge, self-awareness and recognition of relapse in patients. It is also believed that a large part of psychoeducation’s benefit comes by way of its effect of increasing compliance. Patient support organisations such as Aware and Grow are also valuable in helping patients.

Dealing with weight gain

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Dealing with weight gain

Concerns have emerged over the prevalence of the metabolic syndrome with use of antipsychotic medications. Provisional results from an ongoing study in our bipolar disorder clinic show roughly 50% of patients having the metabolic syndrome and a particularly high rate (90%) of central obesity. While many argue that severe mental illness, ie. bipolar disorder and schizophrenia, may give rise to the metabolic syndrome irrespective of medication, nevertheless the newer atypical antipsychotic agents do have a documented propensity for worsening the parameters.

To deal with metabolic problems the following advice is useful. The metabolic syndrome may be silent, so screen regularly for the condition. Weight gain with antipsychotics commonly develops early in treatment and so vigilance is required at this stage. Exercise can help reverse many of the symptoms of the condition, but lifestyle changes are hard to implement. Patients are more informed now, and many are keen to address aspects of the metabolic syndrome.

Shared care in BPAD

The roles of the primary care and psychiatric setting overlap in patient management. Aspects of managing bipolar disorder in primary care should include, but not be limited to, the following:

- Early recognition of symptoms of depression and mania/hypomania in patients with no prior diagnosis of mental health problems
- Appropriate referral to secondary care when needed
- Appropriate use of the Mental Health Act when justified
- Shared care of established patient with a diagnosis of BPAD with regular assessment of mental state and early signatures of relapse
- Encouragement of adherence to medications and abstinence from alcohol and drugs
- Monitoring of medication side-effects and in particular lithium toxicity and metabolic syndrome.

While many people with established and stable bipolar disorder can be managed through primary care, the psychiatry services aim to provide the more comprehensive care needed by some. In addition to standard outpatient and day-hospital care, specialist clinics are now emerging for this condition.

Within our own service based in Coolock Health Centre, Dublin, we operate a specialist bipolar clinic. The specialist clinic permits a particularly focused approach to care for those individuals with more marked illness. Psychoeducation programmes, compliance therapy and specialist counselling for alcohol or substance misuse are available. Regular screening for the metabolic syndrome takes place with the help of a nurse specialist. Senior registrars in psychiatry provide medical review along with the consultant, as part of a special-interest training session. In addition to its benefits for teaching, the clinic’s design also facilitates clinical audit and research.

Ahmed Errasoul is a senior registrar in psychiatry at St Ita’s Hospital, Portrane, Co Dublin (TBC); Ewa Gomercz is a tutor in psychiatry at the Dept of Psychiatry, RCSI; and Robert Daly is a consultant psychiatrist at St Ita’s Hospital, Portrane, Co Dublin and Beaumont Private Clinic, Dublin and is a senior lecturer at the Dept of Psychiatry, RCSI

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