Rapid Cycling Bipolar Affective disorder: Diagnosis and management - A brief review

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Abstract

Bipolar affective disorders are highly prevalent in the general population. The course of bipolar affective disorder is characterised by episodes of mania or hypomania, and periods of depression. One clear-cut manic episode is enough for the diagnosis of bipolar disorder (according to DSM IV criteria) but many patients have two or more episodes. When a patient has 4 or more pathological mood episodes in one year, the course is defined as 'rapid cycling'. It is important to identify rapid cycling in clinical practice as these patients do not respond as well to conventional treatment. Outcomes can be improved by a combination of management of risk factors for rapid cycling and the use of appropriate pharmacological intervention. This article focuses on the diagnostic criteria, clinical features, risk factors and management of rapid cycling bipolar disorder.
Key words: bipolar disorder, rapid cycling, risk factors, treatment.

Introduction

Bipolar affective disorders are highly prevalent in the general population. European studies have reported a prevalence of between 0.1% and 2.4% (1,2,3,4,5). The course of bipolar affective disorder is characterised by episodes of mania or hypomania and episodes of depression. According to DSM IV criteria, one clear-cut manic episode is enough for the diagnosis of bipolar disorder (6). However, many patients have two or more manic episodes.

The term rapid cycling is used to describe a particular course of bipolar disorder. In 1974, Dunner and Fieve (7) studied a group of bipolar patients who had a poor response to lithium and other conventional treatments. Many of these patients experienced at least 4 episodes of mania and/or depression per year. They coined the term 'rapid cycling' to describe this particular pattern. These criteria were validated, incorporated and described in the DSM-IV (6) as a course specifier for bipolar disorder. Rapid cycling has not been described in ICD 10 (8). However many patients who fulfill the diagnostic criteria under ICD 10 code F38.00, i.e. mixed affective episode, are likely to fall into this category.

It is important to clarify the use of the term rapid cycling, because very rapid, i.e. daily alterations in mood episodes, have been described as rapid cycling as well as ultrarapid cycling and ultradian cycling (9) (the term ultradian refers to a cycle of shorter than 24 hours). The relationship between ultradian cycling and rapid cycling bipolar disorder is not yet clear. It is possible that ultradian cycling represents an acceleration of rapid cycling bipolar disorder.

Epidemiology

The prevalence of rapid cycling disorder varies from 13% to 56% of patients with bipolar disorder. This wide range reported could be due to many reasons (9). In particular:

a) The criteria for rapid cycling bipolar disorder could be interpreted differently; using less

stringent criteria, more patients could be described as rapid cycling.

b) The data are derived from studies on patients who are treatment resistant and are inpatients in tertiary care units, where rapid cycling is more common.

Community studies across ten countries showed a 12-month prevalence of rapid-cycling bipolar disorder as 0.3% in the general population. Of patients diagnosed with bipolar disorder, 30-40% fulfilled criteria for rapid cycling. Rapid cycling bipolar disorder was associated with younger age of onset, more severe depressive symptoms, increased number of lifetime episodes and persistence of symptoms. With an increase in the number of depressive episodes experienced, there is an increased risk of suicide. Important predictors for suicide are the change from a manic or hypomanic to a depressive episode (9).

Table: 1 Diagnostic criteria for rapid cycling bipolar disorder

1. The patient should have presented with clinical features meeting the criteria for bipolar disorder
2. There should have been at least 4 discrete mood episodes in the past year; these could be manic, hypomanic or depressive episodes.
3. Between the episodes there should have been a remission period of 2 months or a switch of mood episode to the opposite pole e.g. depression to mania or hypomania.
(Adapted from: Diagnostic and Statistical Manual of Mental Disorders DSM IV. American Psychiatric Association, 2000.)

Table: 2 Risk factors associated with rapid cycling bipolar disorder

1. Bipolar II disorder.
2. Depressive episode in bipolar disorder.
3. Antidepressant therapy for depression in bipolar disorder.
4. Comorbid alcohol and substance misuse.
5. Significant life events.
6. Presence of brain injury.
7. Hypothyroidism.
8. Female sex.
9. Increasing age.
10. Number of previous episodes.

Aetiology of rapid cycling

The aetiology of rapid cycling bipolar disorder remains unclear. Studies investigating the development of this disorder have so far failed to identify genetic factors that differentiate rapid cycling from non-rapid cycling bipolar disorders. Biological factors, such as like medical illnesses, hypothyroidism and substance misuse, are associated with an increased risk of rapid cycling bipolar disorder. Among the hypotheses for rapid cycling pathoaetiology, two of the most commonly accepted are kindling and sensitisation (2).

1. Studies have shown that the risk of rapid cycling increases with the number of previous episodes. Post et al. (11) analysed this subset of patients and found that, initially, relapse of episodes was associated with similar social circumstances or life events and the presenting symptoms were similar. As the illness progressed, these episodes started to occur more spontaneously. This was similar to the kindling phenomenon seen in animal models of epilepsy. The hypothesis is that changes occur in the brain with psychosocial stressors leading the precipitation of mood episodes. After a few episodes, these brain changes might persist, leading to spontaneous mood episodes. The changes could be

electrophysiological or neurochemical.
2. Sensitisation is a learning phenomenon in which repeated exposure to a stimulus heightens the behavioural response to it. It is best understood in drug abusers, especially amphetamine users. With repeated use of amphetamines there is an exaggeration of behavioural responses to the drug and to drug associated stimuli. The phenomenon of sensitisation is also studied with respect to antidepressants.

In bipolar disorder, repeated exposure to psychosocial stressors may cause sensitisation, resulting in greater shift in mood and perhaps contributing to the development of rapid cycling (11).

Management

Rapid cycling disorder is a complex phenomenon and studies examining long-term treatments show less favourable outcome than in non-rapid-cycling bipolar disorder (12).
A diagnosis of rapid cycling should not be made without first excluding thyroid dysfunction, antidepressant-induced mood switching, suboptimal medication regimes and poor compliance with medication (13).

Treatment for bipolar disorder aims to reduce the severity of symptoms, stabilise mood and prevent relapse.

The optimal choice of drug depends on individual variation and response, such as the experience of adverse effects or mood switching. NICE guidelines recommend a combination of lithium and valproate as first-line treatment. However, there are specific considerations for patients with rapid cycling.

Most important, the focus should be on prevention of treatment-induced switching from one pole to another and on long-term outcomes, rather than treating individual episodes.
Many patients with rapid cycling bipolar disorder fall into the category of bipolar II and a high proportion of these patients are likely to be taking a combination of mood stabilisers and antidepressants. Antidepressant therapies have been associated with mood switching; treatment regimes should seek to avoid mood switching in rapid cycling bipolar disorder. NICE guidelines suggest antidepressants should not be used in individuals with rapid cycling, but rather recommend an increase in dose of an anti-manic agent or the addition of another mood-stabilising agent such as lamotrigine. If antidepressants are used in rapid cycling, these should be reviewed and stopped when no longer necessary, i.e. when in remission after a depressive episode, to reduce the risk of inducing mania.

Trials of medications should last at least 6 months, unless severe adverse effects are experienced. This reduces the risk of inducing rapid mood switching.
A specific history of possible risk factors should be taken. These are listed in Table 2, and include substance misuse or comorbid medical conditions. The patient should, with appropriate support, try to minimise, manage or eliminate any risk factors.

Course and Prognosis

Rapid cycling bipolar disorder responds poorly to pharmacological management. Although the STEP-BD study (14) reported that out of 1742 patients who entered the study with a diagnosis of rapid cycling bipolar disorder, only 5% experienced four or more discrete mood episodes over the next year, it should be noted that 61% of rapid cycling patients did experience between one and three discrete mood episodes in the next year. A younger onset of disease, more severe initial symptoms and the use of antidepressants were associated with an increased likelihood of experiencing a mood episode in the follow-up year. These results suggest that cycling may represent a continuum and that treatment may reduce the rate at which cycling occurs. Only a small proportion of patients still qualified as 'rapid cycling' after a year, but care should still be taken to avoid medication-induced mood switching, even when the patient no longer appears to be rapid cycling. This evidence is also in accordance with NICE

guidelines that warn against the use of antidepressant therapies in individuals with rapid cycling.

Conclusion

Rapid cycling refers to one particular course of bipolar disorder. Rapid cycling bipolar disorder responds poorly to medication and many of these patients have comorbid medical conditions. Minimising the use of antidepressants and increasing the use of antimanic agents may reduce the frequency and severity of the pathological mood episodes.

GP Comment

What have I learned from this paper?

Patients with rapid cycling will inevitably be heavy users of both primary and secondary care services and so identifying such patients and providing early intervention are vital.

I was interested to note the association with hypothyroidism, antidepressant-induced mood switching and sub-optimal medication regimes. Such patients need close co-operation between GPs and mental health services.

Dr Stephen Cakebread, GP, Bedfordshire.

References

1. Regeer EJ, Ten Have M, Rosso ML, Hakkaart van Roijen L, Vollebergh W, Nolen WA. Prevalence of bipolar disorder in the general population: a Reappraisal Study of the Netherlands Mental Health Survey and Incidence Study. Acta Psychiatrica Scandinavica 2004;110 (5):374-382.
2. ten Have M, Vollebergh W, Bijl R, Nolen WA. Bipolar disorder in the general population in The Netherlands (prevalence, consequences and care utilisation): results from The Netherlands Mental Health Survey and Incidence Study (NEMESIS). Journal of affective disorders 2002;68 (2):203-213.
3. Szadoczky E, Papp ZS, Vitrai J, Rıhmer Z, Füredi J. The prevalence of major depressive and bipolar disorders in Hungary: results from a national epidemiologic survey. Journal of affective disorders 1998;50 (2):153-162.
4. Faravelli C, Degl'Innocenti BG, Aiazzi L, Incerpi G, Pallanti S Carlo Faravelli, Benedetta Guerrini Degl'Innocenti, Leandro Aiazzi, Guya Incerpi, Stefano Pallanti. Journal of Affective Disorders 1990;20 (2):135-141.
5. Pini S, de Queiroz V, Pagnin D, Pezawas L, Angst J, Cassano GB, Wittchen HU. Prevalence and burden of bipolar disorders in European countries. European Neuropsychopharmacology 2005;15 (4):425-434.
6. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. American Psychiatric Association. American Psychiatric Publishing Inc; 2000.
7. Clinical Factors in Lithium Carbonate Prophylaxis Failure David L. Dunner, MD; Ronald R. Fieve, MD Arch Gen Psychiatry 1974;30 (2):229-233.
8. World Health Organization The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. World Health Organization; 1992.
9. Kramlinger KG, Post RM. Ultra-rapid and ultradian cycling in bipolar affective illness. The British Journal of Psychiatry 1996;168 (3):314-323.
10. Lee S et al. Rapid-cycling bipolar disorder: cross-national community study: BJP 2010:196:217-225.
11. Post RM, Rubinow DR, Ballenger JC. Conditioning and sensitisation in the longitudinal course of affective illness. The British Journal of Psychiatry 1986;149 (2):191-201.
12. Schneck CD. Treatment of rapid-cycling bipolar disorder. The Journal of clinical psychiatry 2006;67:22.
13. Bipolar disorder: The management of bipolar disorder in adults, children and adolescents, in primary and secondary care.NICE Guidance 2006;CG38.
14. Schneck CD et al. The Prospective Course of Rapid-Cycling Bipolar Disorder: Findings From the STEP-BD: American Journal of Psychiatry 2008; 165:370–377.