Case report

Long-term prospective mood self-rating and antidepressant treatment

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Abstract

The use of antidepressants in bipolar illness remains controversial. This controversy continues to be fuelled by short-term studies that inconsistently report efficacy or no benefit. However, long-term studies have been consistently unfavourable, suggesting that understanding the long-term course of the illness in the setting of antidepressant treatment is important. This is an extraordinary case in which prospectively collected daily mood ratings were available in a type I bipolar individual who had experienced minimal medication changes over a 21-year period was reviewed. Data regarding the number of euthymic days in the setting of antidepressant use and after antidepressant discontinuation were collected.

Induction of cycling and increase in the number of depressed days occurred after five years of continuous serotonergic antidepressant administration. Discontinuation of antidepressants after 11 years of continuous use was associated with only a partial improvement which had a delayed onset. Cycling and increase in depression was noted after years of continuous use of serotonergic antidepressant treatment. Antidepressant-associated destabilisation may occur after long-term exposure and may be associated with prolonged worsening even after antidepressant discontinuation.

Key words: Antidepressants; Bipolar disorder; Long-term outcome; Rapid cycling.

Introduction

Antidepressants are the most commonly used pharmaceutical agent in the treatment of bipolar disorder.[1] However, recent controlled studies suggest that antidepressants added to mood stabilisers may not have significant acute efficacy,[2] nor significant prophylactic effect.[3,4] Furthermore, antidepressant use has been associated with manic induction, rapid cycling, and chronic irritable dysphoria.[5] Most of these deleterious effects of antidepressants appear at any point after onset of antidepressant treatment and may not be noted by either the patient or the clinician (an average duration of antidepressant treatment of 1.7 months among the original 35 patients described).[6]

We herein report a case of a patient who recorded daily mood ratings continuously for 21 years. The case suggests that destabilisation with antidepressant treatment may occur slowly after prolonged treatment, while improvement after antidepressant discontinuation may also occur slowly after prolonged abstinence from antidepressants.

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Case report

B is a 55-year-old man and a former practicing attorney with a history of bipolar illness since age 26. He has maintained a daily mood chart from 1989 to the present time. The mood chart recorded the predominant mood of each day with on a nine point scale: '0' was defined as euthymia (well), depression ranged from mild (-1), moderate (-2), severe (-3), and extreme (-4). A similar scale was used for hypomania, and mania. The patient self-defined the severity and polarity of mood without any input from the treating psychiatrists. Prior to 1989, the treatment history is not adequately recorded, and while the patient received lithium consistently, use of antidepressants was intermittent.

Beginning 1989 through the present, B has been treated by only two psychiatrists, with the switchover occurring in 2000. The first psychiatrist used antidepressants as a cornerstone of B's treatment, while the subsequent psychiatrist has attempted to minimise antidepressant use. B prospectively maintained daily mood records continuously for 21 years.

B's baseline illness consisted of infrequent mania, and frequent depressions and hypomanias that consumed approximately one third of his time *(see Figure 1)*. Treatment consisted of antidepressants (sertraline, fluoxetine, paroxetine, citalopram, escitalopram, venlafaxine, amitriptyline, and imipramine from 1989-2000), mood stabilising medications (carbamazepine 600-1400mg daily started 1988, lamotrigine 300-600mg daily started 1998), anxiolytic medications (clonazepam 1mg daily started 1988), antipsychotic (quetiapine 600mg started 2006), stimulant medications (methylphenidate 5-20mg daily started 2006).

Additionally, B utilised marijuana daily with the exception of a two-year period of incarceration and probation for a crime committed during a manic period (2000-2001). Medications have remained fairly consistent with the exception of minor and short-lived changes.

In 2000, despite ongoing frequent depressions, antidepressant medications were discontinued. B remained off antidepressants with the exception of a one month period in 2006 (bupropion 100mg daily), and a three month period in 2007 (escitalopram 10mg daily). Other events occurred in B's life through this period. These include a marriage and divorce, several other significant relationships, moves among five different apartments, successful publication of two books, and a brief run as a host of a local television show. However, all of these events were randomly distributed through the study period. There was never a run of several adverse events

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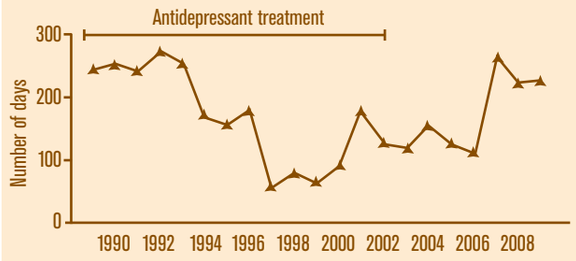
or several high points occurring continuously over several years

Figure 1 depicts the annual number of well days. Mr. B's baseline (1989-1993) included an average of 254 euthymic days/year. After five years of antidepressant treatment, B began to experience a decline in the number of well days reaching the nadir of an average of 71 well days/year from 1997 through 2000. The decline in euthymia was associated with an increase in the number of depressed days and the induction of rapid cycling. Following discontinuation of the antidepressant treatment, B began to experience slow and gradual reduction in the number of ill days and increase in the number of well days reaching an average of 139 well days/year from 2001 through 2007 *(see Figure 1)* and a consistent 230 euthymic days/year for 2008 and 2009.

Figure 1: Annual number of well days collected prospectively for 21 years (1989-2009)

The duration of antidepressant treatment is indicated by the black bar. The number of well days begins to decline after five years of antidepressant treatment and remains low until antidepressants are discontinued. Recovery does not begin until four years off antidepressants.



Discussion

The current case of mood ratings collected prospectively over 21 years in a patient whose medication regiment had remained stable of long periods of time provides insight into the time course of potential antidepressant effects. The destabilisation in the course of the patient's illness began over five years after continuous antidepressant treatment. The patient experienced more ill days including more depressive days despite antidepressant treatment.

Over one year after discontinuation of antidepressant treatment, the number of ill days began to decline. Five years after antidepressant discontinuation, the number of euthymic days had increased, but remained well below the initial baseline. In 2006, after the introduction of methylphenidate and quetiapine, two agents with purported antidepressant action,[7,8] the number of euthymic days increased to a number that is nearly the same as at the initiation of antidepressant treatment.

The role of antidepressant treatment in bipolar illness remains controversial. Gijsman and associates[9] reviewed the literature and concluded that antidepressant treatment should be part of care of bipolar patients, while other authors reviewed the same data and concluded that antidepressant use should be minimised.[1,5,10] Antidepressants may be advantageous for a short term period of 4-10 weeks, but not more so than mood stabilisers used alone.[2] More importantly, antidepressants do not appear to have prophylactic efficacy in bipolar patients.[1,5] Additionally, continuation of antidepressant treatment through periods of euthymia and greater than one year has been associated with greater incidence of cycle acceleration.[6]

This pattern is also seen in this case. Additionally, this case suggests that this antidepressant-related cycle acceleration may be reversible in the absence of antidepressant, but reverses slowly and gradually.

The mechanism of antidepressant related destabilisation is unknown. Recently, an association between the short form of the serotonin transporter promoter and antidepressant-related cycle acceleration has been reported.[11] The patient described herein had received serotonergic antidepressants for most of the period of antidepressant exposure. Utilisation of quetiapine and methylphenidate, which may have antidepressant properties[7,12,13] but which do not have significant serotonergic reuptake inhibition, was associated with a significant increase in well days in 2006 *(see Figure 1)*. Combined serotonin and norepinephrine reuptake inhibiting agents such as venlafaxine and tricyclic antidepressants may be more likely to induce mania/hypomania than a specific serotonin reuptake inhibiting antidepressant, but the dopaminergic antidepressant bupropion carries the least liability for destabilisation.[14]

The observation that non-serotonergic agents carry the least liability for destabilisation while the mixture of serotonin reuptake inhibition with other dopamine or norepinephrine increases the risk, suggests that serotonin reuptake inhibition may be a requirement for antidepressant-related destabilisation. If this is accurate, then the absence of a serotonergic agent after 2000 may have allowed for the partial improvement.

It is important to remember that this patient's progress over a two decade interval is being interpreted through a single variable: administration of antidepressants. The patient experienced other medication changes which could have contributed to the patient's improvement in 2006. Additionally, other aspects of the patient's life (social, economic, medical) may, have impacted his course – both the increased ill days, and the subsequent improvement.

Extraordinary individual case reports serve as hypothesis generating tools. The current case is extraordinary in the availability of prospectively collected mood ratings for a 20 year period with minimal medication changes. The data are consistent with previous reports that destabilisation with antidepressants may occur after prolonged exposure, and suggests that reversal of that process is equally slow – requiring years to reverse, and may be not fully reversible. Examination of antidepressant outcome should be done over prolonged time intervals.

Declaration of Interest: None.

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Case report

First episode psychosis and an underlying cerebellar tumour

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Abstract

We report on the case of a middle aged lady who was referred by her GP with what appeared to be a case of first episode psychosis. Following assessment and investigation an underlying cerebellar tumour was identified. Our aim is to draw attention to the ongoing debates regarding the possible role of the cerebellum in psychosis and cognition and on neuroimaging as a diagnostic modality in cases of first episode psychosis.

Key words: First episode psychosis; Cerebellar tumour; Neuroimaging.

Case history

Ms XX is a 45-year-old factory worker referred by her GP on account of episodes of bizarre behaviour and utterances of recent onset. At assessment, XX described déjà vu phenomenon. She felt that she had attended the interview previously with things arranged in the same way in the office. She expressed persecutory delusional ideas in relation to her work colleagues and was convinced that her house mates were poisoning her food. She denied any olfactory, gustatory or auditory hallucinations or any passivity phenomena. She denied any symptoms of depression or elation.

XX complained of intermittent bouts of headache, predominantly localised around her fronto-temporal and occipital head regions, with worsening during micturition but no associated vomiting. She described intermittent episodes of perceived darkness in the left part of her left visual field and seeing 'shadows of people' in the absence of any visual stimulus. XX reported that she had developed increasing forgetfulness in the six months prior to presentation. She denied any previous history of head trauma. Additionally, XX denied any history of alcohol or recreational drug misuse. There was no previous personal or family history of psychiatric illness. Even though her GP had alluded to the possibility of a past history of non-epileptic seizure, this was not corroborated by XX or her neighbour who accompanied her to the assessment. XX reported that she had been in good physical health prior to her recent complaints.

Collateral from XX's daughter confirmed that these symptoms started approximately two years prior to presentation and had gradually increased in the intervening period. She reported that XX had experienced intermittent episodes of forgetfulness and a tendency to repeat herself in conversation.

XX's neighbour of four years also corroborated her history with more elaborate accounts of escalating bizarre behaviour and utterances. Of note, XX was said to have

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