

PREGABALIN INDUCED MOOD ELEVATION IN BIPOLAR PATIENTS: CASE-REPORTS

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received: 30.10.2020;

revised: 22.12.2020;

accepted: 30.12.2020

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INTRODUCTION

Hagop Souren Akiskal, noticed the patients who exhibit hypomania and manic manifestations following taking antidepressant treatments (Akiskal & Pinto 1999). This condition was more prevalent among those with cyclothymic temperamental tendencies (Akiskal et al. 1979). He categorized these group of patients as bipolar type III (Akiskal & Pinto 1999). The same phenomena was also recognizable in some patients following the substance or alcohol use. Bipolar III/2 type was introduced to describe these patients (Akiskal & Pinto 1999). Since then numerous drugs has been proposed for be the main cause in mood switch among the bipolar patients (Henry & Demotes-Mainard 2003), however the precise underlying biological mechanism has not discovered yet. Of the proven drugs responsible for mood switches in bipolar disorders can name the TCA (eg, imipramine) (Prien et al. 1973, 1984), SSRI (eg, Fluoxetine) (Henry & Demotes-Mainard 2003), MAOI (Stoll et al. 1994), Bupropion (Shopsin 1983, Haykel & Akiskal 1990) and other new antidepressant treatments (eg, Venlafaxine) (Amsterdam 1998).

Pregabalin is a new synthetic molecule is a derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). The drug is used as monotherapy or adjunctive treatment in many psychiatric disorder (Marks et al. 2009), hence few studies has assessed the possible consequences of this drug in mood disorders.

We present two cases of bipolar mood disorder who experienced elevated mood switch after receiving pregabalin. We obtained written consent from our patients. Ethical approval is not required for case reports according to our university polices.

CASE PRESENTATION

Case 1

A 21 years-old woman, university student, presented with irritability and depressed mood. In assessing the past psychiatric disorder two years before coming up to our clinic she experienced a few months period of elevated mood, increased libido and increased rate of speech (excessive talkativeness) was noticeable which was followed by a period of depressed mood, increasing in

sleep duration and also her appetite two years earlier. The patient was diagnosed as Bipolar Mood Disorder (BMD) in another center. Pharmacological therapy was started with lamotrigine, aripiprazole and bupropion and partial remission was obtained. Few months after wards, she frequently experienced brief periods of depression (lasted for days to few months) with elevated mood intervals. She visited us and we took a thorough history. When asked about the sexual history, she confessed to having high risk sexual behaviors (unprotected sex, having multiple sex partners and public sex). She was abusing various types of stimulant and opioid drugs. She complained about sleep problems in the form of sleep inversion and reversal of sleeping tendencies. She reported the history of two previous attempted suicide.

On mental status examination the only finding was the only finding was a heavy makeup. Other aspects such as psychomotor activities, form and content of thought, cognitive state all were intact. This time we started lithium and lamotrigine with the same diagnosis of BMD. One month afterwards, she was visited again while taking her medication regularly. The mood fluctuations were handled near to completely but she expressed dissatisfaction with moderate level of anxiety. We decided to omit lamotrigine from the treatment plan and added pregabalin. We recommended to revisit her after one month but after 2 weeks she came back because of overuse the prescribed pregabalin as it gave her more energy and increased libido. Pregabalin was discontinued and carbamazepine added to treatment regimen. One month later, the mood fluctuations were almost controlled and there was no relapse in pregabalin abuse anymore. Her mood swings, while being on these medication, became nearly controlled for the next 4 months. During this period of time, two lapses in pregabalin abuse happened each time precipitated increased energy level, irritability and high sexual desire. Furthermore she endured brief depression episodes for 2-3 days without suicidal idea. We asked for the lithium level which came back 0.7, within the therapeutic range. She continued to take lithium and carbamazepine and the mood swings nearly stopped.

Case 2

A 35 years-old woman came up to outpatient clinic because of obsession and depression. Her obsessive

thoughts began years ago after testing positive for HIV. She estimated that she has been infected because of having unprotected sex with multiple partners due to her high sexual desire. She continued having herself and also her partners tested repeatedly for HIV all these years. Besides she reported mood swings for the previous 2 years. Sertraline, 50 mg per day, was prescribed for her obsessional compulsive disorder (OCD). By passing less than one week, her obsessional thoughts were diminished significantly but she experienced a rapid mood elevation and also mood changes in less than 24 hours. She committed suicide with her medications and also 40 mg of clonazepam at the time she was distressed and frustrated. In assessing her family history, we noted a history of major depression accompanied by a suicide attempt in her maternal uncle and also a postpartum depression in her mother. We decided to start lithium carbonate (300 mg twice daily), and carbamazepine (200 mg at night) with the BMD diagnosis. She was revisited 28 days later and we added pregabalin (50 mg three time per day) as she felt anxious. Ten days later she made a phone call and reported having a good feeling toward her recent medication regimen since the state of her mood was the same as the time she was taking sertraline. We recommended to stop the pregabalin with the impression of mood switch. She called back 20 days later and complained about restlessness and anxiety. Her condition and medications was asked more in detail and we noticed the continuation of taking pregabalin, despite our recommendation, because of the overwhelming feeling of happiness and joy pregabalin was giving her. Hence the pregabalin was discontinued and consequently her restlessness and anxiety resolved.

DISCUSSION

The term mood stabilizer has been defined dissimilarly in different era. In 1950 mood stabilizers were consisted of amphetamine-barbiturates (Ghaemi 2003). In 1960s, the positive effects of antiepileptic drugs (AEDs) on mood disorder was discovered and gradually it was used as mood stabilizing agents (Grunze 2008). In 1967, first paper published by Turner and for the first time the effects of antiepileptic drugs on mood, separated from their antiepileptic efficacy (Turner 1967). AEDs are classified as the conservative mood stabilizers with both antidepressant antimanic efficacy (Ghaemi 2003). The effectiveness of other AEDs such as carbamazepine (Okuma et al. 1973) or valpromide (Lambert & Venaud 1966) was figured out one by one on mood disorders. The exact mechanism of the AEDs on mood regulation is still unknown, but the regulation effects on ion fluxes (specially the sodium and calcium channels) was proposed as the possible mechanism (Rogawski & Löscher 2004). Mood swings and mania induction by anticonvulsants are uncommon and infrequently reported. Few studies declared the mood elevation following the treatment with topiramate (Kaplan 2005), gabapentin (Short & Cooke 1995, Sansone & Sansone 2005) and lamotrigine (Sansone &

Sansone 2011). The anticonvulsants with γ -aminobutyric acid (GABAergic) effect, pregabalin and gabapentin, may be more applicable for some anxiety states (Strawn & Geraciotti 2007).

Pregabalin (PGB) is a newer gabapentinoid, adjuvant anti epileptic drug, and its structure is similar to gabapentin (Toth 2014). PGB often use in treatment of anxiety (Feltner et al. 2003) and other medical conditions such as neuropathic pain (Arezzo 2008). Primary studies indicated that the pregabalin may have some antidepressant effects (FDA. 2020). However one case was introduced for severe depression and appearance of suicidal thoughts after taking PGB (Schaffer et al. 2013). In one open study it was suggested that pregabalin can be administered as a safe and effective mood stabilizing drug in some treatment-resistant with anti manic effects (Stein et al. 2008). However few studies highlighted the mood switch effects of PGB (Kustermann et al. 2014).

The development of mania symptoms in our patient was noticeable following the PGB administration.

In our first case, carbamazepine which was started before PGB could not be the possible agent to be blamed for mood swing as it is a common mood stabilizer in bipolar patients and that phenomenon has not been reported following carbamazepine. Likewise, the mania symptoms had been subsided after discontinuation of PGB. The same mood elevation symptoms relapsed when she restarted PGB abuse and ultimate mood regulation achieved while PGB was totally omitted from her medication regimen. The second case we reported had experienced the mood elevation symptoms following the SSRI administration which can be categorized as type III bipolar disorders according to the Akiskal classification (Akiskal & Pinto). Also the restlessness and anxiety was resolved following the PGB discontinuation in this patient too.

CONCLUSION

Our observation showed the emergence of hypomania following the PGB administration. This also support the previous case report in a patient presented with conversion (Yukawa et al. 2013). As pointed previously this effect is similar to antidepressants in bipolar disorder patients. It is clear that the antidepressant drugs doesn't have long-term benefits, and even sometimes could result in uncontrolled mania and suicide as well (Ghaemi et al 2008, Liu et al 2007). Therefore, it is advisable to prescribe PGB more cautiously in bipolar disorder.

Acknowledgments: None.

Conflict of interest: None to declare.

Contribution of individual authors:

Seyed Mehdi Samimi Ardestani: study design.

Pegah Seif: data collection, first draft.

All authors give final approval of the version to be submitted.

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