Switch to a manic episode after desvenlafaxine discontinuation in bipolar disorder

Omar W Muquebil Ali Al Shaban-Rodríguez[1]
Enrique Álvarez de Morales[2]
Celia Rodríguez-Turiel[1]
María A. Fernández-Menéndez[3]
Gabriel García-Álvarez[1]

[1]Hospital Universitario San Agustín. Servicio de Psiquiatría. Avilés, Asturias, España
[2]Centro de Salud Mental El Coto. Gijón, Asturias, España
[3]Monash University. Melbourne, Australia

Correspondence:
Omar Walid Muquebil Ali Al Shaban Rodríguez
Hospital Universitario San Agustín.
Servicio de Psiquiatría.
Camino de Heros, 4. 33012 Avilés (Asturias)
Tel. 679225311
E-mail: muquebilrodriguez@gmail.com

Dear Editor,

It is well known that there is a risk of switch to mania in the treatment of bipolar depression with antidepressants (as well as an increase in chances of rapid-cycling), which is more important in the case of tricyclic and dual action antidepressants[1]. A less frequent clinical situation, although some cases are reported in literature, is the switch to mania that occurs inmediately after antidepressant discontinuation[2,3].

We report the case of a 44-year- old female, diagnosed with bipolar disorder type I, who developed a switch to mania after 100 mg desvenlafaxine discontinuation. The woman had been diagnosed at 23 years of age and presented no other medical or surgical history of interest. At the beginning of her illness she had been treated with lithium carbonate, which was retired after some years due to a severe autolytic attempt through drug-induced autointoxication with this medicine -this episode required ICU admission. Throughout the course of her illness she experienced two manic episodes that required hospital admission, and at least 6 confirmed depressive episodes treated with drugs, the two last ones with desvenlafaxine up to 100 mg/day. The treatment consisted on extended-release valproic acid (100 mg/day), clonazepam (from 1.5 to 2 mg/day), extended-release quetiapine (200 mg/day) and desvenlafaxine (100 mg/day), this one being incorporated to the treatment due to a moderate depressive episode about 3.5 months before discontinuation.

After this period, and having remained clinically stable for about 3 months, desvenlafaxine was withdrawn (according to time-relating recommendations that consider that the antidepressant treatment of bipolar depression should be short-term, precisely in order to avoid the risk of switching to mania[1]). The treatment was suppressed without considering gradual discontinuation for various reasons: the desvenlafaxine dose was regarded as a medium dose, the tablets are not divisible and also because during a previous depressive episode the drug had been withdrawn in a similar way with no clinical incidence. Within 3-4 days of withdrawal, she developed a case of expansive mood, delusions of grandeur, decreased sleep and flight of ideas, posing a manic disorder which was controlled in an acceptable way adding asenapine up to 15 mg/day to the treatment, levomepromacine from 25-50 mg daily and encreasing the daily dose of clonazepam up to 3-4 mg. Nevertheless, although attenuated by the treatment, the symptoms lasted for more than 10 weeks.

Noradrenaline has been identified as a key substance for mania switch; however, the efficiency of antidepressants with noradrenergic activity in the treatment of bipolar depression is high and for this reason they are commonly used substances for this condition[4]. It must be stressed that disputes about the treatment of bipolar depression are on the frontline at clinical level. Most approved recommendations include the use of antidepressants combined with mood stabilizers for short periods of time, withdrawing the antidepressant as soon as possible and basing the strategies on the pharmacological properties of antidepressants, like the constant dissociation from the values of the equilibrium dissociation constant for noradrenaline transporter[2-4].

The significance of the case lies in two facts: it is the first identified case of switch to mania after desvenlafaxine withdrawal -however, cases induced by the introduction of this treatment have been reported[5]- and also because of the low number of published cases relating to antidepressants in other groups, although cases relating to the appearance of manic symptoms in patients with no previous history of this kind have been published, together with reported cases of unipolar depression after the withdrawal of selective serotonin reuptake inhibitors[6] .

The complexity of the treatment of bipolar depression is still a major medical challenge and, as an overall indication, it seems important to emphasise the advisability of introducing and withdrawing antidepressants gradually.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

REFERENCES

1. Antosik-Wójcińska AZ, Stefanowski B, Święcicki Ł. Efficacy and safety of antidepressant's use in the treatment of depressive episodes in bipolar disorder - review of research. Psychiatr Pol. 2015;49(6):1223-39.
2. Narayan V, Haddad PM. Antidepressant discontinuation manic states: a critical review of the literature and suggested diagnostic criteria. J Psychopharmacol 2011;25(3):306-13.
3. Ali S, Milev R. Switch to mania upon discontinuation of antidepressants in patients with mood disorders: a review of the literature. Can J Psychiatry 2003;48(4):258-64.
4. Kurita M. Noradrenaline plays a critical role in the switch to a manic episode and treatment of a depressive episode.

Neuropsychiatr Dis Treat 2016;12:2373-80.
5. Kalia R, Magsalin RM, Khan AY, Kahn DA. Mania possibly induced by desvenlafaxine. J Psychiatr Pract. 2010;16:58-62.
6. Baeza S, Quijada J, Santander J. Síndrome de discontinuación de antidepresivos. Rev Chil Neuro-psiquiatr. 2002;40:56-66.

Mania and energy drinks

Cristina Casas-Gómez[1]
María J. Muñoz-Molero[1]
Rosario Guerrero-Sánchez[2]
Fátima Martínez-León[1]

[1]Psiquiatra, Unidad de Gestión Clínica de Salud Mental Valme, Sevilla, España
[2]Enfermera, Unidad de Gestión Clínica de Salud Mental Valme Sevilla, España

Correspondence:
Mª Cristina Casas Gómez
Unidad de Gestión Clínica de Salud Mental Valme
Av. de Bellavista s/n, 41014 Sevilla
Tel.: 955 015 740
E-mail: ccasaspsiq@gmail.com

Dear Editor,

Caffeine is the main ingredient of energy drinks, considered by some authors as emerging drugs[1]. Energy drinks market has grown exponentially since Red Bull was first introduced in Austria in 1987[2,3]. They are marketed for their properties related to the increase in the level of alertness, memory, humor and energy[2,4]. The increase in consumption among more and more young people, primarily in relation to sports practice and entertainment[5] has created concern among the scientific community and public opinion.

Case report

we present the case of a 22-year-old male attended in the emergency department of a general hospital. He had no somatic, surgical or toxic background of interest, he was not a caffeine or energy drinks consumer and did not undergo any treatment. He had no known personal or family psychiatric history. Single, son of separated parents, the eldest of two brothers. He lived with his father.

He went to the hospital with insomnia and anxiety symptoms. During the previous month he had been working in another country where he was in contact with relatives and close friends, who didn´t report disorders or changes in their functionality. Five days before the consultation, and worried about a trip by plane that he had to make, he ingested 20 cans of 250 cc of an energy drink in 24 hours. This energy drink was composed of 80 mg of caffeine, taurine, inositol and vitamin B complex. Since then he had been nervous, restless, unable to sleep (he had slept a total of 8 hours in 5 days), with "many thoughts in his head" and verbalizing multiple projects related to business and excessive purchases. He described himself as a very calm person, but at the moment he had many things to say and he was in an excellent mood. According to his relatives, he was very nervous, he talked nonstop and moved from one topic to another.

Somatic exploration in the casualty room was reported as follows: good general condition, conscious, oriented, cooperative. Well hydrated and perfused, normocoloured, afebrile, eupneic. Isochoric and normorreactive pupils, without neurological focus to the global exploration. Rhythmic cardiac sounds and good vesicular murmur at pulmonary auscultation. Systolic blood pressure 120, diastolic 63. Heart rate 77 bpm. 98% oxygen saturation. The urine toxic test was positive for benzodiazepines, which had been administered at his health center, and negative for amphetamines, cocaine, cannabis, tricyclic antidepressants, barbiturates, methadone, methamphetamines, opiates and MDMA. In the analytical, he did not show alterations. To the psychopathological exploration, the patient was conscious, self oriented and alopsychically, cooperative, syntonic, hyperalert. His affective state was hyperthymic, expansive, with exaltation of self-esteem, tendency to the loss of limits and disinhibition. He presented tachypsychia, flight of ideas, verbosity, high pressure of speech, with discourse centered on disproportionate plans. No delirious contents or sensoperceptive disorders were evident. He denied tanatic or self-injurious thoughts. He had presented hyperphagia during the last few days, with weight loss and global insomnia. During the evaluation, psychomotor restlessness and a partial awareness of illness were observed.

It was established as initial diagnosis probable mania induced by the use of caffeine at high doses.

10 mg oral olanzapine was administered and was kept under observation for 8 hours. Later he was calmer, he had slept; hyperthymia, expansiveness and megalomaniac thought contents persisted. There were no adverse effects to the treatment administered. In this clinical situation, treatment with olanzapine 10 mg at bedtime and diazepam 10 mg conditional on anxiety was prescribed and abstinence from caffeine was recommended. He was discharged from hospital for follow-up by the reference mental health unit. After two weeks it was necessary to adjust the dose of olanzapine from 10 to 20 mg/day due to the persistence of manic symptoms.

Two months later, it was necessary to reduce the dose of antipsychotic to 10 mg/day by sedation in order to facilitate therapeutic adherence. Hypomanic clinic then persisted. Since the assistance in the emergency room he maintained abstinence from caffeine.

Discussion

Caffeine is a methylxanthine derivative that binds to the A1 and A2a receptors of adenosine, acting as competitive an-

tagonists. In the brain, adenosine receptors inhibit the release of numerous neurotransmitters (GABA, acetylcholine, dopamine, glutamate, noradrenaline and serotonin), so that caffeine will produce the opposite effect[5,6]. Thus, obstruction of the 2A receptors by caffeine the adenosinic A2 receptor blockage would produce an increase in dopaminergic neurotransmission with the consequent stimulating properties[5-7]. Its use has been related to various systemic effects, among which cardiovascular, respiratory, musculoskeletal, the central nervous system, and psychiatric effects[5,7-10]. Among the latter, excessive consumption is associated with anxiety disorders[6-9,11], insomnia[5,10], onset and decompensation of psychosis[5,7,8,10] and mania[2,5,7,8,11]. However, the international classifications of diseases and mental disorders, ICD-10[12] and DSM-5[13], although they recognize disorders derived from the consumption of caffeine (intoxication, abstinence, anxiety disorder and sleep disorder), they don´t consider mood disorder induced by this substance[7].

A can of energy drink can contain up to 500 mg of caffeine[7]; in addition to other components such as taurine or inositol. Taurine is a sulfuric amino acid with a neuroprotective role in muscle and brain contraction, producing increased concentration[14]. Inositol is a natural substance that is present in animal tissues, mainly in the heart and brain, involved in the regulation of cellular responses[15]. Both are related to certain psychoactive properties[7], without the literature being directly related to the appearance of affective disorders, although the acute and long-term effects that result from the excessive and chronic consumption of these additives alone and in combination with caffeine, do not know each other completely.

In this case, the patient ingested 1,600 mg of caffeine acutely, since a 250 cc can of Red Bull (brand of ingested beverage) contains 80 mg of caffeine, 1 g of taurine and 50 mg of inositol[2]. Considering the scientific evidence, the abusive consumption of caffeine could be related to the manic symptoms that he presented.

The diagnosis of the disorders related to the consumption of caffeine is based on the anamnesis, the somatic exploration and the complementary tests, which should be performed according to the clinic, and which in this patient were normal. Its treatment is symptomatic, at the beginning a benzodiazepine is recommended, since seizures have been described after doses of abuse[1]. In our case, given the intensity of the symptoms, its marked manic character, as well as the time elapsed after the consumption, we opted for the administration of an antipsychotic, with which initially favorable response was obtained, as well as the indication of the suspension of caffeine intake.

Conclusions

Energy drinks could represent a public health problem due to their potentially serious effects, especially in more vulnerable people, such as children and teenagers, and people with mental disorders. The consumer should be informed of the risk of the intake, mainly if it is carried out in large quantities or associated with other substances such as alcohol or cannabis[5,7].

Caffeine can induce maniac states, both in people with a previous diagnosis of bipolar affective disorder, and in people without a history[11]. There are few cases described, perhaps because the background of caffeine intake is not often recorded, since it is considered harmless[7,11], and its consumption should be explored due to its potential toxicity and its relation to psychiatric disorders.

CONFLICTS OF INTEREST

The authors declare that there are no competing interests regarding the publication of this paper.

REFERENCES

1. Pereiro Gómez C. Manual de adicciones para médicos especialistas en formación. Barcelona: Socidrogalcohol; 2010.
2. Sharma V. Red bull and mania. Ger J Psychiatry. 2010;13(4):178-80.
3. Reissig CJ, Strain EC, Griffiths RR. Caffeinated Energy Drinks -- A Growing Problem. Drug Alcohol Depend. 2009;99(1-3):1-10.
4. Rizkallah E, Bélanger M, Stavro K, Dussault M, Pampoulova T, Chiasson J-P, et al. Could the use of energy drinks induce manic or depressive relapse among abstinent substance use disorder patients with comorbid bipolar spectrum disorder? Bipolar Disord. 2011;13(5-6):578-80.
5. Hernandez-Huerta D, Martin-Larregola M, Gomez-Arnau J, Correas-Lauffer J, Dolengevich-Segal H. Psychopathology Related to Energy Drinks: A Psychosis Case Report. Case Rep Psychiatry. 2017 [citado 2 de abril de 2017];2017.
6. Lozano RP, García YA, Tafalla DB, Albaladejo MF. Cafeína: un nutriente, un fármaco, o una droga de abuso. Adicciones. 2007; 19(3):225-38.
7. Cruzado L, Sánchez-Fernández M, Cortez-Vergara C, Rojas-Rojas G. Manía inducida por bebidas energéticas con alto contenido de cafeína. Actas Esp Psiquiatr. 2014;42(5):259-66.
8. Wang HR, Woo YS, Bahk W-M. Caffeine-induced psychiatric manifestations: a review. Int Clin Psychopharmacol. 2015; 30(4):179-82.
9. Richards G, Smith AP. A Review of Energy Drinks and Mental Health, with a Focus on Stress, Anxiety, and Depression. J Caffeine Res. 2016;6(2):49-63.
10. Temple JL, Bernard C, Lipshultz SE, Czachor JD, Westphal JA, Mestre MA. The Safety of Ingested Caffeine: A Comprehensive Review. Front Psychiatry. 26 may 2017;8. Available in: http://journal.frontiersin.org/article/10.3389/fpsyt.2017.00080/full
11. Ogawa N, Ueki H. Secondary mania caused by caffeine. Gen Hosp Psychiatry. 2003;25(2):138-9.
12. España, Ministerio de Sanidad PS e I. CIE-10-ES: Clasificación Internacional de Enfermedades, 10ª revisión. Madrid: Ministerio de Sanidad, Política Social e Igualdad, Secretaría General Técnica Boletín Oficial del Estado; 2016.
13. DSM-5 Manual Diagnóstico y Estadístico de los Trastornos Mentales. Editorial Médica Panamericana; 2014.
14. Görgülü Y, Taşdelen Ö, Sönmez Mb, Köse Çinar R. A Case of Acute Psychosis Following Energy Drink Consumption. Nöro Psikiyatri Arş. 2014;51(1):79-81.
15. EBSCO CAM Review Board. Inositol as a dietary supplement. Salem Press Encycl Health. 2015.