CASE REPORT

Sulbutiamine, an ‘innocent’ over the counter drug, interferes with therapeutic outcome of bipolar disorder

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Abstract

A case of a patient with bipolar disorder with a history of hospitalizations and addiction to sulbutiamine is presented. Sulbutiamine is a precursor of thiamine that crosses the blood–brain barrier and is widely available without prescription in most countries or over the internet. Because of this patient’s need to consume ever increasing quantities of sulbutiamine, his psychiatric care was severely compromised through him defaulting appointments and frequent changes of psychiatrists. This paper reviews the current scientific knowledge about sulbutiamine, and some of the information and claims available on the web about its use and potential. It is argued that doctors need to be aware of the potential misuse of medication available over the counter or on the internet and its potential harmful influence.

Key words: Sulbutiamine, bipolar disorder, addiction

Introduction

Healthy adult men and healthy adult non-pregnant, non-lactating women consuming a usual, varied diet do not need vitamin supplements. Vitamins in therapeutic amounts may be indicated for the treatment of deficiency states, for pathological conditions in which absorption and utilization of vitamins are reduced or requirements increased, and for certain non-nutritional disease processes. The decision to employ vitamin preparations in therapeutic amounts clearly rests with the physician (Council on Scientific Affairs 1987).

ICD-10 has a special category for abuse of non-dependence-producing substances, such as vitamins. Although the medication may have been medically prescribed or recommended in the first instance, prolonged, unnecessary, and often excessive dosage develops, which is facilitated by the availability of the substances without medical prescription. Attempts to discourage or forbid the use of the substance are often met with resistance. Although it is usually clear that the patient has a strong motivation to take the substance, no dependence or withdrawal symptoms develop as in the case of the psychoactive substances specified in mental and behavioural disorders due to psychoactive substance use (World Health Organization 1993).

Patients with psychiatric disorders are more likely to use over the counter drugs than those with other diseases (Mamtani and Cimino 2002). Substance abuse is a major comorbidity in bipolar patients (Strakowski and DelBello 2000; Cassidy et al. 2001). In fact, as many as 50% of individuals with bipolar disorder have been found to have a lifetime history of substance abuse or dependence (Sonne and Brady 1999). Although rates decrease in older age groups, substance abuse is still present at clinically important rates in the elderly. Bipolar patients with comorbid substance abuse may have a more severe course (Cassidy et al. 2001).

The case report, presented below, shows the relationship between the abuse of sulbutiamine, an over the counter ‘psychoactive’ substance, and the outcome of bipolar disorder.

Case report

Mr Z is a 42-year-old single man who works in the local municipal services and lives with his parents. At the age of 18 he suffered a manic episode with agitation, aggressive behaviour and paranoid
ideation that required admission to a psychiatric hospital. He subsequently suffered a depressive episode that led to a serious suicide attempt. Following this he had three further manic episodes that required involuntary hospitalization. Apart from the depressive and manic episodes his life was organized, he had a steady job and managed to have additional income from playing the stock market. His latest admission was due to a manic episode and he was discharged in January 2004 normothymic on two mood stabilizers (lithium and carbamazepine), as well as a combination of two different antipsychotics in high doses (haloperidol 20 mg and olanzapine 20 mg OD), benzodiazepines (diazepam 40 mg and temazepam 10 mg OD) and antiparkinsonics (biperiden 4 mg OD). Following this discharge he has been followed-up by our outpatient psychiatric department of our hospital. Mr Z was first seen in March 2004 and has kept regular contacts since. On assessment he presented as a physically healthy man with mild pressure of speech and flight of ideas, expressing grandiose ideas that he did not act upon. During this session he also mentioned that he had started receiving sulbutiamine (Arcalion) by a private prescription 4 months before his latest admission. He was given this medication when he complained of ‘lack of energy’ and ‘slowing down’. He found the medication helpful and on his own increased the dose. Before his last admission he was taking ‘much more’ than he was prescribed when assessed. Mr Z was adamant that this prescription should be continued, although sulbutiamine was not included in the Greek national formulary. He was advised that according to medical opinion there was no reason for him to receive sulbutiamine and was also informed that the dose would be gradually reduced and finally stopped. Subsequent appointments revealed that the main reason for attending his outpatient appointments was to have prescriptions of sulbutiamine that he consumed in vast quantities (more than 2 g/day). It also emerged that one of the reasons he decided to approach our services was the fact that his previous psychiatric carers were unwilling to prescribe sulbutiamine. It transpired that he requested similar prescriptions from other clinics as well. When confronted about his behaviour he became evasive and agitated. He claimed that he used ‘Arcalion’ because it gave him ‘a high’, it raised his body temperature and gave him a ‘warm feeling’. He also felt stronger and consumed the medication before swimming in the sea as it increased his stamina but also made him withstand the cold water for a long period that he could not tolerate otherwise (he is a winter swimmer). It is worth noting that Mr Z never overused the benzodiazepines prescribed and was also willing to reduce the dose of diazepam he was receiving so that he could continue the same amount of sulbutiamine ‘while taking fewer pills on the whole’.

Attempts to reduce the dose of sulbutiamine failed and the patient managed to acquire prescriptions from other doctors. This confrontation was the main reason for repeated missing appointments, unwillingness to perform regular blood tests and non-compliance with the medication. On March 2005, after having missed several appointments, he was urgently referred to our department. His clinical picture was characterized by grandiose ideas, irritability, restlessness, pressure of speech, offensiveness and inappropriate familiarity (he was hypomanic). He was not taking his psychotropic medication regularly, and insisted that medication was not helpful. He kept saying: ‘the only drug that makes me feel good is “Arcalion”.’ Reinstitution of his previous medication and regular follow up led to normothymia within 1 month.

Whenever sulbutiamine was reduced, he denied experiencing somatic withdrawal symptoms, but maintained that without sulbutiamine he felt less energy, drowsiness and ‘unlike his normal self’. Eventually, he agreed to a gradual reduction and now he receives 600 mg of sulbutiamine (initial dose 2 g) and 10 mg of diazepam (initial dose 40 mg) without a change in his mental state and activities, although he is complaining of feeling ‘less energetic’.

Discussion

Sulbutiamine is a hydrophobic molecule that easily crosses the blood–brain barrier and gives rise to thiamine and thiamine phosphate esters in the brain (Van Reeth 1999). It does not have psycho-stimulant properties or antidepressive effect, but it can hasten the resorption of psycho-behavioural inhibition occurring during major depressive episodes and thereby facilitate the rehabilitation of patients in their social, professional and family life functioning (Loo et al. 2000). Sulbutiamine may be a useful adjunct to specific anti-infective treatment (Shah 2003).

Information on the effects of sulbutiamine in human brain is lacking. There is only one study in which it was shown that acute sulbutiamine injection led to a significant decrease of the dopamine levels in the prefrontal cortex and 3,4-dihydroxyphenylacetic acid levels (DOPAC) in both the prefrontal and the cingular cortex in rats, although homovallinic acid (HVA) concentration did not differ from the controls in these two areas. Regarding glutaminergic transmission, acute administration of sulbutiamine induced no change
of density of N-methyl-D-aspartate (NMDA) and \( \alpha \)-amino-3-hydro-5-methyl-4-isoxazole propionic acid (AMPA) receptors in cingular cortex, but significantly decreased in the kainate binding sites (Trovero et al. 2000). The authors postulate that sulbutiamine might exert a modulatory effect on glutamnergic and dopaminergic transmission within the prefrontal cortex. This could play a role in the psychoactive effect of sulbutiamine. In this context, it can be argued that it might also affect the mechanism of action of the antipsychotic medication. It is also noted that searching in the literature did not reveal any report of pharmacokinetic interaction between sulbutiamine and psychotrophic medication.

Thiamine deficiency in both man and animals is known to produce memory dysfunction and cognitive disorders which have been related to an impairment of cholinergic activity. Sulbutiamine is considered to improve memory formation in mice and this behavioural effect could be mediated by an increase in hippocampal cholinergic activity (Micheau et al. 1985). In rhesus monkeys, sulbutiamine showed effect upon the mechanisms regulating waking and light sleep, facilitating a state of wakefulness (Balzamo and Vuillon-Cacciuttolo 1982). There are no reports of any impairment caused by overuse of sulbutiamine or other vitamins of the B complex group except pyridoxine. It is reported that one patient developed a severe sensory and a mild motor neuropathy due to massive and prolonged ingestion of pyridoxine (B6) (10 g daily for 5 years) (Morra 1993).

A Google search on the internet showed almost 14,000 sites in which sulbutiamine (Arcalion) is discussed. Some of them say that ‘(Arcalion) speeds up the reflexes and reaction times in clinical tests, promotes wakefulness and alertness’. In other sites sulbutiamine is being sold among sexual merchandise. Though sulbutiamine has no specific therapeutic indication or clinical use, and it does not appear to have an addictive profile, it seems to be used as a great deal by individuals. The same happens with most vitamin preparations (Council on Scientific Affairs 1987). It is well known that bipolar disorder is associated with substance abuse and addiction (Sonne and Brady 1999; Strakowski and DelBello 2000; Cassidy et al. 2001). Our patient fulfilled the DSM-IV criteria for abuse and addiction of this substance. His addiction to sulbutiamine interfered with his treatment for bipolar disorder and the therapeutic relationship with his doctors. Furthermore, it should be noted that the patient increased, on his own, the sulbutiamine dosage by more than 2 g/day. This was temporarily associated with the emergence of the manic episode. In this regard the large dose of sulbutiamine may have contributed to the manic relapse. The widespread use of sulbutiamine can lead to the assumption that individuals with mental illness can use it as well without their doctors’ knowing. Bearing in mind the case presented, it might be clinically relevant to enquire of psychiatric patients of young age about the use of sulbutiamine.

Statement of interest

The authors have no conflict of interest with any commercial or other associations in connection with the submitted article.

References


