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# Severe abstinence zolpidem

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The safety profile of zolpidem is good if it is administered according to the data sheet recommendations. It is considered to have few adverse effects. Plasma concentration of zolpidem is 40% greater in women than in men. This fact could explain both its greater toxicity<sup>1</sup> and that lower doses are indicated in women<sup>2</sup>. Risk of abuse is considered to be low<sup>3-5</sup>. Most of the cases recorded refer to patients who began to use it with medical prescription to treat their insomnia and who ended up with abusive consumption due to its anxiolytic and stimulating effect that helped them to cope with their daily activities<sup>6</sup>. Cases of tolerance to the hypnotic effects of zolpidem in patients who have taken high doses for several years<sup>3,7,8</sup> as well as a considerable number of cases of dependence on it are found in the literature<sup>6</sup>. The doses used in these patients were superior to those indicated and most of the patients also had psychiatric comorbidity or a history of substance abuse<sup>5</sup>. Symptoms similar to those of benzodiazepine abstinence are included in the abstinence period. Seizures after withdrawal of supratherapeutic abuse doses<sup>7-10</sup> and *delirium*<sup>9</sup> have also been described.

A case of severe abstinence symptoms (seizures listed as epileptic and *delirium*) after the sudden withdrawal of the prolonged abuse dose of zolpidem is presented.

This is a 54 year-old woman who was referred urgently by her primary health care physician to a mental health care site with the diagnostic orientation of conversive seizure.

Somatic background is non-relevant, without known toxic habits. She was diagnosed of dysthemia. Approximately over the previous 14 years, she had slowly initiated abusive consumption of zolpidem, which was partially unknown by those around her, within the context of sleep disorders. She had reached a dosage of between 100 to 200 mg/day for anxiolytic and hypnotic purposes, developing tolerance and

dependence phenomena as well as a disadaptive consumption pattern.

She discontinued the prescription of zolpidem during the 10 days prior to the visit to her primary health care physician. Her family reported that she had general malaise, nausea, vomiting, expression of rare thought contents and negativism during the first days of abstinence. During the following days, sweating, tachycardia, tremor and a seizure listed as epileptic were added. She was finally sent urgently to the mental health care site.

The psychopathological examination showed awareness disorder, with decreased alertness and attention level, temporal and spatial disorientation, bradypsychia, incoherent speech, dysphasia, repeating the words «mono» and «paella», it not being possible to rule out the presence of sensorial-perceptive disorders and psychomotor slowing. She was diagnosed of acute confusional syndrome (*delirium*) within the context of an abstinence syndrome to zolpidem. She was referred to a general hospital to clarify the diagnosis and pertinent treatment. This somatic and neurological examination as well as the complementary tests (complete blood test, biochemistry test, routine urine analysis, brain CT scan, electroencephalogram and cerebrospinal fluid study) did not reveal any pathological findings. She had been diagnosed successively of benzodiazepine poisoning, abstinence to them and epileptic seizure, among others.

After the last referral, she was prescribed 45 mg/day of dipotassium clorazepate and 100 mg of trazodone, maintaining the 30 mg/day of citalopram that had already been prescribed. She evolved towards the complete disappearance of the symptoms reported. Two weeks later, there were no relevant data on examination, reporting global amnesia of the episode, a clinical condition that remained at eight months of follow-up.

The patient in question had very long evolution abusive consumption of zolpidem, between 10-20 times the recommended dose. The abuse was maintained for anxiolytic purposes, developing tolerance to the hypnotic effects and dependence on it after several years. She also had psychiatric comorbidity.

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She had variable symptoms of severity during the abstinence period. There are very few bibliographic references to *delirium* within the context of abstinence. However, cases of psychotic symptoms with subsequent amnesia have been described, that can be understood to have a component of confusional nature, after taking a therapeutic dose<sup>1,2</sup>. Dipotassium clorazepate, long half-life benzodiazepine and trazodone, a sedative antidepressant often used in the treatment of insomnia were prescribed.

In this case, the risk of developing severe abstinence symptoms was increased due to lack of knowledge in her setting of the real doses consumed. This fact also hindered and delayed the correct diagnosis and therapeutic management.

In view of the international information on abuse, dependence and risk of severe abstinence to zolpidem, in March 2002, this was included in the Spanish List IV of Annex 1 of the Royal Decree 2829/1977 that regulates manufacturing, distribution, prescription and dispensation of psychotropic substances and preparations.

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