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LETTER TO THE EDITOR

Interactions of *Valeriana officinalis* L. and *Passiflora incarnata* L. in a patient treated with lorazepam

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Interactions of *Valeriana officinalis* L. and *Passiflora incarnata* L. in a patient treated with lorazepam

MC Carrasco, JR Vallejo, M Pardo-de-Santayana, D Peral, MA Martín, J Altimiras

ABSTRACT

There is an increasing interest in the health risks related to the use of herbal remedies. Although most consumers think that phytomedicines are safe and without side-effects, interactions between complementary alternative–and–conventional medicines are being described.

The aim of this clinical-case-report is to highlight the importance of the safe use of herbal remedies by providing a clinical interaction study between pharmaceutical medicines and herbal medicinal products.

The case of a patient self-medicated with *Valeriana officinalis* L. and *Passiflora incarnata* L. while he was on lorazepam treatment is described. Handshaking, dizziness, throbbing and muscular fatigue were reported within the 32 hours before clinical diagnosis. The analysis of family medical history ruled out essential tremor, Parkinson's disease, Wilson's disease and other symptom-related pathologies. His medical history revealed a Generalized Anxiety Disorder and medicinal plant consumption but no neurological disorder. Appropriate physical examination was carried out.

An additive or synergistic effect is suspected to have produced these symptoms. Valerian and passionflower active principles might increase the inhibitory activity of benzodiazepines binding to the GABA receptors, causing severe secondary effects.

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Due to the herbal−product−self−medication increase, the use of herbal remedies should be registered while taking personal clinical history. Multidisciplinary teams should be created to raise studies on medicinal plants with impact on medical praxis.

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Keywords: herbal remedies, interactions, benzodiazepines, valerian, passionflower

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Introduction

The simultaneous consumption of medicaments and herbal remedies (including dry or fresh medicinal plants and phytopharmaceuticals or vegetable drugs), might cause interactions, much of which are not described nowadays (Farah *et al.,* 2000).

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Nowadays, there is an increasing interest on health risks related to the use of herbal remedies. There is uncertainty with regard to their quality, safety and efficacy. Besides, the increasing trend of self-medication and consumers' perception that phytopharmaceuticals are always safe and have no side-effects, can lead to an increase of the incidence of adverse effects associated to the consumption of herbal medicines (Elvin-Lewis, 2005; Williamson, 2005).

During the visit to the general practitioner in Guadiana del Caudillo (Badajoz, Spain), we reported a clinical case (not previously described in available scientific literature) of a 40 years old male patient self-medicated with valerian (*Valeriana officinalis* L.) and passionflower (*Passiflora incarnata* L.) while on lorazepam treatment.

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Results: Clinical Case

Handshaking, dizziness, throbbing and muscular fatigue were reported within the 32 hours before clinical diagnosis. No other neurological symptoms such as cephalea, paresthesia, loss of any extremity strength neither language nor walking gait alterations were reported.

Family medical history ruled out essential tremor, including Parkinson's and Wilson's disease. Clinical history revealed a generalized anxiety disorder (GAD) and dream disorders. No endocrine-metabolic pathologies, hepatopathies, nephropathies, breathing problems neither personal history of neurological pathologies, consumption of toxic substances, high blood pressure or drug allergies were reported. The patient only mentioned that he had recently consumed medicinal plants.

Since two months ago and without side effects, the patient was following a 2mg/24 h lorazepam treatment. Approximately two hours before bedtime and during two days in a row, the patient took the infusion of valerian subterranean parts. Just before going to bed the patient took the same infusion mixed with unlimited-quantity of passionflower dry herb without side effects. The estimated dose for an infusion is 300 mg. Instead of taking an infusion, the third day before going to bed, the patient took a similar dose of the plants but in tablets of dry extract from valerian rhizomes and roots and aerial parts of passionflower. Each tablet contained 300 mg of valerian and 380 mg of passionflower extract according to the product label. The patient took three tablets at one-hour intervals before going to sleep. Nerves and light-and-rhythmical shaking disappeared shortly after going to bed, followed by a strong drowsiness. As the fourth day the phytopharmaceutical treatment was repeated, strong handshaking, dizziness and palpitations appeared before going to bed, followed by a heavy drowsiness which made

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him fall asleep.

Along the physic exploration, nervousness while speaking and anxiety gestures without shaking were observed. The cardio respiratory auscultation was normal and rhythmical, with a frequency of 60 beats per minute. Goiter on palpation of the neck region was not detected. Blood pressure was 128/74 mmHg. During the neurologic exploration, no communication or understanding problems were observed, cranial pairs were normal, neither meningeal signs nor alterations in tone or muscular strength were detected. Reflexes were normal, Romberg sign was negative and cerebellar function normal. No sensitivity or movement alterations appeared when the patient was invited to walk through the doctor's office.

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First of all the patient was calmed down, then he was explained that the episodic movement disorder he suffered, could be due to an interaction between the herbal and conventional medicines taken. He was also advised that control and monitoring was needed. He continued taking lorazepam and stopped consuming valerian and passionflower and symptoms disappeared.

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Discussion and Conclusions

Lorazepam and other benzodiazepines are described as causing-and-aggravating drug-induced tremor (Sweetman, 2006). Moreover, although valerian drug have low toxicity, when their intake exceeds 20 times the 2-3 g therapeutic doses, intoxication takes place. Its symptoms that include handshaking or fatigue, abdominal cramps, chest tightness, dizziness and mydriasis, disappear within 24 hours (Villar del Fresno and Carretero, 2001; Willey *et al.,* 1995).

The examined patient suffered from excessive drowsiness and dizziness, which can be related to the increase in the sedative effect of valerian observed in animal's clinical trials that had been previously treated with benzodiazepines and other barbiturics. No valerian-benzodiazepine human-related interactions had been previously reported (Castillo and Martínez, 2007).

However interactions between benzodiazepines (alprozolam) and sedative plants such as kava (*Piper methysticum* G. Forst.) have been already described (Almeida and Grimsley, 1996).

Passionflower drug, normally prescribed for the treatment of anxiety and insomnia, has a sedative effect that may also increase when combined with other sedative drugs. It provokes nausea and dizziness when doses are high (Castillo and Martínez, 2007). This was one of the patient's symptoms.

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It can be suspected that the symptoms of the case were caused by an interaction between the herbal remedies and lorazepam. The symptoms disappeared when the patient stopped the herbal treatment. An additive or synergistic effect on the central nervous system (CNS) is suspected to have produced these symptoms. Benzodiazepines facilitate the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) by binding to the alpha subunit of the GABA receptor (Bowery and Smart, 2006). Valerian and passionflower might increase the inhibitory activity of benzodiazepines binding to the GABA receptors, causing severe secondary effects as well.

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Due to the increase in the use of herbal remedies, it seems advisable for the general practitioners to ask on the habit of consuming these remedies while taking personal history and anamnesis. This could be a difficult task, since many patients hide

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these uses in order to avoid being misunderstood by the doctor. Most Spanish practitioners lack an adequate training on phytotherapy and although many reject it, there is an increasing acceptability of herbal medicine.

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In this sense we are conducting a Health Program in Guadiana, in which we inform the local population on the need of making an adequate use of traditional and modern herbal remedies. In addition, we are promoting preventive measures to avoid intoxifications (Vallejo et al. 2008a) and interactions of herbal remedies with medicaments. We give short and concise information to the patients of the primary health care centre on the risks on consuming herbs and herbal products inadequately. Meanwhile, we have put posters in the health centre that induce reflexion when using herbal remedies and that promote asking the general practitioner before consuming them. We have also conducted an ethnopharmacological survey compiling all the traditional remedies of the area in order to contribute to health planification (Vallejo et al., 2008b). ¶

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