

LETTER TO THE EDITOR

Interactions of *Valeriana officinalis* L. and *Passiflora incarnata* L. in a Patient Treated with Lorazepam

María Consuelo Carrasco¹, José Ramón Vallejo², Manuel Pardo-de-Santayana^{3*}, Diego Peral², Miguel Ángel Martín² and Jacinto Altimiras²

¹Consultorio Local Nuestra Sra. de la Soledad de Guadiana del Caudillo, Centro de Salud Pueblonuevo del Guadiana (Badajoz), Travesía de la Constitución s/n. 06184 Pueblonuevo del Guadiana, (Badajoz), Spain

²Grupo de Investigación en Humanidades Médicas, Facultad de Medicina, Universidad de Extremadura, Avda. de Elvas s/n. 06071 Badajoz, Spain

³Departamento de Biología (Botánica), Universidad Autónoma de Madrid, c/ Darwin 2, Campus de Cantoblanco, 28049 Madrid, Spain

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 h 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. The active principles of Valerian and passionflower might increase the inhibitory activity of benzodiazepines binding to the GABA receptors, causing severe secondary effects.

Due to the increase in herbal product self-medication, the use of herbal remedies should be registered while taking the personal clinical history. Multidisciplinary teams should be created to raise studies on medicinal plants with impact on medical praxis. Copyright © 2009 John Wiley & Sons, Ltd.

Keywords: herbal remedies; interactions; benzodiazepines; valerian; passionflower.

INTRODUCTION

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

Nowadays, there is an increasing interest in the 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 the consumers' perception that phytopharmaceuticals are always safe and have no side-effects, can lead to an increase in the incidence of adverse effects associated with the consumption of herbal medicines (Elvin-Lewis, 2005; Williamson, 2005).

After a visit to the general practitioner in Guadiana del Caudillo (Badajoz, Spain), we report a clinical case

(not previously described in available scientific literature) of a 40-year-old male patient self-medicated with valerian (*Valeriana officinalis* L.) and passionflower (*Passiflora incarnata* L.) while on lorazepam treatment.

RESULTS: CLINICAL CASE

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

The 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 or a 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.

* Correspondence to: Manuel Pardo de Santayana, Departamento de Biología (Botánica), Universidad Autónoma de Madrid, c/ Darwin 2, Campus de Cantoblanco, E-28049 Madrid.
E-mail: manuel.pardo@uam.es

Since two months ago and without side effects, the patient had been following a 2 mg/24 h lorazepam treatment. Approximately 2 h before bedtime and for 2 days in a row, the patient took an infusion of valerian subterranean parts. Just before going to bed the patient took the same infusion mixed with an 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 from the 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 1 h intervals before going to sleep. Nerves and light-and-rhythmical shaking disappeared shortly after going to bed, followed by a strong drowsiness. On the fourth day the phytopharmaceutical treatment was repeated and strong handshaking, dizziness and palpitations appeared before going to bed, followed by a heavy drowsiness which made him fall asleep.

Along with the physical 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 neurological 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 was normal. No sensitivity or movement alterations appeared when the patient was invited to walk through the doctor's office.

First of all the patient was calmed down, and then it 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 the symptoms disappeared.

DISCUSSION AND CONCLUSIONS

Lorazepam and other benzodiazepines are described as causing and aggravating drug-induced tremor (Sweetman, 2006). Moreover, although valerian drug has low toxicity,

when the intake exceeds 20 times the 2–3 g therapeutic doses, intoxication takes place. The symptoms that include handshaking or fatigue, abdominal cramps, chest tightness, dizziness and mydriasis, disappear within 24 h (Villar del Fresno and Carretero, 2001; Willey *et al.*, 1995).

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

However, interactions between benzodiazepines (alprazolam) and sedative plants such as kava (*Piper methysticum* G. Forst.) have already been 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.

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 (Bowers and Smart, 2006). Valerian and passionflower might increase the inhibitory activity of benzodiazepines binding to the GABA receptors, causing severe secondary effects as well.

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

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