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SCIENTIFIC LETTER

The role of chronic nutritional supplements consumption in a fulminant serotonin syndrome due to citalopram intoxication

El papel del consumo crónico de suplementos nutricionales en un síndrome serotoninérgico fulminante debido a intoxicación por citalopram

Dear Editor:

Selective serotonin reuptake inhibitors (SSRI) are the most frequently prescribed antidepressants and are included among the most frequently found drug in overdose.[1] Serotonin syndrome (SS) is an adverse drug reaction caused by excessive activation of postsynaptic serotonin receptors and characterized by altered mental status, autonomic hyperactivity and neuromuscular abnormalities (tremor, myoclonus or hyperreflexia).[2–4] Although SS may result in death, most patients recover completely only with the suppression of the treatment and supportive care. SS occurs as an idiosyncratic drug reaction[3] or as a result of the interaction of two or more drugs that enhance serotonin transmission, being the association of SSRI with monoaminoxidase inhibitors the most frequent one. Drug combinations involved with SS include SSRI, tricyclic antidepressants, monoamine oxidase inhibitors, serotonin norepinephrine reuptake inhibitors, triptans, trazodone, opioids, buspirone, linezolid, L-tryptophan or methylenedioxymethamphetamine.[2–5] Interestingly, over-the-counter drugs, nutritional supplements or naturopathic treatments together with SSRI may also be involved with the serotonin syndrome.

We report the case of a previously healthy 42-year-old man with a history of chronic tobacco and alcohol consumption who was recently diagnosed for depression. He was treated with a daily dose of 20 mg of citalopram for the last four days. He regularly practiced sport in a gym centre and he routinely consumed tryptophan-rich supplements at a daily dose of 600 mg of tryptophan and one or two litres of stimulating taurine-rich drink (Red Bull®).

The patient was attended in the emergency department following voluntary ingestion three hours before of 480 mg of citalopram and alcohol with autolytic intention. Initially, he was awake, conscious but showing a marked hyperactivity with diaphoresis, sialorrhea and bilateral and reactive mydriasis. His blood pressure was 168/100 mmHg, heart rate 110 bpm, respiratory rate 48 bpm and axilar temperature of 36 °C. Sublingual benzodiazepine treatment was administered without response. Initial haematological and biochemical analysis were normal, blood ethanol was 56 mg/dL, and analysis of toxics in urine were negative (cocaine, cannabis, benzodiazepines, opiates, amphetamines and barbiturates).

Patient evolution was fulminant with progressive deterioration of his agitation and increasing muscular rigidity and myoclonus, Babinsky bilateral sign, 39 °C temperature, and increasing tachycardia and tachypnea. The patient was admitted to the Intensive Care Unit where he was intubated and connected to mechanical ventilation. A multiorgan failure established itself in a few hours with refractory shock, lactic acidosis, acute renal failure (creatinine 4.5 mg/dL) requiring continuous hemodiafiltration, acute respiratory failure and disseminated intravascular coagulation. Analytic evolution showed hypoglycaemia, cytolysis, rhabdomyolysis (LDH 4370 U/L, GOT 12,989 U/L, GPT 7177 U/L, CK 10,935 U/L) and leukopenia (1700/cc). All of microbiological cultures were negative. After 72 h death was confirmed. The clinical autopsy has not been performed.

Our case is of particular interest because chronic tryptophan ingestion by means of non-pharmaceutical substances was probably the unknown predisposing and crucial background factor associated to bad outcome. As a serotonin precursor, tryptophan led to an increase in serotonin production.

Fatality from SS with pure citalopram overdose is rare due to the very safe range of plasmatic levels of SSRI, even in overdose situations. Our patient took a moderated overdose of citalopram (below 30 times the common daily dose) that has been associated with mild or no symptoms.[6,7] Larger pure citalopram overdoses (more than 840 mg) and/or with combination with other drugs have been associated with life threatening SS.[6–9] According to the World Health Organization (WHO) tryptophan recommended diet requirements are 4 mg/kg/day. In some gym environments it is proposed an additional daily dose of 600 mg of tryptophan as nutritional supplement. This means that for a subject of 75 kg the daily tryptophan intake would be threefold the WHO recommended dose. Moreover, the patient consumed

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regularly large doses of taurine with the energetic drink (4–8 g per day) that could also have serotoninergic activity.[10] All these conditions could predispose the fatal SS, being the citalopram overdose probably the trigger.

Gym products consumed for its energizing or body building properties generally contain large amounts of tryptophan or derivates. These substances are not considered drugs but nutrients, and do not need pharmacological or medical control. It is worth remarking the importance of a meticulous anamnesis to detect the consumption of over-the-counter drugs or substances (sportsmen, naturopathy treatments, ...) before prescribing SSRI or when SS is suspected, in addition to check pharmacologic interactions with other drugs that the patient could take.

Availability of data and material

The data supporting the findings of this case are included in this manuscript.

Authors' contributions

ID and GR analyzed and interpreted the present case, reviewed bibliography and wrote a first draft. SF and MR contributed in writing the manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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