

JAW STIFFNESS AND DENTAL EXTRACTIONS DUE TO PHARMACODYNAMIC INTERACTION BETWEEN MIRTAZAPINE AND CHLORPROMAZINE

BRUXISMO Y EXTRACCIONES DENTALES DEBIDO A LA INTERACCIÓN FARMACODINÁMICA ENTRE MIRTAZAPINA Y LA CLORPROMAZINA

Received: 30 July 2013 Accepted: 27 May 2014

DEAR EDITOR

A comprehensive assessment of the patient's drug related needs allows identifying health problems drug-induced. It has been demonstrated that each dollar spent on clinical pharmacy services reduces the pooled median cost of health by 4.81 dollars (1).

Jaw stiffness (bruxism) can be a serotonergic manifestation related to drugs with serotonin reuptake inhibition activity. Clinical manifestations also include: agitation, tachycardia, high blood pressure, tremor, fever, dyspnea, diarrhea, mental confusion and insomnia (2-5). It affects almost 17% of patients with migraine, depression, panic disorder and anxiety (4-5), and can be caused by several mechanisms, such as: an increase in the synthesis or release of serotonin, direct receptor stimulation or inhibition of serotonin reuptake (6). In this context, we report a drug therapy problem which could be related with unnecessary dental extractions in a 57-year-old man with schizophrenia, prostatic benign hypertrophy, and hypertension.

Case report: Patient 57-years-old arrived at a Unit for Drug- therapy Optimization reporting cold, slight hyperthermia (37.8°C), severe pain in his mouth arising from gnashing creak of teeth, dry mouth, tachycardia (108 beats per minute), and high blood pressure (150/98 mmHg). His family doctor had referred him to a dentist, who was pulling out his teeth. The pharmacotherapy used was: enalapril 20 mg (1-0-0), omeprazole 20 mg (1-0-0), mirtazapine 15 mg (1-0-0), chlorpromazine 25 mg (1-1-1), alprazolam retard 1mg (1-1-1), mirtazapine 30mg (0-0-1), lormetazepam 2mg (0-0-1) and tamsulosin 0.4 mg (0-0-1).

A complete and integral pharmacotherapy assessment was performed according with Strand *et al.* (7). Once problems were detected, a report was sent to his psychiatrist with proposals of changes and adjustments of patient's treatment.

A potential pharmacodynamics interaction between mirtazapine and chlorpromazine was detected. The risk of drug-drug interaction is classified as C (Lexicomp interactions), indicating the need of follow up, due to probability of serotonergic syndrome. Therefore, we proposed to the psychiatrist, based on a guideline (2), the replacement of mirtazapine and chlorpromazine by mianserin, and dosage adjustment of alprazolam (9 mg/day).

A week later, patient referred improvement of bruxism, hyperthermia, tachycardia, hypertension and dry mouth. However, he started to experience confusion, stumble and falls which were solved by reducing dosage of alprazolam to 6 mg/day.

Data suggest a possible serotonergic syndrome experienced by patient, since after pharmaceutical intervention, clinical manifestations disappeared within one week. This period coincides with the period of washout of mirtazapine (seven half-lives of decay of drug in organism), indicating complete excretion by kidneys. Therefore, there is a plausible temporal relationship between the withdrawal of mirtazapine and the consequent improvement of clinical conditions. Causal association was evaluated with Adverse Drug Reaction Probability Scale and the likelihood obtained was possible (score four).

After detection of serotonergic syndrome, no changes in antihypertensive medication were needed and dental extractions were discontinued. The only new dosage adjustments was related to alprazolam, since patient experienced confusion,

stumble and falls, exactly in the period correspondent of mirtazapine washout. These symptoms were resolved by reducing dosage of alprazolam from 9 mg/day to 6 mg/day.

Our findings corroborate that pharmaceutical intervention contributed to avoid other unnecessary dental extractions. Patient could have preserved all his teeth whether a comprehensive assessment of pharmacotherapy had been done prior to his routing to the dentist. The use of avoidable and invasive therapeutic approaches increased the economic costs of health care, and worsened the patient's quality of life. Therefore, health care providers must consider the contribution of pharmaceutical care practitioners in the health care system, in order to promote safety use of medicines.

Patricia de Carvalho Mastroianni, PhD. Assistant Doctor Professor at the Department of Drugs and Medications at the School of Pharmaceutical Sciences of the Universidade Estadual Paulista Júlio de Mesquita Filho – UNESP (Araraquara, SP, Brazil). E-mail: patriciamastroianni@yahoo.com.br

Fabiana Rossi Varallo, PhD student at the Department of Drugs and Medications at the School of Pharmaceutical Sciences of the Universidade

Estadual Paulista Júlio de Mesquita Filho – UNESP (Araraquara, SP, Brazil).

Manuel Machuca, PhD in Pharmacy. Clinical Pharmacist. Unit of Optimization of the pharmacotherapy. Sevilla-Spain.

REFERENCES

1. Perez A, Doloresco F, Hoffman JM, Meek PD, Touchette DR, Vermeulen LC, et al. Economic evaluation of clinical pharmacy services:2001-2005. *Pharmacother*, 2008; 28(11): 285-323.
2. Chu J, Wang RY, Hil, NS. Update in clinical toxicology. *Am J Respir Crit Care Med*, 2002; 166(1): 9-15. Available at: https://secure.muhealth.org/~ed/students/articles/AmJResp_166_p0009.pdf. Accessed December 12, 2012.
3. Jackson N, Doherty J, Coulter S. Neuropsychiatric complications of commonly used palliative care drugs. *Postgrad Med J*, 2008; 84 (989): 121-6.
4. Schuman E. Is an FDA alert harming patients? *JAAPA*. 2009a; 22 (5): 55.
5. Schuman E. Serotonin toxicity revisited. *Headache* 2009b; 49 (5): 784-78.
6. Nelson EM, Philbrick AM. Avoiding serotonin syndrome: the nature of the interaction between tramadol and selective serotonin reuptake inhibitors. *Ann Pharmacother*, 2012, 46: 1712-1716.
7. Strand LM, Cipolle RJ, Morley PC, Frakes MJ. The impact of pharmaceutical care practice on the practitioner and the patient in the ambulatory practice setting: twenty- five years of experience. *Curr Pharm Des*, 2004; 10 (31): 3987-4001.