OXYCODONE ABUSE DURING PAIN-RELIEF PRESCRIPTION: AN UNUSUAL BUT IMPORTANT CAUSE

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Introduction: To describe the mechanisms of oxycodone abuse in an adult treated for low-back-pain. Oxycodone is a widely used μ-opioid receptor agonist for the treatment of acute and chronic pain. The N-demethylation via CYP3A4/A5is quantitatively the most important route of oxycodone metabolism: noroxycodone (80% circulating metabolite) has a weak antinociceptive effect. Moreover, CYP2D6catalyzes the O-demethylation to oxymorphone (approximately 13% of the metabolism), that has a μ-opioid receptor affinity 10-40 times higher than oxycodone and has a very potent antinociceptive activity. The polymorphism of cytochrome P450 isoenzymes (CYPs) gives rise to important interindividual and interethnic variability in metabolism and in clinical response to this drug.

Case report: A 53-year-old Caucasian male was evaluated in our unit for oxycodone abuse started following a therapy prescribed to control chronic low-back-pain (scoliosis and spondylolisthesis L5-S1). History was positive for HIV (treated with Emtricitabine-Tenofovir 200 mg / 245mg QD, Atazanavir 300 mg QD and Ritonavir 100 mg QD) and hypertension (treated with losartan, 12.5mg QD). Patient increased progressively oxycodone dosage to obtain analgesic effect: at first admission patient was taking 320 mg/die of oxycodone in association with acetaminophen 3g/die. Despite this dosage, the patients experienced withdrawal symptoms (sweating, nausea, agitation and diarrhea). At admission, blood oxycodone, oxymorphone, noroxycodone and noroxymorphone levels were 70.42, 0.0, 9.4, and 0.67ng/ml, respectively. Oxycodone concentration decreases progressively according to the stop of the drug intake. During hospitalization the addiction symptoms were successfully controlled by clonidine and benzodiazepines. To obtain a low-back-pain control, the patient underwent two peridural injections of depo-medrol 80 mg and ropivacaine 6mg. A surgical treatment of spondylolisthesis was finally suggested. Genotyping for CYP2D6was performed showing that our patient was poor metabolizer (PM); CYP3A4activity was normal.

Discussion and conclusion: In our case, CYPs polymorphism (CYP2D6PM) was the cause of the lack of response to the analgesic therapy that led the patient to progressively increase oxycodone dose. Oxycodone level was higher than usually detected in treated patients, even if subtoxic. Undetectable levels of the main analgesic metabolite (oxymorphone) is the cause of the lack of clinical response to analgesic treatment. Clinician should be aware that the lack of response to the prescribed therapy can be a subtle cause of drug abuse. Drugs interactions evaluation and CYPs polymorphism genotyping is advisable to choose the best therapy and the targeted dose for each patient.