Opioid Withdrawal after Sufentanil-induced Anesthesia

Michel Bourin*

Neurobiology of Anxiety and Mood Disorders, University of Nantes, France

Abstract

This clinical case reports a withdrawal syndrome following intravenous administration of sufentanil to a young woman for short-term anesthesia. Hypotheses are issued and documented. The first, being the fact that the patient had a low liposuction-related fat mass resulting in fast lipid release of sufentanil. The second was a relative overdose of sufentanil leading to non-release of encephalin.

Keywords

Sufentanil; Withdrawal syndrome; Opioids

Introduction

I observed a morphine withdrawal following a gynecological procedure on a small uterine polyp. Anesthesia procedure consisted of: propofol 200 mg, sufentanil 10 mg, droperidol 1.25 g, administered intravenously. The symptoms observed in the 37-year-old woman, 8 hours after surgery, were: derealization, hyperthermia, paresthesia and myoclonus of the upper and lower limbs, gastric embarrassment [1]. The duration of the symptoms for about 3 hours was more representative of a morphine withdrawal; if some symptoms are closed to a panic attack the duration is different. In case of a panic attack the cessation of symptomatology is around 20 minutes. In front of these symptoms, I administered to the patient sublingual prazepam 20 mg. Attenuation of the symptomatology was manifested about 2 hours after taking prazepam and the patient was able to fall asleep. She woke up 4 hours after, the symptomatology of weaning was still present but moderate, and a new 20 mg prazepam tablet did away with the symptoms. The fact that prazepam that acts at the level of GABA receptors could not stop weaning symptoms rapidly suggests that weaning is not related to propofol [2]. Although the mechanism of pharmacological action of propofol is poorly known, it is attributed to a GABAergic action [3]. On the other hand, the patient had no history of taking opioids or other abusive substances such as cannabinoids, alcohol or tobacco.

How to explain this opioid withdrawal?

The patient is 1.64 m tall for 54 kg. Its fat percentage is 11% when it should be between 13, 5 and 17% [4]. One probable explanation is that the patient had undergone liposuction of abdominal fat and thighs 2 years previously. Two of the prescribed drugs (propofol and sufentanil) are eminently fat-soluble and, because of the changed fat/ water ratio, have probably been overdosed, which the protocols of the anesthesiologists do not provide. The diffusion in the fats of sufentanil is carried out in 3 phases, which explains quite well the chronology of the weaning in two stages [5]. Fats used as dampers for the release of products into the blood.

Another explanation is that sufentanil is 500 times more potent for mu receptors than morphine. Sufentanil is the most potent of the opioids currently available for use in man; it has a very high binding affinity for the mu-opioid receptor. The duration of the pharmacological effect is determined by the time of dissociation of stereospecific drug-receptor binding and also by pharmacokinetic half-life; the recovery would be expected in consideration of the different terminal half-times. Moreover, the binding affinity of sufentanil for delta-type binding sites labelled by [3H] [D-Ala2, D-Leu5] enkephalin was found to be 100 times lower than its binding affinity for the mu-receptor sites [6]. [3H] Sufentanil was used for a detailed investigation of the regional distribution of mu-opiate receptor sites in the brain; Bmax and KD values were measured in the dorsal and ventral spinal cord. There is no relationship between binding affinities and lipophilicity and degree of ionization of the compounds. So the endorphinic system is suppressed when a potent exogenous opioid like sufentanil is prescribed with a relative high dosage due to the very low rate of patient fat [7]. Observations with remifentanil show that withdrawal syndrome can be observed [8].

On the other hand, combination of propofol and sufentanil should be reconsidered as studies show some of the dose combinations considered, the hypnotic depth obtained is not improved even if the analgesia seems better [9]. It may be warranted to use fentanyl less...
fat soluble than sufentanil in low fat individuals, as well fentanyl has less affinity to mu opioid receptors than sufentanil. Cumulative dose and length of analgesedative therapy with sufentanil significantly increases the risk of withdrawal syndrome in critically patients with low fat index that is the case of pediatric patients [10].

Opioid weaning after intravenous anesthesia should not be so rare, indeed patients are usually not hospitalized and although surprised to experience “anxiety” do not call a doctor in emergency. A documented post-operative questionnaire would answer this question.

References
1. Cammarano WB, Pittet JF, Weitz S, Schlobohm RM, Marks JD. Acute withdrawal syndrome related to the administration of analgesic and sedative medications in adult intensive care unit patients. Crit Care Med. 1998 Apr;26:676-684.
2. Au J, Walker W, Scott D. Withdrawal syndrome after propofol infusion. Anaesthesia. 1990 Sep;45:741-742.
3. Tang P, Edenhoff R. Recent progress on the molecular pharmacology of propofol. F1000Res. 2018 Jan;7:123.
4. Rhodes SK, O’Neil PM. Effects of body fat distribution on body size estimation accuracy among obese women. Int J Obes Relat Metab Disord. 1997 Mar;21(3):250-253.
5. Scholz J, Steinfath M, Schulz M. Clinical pharmacokinetics of alfentanil, fentanyl and sufentanil. An update. Clin Pharmacokinet. 1996 Oct;31:275-292.
6. Leysen JE, Gommeren W, Niemegeers CJ. [3H] Sufentanil, a superior ligand for mu-opiate receptors: binding properties and regional distribution in rat brain and spinal cord. Eur J Pharmacol. 1983;87:209-225.
7. Korak-Leiter M, Likar R, Oher M, Trampitsch E, Ziervogel G, et al. Withdrawal following sufentanil/propofol and sufentanil/midazolam. Sedation in surgical ICU patients: correlation with central nervous parameters and endogenous opioids. Intensive Care Med. 2005 Mar;31(3):380-387.
8. Delvaux B, Ryckewaert Y, Van Boven M, De Kock M, Capdevila X. Remifentanil in the intensive care unit: tolerance and acute withdrawal syndrome after prolonged sedation. Anesthesiology. 2005 Jun;102:1281-1282.
9. Schraag S, Mohl U, Bothner U, Georgieff M. Interaction modeling of propofol and sufentanil on loss of consciousness. J Clin Anesth. 1999 Aug;11:391-396.
10. Hronova K, Pokorna P, Posch L, Slanar O. Sufentanil and midazolam dosing and pharmacogenetic factors in pediatric analgesedation and withdrawal syndrome. Physiol Res. 2016 Dec;65:S463-S472.