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LETTER TO THE EDITOR

Striking cessation of cataplexy by opioids

An exceptional clinical observation was made in a patient with type I narcolepsy that supports the findings of a recent published study in which cataplexy is reduced by morphine in a mouse model of narcolepsy.

Our patient was born in 1936, and developed symptoms of narcolepsy at about 20 years old. Typical cataplexy developed 10 years later. He had sporadic hypnagogic hallucinations, a disturbed nocturnal sleep, but no sleep paralysis. His medical history included hypertension, gout and benign prostate hypertrophy. He was diagnosed with narcolepsy with cataplexy in the late 1970s, and this diagnosis was confirmed by a narcolepsy specialist in 2006 (GJL). He had a sleep-onset rapid eye movement (SOREM; 5 min) on nocturnal polysomnography, and slept on four naps during the Multiple Sleep Latency Test with sleep-onset latency of 6.5 min and one SOREM. In addition, he is HLA DQB1*06:02 positive. Cataplexy mostly occurs in funny situations, when making a witty remark, but also when he is nervous, and with a lower threshold when he is tired. When on sodium oxybate (SXB) he did not have cataplexy attacks every day, but at least once a week, involving head, neck, arms and leg muscles as well as muscles related to speech. SXB has been used, since 2010, for nocturnal sleep disturbances and to reduce cataplexy. He used Modafinil 50 mg bid from 2014 until 2016, but quit and chose to take ad libitum naps afterwards.

In March 2017, he woke up during the night, 1.5 hr after SXB ingestion, and walked to the toilet while groggy from his SXB dose and fell, resulting in a stable C2 fracture. No surgery was needed and the patient was treated with a hard collar immobilization and initially with oxycodon 5 mg qid and oxycodone controlled-release 10 mg bid, later he received oxycodone 10–60 mg dd for about 14 days during hospitalization. SXB was discontinued on the day of the fracture. He was transferred to a rehabilitation centre where he received the buprenorphine patch, and kept it for 6 months. After a week or two he noticed that his cataplexy had extremely reduced and finally disappeared, although he still was in situations that he says would have elicited cataplexy previous to the opiate treatment. He was cataplexy free for 6 months. On the day he discontinued taking the buprenorphine patch, cataplexy re-appeared. It returned at a frequency of four–five times a day. Immediately after discontinuation of the buprenorphine, he restarted SXB 2.25 g twice a day, with a cataplexy reduction to once a week as a result.

The effect of opioids on narcolepsy was first described by Harper (1981). In this case, a patient noticed a symptom reduction on codeine phosphate, and a recurrence of cataplexy 5 days after discontinuation. Benbadis reported improvement of cataplexy on codeine as well (Benbadis, 1996). Fry reported five patients with a self-reported positive effect of narcolepsy symptoms on codeine, but this was not confirmed in a double-blind placebo–codeine trial performed in eight patients for 1 week (Fry, Pressman, DiPhilippo, & Forst-Paulus, 1986). A reduction of cataplexy on tramadol was noted by Wichniak, Brunner, Friess, and Pollmächer (2003). Inhibition of REM sleep by opiates was given as a possible explanation for this finding (Nishino & Mignot, 1997). Impact on the noradrenergic and/or serotonergic system could possibly explain this. However, a recent finding from Thannickal et al. (2018) shed new light on the mode of action of opiates in narcolepsy. They discovered that human heroin addicts have, on average, 54% more hypocretin-producing cells than controls. In addition, morphine administration increased the population of detected hypocretin cells in 30% depleted mice to normal, and decreased cataplexy in a mouse model of narcolepsy.

This is the first description of symptom reduction in narcolepsy on buprenorphine. Together with the previous findings it is likely that opiate agonists may have an important role in the treatment of narcolepsy. It cannot be ruled out that systems other than the hypocretin system are involved, and therefore more research is needed. Placebo-controlled trials in human narcolepsy are required to validate this treatment.

CONFLICT OF INTEREST

The authors report no conflict of interest for this letter.

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