Short Communication

A CASE REPORT OF PROPOFOL DEPENDENCE IN A PHYSICIAN

Udo Bonnet, M.D.*
Jörg Harkener, M.D.**
Norbert Scherbaum, M.D.***

Abstract—Propofol is a widely used general anaesthetic with multisite mechanisms and especially ultrashort activation of certain central GABA-A receptors. Since its introduction into the market in the mid 1980s this is the seventh report on propofol dependence in the literature. The present case shows for the first time that craving for propofol can be quite intense and able to induce addictive behaviour.

Keywords—dependence, propofol, sedatives

Propofol is an ultrashort acting, general intravenous anaesthetic (Barr 1995) with growing off-label usage, e.g. for treatment of refractory delirium tremens (McCowan & Marik 2000) or some types of refractory headache (Krusz, Scott & Belanger 2000). Furthermore, propofol anaesthesia is advantageous in ultra rapid opiate detoxification (Kienbaum et al. 2000). Propofol primarily works by rapid activation of special central GABA-A receptors containing β1 or β3 subunits (Grasshoff, Rudolph & Antkowiak 2005; Krasowski et al. 1998) and appears to have mainly anticonvulsant activity (Barr 1995). In this context, propofol shares a lot of pharmacological features with sedative hypnotics, such as clomethiazole and benzodiazepines. (In Germany, clomethiazole is commonly used to treat acute alcohol withdrawal of inpatients; see Bonnet et al. 2003). A longer lasting intake of these hypnotics is characteristically combined with the development of a chemical dependency consisting of typical physical and psychological symptoms (O´Brien 2005; Rickels et al 1999). Six anecdotal cases of dependency for propofol have been reported in the literature so far (Fritz & Niemczyk 2002; Schneider et al 2001; Odell 1999; Soyka & Schuetz 1997; Follette & Fareley 1992; Guendel & Kuhs 1992). However, none of them emphasized craving. The present case shows for the first time that craving for propofol indeed can be quite intense and able to induce addictive behavior.

CASE REPORT

A 30-year old physician working at an intensive care unit was admitted to a surgery unit after a car accident. He did not suffer from head trauma but developed symptoms reminiscent of benzodiazepine withdrawal, such as fluctuating and later decreasing tachycardia, hyperhidrosis, lack of concentration, anxiety and insomnia overlapping with increasing restlessness. Physical and laboratory examinations as well as urine drug screening were normal with the exception of a broken thighbone and multiple fresh and older puncture marks above superficial and deeper veins of the left upper extremity of the right-handed man. Throughout a three-week psychiatric consultation treatment the withdrawal-like symptoms improved by treatment with gabapentin.

His medical history reveals a current dependency on cigarettes and propofol. He had consumed tobacco since his early adolescence, and it was later combined for over two years with marijuana. In addition, he experienced a period of alcohol abuse in his early adulthood which was allegedly stopped due to the development of a cluster headache. Further experiences with illegal drugs or hypnotics were not reported. As an intern he discovered the use of intravenous midazolam to soften periodic cluster attacks and calm down after hard work. Midazolam was totally replaced by propofol as he felt more pleasant and euphoric under subanaesthetic doses of this drug; he consumed it solely for a year on a nearly daily basis in several sessions per day. He felt increasingly controlled by propofol and finally increased the daily amount up to two ampoules of 200 mg stolen from the clinic stock. At that time the frequent propofol sessions (up to 15 times a day) were increasingly associated with unwanted,

*Senior Physician and Assistant Medical Director, Rhine Hospital of Essen, Department of Addictive Behaviour and Addiction Medicine, & Associate Professor, Department of Psychiatry and Psychotherapy, University of Duisburg/Essen, Essen, Germany.

**Senior Physician, Department of Trauma Surgery and Reconstructive Surgery, University of Duisburg/Essen, Essen, Germany.

***Medical Director, Rhine Hospital of Essen, Department of Addictive Behaviour and Addiction Medicine, & Professor, Department of Psychiatry and Psychotherapy, University of Duisburg/Essen, Essen, Germany.

Please address correspondence and reprint requests to Prof. Dr. med. Udo Bonnet, Rheinische Kliniken Essen, Klinik für Abhängiges Verhalten und Suchtmedizin & Klinik für Psychiatrie und Psychotherapie der Universität Duisburg/Essen, Virchowstr. 174, D-45147 Essen, Germany. Email: udo.bonnet@uni-due.de

very short lasting attacks of unconsciousness followed by amnesia.

In the beginning of his daily propofol consumption he remembered a voluntary drug holiday lasting two weeks which was associated with mild anxiety, lack of concentration, increasing sleeplessness and a strong desire for propofol before relapsing. Restlessness was reported to result mainly from intense craving for propofol.

Unfortunately, he could not be moved to a weaning therapy during the psychiatric consultation treatment. A few months after his discharge from the surgery unit he lost his job when he was caught while self-injecting propofol. A few days later he again was caught while breaking into a hospital to acquire this drug. He then entered a long-term abstinence-oriented weaning therapy.

It is recommended that off-label administrations of propofol be closely checked for addictive incentives. In this context, no cluster attack occurred in the patient during the three-week psychiatric consultation treatment. Although the course of the acute type of this headache is typically periodic with often long intervals free of symptoms, some doubts about the validity of this self-made diagnosis remained because the patient reported that he had not consulted a headache specialist prior to using propofol.

DISCUSSION

In this case all main ICD-10 criteria required for a diagnosis of dependency on sedatives were fulfilled (O´Brien 2005). This includes psychological (craving for propofol, loss of control) and physical (tolerance, withdrawal syndrome with hyperhidrosis, tachycardia, anxiety and insomnia) components and negative social sequelae, such as burglary to acquire propofol. Physical symptoms were decreasing during the three -week consultation in contrast to psychological symptoms, which were increasing and finally led to the addictive behavior (e.g. burglary).

Although propofol has only ultrashort pharmacological action the frequent stimulation of central GABA-A receptors might be strong enough to evoke counteradaptive changes in central neurotransmission explaining the development of physical dependence (chiefly tolerance, withdrawal) (Heinz et al. 2003). The rapid activation of mesolimbic GABA-A receptors, however, might be responsible for the striking psychological dependence (chiefly craving, addictive behavior). It is assumed that rewarding dopamine and/or endorphin systems (Ikemoto & Wise 2004; Heinz et al. 2003) could be immediately sensitised by a rapid GABAergic input. A slower activation of central GABAergic interneurones (by using physiological routes, such as increasing the GABA level in the synaptic clefts) is presumably not associated with the psychological dependence that builds the main fundament of addiction (Ikemoto & Wise 2004). This idea is supported by the observation that there are no reports of addiction due to GABAergic anticonvulsants, such as gabapentin, vigabatrine or tiagabine so far (Besag 2004; Ashton & Young 2003).

The present case is the seventh in literature to mention propofol dependence since propofol's introduction into the market in the mid 1980s. Five of them were related to professionals (Odell 1999; Soyka & Schuetz 1997; Follette & Fareley 1992; Guendel & Kuhs 1992) and the remaining two to lay persons (Fritz & Niemczyk 2002; Schneider et al. 2001). To date, there are no signs of illegal deals with propofol on the black market and additionally, there exists only scarce evidence for propofol to be a relevant public health risk (Schneider et al. 2001). It must be emphasized that propofol has an excellent safety record and several millions of patients anaesthetised with propofol did not develop any signs of addiction. But one should be aware of the addictive dangers of propofol, especially for professional persons working near anaesthetic stocks and with a current or former history of alcohol or other drug abuse (Kintz et al. 2005).

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