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Review

The fine line between occupational exposure and addiction to propofol

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ABSTRACT

Addiction is considered as an occupational hazard, especially in anesthesia units in hospitals. Professionals in anesthesiology clinics have easy access to a wide range of potent psychoactive drugs, causing them to have a higher risk of drug abuse compared to other healthcare personnel. Recent studies and case reports have shown that abuse of anesthetic drugs used in these units has become a problem among health professionals, and awareness of the problem has increased. Propofol is widely used in anesthesia as a sedative-hypnotic prescription drug and in the literature, propofol abuse is mostly referred to in connection with medical and paramedical personnel. In this manuscript, we reviewed the pharmaco-kinetics, -dynamics effect of propofol, discussed toxicological outcomes of propofol abuse and possible institutional measures to be taken against addiction.

Keywords: Propofol, addiction, abuse, anesthetics

INTRODUCTION

Propofol (2,6-diisopropylphenol) is an intravenous anesthetic agent used for induction of moderate-to-deep sedation prior to surgical operations and distressing medical interventions (Klausz, Rona, Kristóf, Töro, 2009; O'Malley, 2010; Bryson & Frost, 2011). The chemical formula of propofol is $C_{12}H_{18}O$ and its structure is given in Figure 1 (Feng, Kaye, Kaye, 2017). In clinical settings, propofol is safe for providing procedural sedation and it has been used to induce and maintain general anesthesia since 1985 (Kirby, Colaw, & Douglas, 2009; Levy, 2011). In intensive care units (ICU), some advantages like rapid onset, short action time and rapid recovery make propofol an excellent agent for anesthesia and sedation (O'Malley, 2010). Because of its high lipophilicity, propofol has a rapid onset of action and a short-term narcotic effect (Klausz et al., 2009; Levy, 2011). Its minimal residual effects on the central nervous system (CNS) and the rapid return of the patient's consciousness are further advantages of propofol, and with this effect, it is ideal for use in plastic surgery (McCarver & Spear, 2010). Besides induction and/or maintenance of anesthesia, propofol is also used in clinics for procedural sedation and in ICU for sedation in intubated and mechanically ventilated patients. Furthermore, propofol has off-label uses for management of refractory status epilepticus in children and adults and for the treatment of refractory postoperative nausea and vomiting (Folino, Muco, Safadi, & Parks, 2022; Drugbank Online, 2022). In addition to its anesthetic effects, propofol is also used in cases of resistant seizures, resistant migraine and tension headaches, severe alcohol withdrawal and delirium tremors, and to facilitate rapid opiate detoxification (Bonnet, Harkener, Scherbaum, 2008; Sarff & Gold, 2010; Levy, 2011). However, though propofol is not currently classified as a controlled substance, numerous case reports and

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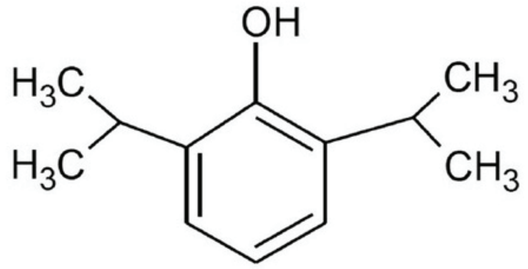

Figure 1. The chemical structure of propofol.

case studies present the abuse potential and addiction risks of propofol (Welliver, Bertrand, Garza & Baker, 2012 ; Han, Jung, Baeck, Lee & Chung, 2013; Gwiazda et al., 2021).

Substance use disorders are not only a major social problem but also a part of a global public health crisis and a serious health concern (Onaolapo et al., 2022). Substance abuse is defined in the American Psychological Association (APA) dictionary (APA, 2022a) as "a pattern of compulsive substance use marked by recurrent significant social, occupational, legal, or interpersonal adverse consequences, such as repeated absenteeism from work or school, arrests, and marital difficulties". According to the Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition (DSM-V), substance abuse and dependence is defined as "substance use disorder" and diagnosing the disorders has been revised (APA, 2022a; Dugosh, 2022). DSM–V–TR places alcohol-, caffeine-, cannabis-, hallucinogens-, inhalants-, opioids-, sedatives-, hypnotics-, anxiolytics-, stimulants-, and tobacco-related disorders under substance-related and addictive disorders, and propofol addiction falls under the category of "sedative-, hypnotic-, or anxiolytic-related disorders." (APA, 2022b). According to Kirby et al., certain criteria can be used in the diagnosis of substance use disorders. These are: i. Compulsion or craving to use a substance; ii. loss of control over the amount or frequency of the substance used; iii. continued use of the drug despite adverse consequences and ensuing problems in relationships; and iv. neglecting normal life necessities (Kirby et al., 2009).

In this manuscript, after summarizing the pharmacological properties (pharmacokinetics, pharmacodynamics, adverse effects) of propofol, the toxicological outcomes including addiction are discussed.

Pharmacokinetic profile of propofol

A three-compartment linear model has been defined for propofol pharmacokinetics: i. a large central compartment ii. peripheral compartment with lower perfusion (lean tissues) iii. deep compartment with low perfusion (fatty tissues) (Iwersen-Bergmann, Rösner, Kühnau, Junge, Schmoldt, 2001; Kranioti, Mavroforou, Mylonakis, Michalodimitrakis, 2007; Klausz et al., 2009; Levy, 2011; Budic et al., 2022). For induction of anesthesia, 1.5-2.5 mg per body weight as kg dose of propofol is sufficient to produce unconsciousness. Children need greater doses while the elderly need smaller doses because of the pharmacodynamic variances (e.g., central distribution volumes and clearance rates) (McCarver & Spear, 2010). There is a sharp decrease in brain concentrations due to the redistribution from the central compartment into peripheral compartments, and this may result the patient waking up from anesthesia (Iwersen-Bergmann et al., 2001).

Propofol has a bitter taste and low oral bioavailability (high first pass effect and high hepatic extraction rate). Therefore, it can only be used intravenously. After intravenous administration, propofol is significantly bound to plasma proteins (mostly albumin) with 97-99% rate and erythrocytes (Budic et al., 2022). Propofol is metabolized very rapidly, and it leaves the tissue storage areas. Thus, plasma concentrations never increase (McCarver & Spear, 2010; Levy, 2011). Propofol is biotransformed to inactivate metabolites with UDP-glucuronosyltransferase (70%) and CYP2B6 and CYP2C9 (29%) enzymes to form either glucuronide or sulfate conjugates in the liver and then excreted by the kidney (1%) (Figure 2) (Iwersen-Bergmann et al. 2001; Kranioti et al., 2007; Klausz et al., 2009; McCarver & Spear, 2010; Levy, 2011; Dinis-Oliveira, 2018; Budic et al., 2022). Polymorphisms in these enzymes are responsible for the individual variables of propofol anesthetic effect like the unpredictable effects of standard doses or prolonged recovery time from anesthesia. The small intestines are also active in the metabolism of propofol with an 24% extraction ratio (Budic et al., 2022). Less than 1% is excreted unchanged in the urine and 2% in the feces. Since kidney and liver diseases do not affect propofol's excretion, it does not accumulate even in patients with those diseases (Levy, 2011). The elimination of propofol does not cause cirrhosis or renal failure, and its elimination half-life is between 0.5 and 1.5 hours (McCarver & Spear, 2010; Levy, 2011). Because of its high lipophilicity, propofol easily crosses the placental barrier and may cause neonatal CNS and respiratory depression (McCarver & Spear, 2010; Dugosh &Cacciola, 2022). If the neonates are exposed to propofol, they should be monitored for hypotonia and sedation (Dugosh &Cacciola, 2022). Animal studies have shown that blocking NMDA receptors and/or potentiate gama-aminobutyric acid (GABA) activity with the use of general anesthetic and sedation medications may affect brain development. Fetal exposure to propofol requires benefit/risk analysis if the exposure duration is greater than 3 hours (Olutoye, Baker, Belfort & Olutoye, 2018; Dugosh &Cacciola, 2022).

Only a small amount of propofol may be excreted to the milk and it is not expected to be absorbed by the infant. Mothers can breastfeed after sufficient recovery from general anesthesia, thus discarding the milk is unnecessary (LactMed, 2021).

Pharmacodynamic profile of propofol

Propofol exerts its pharmacological effect by increasing the chloride ions current at the GABA type-A receptors located in different areas (the reticular activating system, the chemoreceptor trigger zone, the medullary and pontine ventilator centers) (Roussin, Montastruc, Lapeyre-Mestre, 2007; Klausz et al., 2009; McCarver & Spear 2010; Sarff & Gold, 2010; Bryson & Frost, 2011; Levy, 2011) and it activates GABA to produce hypnosis (Budic, 2022). It may also interfere with and inhibit the functions of the N-methyl-D-aspartate receptors (NMDA), α-amino-3-hydroxy-5-

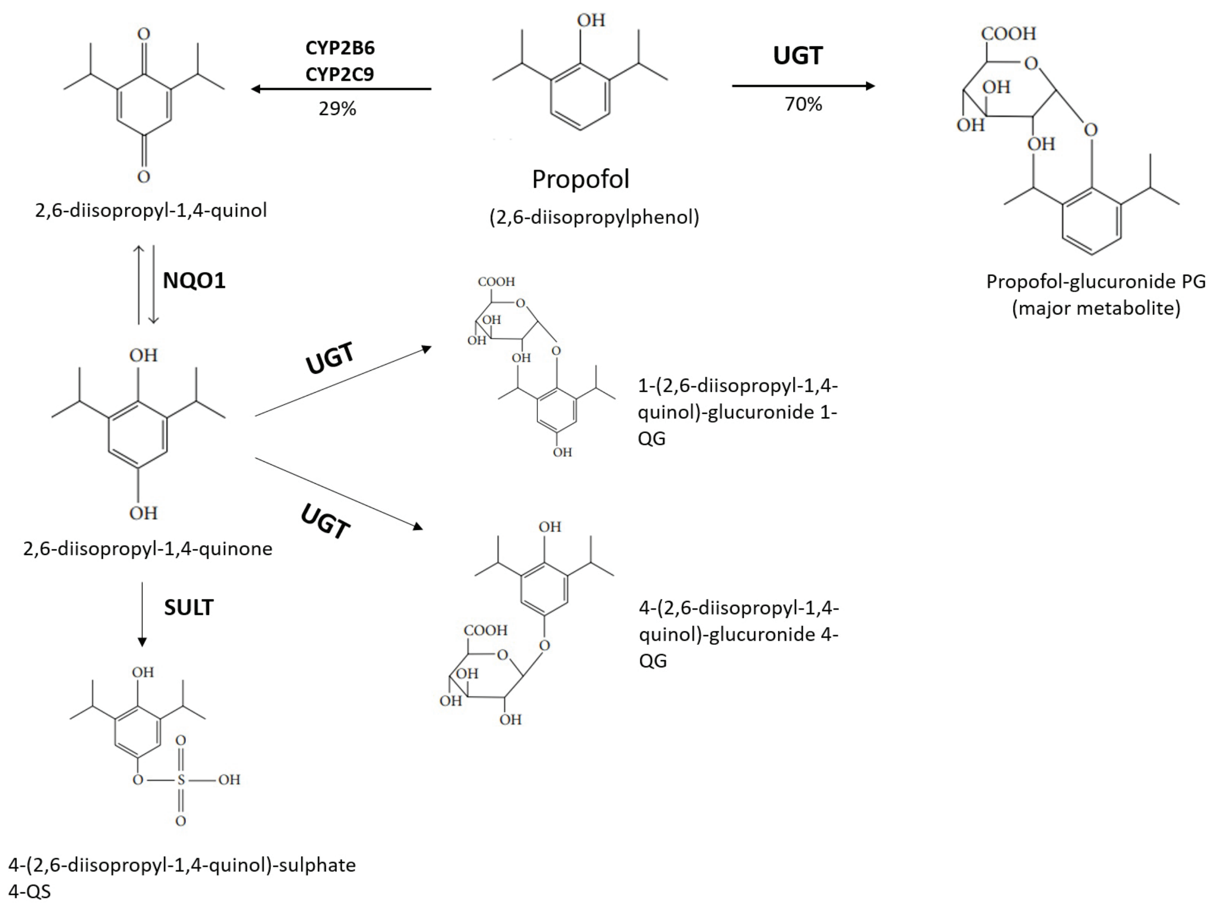

Figure 2. Metabolic pathway of propofol (Dinis-Oliveira, 2018).
SULT: sulfotransferase; UGT: UDP-glucuronosyltransferase; NQO1: diaphorase; CYP: cytochrome P450.

methyl-4-isoxazolepropionic acid (AMPA) receptors, and nicotinic acetylcholine receptors. Moreover it activates inhibitory glycine receptors at the spinal cord level (Roussin et al., 2007; Sarff & Gold, 2010; Bryson & Frost, 2011; Levy, 2011; Feng et al., 2007; Budic et al., 2022). Propofol causes dissociation of GABA from receptors slowly and an increased duration of GABA-activated opening of chloride channels. The opening of chloride channels leads to hyperpolarization of cell membranes which in turn leads to non-response to external stimuli (McCarver & Spear, 2010; Budic et al., 2022). It also has effects on cerebral oxygen requirements, cerebral blood flow and intracranial pressures. Other pharmacological effects include anticonvulsant, antioxidant, anti-inflammatory and bronchodilator effects (Kranioti et al., 2007; McCarver & Spear, 2010).

It is reported that propofol has significant amnesia effects and that it reduces postoperative nausea and vomiting in plastic surgery. Thus, small doses of propofol may be effectively used in post-anesthesia care to treat vomiting and nausea. These small doses do not produce sedation and their anti-emetic action may exert a depressing effect on CNS structures including subcortical areas. Vomiting may also be directly depressed by propofol (McCarver & Spear, 2010).

Adverse effects of propofol

Propofol must be administered by experienced and qualified clinicians (Levy, 2011). However, some complications (e.g., bacteremia, sepsis, hypertriglyceridemia, pancreatitis and a propofol-infusion syndrome) have been found to be associated with its use and these complications are both severe and life-threatening (Sarff & Gold, 2010; Levy, 2011). However, asystole seems to occur only rarely with the administration of propofol. In the elderly, hypovolemia further enhances the hypotensive effects of propofol. Propofol causes a dose-dependent ventilator depression with apnea in 25-35% of inductions of anesthesia. Larger propofol doses can cause respiratory depression and even apnea, also benzodiazepines have sufficient cumulative effects resulting in apnea (McCarver & Spear, 2010). Respiratory and cardiovascular depression are major adverse reactions which have been observed in propofol use. It is clear that the use of propofol requires medical assistance (Roussin et al., 2007). Propofol may become potentially harmful and lethal when injected by incompetent personnel or self-administered because of its potent pharmacodynamics effects on the cardiovascular and respiratory systems (Levy, 2011). Increased rapidity of injection can lead to respiratory depression, and without ventilatory assistance this can lead to death (Roussin et al., 2007).

Because its lipid emulsion formulation can lead to growth of microorganism including *Escherichia coli*, Pseudomonas, *Staphylococcus aureus*, *Candida albicans,* it is important to pay attention to aseptic use when opening propofol vials and to apply it as soon as possible (McCarver & Spear, 2010; Levy, 2011).

Another potential side effect of propofol is hypertriglyceridemia (Roussin et al., 2007; Levy, 2011). When lipid emulsion is used (containing 0.1 g/ml fat infused for >72 h in ICU it can cause hyperlipidemia. Pancreatitis is the result of an increased dose in serum triglycerides (Levy, 2011). Propofol-infusion syndrome is another adverse effect characterized by severe metabolic acidosis, rhabdomyolysis, dyslipidemias, acute renal failure, hypotension, myocardial failure, bradyarrhythmia, and cardiac arrest. Risk factors associated with propofol include situations when propofol infusion (more than 4-5 mg/kg per hour for > 48 h or 67-83 mcg/kg/minute) is given with concomitant use of high dose steroids and catecholamine vasopressors. Other risk factors are cumulative doses of propofol, high fat low carbonhydrate intake, young age (<18 years), critical illness (airway infection, severe head trauma, sepsis, etc.) and inborn errors of mitochondrial fatty acid oxidation. People at particular risk are those on a ketogenic diet or those with carnitine deficiency (Levy, 2011; Diedrich & Brown, 2017; Fong et al., 2008; Mirrakhimov, Voore, Halytskyy, Khan & Ali, 2015). In addition, severe neurological damage, which may cause stress with increased catecholamines and glucocorticoids in circulation, may also be trigger factors in the development of propofol infusion syndrome (Hemphill, McMenamin, Bellamy & Hopkins, 2019)

Propofol abuse

Abuse of propofol is increasing due to its rapid onset of action (<1 minute) and short duration of action (5-10 minutes) (Kirby et al., 2009). Propofol has not typically been listed as a controlled substance (Kirby et al., 2009; McCarver & Spear, 2010; O'Malley, 2010; Levy, 2011) and it is used in operating rooms and ICU. (McCarver & Spear, 2010). Only a small dose required for pleasure, easy access, short duration for action, and without long term side effects make it preferable for those who abuse propofol (O'Malley, 2010; Kirby et al., 2009). Welliver et al. (2012) reported two cases of propofol abuse. The first case was an anesthesiology nurse without a history of substance abuse. After an abdominal hysterectomy, the nurse was given an infusion of fentanyl 4-5 times of the normal dose as a result of a prescription error. The nurse self-administered intravenous (iv) fentanyl within 2 weeks of returning to work. At the end of 7 months, she started to use propofol due to the difficulty in obtaining increased fentanyl doses and in order to reduce the withdrawal syndrome caused. Propofol caused both a decrease in leg shaking, which is a symptom of fentanyl withdrawal syndrome, and euphoria. The nurse continued to use propofol, gradually increasing the dose to experience euphoria, and had a serious car accident after using the substance. After she was found unconscious in the vehicle, she was treated at the rehabilitation center on suspicion of drug abuse. In the second case, the propofol abuser was also an anesthesiology nurse. She used ketorolac after a painful ankle injury but switched to opioids due to the need for more pain relief. She used fentanyl and morphine in increasing doses for 4-6 months, and when it became difficult to obtain these agents, she started using propofol due to its easy access. She continued to use it in the hospital, and her unsteady gait, incidents of falling, and black eyes made her colleagues suspect something which caused them to intervene. The nurse accepted that she had a problem and was directed to therapy. But just after her treatment, she went back to one of the operating rooms in her workplace and used propofol again. After this she received treatment voluntarily. In both cases, each person preferred propofol because of its ease of access. In addition, they could not stop using propofol despite personal injuries and occupational impairments (Welliver et al., 2012)

Two hypotheses arise in the field. The first assumes that patients do not generally know which drug is used for the induction of anesthesia and in most patients who are exposed to propofol, dependency is not a matter of concern. The other hypothesis focusses on some underlying psychiatric pathology or a previous history of drug addiction (Fritz & Niemczyk, 2002). In many cases, the patient history includes drug dependency (Levy, 2011). Propofol addicts cannot cope with the pharmacological effects of the drug, and they may fall and injure themselves after administration (McCarver & Spear, 2010).

A survey made by Wischmeyer et al. searched the information about individuals abusing propofol over the last decade in the USA. They reported that 18% of the hospital departments had one or more people abusing propofol, and two of these departments had more than one incident. There were seven reported deaths linked to propofol abuse, and in each case evidence o abuse could only be discovered when the person was found dead (Wischmeyer et al., 2007). The study results also highlighted an age-related increase in the incidence of suicide in anesthesiology, and a decrease in drug-related deaths due to age. Propofol's short half-life and narrow safety window make its abuse difficult to detect (Wischmeyer et al., 2007). A systematic review on suicide in anesthetics stated that the proportion of anesthetists dying by suicide had increased, and it was emphasized that anesthetic drugs, especially propofol had been used. The study was not specifically conducted to investigate substance abuse or addiction among anesthetists, however propofol was notably seen to be a suicidal drug of abuse among anesthetists. An internet search of deaths due to propofol abuse found that 18 (86%) of 21 fatal cases among healthcare workers were in anesthesia units most of whom were medical or nurse anesthetists (Plunkett, Costello, & Yentis, 2021)

A case from Turkiye was reported in 2015. An emergency medicine doctor who used propofol help relieve his pain caused by nephrolithiasis, was admitted to the psychiatry clinic because of his propofol addiction. After two weeks he refused therapy and left the clinic. Two years later he was found dead due to suspected propofol overdose in the hospital where he had worked (Köroğlu & Tezcan, 2015). In a study by Han et al. the prevalence of propofol abuse was researched using data on blood concentrations of all autopsy cases performed at Korea's National Forensic Service in 2005-2010. Of the 14,673 autopsy cases, propofol was detected in 131, and among these, it was documented that 16 deaths had occurred because of propofol abuse. Also, it was found that nurses and physicians were involved in half of the cases. Moreover, the same study reported that propofol was used more frequently by female healthcare professionals within the 20-30 age range (Han et al.,2013). The results of a retrospective study conducted in Australia and New Zealand by Fry et al.

in 2004-2013, showed that substance abuse was a major problem and associated with a high mortality rate. The mortality rate associated with abuse of propofol was 45% (Fry, Fry & Castanelli, 2015). Furthermore, Gwiazda et al. reviewed two recent case reports for awareness of propofol abuse in Ireland. The first case was a woman found dead at the institution where she worked as a healthcare worker. During the autopsy, it was found that she had old needle puncture marks and an intravenous cannula. Propofol was found in the intravenous infusion bag. However, propofol had not been detected in the post mortem femoral blood and urine samples. This may be explained through the short-acting profile of propofol and inter-individual pharmacokinetic variability. The second case was of a healthcare worker who was found dead in his bed. Used propofol vials were noted in the scene investigation. In the toxicological analysis, both propofol and its glucuronide conjugate were detected in the femoral blood sample, of note with a lethal concentration of propofol (Gwiazda et al., 2021).

A number of factors including access to these addictive drugs and the relative ease of reserving them in small amounts for personal use, as well as high-stress at work, and occupational exposure-related sensitization and stimulated reward pathways in the brain may explain the higher incidence of drug use among anesthetists (Bryson, Silverstein, Warner & Warner, 2008; Merlo, Goldberger, Kolodner, Fitzgerald & Gold, 2008). The largest cohort of known propofol abusers is represented by medical professionals and healthcare workers (Levy, 2011). Propofol abuse by these people has increased, especially among anesthesiology professionals who are younger than 35 years of age and have easy access to the drug (Roussin et al., 2007; Li, Xiao, Xiong, Delphin & Ye, 2008; Merlo et al., 2008; McCarver & Spear, 2010; O'Malley, 2010; Levy, 2011) According to Mensch and Kandel, certain personality characteristics like being highly achievement-oriented, self-controlled, independent, and less comfortable asking for help from others are common for anesthesiologists, and this may contribute to their increased risk of addiction (Mensch & Kandel 1988). A literature review on fatal cases involving propofol abuse revealed that 86% of the cases were healthcare professionals, especially anesthesiologists and nurse anesthetists. Moreover, most of these cases were documented as accidental (81%), with only 9.5% being represented by homicide, and only 9.5% by suicide (Diaz & Kaye, 2017). In another retrospective case study conducted by Earley et al. medical records of healthcare professionals treated at an addiction center were examined. According to the records, 50% of the healthcare personnel had used propofol and most of the propofol abusers worked in the operating room, being women and anesthesiologists. Of note, people who were dependent on propofol often had a history of depression (Earley & Finver, 2013). Propofol, which has the potential for abuse, has taken its place among controlled substances in South Korea since 2011. In this context, Cho et al. conducted a study, using the South Korean Supreme Court database to analyze the criminal cases related to the abuse of propofol by healthcare professionals between 2013-2020. In this study, criminal cases related to the abuse of propofol by healthcare professionals were analyzed. Finally, it was concluded that propofol abuse in this study was the most common among nurses (Cho, Hwang, Shin, Yoon & Lee, 2022).

Psychological addiction is observed to be more common than physical addiction due to various factors such as associated euphoria, relief from stress and tension, post-injection, and post-waking sexual fantasies and dreams. These effects lead to drug craving and loss of control over the amount and frequency of propofol injection which defines psychological dependence (Levy, 2011). It is assumed that psychological dependence might be a result of the rapid activation of mesolimbic GABA-A receptors (Bonnet et al., 2008). Moreover, repeated injections exceeding one hundred per day were reported in chronic propofol abusers (Levy, 2011). Xylocaine significantly reduces pain when administered intravenously but does not alter the effects of propofol (Kranioti et al., 2007).

Like most drugs of abuse, propofol also increases dopamine levels by directly blocking dopamine release or dopamine reuptake from presynaptic nerve terminals (Roussin et al., 2007; Bryson & Frost, 2011; Levy, 2011). This effect may be the underlying factor for the abuse potential of propofol. Propofol is known to cause visual hallucinations by inhibiting NMDA receptors in the brain, similar to ketamine, another abused anesthetic (Levy, 2011). Reported effects range from feeling intense pleasure, vivid dreams related to sex, relaxation, disinhibition and euphoria to unconsciousness and apnea (Roussin et al., 2007; Klausz et al., 2009; McCarver & Spear, 2010; O'Malley, 2010; Levy, 2011). There are some reported reasons which typically lead to the self-administration of propofol for recreation, stress reduction or preventing insomnia (Roussin et al., 2007; O'Malley, 2010).

Occupational exposure to propofol used during surgery may sensitize anesthetists and surgeons to its effects and may subsequently lead to it being abused. (Wischmeyer et al., 2007). Gold et al. suggested that anesthetists who become addicted because of occupational exposure may continue to use agents to mitigate drug withdrawal effects when away from exposure (Gold et al., 2006). In this regard, operating rooms may be regarded as a toxic working environment for anesthesiologists. Because some individuals are more vulnerable to second-hand exposure than others, many anesthetists may become addicted due to susceptibility (Merlo et al., 2008). In addition, recent studies suggest that occupation-related second-hand exposure to intravenous drugs, including propofol (McAuliffe et al., 2006; Levy, 2011), may occur. McAuliffe and colleagues tested this hypothesis and showed that second-hand exposure may increase the risk of substance addiction. Occupational exposure to anesthetics and opiates due to increased indoor air concentration in the workplace sensitizes the brain and this may increase the risk of addiction. In the operating room, the levels of propofol or fentanyl cannot be readily detectable; however, it was suggested by McAuliffe et al. that intravenously injected fentanyl or propofol can be found in the operating room environment but may only be detected using highly sensitive techniques. Such an occupational exposure can lead to addiction and, in the end, people who work in operating rooms may experience withdrawal symptoms (McAuliffe et al., 2006). These possible outcomes were also confirmed by Merlo et al. (Merlo et al., 2008).

There are symptoms which indicate substance dependence such as reducing or completely stopping indispensable activities, intaking an increased amount of the substance, spending excessive time to obtain it, inability to control its use, using the substance or recovering from its use, drug tolerance, withdrawal symptoms, and continuing its use despite adverse consequences. If three or more of the above symptoms occur within one-year period substance dependence is defined (McAuliffe et al., 2006). Patients who use propofol against symptoms such as chronic headaches or migraines may develop psychological dependence. This is an underlying psychological imbalance or disorder with or without dependence on other drugs. Most abusers do not develop true dependence on propofol because there is no evidence of tolerance (Kranioti et al., 2007). However, tolerance may also occur if the frequency of injections is significantly increased (> 100 times a day) (Iwersen-Bergmann et al., 2001).

There are no physical dependence characteristics to define propofol addiction (Roussin et al., 2007). However, symptoms of addiction in healthcare professionals are summarized as follows (i) unusual behavior changes, (ii) mood changes including euphoria, and depression; (iii) desire to work alone and without taking a break; (iv) volunteering for extra cases and withdrawing from social environments with family and friends, avoiding social activities; (v) increase in anger and irritability; (vi) going to work early and/or leaving work late even when off duty; (vii) physical changes like weight loss and pale skin, frequent desire to take breaks while working; (viii) requesting inappropriate and/or increasing amounts of abused substance (Kirby et al., 2009; O'Malley, 2010; Bryson & Frost, 2011). Also, the half-life of the abused drug may affect the tolerance rate (Bryson & Silverstein, 2008).

Measures taken for propofol

Addiction is a significant problem among health professionals with serious implications for public health (McAuliffe et al., 2006; Merlo et al., 2008). Increase in suicide and general mortality rates among physicians with substance abuse may affect their job performance and can harm their patients (Merlo et al., 2008). Monitoring the level of the possible exposure in the biological materials of healthcare professionals may be a way to take some precautions against second-hand occupational exposure. For this purpose, a variety of analytical methods have been developed for the detection and quantification of propofol in different sample types obtained from abusers. High-performance liquid chromatography and gas chromatography are widely used techniques for detection (Levy, 2011). In order to demonstrate chronic abuse, hair analysis of propofol has become an accurate and preferred method (O'Malley, 2010). Also, Kwon et al. (2020) developed and validated a simple, fast, and sensitive LC-MS/MS method for the determination of propofol-glucuronide in hair samples to identify chronic use of propofol. The study also sought to investigate the relationship between dose and hair concentration. While a positive relationship has been observed between dose and hair concentration in some subjects, others with recent hair treatment presented uncorrelated results which has been attributed to variations between individuals like irregular hair growth, hair treatment or contribution from sebum (Kwon, Kim, Cho, Lee & Han, 2020)

Anesthesia locations, ICUs, hospital pharmacies and emergency departments are potential places where drug abuse is common in hospitals. In recent years, many pharmacies in hospitals and anesthesia units have created systems to prevent diversion since propofol abuse is being recognized around the world. Furthermore, some hospitals have installed systems that allow pharmacies to use a fingerprint identification system to track access. These systems keep track of the number of drugs in the pharmacy and frequency of use. Moreover, some healthcare institutions keep pharmacy and anesthesia records in order to detect inconsistencies. Others consider that propofol should be a controlled substance and recommend routine testing of propofol in suspected or at-risk individuals with potential for addiction (Levy, 2011). Treatment for addiction is multifaceted and includes detoxification, follow-up abstinence, as well as education and psychotherapy. During this period, patients are kept away from stress and from access to medication (Bryson & Silverstein, 2008).

CONCLUSION

Propofol is a short acting anesthetic agent used intravenously for sedation against painful or uncomfortable procedures. Propofol abuse has been increasing in recent years for various reasons such as its property of rapid onset, the small dose required for pleasurable effects, the short duration of action, and ease of access. However, when propofol is used for purposes of abuse, it can cause psychological dependence, and this can lead to mortality. Generally, propofol is a drug used in operating/anesthesia rooms and ICUs and is not listed as a controlled substance. Furthermore, several published articles and case reports have shown the problems experienced by propofol abusers. Studies and various case reports have proved that propofol abuse is prevalent among healthcare specialists. In this context, it is mainly anesthetists and nurse anesthetists who are at risk. Considering the increase in propofol abuse by healthcare professionals and the potential risk for job interruptions, increased morbidity and mortality, accidents, and deterioration of public health caused by this abuse, new regulations should be made for the safe and controlled use of propofol.

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