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The Misuse and Abuse of Propofol

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Abstract

Media attention on the misuse of propofol increased significantly when the drug was implicated in the death of pop music superstar Michael Jackson in 2010. The misuse and abuse of propofol among healthcare providers has been reported worldwide, with some misuse resulting in death. Propofol policies guiding healthcare worker re-entry into the workplace after misusing propofol have received rare attention in the research literature. The paucity of information regarding propofol-specific re-entry policies suggests that little research has addressed this problem and the lack of research and policy guidance can contribute to unsafe re-entry and even death. This paper focuses on healthcare providers because they have an easy access to propofol and therefore are vulnerable to misusing or abusing the drug. To accomplish this, the pharmacology and misuse/abuse potential of propofol and the influence of the 12-step recovery paradigm in the re-entry literature are reviewed. In conclusion, existing research and policy are drawn upon to suggest employment re-entry guidelines for healthcare workers.

RéSUMÉ

L'attention médiatique portée à la mauvaise utilisation du propofol a augmenté de manière significative lorsque ce médicament a été mis en cause lors du décès en 2010 de la superstar de pop musique Michael Jackson. La mauvaise utilisation et l'abus du propofol parmi les professionnels de santé ont aussi été constatés à l'échelle mondiale, avec des conséquences telle que la mort. Les règles de conduite encadrant la réinsertion dans le milieu de travail d'un employé ayant un problème d'abus du propofol a jusqu'ici reçu peu d'attentions. La pénurie d'informations concernant les règles spécifiques de réinsertion de professionnels suggère que peu d'études ont examiné ce problème et ce manque de données et de directions peuvent contribuer à une réinsertion dangereuse pouvant même entraîner la mort. Cette étude se concentre sur les professionnels de santé parce qu'ils ont facilement accès au propofol et par conséquent peuvent

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Declaration of Interest

The authors claim no conflict of interest with this manuscript.

être davantage tentés de mal l'utiliser ou même d'en abuser. Pour se faire, la pharmacologie, la mauvaise utilisation/l'abus potentiel du propofol et les résultats d'un programme de reprise en 12 étapes dans le domaine de recherche sur la réinsertion professionnelle, sont en cours d'examen. En conclusion, la recherche existante et ses avancées sont utilisées pour encourager la mise en place de règles régulant la réinsertion au travail pour ces employés dans le domaine médical.

RESUMEN

Ha habido una reciente atención en los medios de comunicación sobre el abuso del propofol. Su aumento se produjo cuando la droga fue vinculada con la muerte en 2009, del artista y superestrella de música pop, Michael Jackson. La malversación y abuso del propofol entre los profesionales de la salud se ha diseminado por todo el mundo, además de causar la muerte como resultado del abuso. Las reglas sobre el propofol que guían la reinserción del personal al empleo, una vez que han abusado la droga, han recibido escasa atención en la literatura de investigación. La falta de información sobre la reentrada específica al propofol sugiere que un mínimo de investigación se ha concentrado en este problema, y la carencia de investigación, puede contribuir a un mal restablecimiento, el cual hasta puede resultar en fatalidades. Este informe se enfoca en los proveedores de servicios de la salud, debido a su acceso fácil al propofol, y de acuerdo a su vulnerabilidad para la malversación o abuso de la droga. Para lograr lo dicho, se consideran la farmacología y posibilidad de abuso y mal uso, y la paradig7ática del programa de rehabilitación de 12 pasos en la literatura de reentrada. En suma, se examinan aquí la investigación sobre el abuso y las reglas actuales para sugerir protocolos que guíen la reentrada de proveedores de servicios de la salud.

Keywords

propofol addiction; propofol misuse; propofol abuse; re-entry to work after propofol abuse; propofol re-entry policies; recovering health care providers

Mots-clés

Mots ciés: dépendance au propofol; mauvaise utilisation du propofol; abus du propofol; réinsertion professionnelle après abus de propofol; règles de réinsertion liées au propofol; professionnels de santé oeuvrant dans le domaine de la toxicomanie et/or readaptation

Keywords

Palabras claves: adicción al propofol; mal uso del propofol; abuso del propofol; restablecimiento en el trabajo posterior al abuso de propofol; reglas de reentrada vinculadas al propofol; proveedores de cuidados de salud en estado de recuperación

BRENDA: a FICTIONAL VIGNETTE

The following fictional scenario relays experiences commonly reported among healthcare providers throughout the world. These experiences especially occur in locations where propofol is an unrestricted, unsecured, and unregulated drug, which remains the case in the majority of healthcare institutions (Bonnet, Harkener, & Scherbaum, 2008; Chao, Lo, Chui,

& Koh, 1994; Cirimele, Kintz, Doray, & Ludes, 2002; Fritz & Niemczyk, 2002; Iwersen-Bergmann, Rosner, Kuhnau, Junge, & Schmoldt, 2001; Klausz, Róna, Kristóv, & Tör , 2009; Kranioti, Mavroforou, Mylonakis, & Michalodimitrakis, 2007; Roussin et al., 2006; Ward, 1992).

Brenda was an exceptional nursing student whose attraction to excitement led her to procure a job in an intensive care unit (ICU) after graduation. After a few years of ICU work, she entered a nurse anesthesia school and then joined a group practice as a certified registered anesthetist (CRNA), where she was respected and trusted by her colleagues.

Brenda found her new job stressful and began to experiment with the drugs readily available to her at work to help her cope with working conditions. Although she had access to a wide array of potent narcotics, injectable propofol became her “drug of choice” because it was not accounted for as a controlled substance and was therefore easily accessible. Three weeks after she first started injecting propofol, Brenda was found in respiratory arrest on the operating room floor. Resuscitated successfully by colleagues, she was brought to the emergency department and released once she was medically stable. The manager of her anesthesia group confronted Brenda with the obvious evidence of her misuse of propofol. Brenda was given the option of receiving assistance for her substance use disorder (SUD) or being terminated from her job. Brenda reported to the Employee Assistance Program (EAP), which expedited her admission into an inpatient substance user treatment program the same day.

Brenda believed after 90 days of inpatient treatment that she was ready to return to work; however, the drugmonitoring program in her state and her employer insisted upon additional treatment in an outpatient treatment setting prior to her re-entry into the clinical workplace. Six months after her overdose and after 90 days of intensive outpatient follow-up, Brenda was cleared by the drugmonitoring program to return to a nonanesthesia position with no access to controlled substances. Her EAP collaborated with nursing administration and arranged for Brenda to fill a part-time position in the ICU, allowing her to attend ongoing aftercare and 12-step meetings. The requirement that Brenda had no access to controlled substances was accommodated by assigning other nurses to administer controlled substances to Brenda’s patients while Brenda fulfilled skilled nursing functions on the unit. Despite the careful orchestration of efforts to ensure Brenda’s safe return to practice, her nurse manager found her in respiratory arrest in the ICU staff bathroom four weeks after her return to work. The cause of her second respiratory arrest was once again propofol. Brenda’s colleagues were unable to revive her.

BACKGROUND

Despite the spectacular media coverage that Michael Jackson’s propofol-related death received and evidence of propofol misuse and deaths among healthcare providers (Fritz & Niemczyk, 2002), propofol largely remains an uncontrolled substance. Propofol, in use since 1986, is currently the most widely used anesthesia induction agent (Eger, 2004) and ICU sedative in the world (Wilson & Compton, 2009). Although warnings of propofol’s abuse potential appeared in 1992 (Follette & Farley, 1992), the drug remains readily accessible in

many hospitals. Numerous investigators have shown that propofol misuse and abuse is a problem among healthcare providers (Bell, McDonough, Ellison, & Fitzhugh, 1999; Iwersen-Bergmann et al., 2001; Soyka & Schutz, 1997; Wischmeyer et al., 2007), and that the most common reason for choosing it as a drug of misuse is its ease of access (Stocks, 2009). Not surprisingly, abuse¹ rates decrease when propofol is regulated and similarly accounted for as other controlled drugs (Wischmeyer et al., 2007).

Re-entry of healthcare providers to the clinical workplace who are recovering from propofol abuse has received little attention in the literature. Workplace re-entry is defined as the employer-sanctioned return to work after a period of abstinence from an active SUD. Wilson and Compton (2009) reviewed the literature related to re-entry to work after recovering from any SUD among anesthesia providers. Their review found no studies specifically related to propofol re-entry. Thus, this paper's overall purpose is to increase awareness about the misuse and abuse potential of propofol. To accomplish this, we discuss the pharmacology of propofol, re-entry policy concerns, and the influence of the 12-step paradigm in the re-entry literature. Suggestions for re-entry of healthcare providers recovering from identified propofol misuse are presented to help prevent Brenda's story from becoming a reality. This re-entry discussion centers mostly on healthcare providers because of the largely unrestricted access to propofol found in the clinical work environment; however, the lay public is also misusing the drug.

Current estimates are that the percentage of healthcare providers with substance dependency are from 2% to 10% (Bell et al., 1999; NCSBN, 2001; American Nurses Association, 1984; Moore, Mead, & Pearson, 1990; Hughes et al., 1992; Trinkoff & Storr, 1994; Baldisseri, 2007; Helzer et al., 1990; Siegel & Fitzgerald, 1988; Trinkoff, Eaton, & Anthony, 1991; Trinkoff & Storr, 1998) while misuse and abuse rates are reported from 14% (Baldisseri, 2007; Siegel & Fitzgerald, 1988) to over 20% (Trinkoff et al., 1991). The prevalence of propofol abuse among anesthesia providers ranges from 3% (Stocks, 2011) to 10% (Bell et al., 1999); however, the misuse of the drug appears to be much higher. Propofol is often one of the substances that healthcare providers manifesting an SUD have used recreationally [Scimeca, 2010; Stocks (2011)]. A recent survey utilizing a convenience sample of recovering anesthesia providers found high rates of propofol misuse (Stocks, 2011). Propofol was named as the drug of choice for only four respondents (3.6%); however, the rate of propofol misuse was greater and nearly 33% of respondents reported using propofol at least once.

PHARMACOLOGY AND MISUSE/ABUSE POTENTIAL OF PROPOFOL

Propofol's actions at multiple receptor subtypes account for its potential for misuse/abuse and its lethality in overdose. Propofol alters ventral striatal dopamine, a pharmacologic characteristic shared with other commonly abused medications (Roussin, Montastruc, & Lapeyre-Mestre, 2007; Zacny, Lichtor, Thompson, & Apfelbaum, 1993a; Zacny, Lichtor, Zaragoza, et al., 1993b; Zacny et al., 1996). Propofol's actions on dopamine likely account

¹The journal's style utilizes the category Substance abuse as a diagnostic category. Substances are used or misused; living organisms are and can be abused. Editor's note.

for its addictive properties, and human propofol addiction has been reported in the literature (Chao & Nestler, 2004; Chao et al., 1994; Zacny, Lichtor, Thompson, et al., 1993a; Zacny, Lichtor, Zaragoza, et al., 1993b; Zacny et al., 1996). Propofol acts at gamma-amino butyric acid (GABA) receptors and *N*-methyl-*D*-aspartate (NMDA) type glutamatergic receptors (reviewed in Roussin et al., 2007). Propofol's actions on GABA and glutamate, neurotransmitters that are critical for influencing level of arousal and consciousness, likely account for its anesthetic properties and lethality in overdose.

Subanesthetic doses of propofol can elicit a euphoric response (Patel et al., 2003; Zacny, Lichtor, Thompson, et al., 1993a). Propofol rapidly redistributes from the plasma into highly perfused brain tissue, and rapid redistribution into adipose tissue accounts for its short duration of action. Propofol has an extremely narrow therapeutic index related to the small dosing window between euphoria and apnea. Propofol is metabolized in the liver through glucuronidation and is renally excreted (Iwersen-Bergmann et al., 2001; Roussin et al., 2007).

Despite the strong recommendation to control propofol as a narcotic by the American Association of Nurse Anesthetists (AANA, 2009a, 2009b), propofol is not yet regulated as a controlled substance by the United States Drug Enforcement Agency (DEA) (Wilson, Canning, & Caravati, 2010). However, the DEA has recently requested a public comment on a proposal to schedule propofol as a Schedule III controlled substance. Until this proposal is implemented, regulating propofol access will depend on voluntarily accounting by individual hospitals. Interestingly, fospropofol, a newly released prodrug of propofol (a prodrug is an inactive form of a drug that is converted to an active drug metabolite *in vivo*), is classified as a Schedule IV controlled substance [American Society of Anesthesiologists (ASA), 2009a, 2009b].

CURRENT RE-ENTRY RECOMMENDATIONS FOR HEALTHCARE PROVIDERS

Contracts between an affected healthcare provider and his or her employee are commonly used to delineate the circumstances and rules for a healthcare workers' re-entry into the workplace. The current literature on the re-entry of healthcare providers has predominantly centered on opioid misuse, with the result that most re-entry contracts include opioid restrictions (Monroe, 2009; Monroe, Pearson, & Kenaga, 2009; Roche, 2007). However, unlike opioid misuse, in which the opioid antagonist naltrexone can be used to aid in safer re-entry (Angres, 2001; Farley & Arnold, 1991; Roche, 2007), an easily administered antagonist is not readily available for propofol.

Many recommendations for re-entry contract guidelines appear in the literature. These include one year away from anesthesia practice (Bryson & Silverstein, 2008; Paris & Canavan, 1999), documented attendance at 12-step meetings (Monroe, 2009; Roche, 2007), mandatory drug testing (AANA, 2009a, 2009b; Herrington, Benzer, Jacobson, & Hawkins, 1982; Monroe, 2009; Roche, 2007), and limited work hours with five-year monitoring contracts (Clark & Farnsworth, 2006). If necessary, reentry may include redirection of the affected healthcare worker into another specialty (Collins, McAllister, Jensen, & Gooden,

2005; Fry, 2005; Menk, Baumgarten, Kingsley, Culling, & Middaugh, 1990). Individuals who are unable or unwilling to be rehabilitated may need redirection out of the profession (Monroe, Pearson, & Kenaga, 2008).

RE-ENTRY OF HEALTHCARE PROVIDERS AND THE 12-STEP RECOVERY PARADIGM

The use of a 12-step program to aid in a healthcare provider's recovery is required by most nursing and medical regulatory boards in the United States. For example, the National Council of State Boards of Nursing (NCSBN) conducted surveys of state-administered drugmonitoring programs and found that nearly 80% require that the nurses attend 12-step meetings and 61% require participants to have a 12-step sponsor (NCSBN, 2009, 2010a, 2010b). Nursing regulatory boards are not alone in using the 12-step treatment approach. The Federation of State Physicians' Health Program guidelines recommend that individual physician participants have a contract that includes the requirement to attend 12-step programs such as Alcoholics Anonymous (AA) or Narcotics Anonymous (NA) (DuPont, McLellan, White, Merlo, & Gold, 2009).

The requirement that individuals participate in 12-step programs is supported by several studies showing that these programs augment an individual's recovery. For example, Fiorentine and Hillhouse (2003) found that extensive participation in 12-step program treatment was associated with the reduction of addictive behaviors. A recent study by McLellan, Skipper, Campbell, and DuPont (2008) demonstrated that 79% of 904 physicians in 16 state physician-monitoring programs had no interruption in their recovery from SUDs at an average follow-up of 7.2 years. The authors concluded that participation in 12-step programs, when combined with additional intensive monitoring, benefitted long-term recovery. Twelve-step meeting involvement appears beneficial to facilitate recovery in nurses who were previously addicted (Scimeca, 2010). Between January 2009 and April 2010, 29 nurses from 20 states shared personal stories for a book about recovering nurses. All 29 nurses credited 12-step program participation with their ability to establish an initial foundation in recovery. Six nurses reported re-initiation of substance use and each of them identified a lack of 12-step involvement as the main precipitant of their re-initiation of substance use (Scimeca, 2010). The exact mechanisms resulting in positive outcomes with 12-step involvement are unknown. However, components, such as cognitive restructuring (Steigerwald & Stone, 1999), helping others with recovery (Zemore, Kaskutas, & Ammon, 2004), and lifestyle change and social network enhancement (Owen et al., 2003), appear to contribute to the efficacy of these programs.

RE-ENTRY SUGGESTIONS FOR HEALTHCARE PROFESSIONALS RECOVERING FROM PROPOFOL MISUSE

Our suggestions, as follow, are based on evidence in the literature and on the current requirements of nurse and physician substance abuse monitoring programs in the United States:

1. Screening and evaluation for an SUD with specific recommendations for treatment (inpatient or outpatient).
2. Five years of monitoring for substance use, including random drug screening with appropriate tests to detect propofol.
3. On the basis of enhanced treatment success and multiple mechanisms of efficacy for 12-step programs, some form of active participation in a recovery-based program such as AA or NA and documentation to corroborate weekly attendance for the duration of the five-year contract is recommended.
4. Minimum of one year away from practice in any facility that uses propofol. This means that the practice will be restricted from any facility such as a hospital, an outpatient surgical center, an outpatient endoscopy, a dental office, etc., that stocks or uses propofol sedation *anywhere* within the organization. Preferable options of re-entry to practice may include primary care clinics, long-term care facilities, chronic or acute dialysis centers, etc.

DISCUSSION

The purpose of this paper was to discuss the abuse and misuse potential of propofol. The serious implications of propofol misuse have received insufficient attention in the drug policy literature. Re-entry of healthcare providers with documented propofol misuse or abuse requires heightened scrutiny and careful planning because the drug is generally not regulated. Healthcare institutions should consider voluntary regulation of propofol access until federal requirements are implemented.

Limitations

Our recommendations have limitations. First, our suggestions are based on the notion that an SUD is a disease that can be treated.² This philosophy is often not easily accepted by everyone and options to re-enter work after substance misuse may not be the cultural norm. Second, the majority of the research about re-entering healthcare providers comes from North America. This presents a clear bias of Western ideologies toward SUDs and their treatment. Third, the re-entry plan is influenced by the 12-step paradigm; however, as indicated, nearly all nursing and medical boards in the United States mandate use of this paradigm. We understand that there are many successful treatment programs and that no one philosophy is best suited to any one individual. More empirical evidence about the quality and effectiveness of such programs, and the necessary internal as well as external critical conditions for their achievement and sustainability are urgently needed.

CONCLUSION

Current U.S. and international policy about propofol re-entry needs more attention. Basic re-entry suggestions for healthcare providers with a history of propofol misuse or abuse are

²The reader is reminded that the medicalizing and associated diagnosis of types of psychoactive substance use and selected users is relatively recent and is a consensus-based taxonomy, which is not empirically informed. Editor's note. American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* (4th ed.). Washington, DC: Author.

outlined. By raising awareness of this issue and by offering re-entry guidelines, we hope to help protect the public, save lives, and to assist healthcare administrators and the professional treatment community.

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Biography

Dr. Todd Monroe, Ph.D., is a Research Associate and Postdoctoral Fellow at the Vanderbilt University School of Nursing (VUSN). His fellowship is jointly supervised between the VUSN and the Vanderbilt University Institute of Imaging Science. Dr. Monroe received a BSN degree with honors from the University of Southern Mississippi, an MSN degree from the University of Alabama, and his Ph.D. in Nursing from the University of Tennessee Health Science Center. For more than a decade, Dr. Monroe has worked clinically in both acute and long-term care. Dr. Monroe has spent past several years in researching substance misuse and abuse among healthcare providers and students with an emphasis on policy development. Dr. Monroe's current research is focused on the neurobiology of pain and using functional magnetic resonance imaging to study pain in older adults with cognitive impairments.

Heather Hamza, CRNA, is a Faculty Anesthetist/Clinical Instructor at Los Angeles County Medical Center at the University of Southern California. She received her Master of Science in Nurse Anesthesia from the University of Buffalo. Mrs. Hamza has been interested in healthcare provider substance abuse and re-entry to work policy for several years. She is a national Peer Assistance Advisor with the AANA. Because of her expertise, Mrs. Hamza frequently speaks to healthcare audiences about substance abuse issues among healthcare providers. Mrs. Hamza is also a third-year Ph.D. student at UCLA, where her dissertation research will involve CRNA re-entry, specifically focusing on cue reactivity.

Greg Stocks, J.D., has practiced as a Nurse Anesthetist over the last 21 years in major academic institutions and private practice. He is a former Peer Assistance Advisor for the AANA and holds an Executive Juris Doctor in Health Law. Currently, he provides medical legal consulting services through Law Med Consulting, LLC, a company that he owns in Baltimore, Maryland.

Paula Davies Scimeca, RN, MS, obtained her baccalaureate degree in Nursing from Adelphi University and her master's degree in Psychiatric/Mental Health Nursing from the State University of New York at Stony Brook. Her career has spanned over three decades, with the first 10 years spent in medical, surgical, and critical care nursing. With over 20 years' experience in addiction and psychiatric nursing, her focus has centered on addiction and recovery in nurses since 2003. The author of "Unbecoming A Nurse" and "From Unbecoming A Nurse to Overcoming Addiction," she is an adjunct professor at Wagner College School of Nursing in Staten Island, New York.

Dr. Ronald Cowan, Ph.D., M.D., is an Associate Professor of Psychiatry, and an Assistant Professor of Radiology and Radiological Sciences at Vanderbilt University School of Medicine. He is an Assistant Professor of Psychology at Vanderbilt University. He also serves as the Director of Vanderbilt's Psychiatric Neuroimaging Program and as the Scientific Director of the Vanderbilt Addiction Center. Dr. Cowan received his Ph.D. in Neuroscience from the University of Tennessee Health Science Center and an MD from Weill Cornell University Medical College. Dr. Cowan completed an internship in internal medicine at the Massachusetts General Hospital/Harvard Medical School and a residency in psychiatry at the McLean Hospital/Harvard Medical School. Dr. Cowan directs a research program on addiction, with a focus on the neurobiology of motivated behavior. Clinical areas of interest include addiction, depression, and obesity.

GLOSSARY

GABA

Inhibitory neurotransmitter.

Glutamatergic	Excitatory type neurotransmitter.
Glucuronidation	Process that makes substances more water-soluble, and, in this way, allow for their subsequent elimination from the body.
Uncontrolled drug	A drug not on the list of FDA controlled substances with misuse/abuse potential.
Ventral Striatum	Associated with limbic structures in the brain consisting of the nucleus accumbens and the olfactory tubercle.

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