

Propofol: Dancing with a “White Rabbit”

By C.F. Ward, M.D.

I tend to think that most practicing anesthesiologists skim over educational pieces about drug diversion and addiction the way the general citizenry ignore descriptions of tax-evasion techniques. These subjects have in common two primary qualities: few people seriously engage in either one, and the transgressions do not seem to have a victim with whom to identify easily. Let me suggest, if I may, that the second notion is exceptionally flawed and that this subject requires more awareness than it usually receives. In particular, I would like to call attention to the abuse of propofol that is either actually increasing in frequency or at least is being reported in greater numbers of late.

As someone who initially was trained with thiopental (Pentothal) as the induction agent of choice, propofol represented a significant change in my practice. I even remember my first experience using propofol: a young woman who was emerging from a MAC anesthesia looked at me as though I were a masked Brad Pitt and told me that she felt simply wonderful. This bore no resemblance to my experience with other sedation agents, and I felt then that this might become an issue of concern for propofol. A feeling of euphoria with no residual “hangover” might suggest propofol is a near perfect mood-altering drug, but it is one that possesses a very thin window separating the dreamy state from the nonresponsive. The first case report of which I am aware that reported addiction to propofol appeared in 1992¹ and assured me that I was not the only anesthesiologist to notice this potential application of propofol. Subsequently, research published in 2004 noted that sleep deprivation, a reality of many of our lives, was to some extent erased during propofol anesthesia.² This paper even generated an editorial, the title of which needs little explanation: “Rested and Refreshed after Anesthesia?”³

I should point out that mankind seems to have sought agents to alter the normal state of consciousness for as long as history has been recorded. Alcohol has the longest such track record by far, despite its very narrow “therapeutic window” and significant toxicity. With respect to propofol we simply must accept that diversion has/does/will occur. Moreover, it may perhaps be increasing, although real data, especially beyond academia, is almost non-existent. Most importantly, the dose-response curve for self-administration of propofol is deadly steep. Yes, people die dancing with this “white rabbit,” not necessarily from intent, but from an inability to control a drug that causes abrupt loss of consciousness.

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In October 2006, Wischmeyer reported his early findings on propofol abuse in academic anesthesia programs to the ASA's Occupational Health Committee, and the final results were published in October 2007,⁴ and, again, they were discussed by that important committee. Some might note the training program connection and conclude that this is solely a problem for that setting. Do not be so comforted, as the non-academic majority of the anesthesia workforce is not especially known for the gathering, analyzing, or reporting on such issues. Absence of evidence, however, is not evidence of absence.

So, the purpose of these comments is to introduce or heighten knowledge of this very troubling issue, and to suggest some consideration of the idea of, perhaps, *a better control and accountability of the use of propofol*. (Please, no stoning or strongly worded e-mails.) If this is flatly rejected, then we might well have to encounter corrective edicts from on high, possibly in the near future. You only need to recall the recent issue of droperidol's scientifically unsubstantiated and inappropriate black box warning, effectively removing it from our armamentarium, another example of regulation overcoming reason. As has been the case with opiates, the family of a colleague whose death was caused by propofol abuse will not be much swayed by arguments based solely on rarity of occurrence or inconvenience in practice mechanics. *It is in all of our best interests to deliberate on this dilemma and find an acceptable practical solution.* The current controversy regarding the California Diversion Program suggests that the horizon bodes ill for governmental ignorance, misunderstanding and intolerance of these issues.

A footnote: Physicians and nurses without anesthesia training or experience currently are using propofol for patient sedation, and this problem has not, to my knowledge, been reported from these sources, although a recent review from France hints that might change.⁵ Assuredly, they would not somehow be uniquely immune to drug diversion. Decades ago, Doug Talbott, one of the early experts in physician drug dependence, noted that anesthesia finds problems because it, uniquely, looks for them, strongly inferring that reporting and true incidence are not remotely equivalent. Introspection . . . and corrective measures, despite their rarity in medicine or life in general, are not signs of weakness.

Editors' Comments:

I applaud Dr. Ward for this important warning to all of us. I am, however, concerned about his call for "regulation," even though he anticipated criticism. I think this is a mistake, would be ineffective, and would create another regulatory nightmare for the vast majority of anesthesiologists. I believe that this is not in our members' best interest, and would do nothing

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to help the very few who are at risk from this drug. To me this would be like trying to regulate the inhalational agents we use, and similar to the government trying to contain the methamphetamine epidemic by regulating our access to the drug in our practices.

—Mark A. Singleton, M.D., Associate Editor

I am most appreciative of Dr. Ward's erudite and timely commentary, one based on an unequaled experience and knowledge about the endemic nature of chemical dependence in the practice of anesthesia. Propofol abuse is real, as are the sequelae of ruined careers, ruined lives, significant morbidity and even mortality. Our specialty must deliberate on how to address this human scourge in a thoughtful and practical manner before some far-lesser-knowledged or inappropriately-motivated politician or regulator does so in a draconian manner. Of course, there must be concern about the nature of any regulation that would result in "a better control and accountability of the use of propofol." The daunting challenge, if answered or answerable: to do so for a drug that is used almost universally, and in large volumes.

—Stephen Jackson, M.D., Editor

I clearly see both sides of the regulatory issue, and personally do not want more regulation, as it has no positive impact for me at all. Further, I am aware of academic programs that have lost residents to inhaled sevoflurane, and that would be even more difficult, if not nearly impossible, to track and control. The drug manufacturers will, of course, fight any regulation, until patents expire or profits become insignificant. However, the association of the word "recreational" with an anesthesia induction drug is startling, and given the explosion in propofol's use outside the operating room—and even outside hospitals and real surgery centers—this issue will, in my opinion, get a bigger play over time. Rules rarely ever stop the "truly motivated," but at times, I do think that they can deter the "simply inquisitive."

—C.F. Ward, M.D., in response to Drs. Jackson and Singleton

- 1 Follette JW, Farley WJ. Anesthesiologist addicted to propofol. *Anesthesiology* 1992; 77:817-8.
- 2 Tung A, Bergmann BM, Herrera S, Cao D, Mendelson WB. Recovery from sleep deprivation occurs during propofol anesthesia. *Anesthesiology* 2004; 100:1419-26.
- 3 Nelson LE, Franks NP, Maze M. Rested and refreshed after anesthesia? *Anesthesiology* 2004; 100:1341-2.
- 4 Wischmeyer PE, Johnson BR, Wilson JE, et al. A survey of propofol abuse in academic anesthesia programs. *Anesth Analg* 2007; 105:1066-71.
- 5 Roussin A, Montastruc JL, Lapeyre-Mestre M. Pharmacological and clinical evidences on the potential for abuse and dependence of propofol: a review of the literature. *Fundam Clin Pharmacol* 2007; 21:459-66.