The Black Box Warning for Droperidol

To the Editor.—I read with interest the recent article and accompanying editorial regarding the black box warning on the package insert for droperidol.1,2 Nuttall et al. indicate that droperidol is a safe, effective, and inexpensive antiemetic and that the black box warning on the package insert is not needed. In addition, they seem to believe that their use of droperidol is prevented by the presence of the boxed warning.2

I was surprised that according to their study,2 the use of droperidol completely stopped after the addition of the black box warning. In contrast, midazolam, succinylcholine, and ketorolac all have black box warnings and still appear to be widely used by anesthesiologists.3 Furthermore, the presence of a black box warning on a medication’s package insert is not the same as the withdrawal of a medication, so clinicians are still able to use it if they choose to.

In view of the events surrounding the withdrawal of rofecoxib (Vioxx)4 and other medications, the US Food and Drug Administration should make every effort to protect patients from drugs that may be dangerous and to alert physicians of these dangers.

At my institution, antiemetics other than droperidol seem to be adequate for the prevention or treatment of postoperative nausea and vomiting, so we are able to get along without droperidol. Moreover, ondansetron is now available as a generic medication, so this alternative to droperidol should be cheaper.5

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References

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In Reply.—I thank Doctor Sosis for his thoughtful comments and the journal ANESTHESIOLOGY for the opportunity to respond. As noted in our article,4 the black box warning on droperidol was based solely on case reports of torsade de points associated with droperidol use and the known pharmacologic effect of droperidol to prolong the QT interval. Our manuscript was an attempt to determine, through a retrospective study, the true incidence of torsade de points associated with droperidol administration in patients who received low-dose droperidol for prophylaxis and/or treatment of nausea and vomiting associated with anesthesia and surgery. We found the incidence of torsade de points to be extremely low. This, combined with the fact that droperidol is one of the few very effective rescue therapies for patients who develop nausea and vomiting postoperatively, led to our conclusion that “the Food and Drug Administration black box warning for low-dose droperidol is excessive and unnecessary.”

Dr. Sosis was “surprised” that according to our study, the use of droperidol completely disappeared after insertion of the black box warning. We were not, because this is consistent with what we have observed in our colleagues’ behavior throughout many institutions and expressed at many national meetings. From Dr. Sosis’ comments, I can only assume that he and his institution have continued to use droperidol for their patients despite the black box warning. However, given the last paragraph of his letter, I suspect that this is not true and that he and his institution have also stopped using droperidol. Dr. Sosis is correct that there are black box warnings on midazolam (respiratory depression and arrest), succinylcholine (acute rhabdomyolysis with hyperkalemia), and ketamine (emergence phenomena), and yet anesthesiologists still use these drugs. Most of these black box warning complications are situations that anesthesiologists are comfortable preventing or treating or avoiding via patient selection.

In contrast, the black box warning on droperidol mandates that a 12-lead electrocardiogram be performed before administration of droperidol. If the QTc is greater than 440 ms for males and 450 ms for females (QTc values seen in at least 10% of all adults), droperidol is not to be administered. Further, the patient must have electrocardiographic monitoring for 2–3 h after droperidol administration. Functionally, logistically, and practically, many anesthesiologists do not want to deal with these hassles. They also fear the litigation costs should they use droperidol without following the black box–required electrocardiographic monitoring and should the patient have an adverse outcome.

The withdrawal of rofecoxib (Vioxx) and other medications demonstrates the importance of postmarketing or phase IV safety studies. The goal of our study was to perform a phase IV trial of droperidol. As such, we found droperidol to be a safe, effective, and inexpensive antiemetic.

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Reference

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