A Plea for the Cautious Use of Droperidol

To the Editor:

I read with interest the recent retrospective investigation by Nuttall et al.1 regarding the safety of low-dose droperidol. Apparently to justify the use of droperidol at the Mayo Clinic, Nuttall et al. noted the minutes of an offsite Food and Drug Administration meeting where an employee stated that droperidol’s black box warning does not apply to the use of low doses of this drug.* At the same time, they quoted the following bold print excerpt from droperidol’s extensive boxed warning: “Cases of QT prolongation and/or torsade de pointes have been reported in patients receiving droperidol at doses at or below recommended doses.”† These two positions seem to be at odds. Also, they did not mention the statement from the boxed warning that if the QTc is prolonged, droperidol should not be administered or that the package insert states that it should be used with extreme caution if the patient has any significant heart disease.

In their report, Nuttall et al. listed several patients who were known to have prolonged QTc intervals and even episodes of ventricular tachycardia before receiving droperidol who either died or developed ventricular tachycardia within 48 h of the droperidol administration. The administration of droperidol to these patients is in complete violation of the package insert. On the basis of their failure to uncover the unequivocal development of torsades de pointes, the authors concluded that droperidol was in no way contributory to these outcomes. They do admit that their retrospective study may not have uncovered such arrhythmias in part because of the inability to capture brief episodes of torsades and other problems. Apparently, the patients did not undergo the mandatory 2–3 h electrocardiogram monitoring called for by the package insert, and it was not clear that the droperidol was administered after the failure of other antiemetics as is also called for by the package insert.

My view is that droperidol’s published boxed warning and package insert are more definitive than comments made at a meeting which cannot necessarily be taken as the official position of the Food and Drug Administration. Consequently, I do not believe that the statement in this article entitled “What We Already Know about This Topic” that the drug’s warnings do not apply to low doses is correct.

In summary, the boxed warning and package insert for droperidol must be carefully read, and its cautionary information closely adhered to in order to more safely use this potentially dangerous medication.

Mitchel B. Sosis, M.S., M.D., Ph.D., Campus Eye Group, Hamilton Square, New Jersey. mbs4117@yahoo.com

Reference


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In Reply:

I thank the Editor for the opportunity to respond to the comments put forth by Dr. Sosis regarding our article.1 We did not justify the use of droperidol at the Mayo Clinic based on minutes of an offsite Food and Drug Administration meeting. We actually performed a large retrospective safety study which was published in the journal Anesthesiology in 2007.2 Droperidol was added back to our formulary after that study. I noted that droperidol was frequently being used by my colleagues. We performed our second retrospective safety study to determine whether this behavior was safe. We found no evidence of polymorphic ventricular tachycardia (VT) associated with the use of this drug.

As noted in our article, there were eight patients who died after droperidol administration. All of the eight patients who died were on palliative care and died of their disease. There were four patients with documented VT, but all four patients had previous cardiac conditions: two had preexisting internal cardiac defibrillators, three had episodes of VT before receiving droperidol, and another had preexisting hypertrophic obstructive cardiomyopathy and underwent a septal myectomy. None of the above-mentioned patients had a prolongation of the QT. The back box states “Cases of QT prolongation and/or torsade de pointes, some fatal, have been reported in patients receiving droperidol at doses at or below recommended doses. All patients should undergo a 12-lead electrocardiogram before administration of droperidol to determine whether a prolonged QT interval (i.e., QTc >440 ms for males or 450 ms for females) is present. Do not administer droperidol if there is a prolonged QT interval. Droperidol is contraindicated in patients with known or suspected QT prolongation, including patients with congenital long QT syndrome. Administer droperidol

References


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* Available at: www.fda.gov/ohrms/dockets/ac/02/transcripts/4000 T1.DOC. Accessed February 18, 2013.