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AMERICAN ACADEMY OF EMERGENCY MEDICINE POSITION STATEMENT: SAFETY OF DROPERIDOL USE IN THE EMERGENCY DEPARTMENT

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☐ **Abstract—Background: Droperidol (Inapsine®, Glaxosmithkline, Brent, UK) is a butyrophenone used in emergency medicine practice for a variety of uses. QT prolongation is a well-known adverse effect of this class of medications. Of importance to note, QT prolongation is noted with multiple medication classes, and droperidol increases QT interval in a dose-dependent fashion among susceptible individuals. The primary goal of this literature search was to determine the reported safety issues of droperidol in emergency department management of patients. Methods: A MEDLINE literature search was conducted from January 1995 to January 2014 and limited to human studies written in English for articles with keywords of droperidol/Inapsine. Guideline statements and nonsystematic reviews were excluded. Studies identified then underwent a structured review from which results could be evaluated. Results: There were 542 papers on droperidol screened, and 35 appropriate articles were rigorously reviewed in detail and recommendations given. Conclusion: Droperidol is an effective and safe medication in the treatment of nausea, headache, and agitation. The literature search did not support mandating an electrocardiogram or telemetry monitoring for doses < 2.5 mg given either intramuscularly or intravenously. Intramuscular doses of up to 10 mg of droperidol seem to be as safe and as effective as other medications used for sedation of agitated patients. Published by Elsevier Inc.**

☐ **Keywords—droperidol; Inapsine; QTc prolongation; dysrhythmia; safety**

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INTRODUCTION

Droperidol (Inapsine®, Glaxosmithkline, Brent, UK) is a butyrophenone used in emergency medicine practice for control of psychosis/agitation, as an antiemetic, for vertigo, as an adjunct analgesic (especially in opioid-tolerant patients) and as a treatment for benign headache (1–5). Initially produced in 1961, it has numerous sites of biochemical activity, most notably as a dopamine receptor antagonist (D2). It is injectable as an intravenous (i.v.) and intramuscular (i.m.) medication, giving it utility when dealing with agitated patients where i.v. access may be dangerous or impossible (6). Described dosages used in practice range from 0.625 mg i.v. for control of nausea to much larger for control of violent agitation (10 mg i.m.).

The most common side effects of droperidol are extrapyramidal, such as dystonia or akathisia, and are

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Table 1. The Definitions of the Grades of Evidence of the Articles

Grade A	Randomized clinical trials or meta-analyses (multiple clinical trials) or randomized clinical trials (smaller trials), *directly* addressing the review issue
Grade B	Randomized clinical trials or meta-analyses (multiple clinical trials) or randomized clinical trials (smaller trials), *indirectly* addressing the review issue
Grade C	Prospective, controlled, nonrandomized, cohort studies
Grade D	Retrospective, nonrandomized, cohort or case-control studies
Grade E	Case series, animal/model scientific investigations, theoretical analyses, or case reports
Grade F	Rational conjecture, extrapolations, unreferenced opinion in literature, or common practice

mitigated through administration of an H1-blocker, such as diphenhydramine. Practitioners may elect to prophylactically administer an H1-blocker prior to droperidol. In 2001, the U.S. Food and Drug Administration (FDA) issued a black box warning for droperidol over concerns of QT prolongation and the potential for torsades de pointes (TdP) (7). The FDA stated that an electrocardiogram (ECG) should be obtained prior to droperidol administration and it should not be used if the QTc is > 440 ms in males or > 450 ms in females. The FDA also recommended cardiac monitoring for 2–3 h after droperidol administration. Clinicians familiar with droperidol in practice have questioned this warning because most of the case reports of TdP occurred with large doses of droperidol rarely used in the emergency department (ED) setting (25–600 mg) (7). The FDA listed 277 cases of adverse effects associated with droperidol since its introduction to the market in 1970 (74% of these sent in from outside the United States with many of the reports as duplicate submissions), leaving a total of 65 individual cases. Of these cases, only two described adverse effects possibly caused by droperidol in dosages commonly used in the United States. Only five of these events related to doses of < 2.5 mg (8). In fact, in the year 2000, over 25 million unit doses of droperidol were sold and only 10 adverse cardiac events were related to doses of 1.25 mg or less (4). All 10 of these events had confounding factors that could have explained the cardiac event, such as preexisting cardiac disease or alcoholism. Kao et al. published on this topic and describe nine cases of TdP directly attributed to droperidol in 30 years of use (9). Despite this small number of cases, the black box warning and decreased availability has led emergency physicians (EPs) to a dramatic shift away from use of droperidol (10).

This article seeks to review the medical literature on droperidol use and to offer evidenced-based recommendations to EPs. This work was done at the request of and published as a clinical practice statement by the American Academy of Emergency Medicine Clinical Guidelines Committee.

METHODS

A structured review of the medical literature using MEDLINE was performed and limited to studies published from January 1995 to January 2014. Inclusion criteria were all studies involving human subjects and written in the English language and containing the keywords: droperidol/Inapsine. The abstracts of the articles found in this search were assessed independently by two EPs, to determine which papers should be pulled for more detailed review based on their suspected relevance to the clinical question. Studies included for the final detailed review were limited to randomized controlled trials, prospective trials, retrospective cohort trials, case series, and case reports in human subjects. References of selected articles were also screened for inclusion criteria. Also, articles studying multiple medication adverse interactions including droperidol were not included. General review articles were not included for formal review. Each of the articles selected underwent a Grade of Evidence Review. Each of the selected articles was subjected to detailed review by at least two of the authors. The level of the evidence was assigned a grade using the definitions as noted in Table 1 and were based on reference focus, specific research design, and methodology.

Each of the selected articles was also subjected to detailed review and assigned a Quality Ranking based on a critical assessment with regard to quality of the design and methodology. This includes Design Consideration (focus, model structure, presence of controls) and Methodology Consideration (actual methodology utilized). The definitions of the Quality Ranking scores are included in Table 2.

Table 2. The Definitions of the Quality Ranking Scores of the Articles

Ranking	Design Consideration Present	Methodology Consideration Present	Both Considerations Present
Outstanding	Appropriate	Appropriate	Yes, both present
Good	Appropriate	Appropriate	No, either present
Adequate	Adequate with possible bias	Adequate	No, either present
Poor	Limited or biased	Limited	No, either present
Unsatisfactory	Questionable/none	Questionable/none	No, either present