PGY-4

**Critical Review Form**

 **Therapy**

[Thomas H Jr, Schwartz E, Petrilli R. Droperidol versus haloperidol for chemical restraint of agitated and combative patients. Ann Emerg Med. 1992 Apr;21(4):407-13.](http://pmid.us/1554179)

**Objectives: To compare "equal doses of haloperidol and droperidol used for the chemical restraint of violent and agitated patients." (p. 408)**

**Methods: This randomized, controlled trial comparing haloperidol and droperidol for acute agitation was conducted in the ED of Wake Forest Baptist Medical Center in Wake Forest, North Carolina between April 1990 and January 1991. All adult patients with agitation requiring physical restraint and "constant attention from medical personnel" were evaluated by two physicians; if these physicians agreed that the agitation was not due to a "readily correctible" etiology and that chemical restraint was warranted, the patient was then eligible for enrollment. Exclusion criteria were allergy to either study drug, low initial blood pressure (systolic blood pressure < 110 mmHg or diastolic blood pressure < 60 mmHg), or administration of another psychotropic medication by medical personnel prior to study entry.**

**Patients were randomized to receive either haloperidol (5 mg) or droperidol (5 mg), which were given either IV or IM at attending physician discretion. Combativeness was then assessed on a novel 5-point scale at 15, 30, and 60 minutes after drug administration. If the initial drug remained "ineffective" after 30 minutes, the study drug could be repeated or another sedative agent could be given.**

**During the study period, 68 patients were enrolled; 21 patients received IM haloperidol, 12 received IV haloperidol, 26 received IM droperidol, and 9 received IV droperidol. The median age in these groups ranged from 31 to 36 years and the proportion of female patients ranged from 0 to 52%.**

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| **Critical Review Form: Therapy** |
| Guide | Comments |
| **Are the results valid?** |
| **Did experimental and control groups being the study with a similar prognosis?** |
| Were patients randomized? | No. Patients were analyzed based not only on study medication, but on route of administration. While patients were randomized to receive either haloperidol or droperidol, the route of administration was determined by the attending physician and was not randomized ([selection bias](http://pmid.us/21491415)). |
| Was allocation concealed? Was it possible to subvert the randomization to ensure a patient would be “randomized” to a particular group? | Uncertain. The authors report that "The pharmacy prepared identical-appearing vials of droperidol and haloperidol at a concentration of 2.5 mg/mL, and a random-number generator was used to dispense these vials to the ED." (p. 408) The exact method of group allocation is not well-described here; specifically, the authors do not specify how random numbers were generated (e.g. computer algorithm), how random numbers were used to assign patients to groups, and who actually dispensed the medications. |
| Were patients analyzed in the groups to which they were randomized? | Yes, up to 30 minutes. While few details are provided, it appears that there was no crossover between groups up to 30 minutes once the initial medication was dispensed and that all patients analyzed based on the initial medication received ([intention to treat analysis](http://pmid.us/10480822)). After 30 minutes, patients who remained agitated and required additional study drug or other psychotropic medication were then dropped from the study and from further analysis. |
| Were patients in the treatment and control groups similar with respect to known prognostic factors? | No. The authors provide very little demographic information, do not provide any medical or psychiatric history, and provide no information on intoxication with agents other than alcohol. While patients were similar with respect to age, the proportion in each group who were female varied widely. There was also a wide range of blood alcohol levels (174-250). |
| **Did experimental and control groups retain a similar prognosis after the study started?** |
| Were patients aware of group allocation? | No. As stated, identical-appearing vials of study medication were prepared in the pharmacy. Patients would, however, be aware of the route of drug administration (IV vs. IM). |
| Were clinicians aware of group allocation? | No. See above. |
| Were outcome assessors aware of group allocation? | No. The only outcomes measured were vital signs and level of combativeness up to 60 minutes after study drug administration. These measurements were made by clinicians at the bedside who would have remained blinded to study group allocation. |
| Was follow-up complete? | Purportedly yes. It would appear that outcome data (out to 30 minutes) was available for all patients enrolled. |
| **What are the results?** |
| How large was the treatment effect? | * The authors report a significantly more rapid response to IM droperidol compared to IM haloperidol (p = 0.03).
	+ This difference in combativeness scores was observed at 10 minutes (2.11 vs. 3.00, p = 0.004) and 30 minutes (3.75 vs. 4.43, p = 0.010).
	+ There was no difference in combativeness scores at 5 or 15 minutes.
* There was no significant difference in combativeness scores between the IV droperidol and IV haloperidol groups.
* There were no significant differences in heart rate and blood pressure at each observation time between the study groups.
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| How precise was the estimate of the treatment effect? (i.e. what 95% CIs were associated with the results?) | There were no 95% confidence intervals reported. Based on the data provided, no true measures of effect size or confidence intervals could be calculated. |
| **How can I apply the results to patient care?** |
| Were the study patients similar to my patient? | Uncertain. The authors provide almost no demographic information, provide no information regarding psychiatric history, and provide no information regarding intoxication with substances other than ethanol. I suspect that the majority of patients requiring chemical sedation in our ED for acute agitation are either suffering from a primary psychiatric disorder or are intoxicated with illicit substances ([external validity](http://www.epmonthly.com/archives/features/understanding-external-validity/)). |
| Were all clinically important outcomes considered? | No. The authors measured decrease in agitation based on a novel scale that has not been validated, as well as blood pressure and heart rate. They did not look at need for additional sedation, staff injury, ED length of stay, QT prolongation, cardiac dysrhythmia (e.g. torsades the pointes), or respiratory depression. |
| Are the likely treatment benefits worth the potential harm and costs? | Uncertain. This was a very small study with many methodological problems, including lack of true randomization into IM and IV group, lack of a true [intention to treat analysis](http://pmid.us/10480822), and lack of true [patient-centered outcomes](http://omerad.msu.edu/ebm/Intro/Intro6.html). The authors found a significantly more rapid response to IM droperidol compared to IM haloperidol, however they provide no measures of effect to allow us to quantify this response, however this difference did not hold at all times points. They also found no such difference between the groups who received IV medication. |

**Limitations:**

1. **It is not stated if this was a** [**convenience sample**](https://explorable.com/convenience-sampling) **or a** [**consecutive sample**](http://pmid.us/9754593) **of patients.**
2. **No** [**primary outcome**](http://pmid.us/26528658) **was reported.**
3. **No** [**sample size calculation/power analysis**](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1726174/) **was provided.**
4. **No demographic data, medical history, substance use other than alcohol reported. Given that a large number of patients requiring chemical sedation in our ED suffer from primary psychiatric disorders or intoxication with illicit substances, it is unclear if these results are generalizable to our population (**[**external validity**](http://www.epmonthly.com/archives/features/understanding-external-validity/)**).**
5. **The main outcome reported was based on a novel combativeness scale that has not been validated. Other** [**patient-centered outcomes**](http://omerad.msu.edu/ebm/Intro/Intro6.html)**, including the incidence of torsades de points, were not evaluated.**

**Bottom Line:**

**This small, randomized trial found a significantly more rapid response to IM droperidol compared to IM haloperidol, with no difference between medications when given IV. The use of a non-validated tool as the main outcome measure, small sample size, and lack of proper reporting all severely limit the applicability of these results.**