PGY-1

**Critical Review Form**

 **Therapy**

[Calver L, Drinkwater V, Gupta R, Page CB, Isbister GK. Droperidol v. haloperidol for sedation of aggressive behaviour in acute mental health: randomised controlled trial. Br J Psychiatry. 2015 Mar;206(3):223-8.](http://pmid.us/25395689)

**Objectives: " to compare the effectiveness and safety of droperidol with haloperidol for the sedation of patients with acute behavioural disturbance in an acute mental health unit." (p. 223)**

**Methods: This blinded, randomized controlled trial comparing intramuscular (IM) droperidol with IM haloperidol for acute behavioral disturbance was conducted in the psychiatric intensive care unit (ICU) of a large tertiary care hospital in Newcastle, New South Wales, Australia between August 2011 and June 2013. Patients admitted to the psychiatric ICU involuntarily with agitation or aggression, requiring parenteral medication for sedation (at clinician discretion), were eligible for enrollment. Patients under 18 years of age and those willing to take oral medication for sedation without need for physical restraint or seclusion were excluded.**

**Patients were initially physically restrained and administered droperidol (10 mg IM) or haloperidol (10 mg IM) in a blinded fashion based on block randomization. Following study drug administration, physical restraint was removed. An acute behavioral disturbance chart, the** [**Sedation Assessment Tool (SAT)**](https://pubmed.ncbi.nlm.nih.gov/22151672/)**, was used to record the level of agitation at the time of recruitment; SAT scores and vital signs were then recorded every 10 minutes following trial drug administration for the first hour, then half-hourly until the patient was settled. Additional sedation was recommended if the patient remained agitated after 30 minutes, but this was also at clinician discretion.**

**The primary outcome was the time from study medication administration until the SAT score deceased by 2 or more, or until the score was 0. Failed sedation was defined as failure to achieve the primary outcome in 120 minutes. Additional adverse outcomes included respiratory depression (respiratory rate < 12), hypotension (systolic blood pressure < 90), bradycardia (heart rate < 60), hypoxia (SpO2 < 90%), and development of extrapyramidal side effects.**

**Out of 584 sedation episodes over the study period, 356 were excluded because clinicians chose to give a labeled sedation medication, or due to previous inclusion in the study. This left 228 patients who were randomized to either haloperidol (n = 110) or droperidol (n = 118). The median age in each group was 34 and 33 years, respectively, and 69% and 75% were male.**

|  |
| --- |
| **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? | Yes. "Block randomisation was used. Microsoft Excel was used to randomly create blocks of four (ABAB, AABB, etc.) or six (ABABAB, AAABBB, etc.). The use of different block sizes meant that it was impossible to predict the next treatment. Each A or B allocation was then assigned a study code. The list of study codes with allocations was generated by a research assistant and supplied to the Calvary Mater Newcastle pharmacy, so that the investigators and treating staff remained unaware of the allocations. The pharmacy relabelled the vials of haloperidol or droperidol with study numbers based on the list of allocations. The vials were then supplied to the psychiatric intensive care unit in sequential order." (p. 224) |
| Was allocation concealed? Was it possible to subvert the randomization to ensure a patient would be “randomized” to a particular group? | Yes. The randomization method and the use of random block sizes, as detailed above, should be adequate to maintain [allocation concealment](http://apps.who.int/rhl/LANCET_614-618.pdf). |
| Were patients analyzed in the groups to which they were randomized? | Yes. The authors make no mention of crossover between groups. it appears that an [intention to treat analysis](http://pmid.us/10480822) was used. |
| Were patients in the treatment and control groups similar with respect to known prognostic factors? | Mostly yes. Patients were similar with respect to age, gender, cause of acute behavioral disturbance, and baseline SAT scores. Patients with primary mental illness were somewhat more likely to receive haloperidol (56% vs. 44%) while those with drug-induced psychosis were somewhat more likely to receive droperidol (34% vs. 27%). |
| **Did experimental and control groups retain a similar prognosis after the study started?** |
| Were patients aware of group allocation? | No. "...the haloperidol was purchased from Fagron Ltd (Sydney, Australia) and transferred into vials identical to those containing the droperidol formulation." (p. 224) This should have been adequate to maintain blinding for patients and clinicians. |
| Were clinicians aware of group allocation? | No (see above). There is no risk of [performance bias](http://bmg.cochrane.org/assessing-risk-bias-included-studies) on the part of the clinicians. |
| Were outcome assessors aware of group allocation? | No. "At the completion of the study one investigator (G.I.) still masked to the allocation audited all primary and secondary outcomes using the original data sheets. Another investigator not involved in recruiting patients or coordination of the study (C.P.) was then given the masked data, and separately the group allocations as either A or B by the pharmacy. At this time only the study labels A or B and not the drug names were known to the investigator. This investigator analysed the data independently and presented this to the other investigators. Only then did the pharmacy reveal whether A or B was haloperidol or droperidol." (p.224) |
| Was follow-up complete? | Yes. Outcome data was available for all patients who randomized. |
| **What are the results?** |
| How large was the treatment effect? | * For the primary outcome, median time to sedation was 20 minutes in the haloperidol group (IQR 15-30 minutes) and 25 minutes in the droperidol group (IQR 15-30 minutes).
* Adequate sedation was achieved in 92% or patients in both groups (RR 0.99, 95% CI 0.92 to 1.1).
* Additional sedation was necessary in 13% of haloperidol patients and 5% of droperidol patients (risk difference 7.6%, 95% CI 0.3 to 15%).
* Adverse effects occurred in 1 patient in the haloperidol group (1%) and 6 patients in the droperidol group (5%):
	+ Hypotension occurred in 3 droperidol patients and 1 haloperidol patients.
	+ Desaturation, extrapyramidal side effects, and oversedation each occurred in one patient in the droperidol group.
 |
| How precise was the estimate of the treatment effect? (i.e. what 95% CIs were associated with the results?) | See above. |
| **How can I apply the results to patient care?** |
| Were the study patients similar to my patient? | No. This study was conducted in a psychiatric ICU rather than an emergency department. While a significant proportion of patients presented with drug-induced psychosis (~30%), I suspect that a higher percentage of patients requiring sedation for agitation in our ED are intoxicated. The substances causing intoxication in this study were not detailed, and we likely see a different proportion of drugs in our ED than are seen in the psychiatric ICU in Australia ([external validity](http://www.epmonthly.com/archives/features/understanding-external-validity/)). Additionally, patients in this study received 10 mg of IM haloperidol, whereas we typically give 5 mg IM along with a concomitant dose of IM ativan (typically 2 mg). |
| Were all clinically important outcomes considered? | Yes The authors considered time to sedation, adequate sedation within 2 hours, need for additional sedation, adverse effects, and staff injuries. They did not look at outcomes beyond 120 minutes. |
| Are the likely treatment benefits worth the potential harm and costs? | Uncertain. The two drugs performed with similar efficacy, with only a 5-minute difference in median time to sedation. An equal proportion of patients achieved adequate sedation by 2 hours. There was a somewhat higher number of adverse events in the droperidol group, though the clinical significance of these events was not detailed. |

**Limitations:**

1. **The sedation assessment tool used does not appear to be well-validated.**
2. **Nearly half of eligible patients were not included because clinicians chose to give labeled medication or a different dose of medication from that in the study (**[**selection bias**](http://pmid.us/21491415)**).**
3. **Nine patients (7 in the droperidol group and 2 in the haloperidol group) received IM midazolam in breach of study protocol.**
4. **This study was conducted in a psychiatric ICU in Australia, and the results may not generalized to ED patients in the US (**[**external validity**](http://www.epmonthly.com/archives/features/understanding-external-validity/)**).**

**Bottom Line:**

**This randomized, controlled trial from Australia found no significant difference in mean time to sedation when comparing IM haloperidol (10mg) and IM droperidol (10 mg) for management of acute agitation in a psychiatric ICU.**