

## Droperidol and midazolam, alone or combined, have similar effects on duration of violent and acute behaviour disturbance in emergency department patients

### QUESTION

**Question:** Which drug is most effective at sedation of violent or agitated patients in the emergency department: midazolam, droperidol or a combination of the two?

**Patients:** 79 adults presenting on 91 occasions with violent and acute behavioural disturbance of sufficient severity to require restraint and sedation, as assessed by clinic staff. No exclusions were made on the grounds of suspected cause of behaviour. Most presentations related to alcohol intoxication (70%), 41% were related to deliberate self harm, 9% to drug induced delirium, 5% to acute psychosis and 2% to other causes.

**Setting:** One urban hospital emergency department, Australia; August 2008 to July 2009.

**Intervention:** 10 mg midazolam (29 patients), 10 mg droperidol (33 patients) or 5 mg midazolam plus 5 mg droperidol (29 patients), administered by intramuscular injection.

**Outcomes:** *Primary outcome:* duration of the violent and acute behavioural disturbance episode (defined as the duration of need for attendance of security staff to assist management of the patient). *Secondary outcomes:* included necessity for additional sedation and occurrence of adverse drug reactions. Bayesian time to event analyses was used to assess time to additional sedation; therefore CIs in these analyses represent Bayesian confidence intervals (credible intervals).

**Patient follow-up:** 100% at 90 min, 86.8% (79 presentations) at 6 h.

### METHODS

**Design:** Randomised controlled trial.

**Allocation:** Concealed.

**Blinding:** Triple blind (patients, healthcare providers and investigators blinded).

**Follow-up period:** 6 h.

### MAIN RESULTS

Of 223 patient presentations with violent and acute behavioural disturbance occurring during the study period, 91 were included in the trial. The principal reason for exclusion was successful verbal de-escalation. There was no significant difference in the duration of violent and acute behavioural disturbance between the treatment groups (median duration (interquartile range): 20 min (11-37) with droperidol vs 24 min (13-35) with midazolam vs 25 min (15-38) with droperidol plus midazolam,  $p=0.66$ ). A greater proportion of patients receiving midazolam alone required additional sedation than those receiving droperidol alone (33% (95% CI: 19% to 52%) with droperidol vs 62% (95% CI 42% to 79%) with midazolam vs 41% (95% CI 24% to 61%) with droperidol plus midazolam; HR for midazolam vs droperidol: 2.31, 95% CI 1.01 to 4.71). The incidence of QT prolongation was similar for droperidol and midazolam alone, but was higher with combination therapy (6% (95% CI 1% to 23%) with droperidol vs 7% (95% CI 1% to 24%) with midazolam vs 14% (95% CI 5% to 33%) with droperidol plus midazolam). Drug-related adverse effects were most common in the midazolam group (6% (95% CI 1% to 22%) with droperidol vs 28% (95% CI 13% to 47%) with midazolam vs 7% (95% CI 1% to 24%) with droperidol plus midazolam). Statistical comparisons between groups for adverse event outcomes were not reported.

### CONCLUSIONS

Droperidol and midazolam, alone or combined, have similar effects on duration of violent and acute behavioural disturbance in patients in the emergency department. Although this was a small study where safety was not a primary outcome, there was no evidence of a higher rate of adverse reactions to droperidol alone compared to midazolam alone.

### ABSTRACTED FROM

**Isbister GK, Calver LA, Page CB, et al.** Randomized controlled trial of intramuscular droperidol versus midazolam for violence and acute behavioral disturbance: the DORM study. *Ann Emerg Med* 2010;**56**:392-401.e1.

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Where a person is out of control because of intoxication and/or mental health problems, everyone involved is vulnerable. Healthcare decisions should be based on clear evidence, but where there is none, in these difficult and unsatisfactory situations, attitudes to interventions soon become jaded. Nothing is perfect. People get harmed. Droperidol fell out of favour some years ago after risk-benefit assessments regarding QT intervals. Janssen-Cilag, the company which marketed droperidol, concluded that the injectable form would no longer be commercially viable.<sup>1</sup> Newer (usually more lucrative) drugs are now sometimes evaluated and older ones become half forgotten. There are far too few studies in this area.

This welcome trial highlights key issues. First, it is important and ethical to randomise the underevaluated

accessible treatments even when participants do not have capacity to consent. It is unethical not to randomise. Second, studies can tread the line between explanatory (asking questions such as 'in ideal circumstances does the treatment work?') and pragmatic (with questions such as 'does treatment have applicable clinically important effects?'). The primary outcome was chosen because it was more objective and clinically applicable than scale data. Third, droperidol may have a place. This good study does not, however, prove that droperidol is as safe as other approaches. The size calculation was based on the duration of violent and acute behavioural disturbance and not potentially important adverse effects. Just as the retreat from use of droperidol was probably based on less firm evidence than would have been ideal – a situation not too rare<sup>2</sup> – the rehabilitation of the use of this drug should

not be based on one small trial. 'One swallow does not a summer make' (Aristotle 384-322 BC). One good but small trial should not be the dawning of a new age of use of droperidol. This pioneering and courageous study should be replicated, developed and enlarged – soon.

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**Conflicting interests** None.

### REFERENCES

1. WHO Pharmaceuticals Newsletter 2001, No. 01. <http://apps.who.int/medicinedocs/es/d/Js2261e/>
2. **Clarke A, Deeks JJ, Shakir SA.** An assessment of the publicly disseminated evidence of safety used in decisions to withdraw medicinal products from the UK and US markets. *Drug Saf* 2006;**29**:175-81.