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Droperidol for Acute Agitation

Introduction

1. While verbal de-escalation should always be attempted first, chemical sedation of acutely agitated patients may be required if the patient becomes a danger to themselves or to ED staff.
2. In 2001, the U.S. FDA issued a black-box warning for droperidol and QTc prolongation based on observational after-market data.
3. The majority of these cases were reported at higher doses than those used in the ED (65-300 mg).
4. Multiple prospective studies have demonstrated safe and effective use of droperidol in the ED for acute agitation.

Pharmacology[1,2]	
MOA	Butyrophenone D2 receptor antagonist
Dose	5-10 mg alone 2.5-5 mg coadministered with midazolam
Administration	Routes: IM or IV
PK/PD	Onset: 3-10 min Peak: ~ 30 min Duration: 2-4 hours
Adverse Effects	Mild to moderate hypotension Bradycardia QTc prolongation (dose dependent) Extrapyramidal symptoms (dystonia, akathisia)
Drug Interactions and warnings	Pheochromocytoma: may cause severe hypertension or tachycardia Other CNS depressants- potentiating effect
Compatibility	Compatible with NS, D5W, or LR
Comments	No renal dose adjustments required

(Britany Byrkit & Jimmy@pharmacyfridaypearls.com

Review of the Evidence			
Author, year	Design/ sample size	Intervention & Comparison	Outcome
Martel, 2020[3]	DB, RCT (n=115)	• IM Droperidol 5 mg • IM Ziprasidone 10 mg • IM Ziprasidone 20 mg • IM Lorazepam 2 mg	• **Droperidol was more effective than ziprasidone 10mg or 20 mg,** and lorazepam at 15 minutes o 64% compared to 25%, 35%, 29%
Cole, 2020[4]	Observational (n= 16,546)	• IV/IM Droperidol	• The mean QTc difference was +3.3 milliseconds (ms) after droperidol • **The incidence of torsades des pointes (TdP) was 1/16,546 or 0.006%**
Yap et al, 2017[5]	Subgroup analysis of RCT (n=92)	• IV Midazolam 5 mg + IV Droperidol 5 mg • IV Droperidol 10 mg • IV Olanzapine 10 mg	• **At 10 minutes, significantly more patients in the midazolam-droperidol group** o Midazolam-droperidol 85.3% compared to 46.7% droperidol monotherapy, and 50% olanzapine monotherapy
Taylor et al. 2017[6]	RCT (n= 345)	• IV midazolam 5 mg + IV droperidol 5 mg • IV Droperidol 10 mg • IV Olanzapine 10 mg	• **Midazolam + droperidol was faster than either droperidol or olanzapine alone, and required less rescue doses** o 76.6% compared to 49.6% and 49.2% respectively
Calver 2015[7]	Observational (n= 1,009)	• IM/IV Droperidol 10 mg	• Thirteen of 1,009 or **1.3% patients had an abnormal QT** • Median time to sedation was 20 minutes (IQR 10 to 30 minutes) • **No cases of torsades de pointes**
Chan et al. 2013[8]	DB, RCT (n=336)	• IV Droperidol 5 mg + midazolam • IV Olanzapine 5 mg + midazolam • IV Placebo + midazolam	• Combination of droperidol or olanzapine + IV midazolam resulted in **faster median time to sedation (6, 5 min vs. 10 min) than midazolam monotherapy** • The 3 groups' adverse event profiles and lengths of stay did not differ.
Isbister et al. 2010[9]	DB, RCT (n = 91)	• IM Midazolam 10 mg • IM Droperidol 10 mg • IM Droperidol 5 mg + IM midazolam 5 mg	• IM droperidol resulted in similar security duration as midazolam or midazolam/droperidol combination, • Droperidol required less additional sedation, had a lower rate of adverse effects • **Droperidol had no cases of arrhythmias or QT prolongation**
Knott et al. 2006[10]	DB, RCT (n=74)	• IV Midazolam 5 mg • IV Droperidol 5 mg	• 28.1% more patients were sedated at 5 min with IV midazolam vs. droperidol o **At 10 min ~ 50% of patients were adequately sedated in both the midazolam and droperidol groups**. • Less patients in the droperidol group required additional sedation within 60 min vs. midazolam group

Conclusions

1. Droperidol appears safe and effective at the low doses required for acute agitation in the ED and results in less respiratory depression than midazolam monotherapy.
2. Droperidol does not have to be administered with a benzodiazepine to achieve rapid and adequate sedation.
3. There is a low rate of akathisia with droperidol that can be managed with IV diphenhydramine.

References

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