

The Use of Common Antipsychotics for Acute Agitation

Introduction

1. Antipsychotic medications are used for numerous acute states in the emergency department, especially agitation.
2. IV access is often not available for patients with agitation and alternative routes must be considered; the drug of choice may change depending on the route of administration.
3. This handout will focus on the pharmacotherapy of the most utilized antipsychotics in the emergency department for acute agitation.

Pharmacology

	Haloperidol (Haldol®)	Droperidol (Inapsine®)	Olanzapine (Zyprexa™)	Ziprasidone (Geodon®)
Dose	<ul style="list-style-type: none"> • PO: 0.5-5 mg • IM/IV: 2-5 mg 	<ul style="list-style-type: none"> • IM: 5-10 mg • IV: 2.5-5 mg 	<ul style="list-style-type: none"> • PO: 5-10 mg • IM: 5-10 mg 	<ul style="list-style-type: none"> • PO: 20-40 mg • IM: 10-20 mg
Onset	<ul style="list-style-type: none"> • PO: 30-60 min • IM: 20-40 min 	<ul style="list-style-type: none"> • IV/IM: 5-15 min 	<ul style="list-style-type: none"> • PO (ODT): 15-20 min • IM: 5-10 min 	<ul style="list-style-type: none"> • PO: 45-60 min • IM: 15-60min
Elimination Half-life	10-37 hours	2-4 hours	30-37 hours	2-5 hours
Parenteral Concentrations available	5 mg/ 1mL	2.5 MG/1mL	Powder for Solution: mix with 2.1 mL sterile water to make 5 mg/ 1 mL solution	Powder for Solution: Mix with 1.2 mL sterile water for injection 20 mg/ 1 mL
QTc Prolongation (Dose used in study)	4.7-14.7 mSec (10-15 mg)	+16 mSec women +22 mSec men (4.5 mg)	+6.4 mSec (20 mg)	+15.9 mSec (30 mg)
Comments	Give lower dosage range in elderly Risk of QTc prolongation	BBW for QTc prolongation Frequently on drug shortage	Warning to separate from benzodiazepines administration by 1 hour	Caution for QTc prolongation

Overview of Evidence

Author, year	Design/sample size	Intervention & Comparison	Outcome
Klein, 2018	Observational n=737	<ul style="list-style-type: none"> IM haloperidol 5 mg IM ziprasidone 20 mg IM olanzapine 10 mg IM midazolam 5 mg IM haloperidol 10 mg 	<p>At 15 minutes, midazolam resulted in more patients adequately sedated compared with ziprasidone 20 mg, haloperidol 5 mg, haloperidol 10 mg, and olanzapine.</p> <p>At 15 minutes, olanzapine resulted in more patients adequately sedated compared with haloperidol 5 and 10 mg.</p>
Taylor, 2017	RCT n=349	<ul style="list-style-type: none"> IV midazolam 5 mg + droperidol 5 mg IV olanzapine 10 mg IV droperidol 10 mg 	<p>Ten minutes after the first dose, significantly more patients in the midazolam-droperidol group were adequately sedated compared with the droperidol and olanzapine groups.</p> <p>Patients in the midazolam-droperidol group required fewer additional doses or alternative drugs to achieve adequate sedation.</p>
Hsu, 2010	RCT n=42	<ul style="list-style-type: none"> IM haloperidol 7.5 mg IM olanzapine 10 mg ODT olanzapine 10 mg PO risperidone 3 mg 	<p>IM olanzapine or orally disintegrating olanzapine tablets showed significantly greater improvement in PANSS-EC scores than did patients who received IM haloperidol at points 15, 30, 45, 60, 75, and 90 minutes after injection.</p> <p>There was no significant difference in effectiveness among intramuscular olanzapine, ODT olanzapine, and oral risperidone solution.</p>
Martel, 2005	RCT n=144	<ul style="list-style-type: none"> IM droperidol 5 mg IM ziprasidone 20 mg IM midazolam 5 mg 	<p>There were more patients who remained agitated in the ziprasidone group at 15 minutes than in the droperidol and midazolam group.</p> <p>At 45 minutes, there were more agitated patients in the midazolam group than in the droperidol and ziprasidone groups.</p> <p>No cardiac dysrhythmias were identified.</p>
Nobay, 2004	RCT n=111	<ul style="list-style-type: none"> IM midazolam 5 mg IM lorazepam 2 mg IM haloperidol 5 mg 	<p>The mean time to sedation was 18.3 minutes for midazolam, 28.3 minutes for haloperidol, and 32.2 minutes for lorazepam. (P< 0.05)</p> <p>Time to arousal was 81.9 minutes for patients receiving midazolam, 126.5 minutes for haloperidol, and 217.2 minutes for lorazepam. (P<0.05)</p>
Wright, 2001	RCT n=311	<ul style="list-style-type: none"> IM haloperidol 5 mg IM olanzapine 10 mg IM Placebo 	<p>Significant differences between olanzapine and haloperidol were observed at 15, 30, and 45 minutes after the first injection in scores on Agitated Behavior Scale, and Agitation Calmness Evaluation Scale.</p> <p>Significant differences between haloperidol and placebo were observed from 30 minutes onward on agitation scores.</p> <p>At 24 hours, changes in QTc intervals with active treatments were not significantly different from those with placebo.</p>
Thomas, 1992	RCT n=21	<ul style="list-style-type: none"> IM/IV haloperidol 5 mg IM/IV droperidol 5 mg 	<p>Droperidol decreased combativeness significantly more than IM haloperidol at 10 and 30 minutes.</p> <p>There was no significant difference between the two drugs when given by the IV route.</p>

References

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