

#### Rational Approach To Medicating an Agitated Patient

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# Approach & Goals

- & Recognize and address agitation
  - Verbal de-escalation
  - Immediate needs (pain, hunger, nicotine, not taking meds)
  - Team based approaches work better ("Code [insert number/color]")

#### 🗞 Goal

- Patient and staff safety
- Identify cause of agitation
- Aim for calm, sleepy, but arousable
- & Goldilocks timing of medications





# Chief Complaint

Aggressive Behavior (Menacing a passenger vehicle (tapping window), then "humping the hood" with police, restrained by ems, screaming on arrival, medicated in ambulance bay, not in custody or on hold on arrival.)



#### UCSF ED Adult Severe Refractory Agitation Guideline Based on Initial Antipsychotic

### Cast of characters - Acute Agitation

Drug	Usual Dose	Route	Sedation dynamics	Duration	Comment
Haloperidol (1st) \$3	5 mg	<b>IM</b> , IV*, PO	Onset: 15 min Peak: 30 min	2 hrs	QTc EPS
Droperidol (1st) \$5	5-10 mg	IV, <b>IM</b>	Onset: 5-10 min Peak: 30 min	2-4 hrs	QTc EPS
Olanzapine (2nd) \$40	10 mg	<b>IM</b> , IV*, PO	Onset: 15 min Peak: 30 min	2-4 hrs	IV/IM BZD caution
Ziprasidone (2nd) \$50	20 mg	IM, PO	Onset: 15 min Peak: 30 min	2-4 hrs	QTc
Ketamine \$2	4-5 mg/kg, 1- 1.5 mg/kg	IM, IV	IM: 3-5 min IV: 1-2 min	IM: 15-30 min	Proc. sed. monitoring

Avoid AP in toxin-related causes of agitation (alcohol, anticholinergics, cocaine, stimulants)



### FGAs

#### & Haloperidol

- Potent inhibitor of D2 receptor
- Most commonly used FGA
- Case reports of TdP (higher dosing, IV route)

#### & Droperidol

- Invented in search of morphine replacement
- Similar mechanism to haloperidol
- 1970 Jenssen FDA approval
- $2001 \rightarrow FDA$  Black Box Warning
- & Adjuncts used often (bzd+ach)
- & Extremely rare NMS





Factor	Ν	
Total cases reported	273	
Foreign source of case report	94	
Serious adverse event (AE)	127	
Total deaths reported	89	
Deaths with droperidol dose 2.5 mg or less	2	
Possible cardiac event	74	
Torsade or prolonged QT	17/127	
Excessive/inappropriate droperidol dose	57/74	
Droperidol (2.5 mg or less) likely cause of AE	5	

Table 1. Summary of Cases on Which the Droperidol Warningby the Food and Drug Administration Was Based

Majority of death doses: 25-250 mg (14 doses not reported)

Concomitant issues in patients who died: alcohol intoxication suicide attempts general anesthesia multiorgan dysfunction sepsis

	Α	В	С	D	E	F	G	Н		J	K	L	М	Ν	0	Р	Q	R	S
1	Table 4. P	Patie	nt d	emogr	aphi	cs, clini	ical i	nforr	natior	n, QTc	mea	asurme	ents, lab	orate	ory va	alues,	and	l dru	g intera
2	Patient^	Age	Sex	Race	Weight (kg)	First droperidol dose	First dose route	Total droperidol doses in ED	QTc Pre-droperidol	QTc Post-droperidol	QTc difference	Timing of pre-EKG+	Timing of post-EKG+	Potassium (mEq/L)	Magnesium (mg/dL)	Calcium (mg/dL)	DDI +/-2 hours	DDI home medications	
3	29	32	М	W	63	1.25	IV	1	496	537	41	-4 hr	6 hr	3.7	1.9	7.9	-	-	
4	30	89	М	W	80	0.625	IV	1	*393	*437	44	-6 hr	18 min	4.2	2	9.4	Х	Х	
5	31	41	F	B/AA	75	2.5	IM	1	407	477	70	-24 hr	1 hr	3.5	1.7	8.9	-	Х	
6	32	26	М	W	64	0.625	IV	1	438	515	77	-2 hr	3 hr	3.4	2.1	11.2	Х	-	
7	33	56	F	W	55	0.625	IV	2	430	*510	80	-3 h	15 hr	4.1	2.4	9.6	-	-	
8																			
9	Presence of bundle branch block																		

	А	В	С	
1	Table 3. Droperidol Route and Dosing			
2		IM	IV	
3	First dose, (mg)	70	107	
4	.625	8 (11.4%)	35 (32.7%)	
5	1.25	19 (27.1%)	59 (55.1%)	
6	2.25	1 (1.4%)	0 (0.0%)	
7	2.5	36 (51.4%)	12 (11.2%)	
8	5	6 (8.6%)	1 (0.9%)	

#### FGA Pearls

- & Avoid IV route for haloperidol
- & EPS is common: diphenhydramine for dystonia, bzd for akathisia
- & Droperidol may prolong QTc in certain patients
- & Droperidol is safe at usual n/v/migraine doses: 0.625-1.25 mg
- & Droperidol for agitation is off-label, but decent data supports safety & efficacy
  Br J Psychiatry. 2015;206(3):223-228
- & Good idea NTE 20 mg/day, (maybe even 10mg/day?) Ann Emerg Med. 2010;56(4):392-401 Acad Emerg Med. 2005;12(12):1167-1172 Ann Emerg Med. 1992;21:407-413



### SGAs

#### Olanzapine

- & Oral version available (ODT)
- **\&** Probably as effective as droperidol
- & Maybe > haloperidol
  - Faster sedation, less rescue meds
- & Increased respiratory depression:
  - IV route
  - Parenteral benzodiazepines

#### Ziprasidone

- & Oral version available
- & Commonly used by psych institutions
- & Similar QTc issues as haloperidol, droperidol

Drugs. 2005;65(9):1207



#### SGA Pearls

- & Lower rate of EPS (<1%)
- & Do not give diphenhydramine/anticholinergics
- & Avoid olanzapine with parenteral benzodiazepines
- & Caution with ziprasidone and QTc issues







#### Ketamine Pearls

Reliable, predictable, breathing ok (most of the time)

Negative inotrope

Schizophrenia concern

Bad press

And then what?



- **Paramedics convicted**
- in death of Elijah
- **McClain for giving fatal**
- ketamine overdose



#### Intravenous Dexmedetomidine

- & FDA approval 1999
- & Alpha-2 agonist (clonidine-like)
- & Unlikely respiratory depression
- & Slight analgesic properties
- & Used as adjunct in AWS and agitation
- & Requires IV pump, controlled rate infusion
- & Dosed in mcg/kg/hr



Am J Health-Syst Pharm. 2023;80:526-531



# Sublingual Dexmedetomidine

- 𝔅 FDA approval: 2022
- & Indications: Schizophrenia or bipolar I/II
- **◊** Onset: ~20 minutes
- & Duration: 2.8 hours
- & Common SE: somnolence, hypotension
- & \$180-200 per dose





Sublingual Administration

**Buccal Administration** 

JAMA. 2022 Feb 22;327(8):727-736

#### Where can we use SL dexmedetomidine?

- & Alternative/adjunct to oral antipsychotics?
- & Elderly pts?
- & Movement disorders?
- & CT-scan/MRI?
- & QT-related issues?

# Use of Restraints (violent)

 $\sim$ 2.6% of ED visits involve agitation

Advocacy groups call for reduction/ban

Race may influence restraint use

Black patients associated with:

More frequent restraintLonger restraint



J Emerg Med. 2022 May;62(5):636-647 JAMA Netw Open. 2021;4(1):e2035241.



# In Summary

Haloperidol, droperidol, ziprasidone, olanzapine, benzodiazepines, ketamine have been used in EM for treatment of acute agitation

FGA and SGA take  $\sim$ 30 min for effect, caution with redosing

Adjuncts expedite sedation and may prevent EPS at the cost of recovery time

FGAs and ziprasidone have non-negligible QTc issues

Ketamine will give you immediate control, but agitation may return

