Management of Acute Agitation and Aggression in Children and Adolescents with Quetiapine in the Emergency Department (2ACT)

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Background

- Acute agitation is a state of behavioural dyscontrol that may result in harm to the patient, their family, or health care provider
- Chemical restraints may be necessary to ensure safety
- First-generation antipsychotics (FGAs) and/or benzodiazepines are typically used for managing acute agitation or aggression in the pediatric population
- Recent use of oral immediate-release as needed (prn) quetiapine, a second-generation antipsychotic (SGA), has been observed in the pediatric emergency department (ED) at Surrey Memorial Hospital (SMH) for this purpose
- Evidence on efficacy and safety of prn quetiapine for managing acute agitation and aggression in the pediatric population is limited

Objectives

Primary

- To characterize the dose (mg/kg) of prn oral immediate-release quetiapine used for managing acute agitation or aggression in pediatric patients

Secondary

- To determine the following:
  - Dose (mg/dose) of prn oral immediate-release haloperidol, loxapine, and chlorpromazine used for managing acute agitation or aggression in pediatric patients
  - Proportion of patients whose sign(s) and symptom(s) improved within or at one-hour post-first dose antipsychotic
  - Earliest recorded onset of action post-first dose antipsychotic
  - Mean length of stay (LOS) in the ED for non-admitted patients
  - Proportion of patients admitted
  - ED revisits within or equal to 30 days post-discharge
  - Adverse drug events during antipsychotic therapy

Methods

- **Design:** Retrospective chart review
- **Inclusion criteria:**
  - Age 5 years or greater to less than 17 years old AND
  - Acute agitation or aggression AND
  - At least one oral prn dose of immediate-release quetiapine, haloperidol, loxapine, or chlorpromazine
- **Exclusion criteria:** Subsequent visit to the ED
- **Study period:** January 1, 2012 to December 31, 2016
- **Setting:** Pediatric ED at SMH
- **Analysis:** Descriptive statistics

Table 1: Patient Characteristics

	Quetiapine n = 32	Haloperidol n = 11	Loxapine n = 10	Chlorpromazine n = 16
Age, years, median (IQR)	15 (14-16)	14 (14-15)	15 (15-16)	14 (12-15)
Greater than 12 years, %	84	82	100	56
Female, %	69	45	70	31
Canadian Triage and Acuity Scale score, median (IQR)	3 (2-3)	3 (2-3)	3 (2-3)	2 (2-3)
Mode of admission, %				
Ambulance	9	36	20	19
Family member/caregiver	38	18	20	25
Police	34	36	60	44
Other	19	9	0	13
Documented psychiatric history, %	78	73	80	69
Documented substance use history, %	50	36	60	50
Psychiatric medications prior to visit, %				
FGA (same antipsychotic at home)	3	0 (0)	0 (0)	0 (0)
SGA (same antipsychotic at home)	28 (16)	9	40	31
Benzodiazepine	13	8	0	13
Clonidine	6	0	10	6
SSRI	38	27	30	13
Stimulant	16	27	20	19
Other	22	18	10	13
None or unknown	35	45	30	19
ED physician diagnosis, %				
Psychosis	9	55	30	6
Suicidal ideation	53	9	20	19
Behavioural issue	13	0	0	44
Situational crisis/acute stress	17	0	0	6
Intoxication	9	9	20	6
Other	12	36	40	19
Time to administration post presentation to ED, hours, median (IQR)	4 (2-6) (n = 30)	2 (1-3) (n = 10)	4 (2-8)	2 (1-5)

Figure 1: Type of Agitation versus Proportion of Patients in Each Treatment Arm

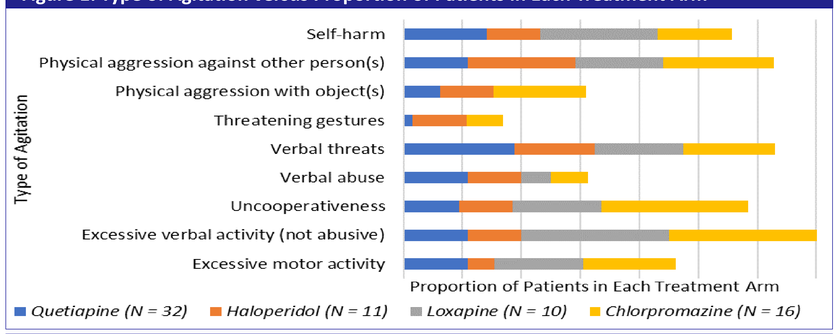

Table 2: Other Medications or Restraints Prior To, With, and Post-First Dose Antipsychotic

	Quetiapine n = 32			Haloperidol n = 11			Loxapine n = 10			Chlorpromazine n = 16		
PRN Medications, n	**Prior**	**With**	**Post**	**Prior**	**With**	**Post**	**Prior**	**With**	**Post**	**Prior**	**With**	**Post**
FGA (same FGA)	0	0	0	0 (0)	0 (0)	1 (1)*	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
SGA (same SGA)	0 (0)	0 (0)	0 (0)	0	0	1	0	0	0	0	0	0
Lorazepam	3	3	0	0	9	1*	0	6	2	1	1	1
Benztropine	0	0	0	0	1	1*	0	3	1	0	1	0
Other	2	2	0	0	0	1	0	0	0	0	1	0
Seclusion room, n	0	0	1	1	0	1	4	1	0	2	2	0
Physical restraints, n	1	0	0	3	2	1	3	0	0	3	0	0

Note: Prior = period prior to administration of first dose antipsychotic post presentation. Post = period post-first dose antipsychotic, up to and at 1-hour post dose. * = intramuscular formulation

Results

Table 3: Dose of Antipsychotic and Outcomes

	Quetiapine n = 32	Haloperidol n = 11	Loxapine n = 10	Chlorpromazine n = 16
First dose, mg/kg, mean ± SD	0.54 ± 0.27 (n = 31)	0.07 ± 0.03	0.20 ± 0.10	0.53 ± 0.24 (n = 14)
First dose, mg, median (IQR)	25 (25-25)	4 (3-5)	10 (10-10)	25 (13-50)
Total 24h dose, mg/kg, mean ± SD	0.71 ± 0.53 (n=31)	0.08 ± 0.04	0.20 ± 0.10	0.78 ± 0.58 (n = 14)
Total 24h dose, mg, median (IQR)	25 (25-50)	5 (3-7)	10 (10-20)	25 (22-56)
Number of doses in 24h, median (IQR)	1 (1-1)	1 (1-2)	1 (1-1)	1 (1-2)
Earliest recorded onset of action, minutes, median (IQR)	90 (40-150) (n = 26)	82 (48-154)	88 (64-104)	70 (35-120) (n=15)
LOS in the ED for non-admitted patients, hours, median (IQR)	15 (9-22) (n = 18)	14 (4-15) (n = 5)	18 (13-21) (n = 4)	5 (2-15) (n = 13)
Admission to inpatient ward, n (%)	14 (44)	6 (55)	6 (60)	3 (19)
ED revisits within or equal to 30 days post-discharge for mental health reasons, n (%)	11 (34)	5 (45)	4 (40)	9 (56)

Figure 2: Response Within or At One-hour Post-first Dose Antipsychotic

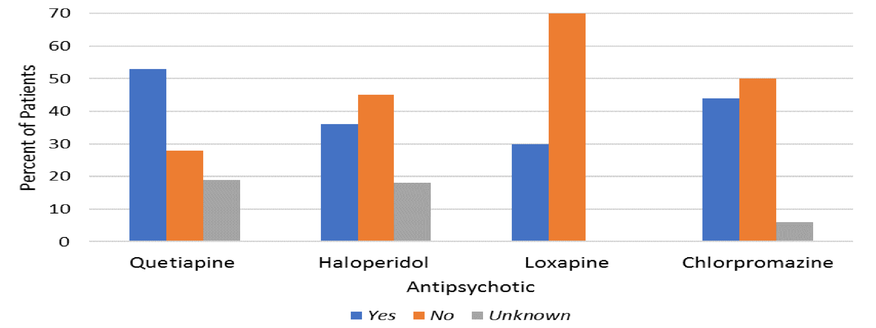

Table 4: Adverse Drug Events (ADEs)

	Quetiapine n = 32	Haloperidol n = 11	Loxapine n = 10	Chlorpromazine n = 16
Headache, n (%)	2 (6)	0 (0)	0 (0)	0 (0)
Nausea, n (%)	0 (0)	1 (9)	0 (0)	0 (0)
Rash, n (%)	1 (3)	0 (0)	0 (0)	0 (0)
EPSE, n (%)	0 (0)	2 (18)	1 (10)	1 (6)

Note: A Naranjo score was determined for each ADE. All events were assessed as having a possible association with the drug. EPSE = extrapyramidal side effects (dystonia, parkinsonism)

Limitations

- Single-centre, retrospective design with small sample size
- Unable to verify accuracy of collected data documented in patient charts
- Difficult to extrapolate findings outside ED setting

Conclusions

- Mean prn quetiapine dose was 0.54 ± 0.27mg/kg, with a median of 25mg per dose. The median number of doses of quetiapine administered in 24h was 1
- Median prn haloperidol, loxapine, and chlorpromazine dose were 4mg, 10mg, and 25mg per dose, respectively
- No noticeable difference in response between quetiapine and FGAs was observed
- Low rates of ADEs were reported in all groups. EPSE were reported with FGAs, but not with quetiapine