JPPT | Retrospective Chart Review

Use of Intramuscular Chlorpromazine Versus Intramuscular Olanzapine for the Management of Acute Agitation and Aggression in Youth

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OBJECTIVES In the inpatient psychiatric setting, one treatment strategy used to manage acute agitation in youth includes administration of IM antipsychotics. The aim of this study was to compare the effectiveness and safety of IM chlorpromazine versus IM olanzapine in treating aggression in youth.

METHODS We conducted a retrospective chart review of patients younger than 18 years hospitalized in the inpatient psychiatric unit who received either IM chlorpromazine or IM olanzapine for acute agitation. Demographic, efficacy, and tolerability data were collected using the electronic health record EPIC. The primary outcome was change from baseline to end point in the Behavioral Activity Rating Scale (BARS) score. BARS was applied retrospectively using nursing and physician documentation to evaluate for clinical response.

RESULTS Among 145 patients who met the inclusion criteria, 72 received IM chlorpromazine, compared with 73 who received IM olanzapine. The mean change in BARS score (before and after IM antipsychotic) was greater with olanzapine (3.58 ± 0.99) than with chlorpromazine (3.07 ± 1.18, $p = 0.006$). The target BARS score of 4 was achieved more frequently with chlorpromazine (45.8%) than with olanzapine (24.7%, $p < 0.008$). Coadministration of IM diphenhydramine occurred significantly more often in the olanzapine group than in the chlorpromazine group (71.2% vs 36.1%, $p < 0.001$).

CONCLUSIONS Management of acute agitation with IM olanzapine resulted in a greater change in BARS score, despite more youth requiring coadministration with diphenhydramine. In comparison, IM chlorpromazine demonstrated a higher likelihood of returning patients to baseline. Study results suggest tolerability of IM chlorpromazine and olanzapine.

ABBREVIATIONS BARS, Behavioral Activity Rating Scale; EPS, extrapyramidal symptoms; IM, intramuscular; RUHS, Riverside University Health System

KEYWORDS adolescents; aggression; agitation; chlorpromazine; injections, intramuscular; olanzapine

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Introduction

On the inpatient psychiatric unit, it is common for children and adolescents to exhibit acute agitation or aggression. Various psychiatric disorders, such as attention-deficit hyperactivity disorder, mood disorders, and conduct disorder, are associated with aggressive behaviors.[1] When acute aggression occurs, it is a behavioral emergency that requires immediate intervention in order to reduce the danger to the patient, staff, and other adolescents in the psychiatric unit.[2]

The use of sedatives and mechanical restraints has been the basis of treatment for agitation for a number of years.[3,4] Because physical restraints have been scrutinized for potentially increasing the morbidity and mortality of patients, many psychiatric hospitals seek to use the least restrictive options, including pharmacologic interventions, to manage severely agitated or aggressive patients.[5–9] Although behavioral techniques, such as verbal de-escalation, are usually the first-line intervention, psychotropic medications with sedative properties are commonly used on an "as needed" basis to treat or prevent acute aggressive episodes.[10] The goal of using pharmacotherapy is to address the underlying distress, and to calm the patient sufficiently to be assessed by the provider.[5] Some psychotropic medications that are used for rapid treatment include IM first-generation or second-generation antipsychotics with or without concurrent benzodiazepines, anticholinergics, or antihistamines. The use of benzodiazepines or diphenhydramine in youth may be less favorable because these medications are more likely to cause paradoxic reactions consisting of behavioral disinhibition.[1,5,11]

Among the second-generation antipsychotics, ziprasidone was the first medication to be available in an injectable form.[12] As a result, ziprasidone is the

most studied IM medication for managing agitation in children and adolescents.[1–3,13–15] Although ziprasidone has the most available data in youth, there are several factors that limit its use in managing agitated patients, including cost and reconstitution time.[14,15] In addition, the American Association for Emergency Psychiatry guideline does not recommend the use of ziprasidone for treatment of agitation in children and adolescents because of its activating potential and the risk of QT prolongation.[5] Instead, the consensus recommends use of chlorpromazine, despite few studies investigating IM administration in youth.[16,17]

Chlorpromazine is a low-potency, first-generation antipsychotic that has been used in the United States since the 1950s to treat adults with schizophrenia, mania, and psychosis, as well as a variety of other medical conditions. In addition, chlorpromazine is approved to treat behavioral problems in children as young as 6 months.[18,19] First-generation antipsychotics, such as haloperidol and chlorpromazine, have been the core treatments for aggression in children and adolescents for many years.[13] One of the benefits of using chlorpromazine in youth is that it is more sedating, and it is associated with less extrapyramidal symptoms (EPS) compared with high-potency, first-generation antipsychotics, such as haloperidol.[10] Extrapyramidal symptoms include acute dystonia, akathisia, parkinsonism, and tardive dyskinesia, which are debilitating adverse effects caused by treatment with antipsychotics. Thus, IM haloperidol is associated with poor tolerability, which may limit its use in young patients who are at a greater risk than adults for developing acute dystonia.[20] The increased risk of EPS may lead practitioners to prefer agents with a lower risk, such as second-generation antipsychotics.

Second-generation antipsychotics, such as olanzapine, are commonly used for the management of acute agitation and aggression in pediatric and adult patients because they are better tolerated and have a reduced risk of EPS.[2,5,21] Many studies in adults have demonstrated the effectiveness and safety of IM olanzapine in the treatment of acute agitation.[2,21,22] Retrospective analyses of IM olanzapine demonstrated that drowsiness was the most common adverse drug event reported when effective doses were used to manage agitated children (5 mg) and adolescents (10 mg).[2] In addition, IM olanzapine exhibits a dose-dependent response in reducing agitation in patients with schizophrenia.[23] Because both first- and second-generation antipsychotics are used for treating agitation, provider preference and knowledge of a particular agent will usually dictate therapeutic decision-making.

In order to measure behavioral changes after administration of IM antipsychotics, some studies have used the Behavioral Activity Rating Scale (BARS) as an assessment tool.[1] The BARS assessment is a high-sensitivity, validated scale that has been reliably used to assess agitation in clinical trials. For example, the BARS tool has been used to assess the rapid effects of ziprasidone on the behavioral activity of acutely agitated youth with psychosis.[24,25] The scale is simple to use and can be implemented in non-medical settings by individuals who are not medically trained.[24]

Although there is increasing use of IM olanzapine in children and adolescents to treat agitation and aggression, IM chlorpromazine continues to be used as a mainstay of therapy in the inpatient psychiatric setting.[5,17] Currently, there are no studies investigating the effectiveness and tolerability of IM chlorpromazine compared with other IM antipsychotics in youth. Many inpatient psychiatric hospitals have a high use rate of chlorpromazine for agitation in youth despite the absence of recent data comparing its effectiveness to that of newer, second-generation antipsychotics. In order to bridge this gap in knowledge, it is necessary to examine the effectiveness of IM chlorpromazine relative to IM olanzapine in children and adolescents.

Materials and Methods

A retrospective chart review was conducted of patients younger than 18 years who received either IM chlorpromazine or IM olanzapine for managing agitation and/or aggression during their hospitalization. Patients were selected using a computerized pharmacy surveillance software, VigiLanz, version 2018 (VigiLanz Corporation, Minneapolis, MN) to identify medication orders for IM chlorpromazine and IM olanzapine in youth hospitalized in the inpatient psychiatric unit. A total of 174 medication orders were identified for patients hospitalized in the inpatient psychiatric unit at the Riverside University Health System (RUHS) Arlington campus between October 1, 2016, and August 28, 2018, which consisted of patients hospitalized in the inpatient psychiatric unit. The psychiatric hospital is a county facility with segregated adolescent and adult units. There are 12 inpatient beds on the adolescent unit, and the patients' treatment is managed by pediatric psychiatrists.

Among youth who received IM chlorpromazine or IM olanzapine for acute agitation, 145 patients met the inclusion criteria for this study. Requirements for inclusion were age less than 18 years, hospitalization at the RUHS Arlington campus, and having received at least 1 dose of IM chlorpromazine or IM olanzapine for acute agitation or aggression. Youth received IM antipsychotics if oral psychotropics were refused by the patient. Exclusion criteria included being 18 years or older, not receiving either IM chlorpromazine or IM olanzapine, or receiving the medication for an indication other than acute agitation or aggression (i.e., court order). Furthermore, patients were excluded if there was insufficient nursing and/or provider documentation before and after IM administration. In the chlorpromazine group, 5 patients were excluded for inadequate documentation

in comparison with 11 youth in the olanzapine group. Patients were not included if concomitant administration of IM chlorpromazine and IM olanzapine occurred. Intramuscular medications for agitation and aggression were verified through documentation in the medication administration record. During the course of the study, more than 20 psychiatrists were involved in the prescribing of IM antipsychotics for acutely agitated youth.

Demographic and clinical data were collected using the electronic health record system EPIC. Baseline data included age, sex, ethnicity, and weight. Clinical data included primary diagnoses, dosage of IM antipsychotic received, presence of scheduled oral antipsychotics, concurrent administration of IM antihistamines or benzodiazepines, time to next IM medication, and vital signs. All diagnoses were made in accordance with the *Diagnostic and Statistical Manual of Mental Disorders,* 5th edition (DSM-5) and the *International Statistical Classification of Diseases and Related Health Problems*, 10th revision codes.[26,27] Safety data were collected using provider and nursing progress notes as well as administered medications to treat side effects associated with the study medication. When documented, vital signs were examined to identify significant cardiopulmonary effects secondary to the study medication.

Because a formal objective agitation rating scale was not available in the existing charts, the Behavioral Activity Rating Scale (BARS) tool was retrospectively applied for each patient based on provider and/or nursing documentation. A single, unblinded investigator assigned BARS scores for each patient in this study. The investigator was a pharmacist with knowledge of BARS scoring criteria. The BARS assessment consists of a single item, 7-point scale that scores a patient's behavioral activity from 1 = *difficult or unable to arouse* to 7 = *violent, requires restraint* (Table 1). The midpoint score of 4 corresponds with a baseline level of activity (i.e., *quiet and awake*). A BARS rating of 4 is the target score after an IM injection is administered. The pre-IM BARS score was defined as the behavior activity level immediately prior to the administration of either IM chlorpromazine or IM olanzapine. The post-IM BARS score was determined after the IM chlorpromazine or IM olanzapine was administered (approximately 30–60 minutes after the injection and prior to any further episodes of agitation or additional injections). Documentation time stamps were used to ensure the consistency of observation time. In addition, the postevent documentation addressed any immediate and delayed effects of the medication.

The primary end point measured to assess effectiveness was the change from baseline to end point in BARS scores. Secondary end points assessed included effectiveness of coadministered IM antihistamines and/or benzodiazepines, achievement of target BARS score, postinjection BARS score, and tolerability of the study agents.

Table 1. Behavioral Activity Rating Scale

Score	Description
1	Difficult or unable to arouse
2	Asleep but responds normally to verbal or physical contact
3	Drowsy, appears sedated
4	Quiet and awake (normal level of activity)
5	Signs of overt (physical or verbal) activity, calms down with instructions
6	Extremely or continuously active, not requiring restraint
7	Violent, requires restraint

All statistical analyses were conducted using SPSS version 25.[28] Standard χ^2 analysis was used to compare categoric data, including sex, race, coadministered IM medications, adverse drug events, and BARS target achievement. Analysis of variance was performed on all continuous variables, including age, weight, IM dose, BARS score measurements, and vital signs, using an $\alpha < 0.05$. Regression analysis was used to adjust for confounding variables in order to assess if the target BARS score of 4 was significantly associated with either study medication when controlling for age, sex, IM dose, and pre-IM BARS score.

Results

At the RUHS inpatient psychiatric hospital, 145 children and adolescents received IM injections for acute agitation, consisting of 72 doses of chlorpromazine and 73 doses of olanzapine. Demographic characteristics were not significantly different between the chlorpromazine and the olanzapine treatment groups (Table 2). Most patients in the chlorpromazine (58%) and the olanzapine (67%) groups were male, and the average age was 14 years. In the chlorpromazine group, 36% were classified as children (age ≤12 years) and 64% were classified as adolescents (age 13–17 years). In the olanzapine group, 18% were classified as children and 82% were classified as adolescents. There was a relatively even distribution between white, African American, and Hispanic patients.

Primary diagnoses were collected for both treatment groups. On discharge, the most common primary diagnosis was mood disorder for both the chlorpromazine and the olanzapine groups (Table 3). Diagnoses classified under mood disorder were disruptive mood dysregulation disorder, major depressive disorder, unspecified bipolar disorder, and unspecified mood disorder. In the chlorpromazine group, disruptive, impulse-control, and conduct disorders were the second most common diagnosis, comprising intermittent explosive disorder, oppositional defiant disorder, impulse control

Table 2. Baseline Demographics

Characteristic	Chlorpromazine (n = 72)	Olanzapine (n = 73)	p value
Age, mean ± SD, yr	14 ± 3	14 ± 2	0.07
Weight, mean ± SD, kg	63.9 ± 22.3	64.3 ± 20	0.91
Male, n (%)	42 (58)	49 (67)	0.27
Female, n (%)	30 (42)	24 (33)	
Ethnicity, n (%)			
White	26 (36)	19 (26)	
African American	22 (31)	25 (34)	0.46
Hispanic	21 (29)	28 (38)	
Asian	3 (4)	1 (2)	

disorder, and conduct disorder. In contrast, psychotic disorders were the second most common diagnosis in the olanzapine group, which included schizophrenia, schizoaffective, and unspecified psychotic disorder. A third of the patients in both groups were taking a scheduled oral antipsychotic prior to the administration of the IM medication. In the olanzapine group, more patients were prescribed scheduled oral olanzapine than any other antipsychotic. In comparison, oral chlorpromazine and risperidone were the most commonly scheduled oral antipsychotics in the chlorpromazine group (Table 3). Although more individuals in the chlorpromazine group required a second injection within 6 hours compared with the olanzapine group, no patients in either group received a second injection within an hour of the first administered dose.

Within both treatment groups, there was an increase in dose administered from children to adolescent patients. The mean IM chlorpromazine dose (IQR, 25–150 mg) administered in children was approximately 25 mg, whereas the mean adolescent dose was 50 mg (Table 4). In comparison, the mean IM olanzapine dose was 5 mg in children and 7.5 mg for the adolescent patients (IQR, 2.5–10 mg). The doses used were clinically appropriate and were based on the patient's weight, level of aggression, and prior exposure to antipsychotics.[2,5] Intramuscular diphenhydramine was more commonly coadministered with IM olanzapine (71.2%) than with IM chlorpromazine (36.1%). Concomitant administration of IM diphenhydramine and IM benzodiazepine occurred in 1 patient in both treatment groups, but no patients in the olanzapine group received IM benzodiazepine alone.

Prior to administering IM chlorpromazine or olanzapine, there was no difference between treatment groups in the BARS score (Table 5). On average, the patients demonstrated signs of overt physical or verbal activity and were not redirectable to instruction by staff. There was a statistically significant decrease in BARS score from prior to the injection to after the medication was administered, with a greater reduction in the olanzapine group than in the chlorpromazine group (3.58 vs 3.07, p = 0.006). Among patients who did not receive concomitant medications, there was a greater reduction in BARS score in the olanzapine group than in the chlorpromazine group (3.33 vs 2.89). Coadministration of IM diphenhydramine and/or benzodiazepines with IM olanzapine led to a greater change in BARS score in comparison with concomitant administration with IM chlorpromazine (3.67 vs 3.36). There was a statistically significant difference in postinjection BARS score between the olanzapine group and the chlorpromazine group (2.71 vs 3.21, p = 0.004).

Youth in the olanzapine group achieved the target BARS score of 4 less frequently than those in the chlorpromazine group (24.7% vs 48.8%, p < 0.008). A greater percentage of patients who received IM chlorpromazine alone (n = 22; 50%) achieved the target BARS score than those who received IM olanzapine alone (n = 6; 28.6%). Similarly, more patients who received concomitant IM diphenhydramine and/or benzodiazepines returned to baseline in the chlorpromazine group (n = 11; 39.2%) than in the olanzapine group (n = 12; 23.1%). Approximately 4.1% of patients in the olanzapine group and 8.3% of patients in the chlorpromazine group required redirection by staff to help settle down. Most patients in the olanzapine group were more sedated than desired (BARS score <4). Regression analysis demonstrated that IM chlorpromazine was significantly better at achieving the target BARS score compared with IM olanzapine (OR = 4.12, p = 0.028), even after controlling for age, sex, IM dosage, and BARS pre-IM score.

There were no clinically significant adverse drug events associated with the treatment medications in either group. The most common adverse event reported in both treatment groups was somnolence. The IM olanzapine group reported a greater frequency of somnolence (71.2%) than the chlorpromazine group (45.8%). Increased incidence of somnolence in the olanzapine group may be attributed to higher rates of coadministered IM diphenhydramine during episodes of agitation and aggression. There was no documenta-

Table 3. Clinical Characteristics

Characteristic	Chlorpromazine, n (%)	Olanzapine, n (%)
Primary diagnosis		
Neurodevelopmental disorders	9 (12.5)	9 (12.3)
Psychotic disorders	10 (13.9)	19 (26.0)
Disruptive, impulse-control, and conduct disorders	20 (27.8)	9 (12.3)
Mood disorders	33 (45.8)	36 (49.3)
Coadministered IM medication		
Diphenhydramine*	26 (36.1)	52 (71.2)
Benzodiazepine	1 (1.4)	0 (0)
Diphenhydramine + benzodiazepine	1 (1.4)	1 (1.4)
Scheduled oral antipsychotic, yes	23 (32)	25 (34)
Oral antipsychotic		
Chlorpromazine	5 (6.9)	0 (0)
Olanzapine	1 (1.4)	10 (13.7)
Risperidone	5 (6.9)	4 (5.5)
Quetiapine	4 (5.6)	1 (1.4)
Aripiprazole	3 (4.2)	5 (6.9)
Ziprasidone	2 (2.8)	1 (1.4)
Lurasidone	1 (1.4)	2 (2.7)
Haloperidol + quetiapine	1 (1.4)	1 (1.4)
Aripiprazole + lurasidone	1 (1.4)	1 (1.4)
Within 6 hr of next IM	6 (8.3)	1 (1.4)

* $p < 0.001$.

tion of dizziness, EPS, or cardiac effects in either treatment group. One patient in the chlorpromazine group was reported to have hypotension after the injection.

Discussion

Based on the results from this study, both IM chlorpromazine and IM olanzapine may be effective for managing episodes of agitation and aggression in children and adolescents in the inpatient psychiatric setting. Intramuscular antipsychotics were used in both treatment groups to control agitated behaviors. The olanzapine regimen produced a greater change in BARS score, although the medication required more coadministration with diphenhydramine. Most patients in the olanzapine group experienced somnolence, and only a quarter of patients were therapeutically calmed after the injection. In comparison, less than half of the patients who received IM chlorpromazine experienced sedation, and nearly twice as many patients returned to their baseline activity level after administration. Similar results were observed among patients who did not receive concomitant diphenhydramine and/or benzodiazepines. The addition of coadministered IM diphenhydramine resulted in a greater reduction of BARS score in both groups compared with when the antipsychotics were given alone. A smaller percentage of patients achieved the target BARS score with IM diphenhydramine present than without concomitant administration.

Although some providers may desire to sedate agitated youth to reduce the risk of harm to others as well as the patient, it is not the preferred outcome because somnolence is an adverse drug event of a medication. By attempting to elicit sedation, the provider is incapable of conducting an evaluation of the patient, and the patient is unable to benefit from group therapy sessions.[5] According to the Joint Commission on Accreditation of Healthcare Organizations, the use of restraints, whether chemical or physical, should not be used as a means of coercion or discipline, and should be discontinued as soon as possible.[29] Excessively sedating a patient with chemical restraints impedes the patient's freedom and prolongs the time until the patient can return to their baseline activity level. Furthermore, overt sedation can be dangerous to the patient, possibly leading to respiratory failure.

In order to prevent prolonged effects of IM medication, the pharmacokinetics and pharmacodynamics of the individual agents should be considered. There are pharmacokinetic differences between IM chlorproma-

Table 4. Administered Doses of Intramuscular Chlorpromazine and Olanzapine

Intramuscular Dose Administered	Chlorpromazine	Olanzapine
Cumulative dose, mean ± SD, mg	43.1 ± 20.2	7.3 ± 2.6
Child dose, mean ± SD, mg	31.7 ± 10.9	5.0 ± 1.8
Adolescent dose, mean ± SD, mg	49.5 ± 21.4	7.8 ± 2.8

zine and IM olanzapine. In children and adolescents, the peak effect of IM chlorpromazine occurs 15 minutes after administration, whereas IM olanzapine ranges between 15 and 45 minutes.[5] Although both medications bind similarly to histamine receptors, chlorpromazine has a stronger affinity for alpha-1 than olanzapine, resulting in sedation. In comparison, olanzapine has a stronger potency for muscarinic receptors than chlorpromazine. The additive effects of antagonizing the histaminic, adrenergic, and cholinergic pathways cause sedation. Thus, the addition of a second agent (i.e., anticholinergic) may not be clinically necessary, and it could be a method for limiting somnolence.

In this study, the use of significantly more doses of diphenhydramine in the olanzapine group than in the chlorpromazine group may be attributed to a variety of factors. The selection of treatment medication may be due to the symptom severity of the patients. Even though the BARS score is considered to be more specific and less subjective than the Clinical Global Impression rating, it does not evaluate the extent of severe agitation and potential for harm.[1] In the chlorpromazine group, slightly more patients required restraints than in the olanzapine group (25 vs 21). However, of those requiring restraints, there was an increased frequency of patients in the olanzapine group who received coadministered IM diphenhydramine (76.2%) than in the chlorpromazine group (36%). Therefore, more doses of diphenhydramine may have been administered with olanzapine because the patients were demonstrating more severe aggression. Psychiatrists consider a number of factors when selecting a medication to manage an acute episode of agitation, including the degree of symptom severity, comorbid conditions, and previous exposure to psychotropics. The combination of IM diphenhydramine with olanzapine allows for a faster onset of action to help settle the patient in a shorter period of time. In addition, selection of each treatment medication may be related to physician preference, with more seasoned psychiatrists favoring older first-generation antipsychotics rather than second-generation antipsychotics. At our institution, psychiatrists are not required to document their rationale for selecting one antipsychotic over another in emergency situations.

When selecting the dose of the antipsychotic, psychiatrists base their decision on the relative size of the individual, the patient's primary diagnosis, and the level of aggression. Youth in the olanzapine group received higher doses than individuals in the chlorpromazine group, based on calculated equivalent doses. The doses of IM olanzapine observed in this study were consistent with those in previous studies.[2,5] Because patients in both treatment groups weighed approximately the same, this suggests that patients in the olanzapine group were more aggressive, although more patients in the chlorpromazine were placed in restraints. An alternative explanation could be that the different etiologies for agitation could result in variable responses to agents. More patients in the olanzapine group had a primary diagnosis of a psychotic disorder in comparison with the chlorpromazine group. Thus, it is possible that those with chronic, more severe disorders were more resistant to treatment and required larger doses with coadministered diphenhydramine. Despite the differences in primary diagnoses between the groups, there was an equal number of individuals who were prescribed scheduled oral antipsychotics prior to receiving the IM medication. More patients taking scheduled oral olanzapine received IM olanzapine than IM chlorpromazine. Similarly, within the chlorpromazine group, more patients were prescribed oral chlorpromazine or risperidone than in the olanzapine group.

Overall, both IM chlorpromazine and IM olanzapine were tolerated in children and adolescents. The increased frequency of somnolence reported in the olanzapine group may be due to the sedative properties of the medication alone or due to the coadministration with diphenhydramine. Clinically significant cardiac effects, including QTc prolongation, were not documented in either treatment group. However, electrocardiograms are not routinely performed in youth in the inpatient psychiatric unit, which may limit the generalization of the study medication tolerability. In addition, underreporting of adverse drug events cannot be excluded.

Although chlorpromazine has been used for decades, there are limited data available investigating the safety and effectiveness of IM administration in children and adolescents for managing acute agitation and aggression. The combination of IM chlorpromazine, meperidine, and promethazine has been well studied in youth as a cocktail used for conscious sedation for cardiac catheterization, neuroimaging, laceration repair, and minor elective surgery.[30–39] In addition, IM chlorpromazine has been used to manage acute amphetamine poisoning in children.[16] In the Swart and colleagues study,[17] chlorpromazine and olanzapine demonstrated effectiveness in "settling" the patient and

Table 5. Comparison of Behavioral Activity Rating Scale (BARS) Score Between Treatment Groups

BARS	Chlorpromazine	Olanzapine	p value
Pre-IM score, mean ± SD	6.26 ± 0.61	6.29 ± 0.46	0.79
Post-IM score, mean ± SD	3.21 ± 1.09	2.71 ± 0.98	0.004
Change in score, mean ± SD	3.07 ± 1.18	3.58 ± 0.99	0.006
Target score achieved, n (%)	33 (48.8)	18 (24.7)	<0.008

prevented further aggressive episodes when used as needed for behavioral control. However, this study examined a variety of administration routes, and it did not focus on the effectiveness and safety of IM administration alone. Despite the lack of data supporting use of IM chlorpromazine in pediatrics, the most recent agitation guideline for children and adolescents recommends its use for managing these acute episodes.[5]

In addition to IM chlorpromazine, the agitation guideline recommends the use of IM olanzapine as an alternative agent.[5] Intramuscular olanzapine has been investigated in children and adolescents for agitation, using doses ranging from 5 to 20 mg.[21,40] The data suggest that olanzapine is safe and effective for acute agitation. When compared to IM ziprasidone, olanzapine was equally effective in treating aggression in youth when examining length of stay, efficacy, number of restraints, and duration of the restraints.[2] Furthermore, in a retrospective study of IM ziprasidone, a similar change in BARS score from baseline to after injection was observed in children and adolescents.[1]

Because of the retrospective design of this study, there are several limitations to note. First, the small sample size of this study limits applicability of the results in all children and adolescents. As a retrospective, single-center study, the results may not represent the general population and may introduce selection bias. In addition, the non-controlled nature of the study may have biased the evaluators in their assessment of the effectiveness of the study medications. The study would be strengthened by having at least 2 raters who are blinded to the interventions. In addition, the results of this study depend on the accuracy and completeness of nursing and provider documentation. Therefore, the possibility of insufficient documentation of vital signs and adverse drug events caused by the IM medications prevents the investigators of this study from making definitive conclusions regarding the tolerability of these treatments in youth. Also, the ability of the BARS tool to demonstrate the effectiveness of these agents for managing agitation and aggression depends on accurate, detailed documentation in the patients' charts. Throughout the study period, patients could have had multiple psychiatrist hospitalizations where emergency antipsychotic injections were administered. Thus, patients could have received both olanzapine and chlorpromazine injections. Based on these limitations, caution is needed in interpreting the study results.

Despite the limitations of a retrospective design, this study contains valuable information on real-world prescribing practices in children and adolescents. Because there are limited data evaluating the effectiveness and tolerability of IM chlorpromazine for agitation in youth, this study may provide appropriate doses for managing aggressive episodes. In addition, the minimal exclusion criteria allow for generalization to a diverse patient population. Future studies using a prospective, randomized, double-blind design may provide additional efficacy and safety data to determine an optimal regimen.

Conclusion

Based on the results of this study, administration of IM olanzapine to manage acute agitation in youth produced a greater change in BARS score, despite more patients requiring coadministration with diphenhydramine. In comparison, IM chlorpromazine demonstrated a higher likelihood of returning patients to baseline and avoiding oversedation. Although IM olanzapine may elicit a greater incidence of sedation, this adverse drug event could be a result of more doses given with diphenhydramine. Furthermore, the results of this study suggest the IM chlorpromazine and IM olanzapine are well tolerated in children and adolescents. Although this study provides some information regarding the effectiveness and safety of IM chlorpromazine and IM olanzapine for managing agitation, more prospective studies need to be conducted.

Article Information

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access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Ethical Approval and Informed Consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and have been approved by the Riverside University Health System Institutional Review Board. Given the nature of this study, informed consent was not required.

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