

Impact of holding home stimulant(s) on agitation in a child and adolescent inpatient psychiatric population

Anupha M. Mathew, PharmD, BCPS¹; Sophie Robert, BPharm, PharmD, BCPP²;
Clint Ross, PharmD, BCPP³; Erin Weeda, PharmD, BCPS⁴; Adrienne Pruitt, MD⁵

How to cite: Mathew AM, Robert S, Ross C, Weeda E, Pruitt A. Impact of holding home stimulant(s) on agitation in a child and adolescent inpatient psychiatric population. *Ment Health Clin* [Internet]. 2021;11(2):50-4. DOI: 10.9740/mhc.2021.03.050.

Abstract

Introduction: This study aimed to compare the rates of agitation-related interventions associated with initial holding versus continuation of home stimulant(s) in a child and adolescent population at the time of admission to an inpatient psychiatric facility.

Methods: This retrospective chart review included patients less than 18 years of age who were admitted to an academic medical center between July 1, 2017, and July 1, 2018. Patients were divided into 2 groups: those continued on their home stimulant(s) and those who had them held. We compared both groups on agitation-related outcomes by examining the difference in the number of level I or II events or as-needed medication administrations. Mechanical restraints and closed-door seclusions were grouped as level I events, and level II events consisted of nonmechanical restraint.

Results: The analysis included 169 patients. In total, 126 (75%) patients were continued on their home stimulant, and 43 (25%) had them held. The occurrence of the composite endpoint of level I or II events or as-needed intramuscular medication administration was numerically higher in the group that had their home stimulant held (27.9% vs 23%; $P=.52$). Level I events were also numerically higher but not statistically significant in the group that had their home stimulant held (16.3% vs 11.9%; $P=.46$).

Discussion: The composite outcome of as-needed intramuscular medication administration and level I or II events was numerically higher in the group that had their home stimulant held. Use of a larger sample size and adjusted analyses may help elucidate covariates that impact agitation-related outcomes.

Keywords: agitation, seclusion, restraint, hold, psychostimulants

¹ (Corresponding author) Clinical Pharmacy Resident, Medical University of South Carolina Health, Charleston, South Carolina, anmathew6@gmail.com, ORCID: <https://orcid.org/0000-0003-2848-7861>; ² Clinical Pharmacy Specialist - Psychiatry, Medical University of South Carolina Health, Charleston, South Carolina; Research Assistant Professor, Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, South Carolina; Adjunct Assistant Professor, Medical University of South Carolina, College of Pharmacy, Charleston, South Carolina, ORCID: <https://orcid.org/0000-0003-4221-0252>; ³ Clinical Pharmacy Specialist - Psychiatry, Medical University of South Carolina Health, Charleston, South Carolina; Affiliate Associate Professor, Medical University of South Carolina, College of Pharmacy, Charleston, South Carolina, ORCID: <https://orcid.org/0000-0002-2684-782X>; ⁴ Assistant Professor, College of Pharmacy, Medical University of South Carolina Health, Charleston, South Carolina, ORCID: <https://orcid.org/0000-0001-7876-5802>; ⁵ Assistant Professor, Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina Health, Charleston, South Carolina, ORCID: <https://orcid.org/0000-0002-6990-7992>

Disclosures: The authors do not have any biomedical financial interest or potential conflicts of interest.

Introduction

Stimulant medications are useful for the treatment of multiple diagnoses and are the gold standard pharmacotherapy treatment of ADHD.¹ ADHD is a neurodevelopmental disorder that is characterized by hyperactivity, impulsivity, and inattention.² Stimulants are used to treat these core features of ADHD; such symptoms may worsen upon stimulant discontinuation. Beneficial effects of stimulants on aggression associated with oppositional

defiant behavior and conduct disorder, frequently comorbid with ADHD, may also be lost with interruptions in therapy.^{2,3}

When evaluating patients for inpatient psychiatric admission, providers may or may not initially continue their home stimulants for a variety of reasons. Reasons to potentially *hold* (discontinue temporarily) these medications include active psychotic illness, mania, seizure disorder, or cardiac disease, among others.⁴⁻⁷ At times, stimulants are held or discontinued for unclear reasons (eg, patient/guardian preference, inability to obtain accurate medication history, delays in obtaining guardian consent). Anecdotally at our institution, holding home stimulants may contribute to agitation (potentially from impulsivity/hyperactivity/inability to focus) requiring intervention in some cases. Although verbal de-escalation is attempted first in cases of agitation, other methods may be necessary, including seclusion, restraint, or as-needed medications.⁸ Current practice regarding the continuation of home stimulant(s) (eg, amphetamine- or methylphenidate-based products) in child and adolescent patient populations being admitted to the hospital is variable based on prescriber discretion. There are no current guidelines, published literature, or standard of care regarding whether home stimulants should be initially continued or withheld upon admission to a psychiatric hospital.

The aim of this study was to compare rates of agitation-related interventions associated with holding versus continuation of home stimulant(s). Agitation-related interventions included the use of seclusion, restraint, or as-needed oral/intramuscular medications (diphenhydramine, hydroxyzine, benzodiazepines, and antipsychotics).

Methods

This retrospective, single center study was approved by the IRB at the Medical University of South Carolina. Participants included patients less than 18 years of age who were admitted to an academic medical center between July 1, 2017, and July 1, 2018, and were prescribed and adherent to home stimulant(s). Patients were included in the study if they were admitted to the psychiatric service, which includes the psychiatric emergency department. Patients with home stimulant(s) started less than 4 weeks prior to admission and those not adherent to these agents were excluded. Data for the first encounter was retained for inclusion in the study for those patients with more than 1 encounter during the study period.

After the application of exclusion criteria, patients were divided into 2 groups: those continued on their home

stimulant(s) and those who had their home stimulant(s) held. To facilitate patient categorization, the date/time was collected for hospital admission and initial stimulant administration. Continuation of home stimulant was defined as the administration of medication within 24 hours of admission. Patients were considered to have their home stimulant continued even if their home regimen was modified to another formulation based on formulary restrictions or modified to a different dose. Patients who were on multiple home stimulants were considered to have their home stimulant(s) continued if 1 of those agents was administered within 24 hours of admission.

Baseline patient characteristics; date/time of hospital admission and initial stimulant administration; information regarding the use of seclusion, restraint, as-needed intramuscular/oral medication administration; and Children's Attention Problem Rating Scale (CAPS) scores were extracted from the electronic medical records. Baseline CAPS score was utilized to assess the patients' disease severity during admission. Per internal psychiatrist consensus at the institution, CAPS scores of 10 and above are considered to reflect a higher disease severity. The duration of and adherence to home stimulant(s) were assessed via review of prescriber documentation in each patient's history and physical. Duration was also verified by utilizing prescription drug fill data.

Data are summarized as counts with proportions for categorical data or median and interquartile range for continuous data. To assess agitation-related outcomes, data regarding the occurrence of seclusion, restraint (mechanical and nonmechanical), and as-needed medication (ie, antipsychotics, benzodiazepines, and diphenhydramine) administrations were collected. This information was obtained if the event occurred within 72 hours of admission. Interventions were divided into 2 categories based on their severity. Mechanical restraints and closed-door seclusions were grouped as level I events as these were considered to be the most restrictive interventions. Level II events consisted of nonmechanical restraints (therapeutic hold and escort). The occurrence of any level I or II event or as-needed intramuscular medication administration served as the primary composite outcome for this study and was compared between the 2 groups. As-needed oral medication administration was not included in the primary outcome because as-needed intramuscular medication administration was found to be a better surrogate for more severe agitation. Data were compared using chi square, Fisher exact, or Mann-Whitney *U* tests when appropriate. The relationship was considered to be statistically significant if the *P*-value was less than .05. Statistical analysis was performed using SPSS version 22.

TABLE: Baseline characteristics of the study

Baseline Variable	No. (%) ^a		P Value
	Home Stimulant Continued n = 126	Home Stimulant Held n = 43	
Age, y	11 (9-14)	13 (10-15)	.13
Male sex	87 (69.0)	29 (67.4)	.85
Race			.20
Black or African American	56 (44.4)	13 (30.2)	
White	62 (49.3)	28 (65.1)	
Other/unknown	8 (6.3)	2 (4.7)	
Any substance use	24 (19.0)	6 (14.0)	.60
Alcohol	6 (4.8)	4 (9.3)	.28
Marijuana	10 (7.9)	2 (4.7)	.73
Tobacco	8 (6.3)	0 (0)	.21
Any concurrent medication	112 (88.9)	33 (76.7)	.05
Alpha-agonists	76 (60.3)	18 (41.9)	.04
Antidepressants	71 (56.3)	22 (51.2)	.56
Antipsychotics	32 (25.4)	7 (16.3)	.22
Atomoxetine	2 (1.6)	0 (0)	>.99
Mood stabilizers	10 (7.9)	3 (7.0)	>.99
Children's Attention Problem Rating Scale score ≥ 10	19 (15.1)	2 (4.7)	.07

^aException noted for age variable, which is median (interquartile range).

Results

A total of 244 patients had 1 or more home stimulant(s) documented on their prior-to-admission medication list during the study period. Of those, 169 patients met the defined inclusion and exclusion criteria and were included in the study. A majority of the patient population was male between the ages of 10 and 15 years. At the completion of data collection, 126 (75%) patients had their home stimulant continued, and 43 (25%) patients had their home stimulant initially held. Differences between baseline characteristics were seen between the 2 groups. Inpatient administration of alpha-agonists was higher in those who had their home stimulant continued (60.3% vs 41.9%; $P < .05$). A baseline CAPS score of 10 or above was more common in those who had their home stimulant continued (15.1% vs 4.7%; $P = .07$). Even though statistically not significant, substance use (ie, tobacco, alcohol, and marijuana) was found to be higher in those who had their home stimulant continued (19.0% vs 14%; $P = .60$). A difference in race was also seen when comparing those who were continued on their home stimulant(s) versus not; reasons for this difference are unclear. Other baseline characteristics are outlined in the Table.

Overall, the composite endpoint of level I or II events or as-needed intramuscular medication administration was 27.9% in the group that had their home stimulant held

versus 23% in those that were continued ($P = .52$; Figure 1). Level I and II events were numerically higher in the group that had their home stimulant held (16.3% vs 11.9%; $P = .46$ and 11.6% vs 6.3%; $P = .32$, respectively). Mechanical restraint was used in 3 patients, all of whom had their home stimulant held during hospitalization. All of the mechanical restraint was used in the emergency department as closed-door seclusion is not routinely available in this area of the hospital. Use of as-needed intramuscular medication for agitation was 7% in the group that had their stimulant held versus 9.5% in those who were continued ($P = .76$). The use of oral and intramuscular antipsychotics, benzodiazepines, and diphenhydramine is outlined in Figure 2. As-needed

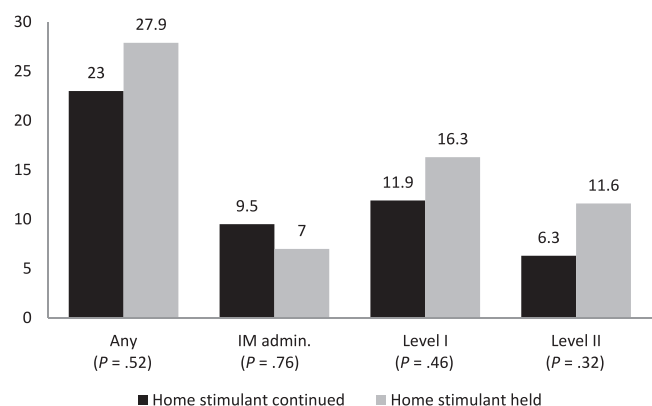


FIGURE 1: Agitation-related outcomes measured (%)

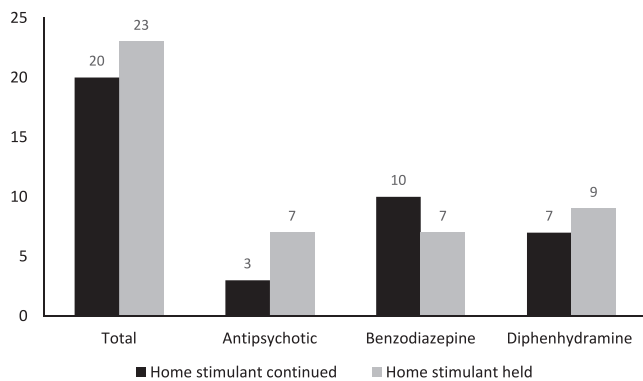


FIGURE 2: Oral and intramuscular as needed/once medication administration (%)

antipsychotic medication administration (both oral and intramuscular) was more commonly seen in those who had their home stimulant held.

Discussion

The lack of literature or guidelines regarding the continuation of home stimulant(s) during hospitalization contributes to the variation in standard of care between hospitals and even clinicians. Worsening agitation could result from holding home stimulants in patients who are adherent to their current regimen. Currently, there are no prospective or retrospective clinical trials looking at agitation-related outcomes associated with holding versus continuing home stimulant(s). The aim of this study was to assess if there is any association between holding home stimulant(s) during hospitalization and agitation-related outcomes.

Overall, when comparing agitation-related outcomes between the 2 groups, a higher occurrence (albeit not significant) of seclusion, restraint (mechanical and non-mechanical), or as-needed intramuscular medication administration was seen in those who had their home stimulant held. Although not statistically significant, any reduction in the use of mechanical restraint and closed-door seclusion can be considered clinically significant as the utilization of mechanical restraint and closed-door seclusion in agitated patients is a highly regulated practice.^{9,10} In some cases, interventions, such as restraint and seclusion, must be utilized to prevent patient and staff injury.¹¹ Mechanical restraint is regulated due to the consequences and its potential to lead to many physical and emotional long-term adverse effects.¹² Multiple protocols are set in place at our institution to minimize the use of restraints and closed-door seclusion. Treatment strategies, such as verbal de-escalation, are applied prior to therapeutic escort, therapeutic hold, and closed-door seclusion. If therapeutic escort/hold and/or closed-door seclusion are used in any pediatric patient, a physician is

required to evaluate the need for these interventions within 1 hour after its initiation. Of note, patients who had their home stimulant(s) continued during admission had a higher disease severity (based on CAPS score), which may have led providers to initiate home stimulant(s) within 24 hours of admission. Despite this higher baseline disease severity, these patients had fewer level I and II events but greater use of intramuscular as-needed medication, perhaps reflecting a beneficial impact of stimulant treatment on reducing the intensity of agitation and related interventions.

Limitations of this study include the retrospective chart review design, single study site, and small sample size. Patients were categorized based on duration of stimulant use prior to admission only; dose modifications were not accounted for, and this may have introduced some confounders. High CAPS score and greater use of as-needed intramuscular medication in the continued group could be accounted for if these patients had their regimen adjusted prior to admission due to uncontrolled symptoms. Reasons for initially holding home stimulants were not assessed during data collection (eg, seizure, cardiovascular-related admission, and acute mania) as these are not consistently documented. The reason for patient admission could have impacted the decision to initially hold home stimulant(s) and led to the need for as-needed antipsychotics. For example, if a patient presented to the hospital in acute mania, the initial strategy would be to hold home stimulant(s), and this may have impacted outcomes. Patient adherence to home stimulant(s) was based on initial physician progress note and medication reconciliation upon admission. Given the retrospective design of the study, we were limited to relying on the prescriber's determination of adherence. Although our child and adolescent psychiatry prescribers are generally very thoughtful in their assessment, the accuracy of determining patient adherence can vary depending on the prescriber. Studies have found physicians' traditional clinical assessment of adherence to be poorly correlated with more objective measures of adherence, such as refill histories.¹³ However, other methods were not readily available. If a patient was not adherent to the home stimulant(s), the discontinuation of medication would not impact symptoms and, therefore, would not have an effect on agitation-related outcomes. For patients with multiple admissions during the study period, data for the first encounter was retained to minimize oversampling bias. However, this may have exposed the study to selection bias.

Other limitations of this study include differences in baseline characteristics that may have influenced treatment decisions at admission and subsequent impact on agitation-related outcomes. Baseline CAPS score was extracted from the electronic medical records to assess disease severity during admission. Patients who had CAPS scores of 10 and greater were considered to be of greater disease severity based on

internal clinical consensus, but this lacks empirical evidence in published literature. As indicated by our baseline characteristics, patients continued on their home stimulant(s) had a higher disease severity at baseline. Additionally, patients continued on their home stimulant(s) had a higher rate of inpatient concomitant alpha-agonist use, which may be another indicator of greater disease severity. Higher disease severity has an impact on agitation-related outcomes and the increased need for as-needed medication utilization as well as restraints and seclusions. Concurrent inpatient use of medications, such as alpha-agonists and benzodiazepines, could have an impact on agitation-related outcomes. Alpha-agonists are used in patients with ADHD for symptom control and can reduce agitation in youth.¹⁴ Unlike alpha-agonists, benzodiazepines can have differential impact based on patient-specific characteristics. This class of medication can reduce anxiety and agitation, but it can also cause a paradoxical reaction and worsen symptoms, such as agitation and anxiety.¹⁵ Our data analyses did not adjust for such potential confounders. If conducting another retrospective chart review, it may be beneficial to apply propensity score matching in a larger sample size to help elucidate covariates that influence treatment decisions and impact agitation-related outcomes.

In conclusion, although not statistically significant, this study found a trend toward reduced agitation-related outcomes when home stimulant(s) were continued. Our findings suggest that the continuation of home stimulant in our pediatric population may be associated with reduced occurrence of level I and II events. Due to the potential consequences of restraint and seclusion, the results of this retrospective chart review suggest that continuation of home stimulant(s) in patients who are adherent to their current regimen may be advantageous. If a patient does not have any contraindications to the continuation of stimulant(s) during hospitalization, considerations should be made to restart medication after verifying dose, formulation, and adherence.

Acknowledgments

E.W. served as the statistical expert for this research. The authors acknowledge the dedication and effort that was provided by Natalie Domis, PharmD Candidate 2019, of Medical University of South Carolina College of Pharmacy. The authors thank the nursing and house staff for answering questions regarding the standard practices.

References

1. Subcommittee on Attention-Deficit/Hyperactivity Disorder; Steering Committee on Quality Improvement and Management; Wolraich M, Brown L, Brown RT, George D, et al. ADHD: Clinical

- practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics*. 2011;128(5):1007-22. DOI: [10.1542/peds.2011-2654](https://doi.org/10.1542/peds.2011-2654). PubMed PMID: [22003063](https://pubmed.ncbi.nlm.nih.gov/22003063/).
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington (VA): American Psychiatric Association; 2013.
3. Connor DF, Boone RT, Steingard RJ, Lopez ID, Melloni RH Jr. Psychopharmacology and aggression: II. A meta-analysis of nonstimulant medication effects on overt aggression-related behaviors in youth with SED. *J Emot Behav Disord*. 2003;11(3):157-68. DOI: [10.1177/10634266030110030301](https://doi.org/10.1177/10634266030110030301).
4. Schelleman H, Bilker WB, Kimmel SE, Daniel GW, Newcomb C, Guevara JP, et al. Methylphenidate and risk of serious cardiovascular events in adults. *Am J Psychiatry*. 2012;169(2):178-85. DOI: [10.1176/appi.ajp.2011.11010125](https://doi.org/10.1176/appi.ajp.2011.11010125). PubMed PMID: [22318795](https://pubmed.ncbi.nlm.nih.gov/22318795/).
5. Viktorin A, Rydén E, Thase ME, Chang Z, Lundholm C, D'Onofrio BM, et al. The risk of treatment-emergent mania with methylphenidate in bipolar disorder. *Am J Psychiatry*. 2017;174(4):341-8. DOI: [10.1176/appi.ajp.2016.16040467](https://doi.org/10.1176/appi.ajp.2016.16040467). PubMed PMID: [27690517](https://pubmed.ncbi.nlm.nih.gov/27690517/); PubMed Central PMCID: [PMC6641557](https://pubmed.ncbi.nlm.nih.gov/PMC6641557/).
6. Greenhill LL, Pliszka S, Dulcan MK. Practice parameter for the use of stimulant medications in the treatment of children, adolescents, and adults. *J Am Acad Child Adolesc Psychiatry*. 2002;41(2):26S-49S. DOI: [10.1097/00004583-200202001-00003](https://doi.org/10.1097/00004583-200202001-00003). PubMed PMID: [11833633](https://pubmed.ncbi.nlm.nih.gov/11833633/).
7. Canadian ADHD Resource Alliance (CADDRA). Canadian ADHD practice guidelines. 4th ed. Toronto (ON): CADDRA; 2018.
8. Hallett N, Dickens GL. De-escalation of aggressive behaviour in healthcare settings: concept analysis. *Int J Nurs Stud*. 2017;75:10-20. DOI: [10.1016/j.ijnurstu.2017.07.003](https://doi.org/10.1016/j.ijnurstu.2017.07.003). PubMed PMID: [28709012](https://pubmed.ncbi.nlm.nih.gov/28709012/).
9. Measure Information Form [Internet]. HBIPS-2 (v2019A); 2019 [cited 2019 Aug]. Available from: <https://manual.jointcommission.org/releases/TJC2019A/MIFo117.html>
10. Measure Information Form [Internet]. HBIPS-3 (v2019A); 2019 [cited 2019 Aug]. Available from: <https://manual.jointcommission.org/releases/TJC2019A/MIFo117.html>
11. Pogge DL, Pappalardo S, Buccolo M, Harvey PD. Prevalence and precursors of the use of restraint and seclusion in a private psychiatric hospital: comparison of child and adolescent patients. *Adm Policy Ment Health*. 2013;40(3):224-31. DOI: [10.1007/s10488-011-0396-2](https://doi.org/10.1007/s10488-011-0396-2). PubMed PMID: [22194033](https://pubmed.ncbi.nlm.nih.gov/22194033/).
12. Evans LK, Strumpf NE. Two decades of research on physical restraint: impact on practice and policy. In: Hinshaw AS, Grady PA. *Shaping health policy through nursing research*. New York: Springer Publishing Company; 2011. p. 167-84.
13. Meddings J, Kerr EA, Heisler M, Hofer TP. Physician assessments of medication adherence and decisions to intensify medications for patients with uncontrolled blood pressure: still no better than a coin toss. *BMC Health Serv Res*. 2012;12:270. DOI: [10.1186/1472-6963-12-270](https://doi.org/10.1186/1472-6963-12-270). PubMed PMID: [22909303](https://pubmed.ncbi.nlm.nih.gov/22909303/); PubMed Central PMCID: [PMC3570326](https://pubmed.ncbi.nlm.nih.gov/PMC3570326/).
14. Cinnamon Bidwell L, Dew RE, Kollins SH. Alpha-2 adrenergic receptors and attention-deficit/hyperactivity disorder. *Curr Psychiatry Rep*. 2010;12(5):366-73. DOI: [10.1007/s11920-010-0136-4](https://doi.org/10.1007/s11920-010-0136-4). PubMed PMID: [20652773](https://pubmed.ncbi.nlm.nih.gov/20652773/); PubMed Central PMCID: [PMC3676929](https://pubmed.ncbi.nlm.nih.gov/PMC3676929/).
15. Robin C, Trieger N. Paradoxical reactions to benzodiazepines in intravenous sedation: a report of 2 cases and review of the literature. *Anesth Prog*. 2002;49(4):128-32. PubMed PMID: [12779114](https://pubmed.ncbi.nlm.nih.gov/12779114/).