Pharmacological Management of Agitation and Delirium in Older Adults: a Survey of Practices in Canadian Emergency Departments

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ABSTRACT

Agitation is a common presenting symptom of delirium for older adults in the emergency department (ED). No medications have been found to reduce delirium severity, symptoms, or mortality, yet they may cause harm. Guidelines suggest using medications only when patients are posing a risk of harm, situations which may arise frequently in the ED. We sought to characterize prescribing patterns of medications for agitation by ED physicians in Canadian hospitals. In this multicenter study, we surveyed physicians in Vancouver, Toronto, and Sherbrooke. Descriptive statistics were used to summarize group characteristics and starting doses were compared to order sets. Fisher exact tests were used for demographic comparison. Ordinal linear regression models were run to identify a relationship between starting dose of medications and location. Of the 137 physicians invited, 77 (56%) completed the survey. Use of order sets was greatest in Sherbrooke and least in Vancouver. The most common medications used across sites were haloperidol, lorazepam, and quetiapine. Benzodiazepines were used across all sites but were used significantly more frequently in Vancouver than the other sites. Practice location was a significant predictor of starting dose of haloperidol, with Sherbrooke and Toronto having a lower starting dose than Vancouver. Higher use of order sets correlated with lower and more consistent starting doses. Benzodiazepines are used across EDs in Canada despite little evidence for efficacy in delirium and risk of harm. Implementation of order sets may be a useful way to standardize ED management of older adults experiencing hyperactive delirium.

Key words: hyperactive delirium, agitation, emergency department, antipsychotics

INTRODUCTION

Delirium is reported in 8–17% of emergency department (ED) visits in Canada among seniors.[1-3] It is associated with multiple poor outcomes including higher rates of admission, longer hospital stays, cognitive decline, and discharge to long term care.[3,4] While most geriatric delirium is hypoactive, some older patients, whether due to delirium or behavioral and psychiatric symptoms of dementia (BPSD), develop psychomotor agitation during their ED stay.[4]

The strongest evidence for inpatient management of delirium supports multicomponent intervention strategies.[4,5] For pharmacological management, benzodiazepines have specific indications including alcohol withdrawal, but cause sedation and may paradoxically increase agitation.[6] Previous research has reported an association between antipsychotics and increased risk of stroke and mortality in patients with dementia.[6] Additionally, in multiple studies and meta-analyses, no antipsychotic medications have been found to reduce delirium severity or symptoms, nor mortality.[1] Guidelines thus suggest using medications only when patients are posing a direct risk of harm to themselves or others.[7] There is a paucity of evidence to guide pharmacologic management of agitation, a common symptom of hyperactive delirium, in the ED. Notably, there have been no studies on the limited or one-time use of antipsychotics in the ED.

Deciding which medication to use is a complex decision that depends on both patient- and physician-dependent factors. One strategy which physicians use to aid decisions in the ED is the standardized order set, which has been shown in non-randomized studies to improve patient outcomes, including decreased length of stay and mortality.[8] The objective of this survey was to characterize prescribing practices for the management of hyperactive delirium and agitation in older adults by Canadian ED physicians, and to describe the impact of standardized order sets on prescribing.

METHODS

Study Design and Time Period

We designed a survey through collaboration among the investigators who include national experts in geriatrics and geriatric emergency medicine (Table 1). Medications were selected to be broad, represent a variety of classes, and included medications that have been studied for delirium management. The survey was distributed via blinded email and remained open for two months. For sites with a less than 100% response rate one month following initial invitation, a reminder regarding participation was sent. The survey was available in English and French. The survey was distributed during September and October 2021.

Population

The survey was distributed to practicing staff physicians in the ED in three Canadian cities. Included in the study were Providence Healthcare (Vancouver, BC), Mount Sinai Hospital (Toronto, ON), and the Centre Hospitalier Universitaire de Sherbrooke (Sherbrooke, QC), which is an American College of Emergency Physicians accredited Geriatric ED.

TABLE 1.
Survey questions

Question	*Answer Choices*
1. Where do you practice?	St. Paul's Hospital or Mount Saint Joseph's Hospital (Vancouver, BC) Mount Sinai Hospital (Toronto, ON) Centre hospitalier universitaire de Sherbrooke (CHUS) (Sherbrooke, QC)
2. How long have you been in independent practice?	< 1 year 1-5 years 5-10 years 10-15 years ≥20 years
3. How do you decide which medications to use for agitated or delirious patients in the emergency department? (Choose as many as apply.)	Order set / Preprinted orders (PPO) Personal clinical judgement Personalized or customized order set or quick orders Recommendation of other team members Other (write-in)
4. Are you familiar with an order set / Preprinted orders (PPO) for agitated or delirious patients in the emergency department?	Yes No
5. If yes—Do you use the available order set / Preprinted orders (PPO) for agitated or delirious patients in the emergency department?	Yes No
6. Which of the following medications do you use for agitated or delirious patients in the emergency department?	Dimenhydrinate (Gravol) Diphenhydramine (Benadryl) Haloperidol (Haldol) Ketamine Lorazepam (Ativan) Loxapine Methotrimeprazine (Nozinan) Midazolam (Versed) Olanzapine (Zyprexa) Quetiapine (Seroquel) Risperidone (Risperdal) Zopiclone (Immovane) Other (write in)
7. Please list the medications you selected to reflect your order of preference. (Drag and drop to re-order. Put the most preferred agent at the top and least preferred at the bottom.)	This carries forward the selected answers from Question 6.

Data Analysis

Data were collected via Qualtrics (Qualtrics, Seattle, WA) via the University of British Columbia's licensing agreement and analyzed in IBM SPSS (Version 28; IBM SPSS Statistics, Armonk, NY).

Descriptive statistics were used to summarize group characteristics and starting doses were compared to order sets available from each site. Fisher-Freeman-Halton exact test was used to identify significant differences between the groups, with non-parametric data with a small sample size of 77. Ordinal logistic regressions using likelihood ratio chi-squared testing were conducted to examine the relationship between starting dose and location for haloperidol. The regression models included years in practice as a covariate, divided into five ordinal categories. Regressions utilized Sherbrooke as the reference variable. *P* value of significance was corrected to .0026 using the Bonferroni correction.

Ethics Approval

Approval was obtained through the Providence Health Care (Study #H21-00426), Toronto Area Health Network (Study #21-0145-E), and Sherbrooke (Study #2022-4445) Research Ethics Boards. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to Participate

Informed consent was obtained from all individual participants.

RESULTS

Of the 137 eligible physicians, 77 (56%) completed the survey (Table 2). The response rate was 29% (20/70) in Vancouver, 69% (22/32) in Toronto, and 100% (35/35) at Sherbrooke. There was no difference in the distribution of years in practice by site, with the average length of time in practice ranging from 10-15 years ($p = .687$).

Vancouver's order set included the most options, including lorazepam, loxapine, haloperidol, risperidone, and olanzapine. Toronto included only haloperidol on their order set, as well as a statement discouraging benzodiazepine use unless delirium is secondary to alcohol or benzodiazepine withdrawal. Lastly, Sherbrooke's order set included a similar statement regarding benzodiazepines, recommendation to avoid antipsychotics in parkinsonism, and dose recommendations for haloperidol and quetiapine.

The use of and familiarity with order sets was statistically greater at Sherbrooke than at Vancouver or Toronto ($p < .001$). However, use of other decision-making parameters, including personalized judgement, personalized order set, and team recommendations, was not statistically different between sites.

Patterns for use of medications were analyzed by site (Table 2). The most frequently used medications across sites were haloperidol (88.3%), quetiapine (53.2%), and lorazepam (42.9%). None of the participants reported use of diphenhydramine, dimenhydrinate, or zopiclone. One physician in Toronto reported diazepam use. Vancouver had less use of haloperidol (Vancouver, 60%; Toronto, 100%; Sherbrooke 97.1%; $p < .001$) and more use of loxapine (Vancouver, 90%; Toronto 18.2%; Sherbrooke, 0%; $p < .001$).

Starting dose of haloperidol was grouped into four ordinal categories: less than or equal to 0.5 mg, greater than 0.5 mg to 2 mg, greater than 2 mg to 5 mg, and greater than or equal to 5 mg. Years in practice was not a significant predictor of starting dose of haloperidol ($p = .748$). Practice location was a significant predictor of starting dose of haloperidol ($p \leq .001$), with Toronto and Sherbrooke having lower starting doses than Vancouver ($p < .001$), despite all three order sets including the same starting dose of 0.5 mg. All participants from Vancouver who used both haloperidol and loxapine reported using loxapine first. We therefore calculated haloperidol dose-equivalents of loxapine.[9] With the addition of loxapine, Vancouver still had higher starting doses than the other sites ($p < .001$).

DISCUSSION

In this multicenter survey investigating prescribing practices for hyperactive delirium in Canadian EDs, we found that across three Canadian cities, choice of medications was similar. Preference for haloperidol versus loxapine was site-dependent, likely reflecting local practice patterns. Although there is evidence for harm, benzodiazepines were used frequently across sites, with lorazepam used by 28–65% of physicians per site.[6] There was a trend towards increased benzodiazepine use in Vancouver, which included lorazepam on its order set. The frequency of benzodiazepine usage in Toronto, which fell between that of Sherbrooke and Vancouver, may reflect pre-existing local practice patterns, as only half of physicians used order sets. In Vancouver, the site with the lowest order set utilization, haloperidol and loxapine starting doses were highest. This correlation highlights the potential benefits of standardized order sets for management of agitation and delirium in the ED.

Overall, systematic reviews do not support use of haloperidol or any other antipsychotic in the management of agitation and delirium in older adults.[10] While there are large bodies of literature characterizing the incidence, diagnosis, and non-pharmacological management of delirium in the ED, there is a paucity of data on management recommendations and practices. To our knowledge, this is the first multi-center survey to investigate pharmacologic management of hyperactive delirium in Canadian EDs.

This study provides a unique perspective on how emergency medicine physicians manage agitation in older adults which, due to differences in setting, resources, and patient presentation, may differ from a geriatric medicine approach. Limitations include variable participation across sites which may have been due to missed communication. Our survey also did not capture whether physicians were using medications alone or in combination. The external validity of our findings is limited as we surveyed ED physicians in three cities. Despite the anonymous nature of the survey, over- and

TABLE 2.
Use of each medication by site

	Total	*Vancouver*	*Toronto*	*Sherbrooke*	*P value*
Total completed survey	79 (56%)	20 (29%)	35 (100%)	22 (69%)	
Physicians using order set	32 (41%)	3 (15%)	26 (74%)	3 (14%)	<.001[a]
Medication use					
Haloperidol	68 (88.3%)	12 (60%)	22 (100%)	34 (97%)	<.001[a]
Ketamine	8 (10.4%)	4 (20%)	4 (18%)	0	.01
Lorazepam	33 (42.9%)	13 (65%)	10 (46%)	10 (29%)	.03
Loxapine	22 (29%)	18 (90%)	4 (18%)	0	<.001[a]
Methotrimeprazine	3 (4%)	3 (15%)	0	0	.016
Midazolam	15 (20%)	8 (40%)	5 (23%)	2 (6%)	.006
Olanzapine	18 (26%)	4 (20%)	9 (41%)	5 (14%)	.08
Quetiapine	41 (53%)	20 (80%)	9 (41%)	16 (46%)	.019
Risperidone	28 (36%)	6 (30%)	3 (14%)	19 (54%)	.006
Median starting dose of haloperidol	≤0.5 mg	≥5 mg	≤0.5 mg	≤0.5 mg	.001[a]
Median starting dose of loxapine or haloperidol (in haloperidol equivalents)	≤0.5 mg	0.5 mg to ≤2 mg	≤0.5 mg	≤0.5 mg	<.001[a]

[a]Indicates reached statistical significance.

underreporting are possible, and the trends observed in our data could be more significant. Furthermore, we note that this study was not designed to assess non-pharmacological interventions, nor relative preference for non-pharmacological versus pharmacological management.

Making prescribing decisions in the ED is complex, with physicians using recommendations of other clinicians, clinical judgement, and order sets to decide which agent to administer. Order sets have been shown to correlate with improved, disease-specific patient outcomes, as well as decreased length of stay.[7] In this survey, we see that use of order sets likely influences prescribing, as medication choice was highly correlated to order set suggestions at Sherbrooke which had the highest reported use of order sets. In Vancouver, where the order set had low utilization, staff had more variable prescribing patterns.

CONCLUSIONS

Pharmacological management of delirium and agitation in the ED is complex, and there is no one "safe" or evidence-based option. In this multicenter survey across Canadian EDs, we found that hospitals with higher use of standardized order sets had less benzodiazepine use and lower starting doses of haloperidol, both of which are supported by evidence and society guidelines. While order sets may encourage uniform prescribing, they need to be part of local culture to become effective.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood the *Canadian Geriatrics Journal*'s policy on disclosing conflicts of interest and declare that we have none.

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