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RESEARCH ARTICLE

Hospitalizations of older people in an emergency department related to potential medication-induced hyperactive delirium: a cross-sectional study

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Abstract

Background Although delirium is one of the most common adverse drug reactions observed in hospitalized older people, it remains underdiagnosed. *Aim* To estimate the prevalence of hospitalization of older people with potential medication-induced hyperactive delirium in the emergency department (ED); to identify the risk factors and the medicines frequently associated with the occurrence of the syndrome. *Method* A cross-sectional, retrospective study was performed with older people (age ≥ 60) admitted in 2018 to a Brazilian ED. The hospitalizations with suspected hyperactive delirium were screened with the aid of trigger-tools: International Code of Diseases-10th Revision, intra-hospital prescriptions of antipsychotics, and trigger-words related to the syndrome. A chart-review and medication review were developed to establish the causality assessment between adverse event and medicine. Logistic regression was used to determine risk factors for occurrence. *Results* Among the hospitalizations included, 67.5% (193/286) were screened by at least one trigger-tool. Of these, potential medication-induced hyperactive delirium was observed in 26.0% (50/193). The prevalence estimated in the ward was 17.5% (50/286). Opioids (31.9%), benzodiazepines (18.8%) and corticosteroids (10.6%) were the commonest medicines associated with delirium. Long-lived patients ($p = 0.005$), potentially inappropriate medicines (PIMs) ($p = 0.025$), and high weighted deliriogenic load ($p = 0.014$) were associated with potential medication-induced hyperactive delirium. *Conclusion* Approximately one in six hospitalizations of older people in the ED showed potential medication-induced hyperactive delirium. Data suggest PIMs and high weighted deliriogenic load, rather than polypharmacy or anticholinergic burden, are considered the most important characteristics of pharmacotherapy associated with avoidable hyperactive delirium among long-lived patients.

Keywords Aged · Drug therapy · Delirium · Emergency service, hospital · Risk factors

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Impacts on Practice

(1) Medication review in EDs may be included in multicomponent strategies performed by multidisciplinary healthcare teams to identify potentially inappropriate medicines that should be deprescribed, due to the increased risk to precipitate hyperactive delirium in long-lived older people.
(2) The prescription of medicines with deliriogenic property may be applied for screening of older people with higher probability to develop medication-induced hyperactive delirium in EDs.
(3) Clinical pharmacists could play an important role in EDs by preventing medication-related hyperactive delirium.

Introduction

Delirium is a serious public health problem and is often associated with increased morbidity and mortality rates [1], longer hospital stays [2], worse physical, cognitive, and social outcomes [3], as well as increased healthcare costs [4].

The development of delirium among older people is multifactorial and involves a complex inter-relationship between contributing factors related to the patient, healthcare assistance, and pharmacotherapy [5, 6]. In Emergency Departments (EDs), urinary catheterization, length of stay more than 10 hours, and the presence of severe pain, rather than the use of opioids, were significantly associated with a higher risk of developing delirium during hospitalization [7].

The rate of developing delirium during hospitalization of older people in EDs ranged from 11 to 27% [7]. It is estimated that 12 to 39% of delirium in older people is related to medicines [8, 9], being one of the most frequent adverse drug reactions (ADR) in hospitals [10].

Although polypharmacy and anticholinergic property of medicines has been described as risk factors for precipitating delirium among older people [6, 11, 12], data are divergent in the literature, probably due to different instruments available [11] and difficulties in applying them as part of routine clinical practice. Rawle et al. [13] and Pasina et al. [14] did not find an association between anticholinergic burden and delirium subtype or delirium-mortality in hospitalized older people. Meta-analysis studies have failed to demonstrate a statistical association with polypharmacy [6, 7] and evidence regarding the use of medications based on the American Geriatric Association (AGS) Beers criteria is very limited in EDs [7].

AIM

To estimate the prevalence of hospitalization of older people with potential medication-induced hyperactive delirium in the ED and, to identify the risk factors related to the occurrence, and to describe the medicines frequently associated with potential hyperactive delirium.

Ethics approval

This study was approved by the Research Ethics Committee of the Faculty of Pharmaceutical Sciences of Ribeirão Preto-USP (Protocol CEP/FCFRP no. 505—CAAE: 10,303,019.7.0000.5403).

Method

Study design and location

A cross-sectional, retrospective study was performed by assessing electronic medical and medication records of older patients admitted to the internal medicine ward attached to an ED in the interior of São Paulo State (Brazil) in 2018.

Study population

All patients aged 60 years or over hospitalized in the internal medicine attached to an ED in the interior of São Paulo, Brazil, from January to December 2018, were included. The recruitment of eligible hospitalizations and suspected potential delirium was carried out using the following strategies (Fig. 1):

(a) In-hospital prescriptions of antipsychotic medicines: screening occurred with the identification of at least one in-hospital prescription of typical or atypical antipsychotic medicine, both for administration and/or for use when necessary. All dosage forms of haloperidol, levomepromazine, olanzapine, quetiapine and risperidone available in the ED were considered.
(b) 10th International Disease Code (ICD-10): screening was carried out by identifying at least one of the diagnostic codes proposed by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) for the diagnosis of delirium [15] (Table 1).
(c) Trigger-words: the documentation of healthcare professionals in electronic medical records were screened by identifying trigger-words suggestive of potential

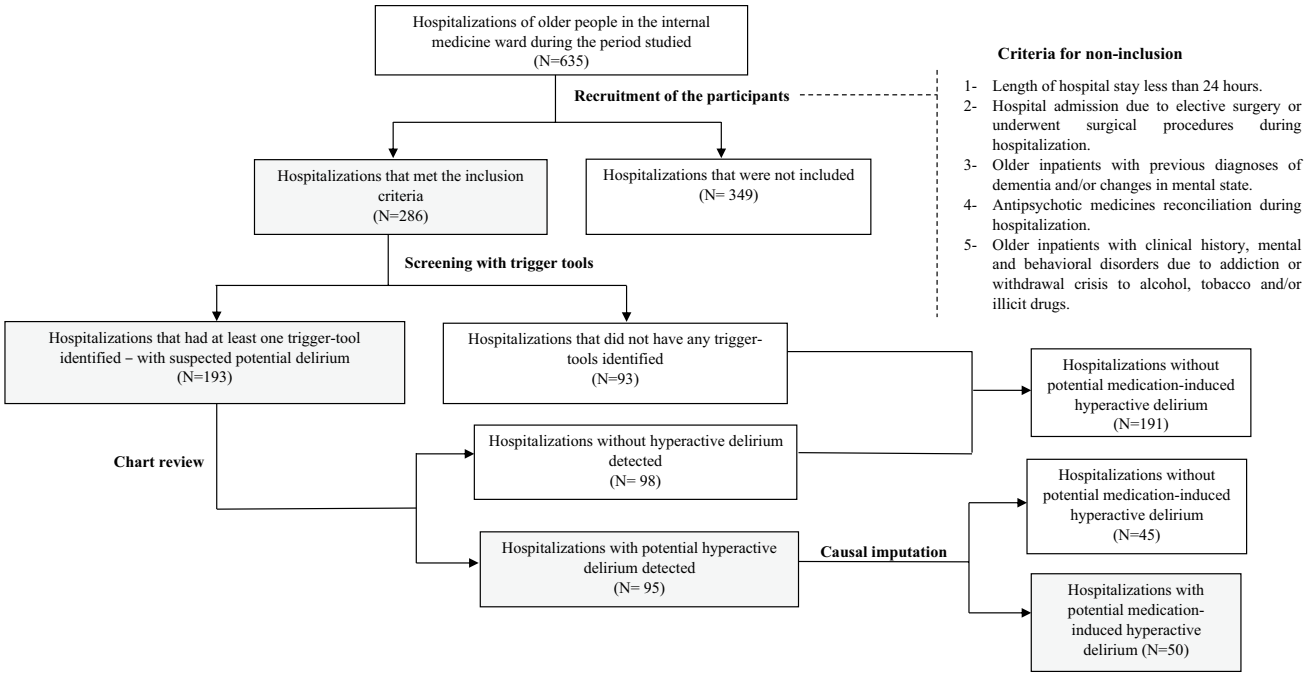

Fig. 1 Flowchart of detection of potential medication-induced hyperactive delirium in the hospitalizations of older people in an emergency department. Ribeirão Preto, São Paulo, 2018 (n = 635)

Table 1 ICD-10 codes proposed by the DSM-5 applied to screening potential delirium. Source: American Psychiatric Association (2013)[17]

ICD-10 codes for delirium					
Related to medicines or substances				Clinical or mixed	Unspecified
Substance	Withdrawal	Intoxication	Medication-induced		
Opioids	F11.23	F11.121; F11.221	F11.921	R41.0	F05
Sedative, hypnotic, or anxiolytic	F13.231	F13.121; F13.221	F13.921	R45.0	
Amphetamine (or other stimulant)	–	F15.121; F15.221	F15.921		
Other classes	F19.231	F19.121; F19.221	F19.921		

delirium. The terms used for the search were based on DSM-5 and the study performed by Puelle et al. [16].

After the screening process, a chart review was performed for hospitalizations that had at least one trigger identified to confirm the presence of potential delirium, as well as to identify the hyperactive subtype and assessing the patient's pharmacotherapy. The following definitions were considered to carry out the research [15]:

Delirium is a complex syndrome characterized by disturbance in attention (reduced ability to direct, focus, sustain, and shift attention), awareness (reduced orientation to the environment), and an additional disturbance in cognition (memory deficit, disorientation, language, visuospatial ability, or perception), which are not better explained by another preexisting, established, or evolving neurocognitive disorder.

Hyperactive delirium occurs when the individual has a hyperactive level of psychomotor activity that may be accompanied by mood lability, agitation, and/or refusal to cooperate with medical care.

Variables

The primary outcome of the study was the hospitalizations with potential medication-induced hyperactive delirium. For this, the following variables were collected:

(a) Sociodemographic: gender, age (young older people: 60 to 79 years old; long-lived older people: ≥ 80 years

old), drinking habits, smoking, and the use of illicit substances (excludes addiction as a cause of delirium).
(b) Clinical: morbidity and comorbidities, length of hospital stay (days of hospitalization), and laboratory parameters.
(c) Pharmacotherapeutic: drug active principle, dosage and dose regimen prescribed, number of medicines prescribed per day according to deliriogenic or anticholinergic properties, potentially inappropriate medicines (PIMs) for older people, weighted deliriogenic and anticholinergic loads, as well as medication regimen complexity index (MRCI).

The identification of medicines with deliriogenic property and the calculation of weighted deliriogenic load were made with the aid of the Delirium Drug Scale (DDS) [17]. The DDS is an evaluation tool designed to assess the risk of delirium attributable to 97 medicines which have ranks from 1 to 2, depending on their potential of inducing delirium.

Data collection and analysis

The medication review consisted of the daily quantification of the medicines prescribed during hospitalization in the internal medicine ward, as well as the classification according to: deliriogenic property [17], anticholinergic property [18], and whether they are considered PIMs for older people [19]. The calculations of the MRCI [20], the anticholinergic load [18], and the weighted deliriogenic load prescribed per day were also performed [17].

The MRCI was calculated with the adapted and validated version tool [20]. Low complexity for the patient's pharmacotherapy was considered when the total daily score was 1.5 to 14.9 points, medium complexity when it was between 15.0 and 28.9 points, and high complexity when it was greater than 29.0 points [21].

To calculate the weighted deliriogenic load [22], the medications prescribed per day for each patient were compared to the DDS [17], and the equations shown below were applied:

$$Weighted\ deliriogenic\ load[22] \sum \left(\frac{administered\ daily\ dose}{administered\ daily\ dose + minimal\ daily\ geriatric\ dose} \right) X\ DDS\ score$$

$$DDS\ score[17] = \sum rankX \left(\frac{administered\ daily\ dose}{administered\ daily\ dose + minimal\ daily\ geriatric\ dose} \right)$$

The identification of medicines with anticholinergic activity and the calculation of anticholinergic load were carried out with the aid of the Brazilian anticholinergic activity scale [18]. The tool lists 125 medicines that present anticholinergic activity ranging from 1 to 3, depending on their anticholinergic activity.

PIMs were classified according to the AGS Beers Criteria [19] which is an explicit list of PIMs that are typically best avoided by older people in most circumstances or under specific situations, such as in certain diseases or conditions [19].

The MRCI is a tool used to measure the complexity of pharmacotherapy of an individual patient, which is divided into three sections: A, B and C. Section A corresponds to the information on dosage forms, section B corresponds to the information on dose frequency, and Section C corresponds to additional information. Each section is scored based on the analysis of the patient's pharmacotherapy, and the complexity index is obtained by adding the points (scores) of the three sections [20].

For deliriogenic medicines described in the literature not included in the DDS scale, rank 1 was considered in the load calculation. These medicines were: acetylsalicylic acid, valproic acid, amantadine, amiodarone, atenolol, benztropine, captopril, digoxin, enalapril, phenytoin, fluoroquinolones, ibuprofen, indomethacin, levodopa, levomepromazine, methyldopa, naproxen, promazine, propranolol, quetiapine, risperidone, selegiline, and verapamil [8, 9, 12, 23–25]. The dosage used for minimal daily dose also proceeds from the Geriatric Dosage Handbook, as recommended by the DDS. The weighted deliriogenic load was considered low when the score obtained was $0 >$ weighted DDS ≤ 1 and high when the score was > 1.0 [22].

The calculation of the anticholinergic load was performed by adding the scores for the magnitude of anticholinergic activity for each prescribed medicine, which vary from 1 to 3. The greater the magnitude of the anticholinergic activity, the higher the score attributed to the medicine [18]. Although there is no consensus in the literature, a daily average of anticholinergic load ≥ 2 is considered high [26].

The degree of causality assessment between the occurrence of potential hyperactive delirium and the use of medicines was performed with the instrument developed by the

World Health Organization in collaboration with the Uppsala Monitoring Center [27]. The cases of medication-induced hyperactive delirium were those with a causality imputation ≥ 'possible' [28].

Hospitalizations that did not have any triggers identified after screening were classified as without potential medication-induced hyperactive delirium. In addition, hospitalizations which were identified by trigger-tools, but after chart review the potential hyperactive delirium was not confirmed, were also considered without delirium.

The medicines associated with potential delirium were classified according to their Anatomical Therapeutic Chemical code, the deliriogenic [17] and/or anticholinergic properties [18], and the AGS Beers criteria [19].

Study size

All hospitalizations of older people in the internal medicine ward of the ED that occurred in the period of the study were enrolled.

Statistical analysis

The independent t-test was used to compare the means of continuous variables (length of hospital stay, age, comorbidities) and the risk of hospitalizations with potential medication-induced hyperactive delirium.

The association between hospitalizations with potential medication-induced hyperactive delirium and all dichotomic variables were analyzed using univariate logistic regression analysis. The model considered the dependent variable (potential medication-induced hyperactive delirium) and all the predictive covariates [gender; age (young older people, long-lived older people); comorbidities (hospitalizations with mean > 4); high weighted deliriogenic load (hospitalizations with mean > 1); high anticholinergic load (hospitalizations with mean ≥ 2.0), high MRCI (hospitalizations with mean ≥ 29.0 points); polypharmacy (hospitalizations with mean of medicines prescribed ≥ 5); PIMs, and medicines with deliriogenic and anticholinergic properties prescribed (yes/no)].

The multivariable logistic regression model was built with the predictive variables with p value ≤ 0.10 in the univariate analysis using the Forward Stepwise Regression method in the Statistical Package for the Social Sciences (SPSS), version 21 (IBM Corp, USA). The C-statistic and the Hosmer–Lemeshow adequacy test were used to evaluate the adequacy of the logistic regression model. Differences were considered significant at p values ≤ 0.05.

Results

In 2018, there were 635 hospitalizations for 551 patients recruited from the studied ward. The greater number of hospitalizations is explained by the fact that a patient may have been admitted to the ED more than once during the data collection period. Two hundred and eighty-six hospitalizations (45.0%) met the inclusion criteria, of which the majority [67.4% (193/286)] had at least one trigger-tool identified (Fig. 1). Most hospitalizations were related to female patients [50.3% (144/286)], with a mean age of 72.0 ± 7.9 years old. It was found that 4.2% of hospitalizations were related to former smokers, 1.8% to former alcoholics, 1.5% to current smokers, and 0.9% to alcoholics.

Potential hyperactive delirium was detected in 49.2% (95/193) of hospitalizations with at least one trigger-tool. After medication review, 52.6% of them were classified as potentially medication-induced (50/95) (Fig. 1). The prevalence of potential medication-induced hyperactive delirium in the ward was 17.5% (50/286).

Furthermore, patients hospitalized with potential medication-induced hyperactive delirium were older when compared with those without delirium (Table 2). Regarding risk factors, the hospitalizations of long-lived older people, with prescriptions of deliriogenic medicines, high weighted deliriogenic load, PIMs, and high MCRI were significantly associated with potential medication-induced hyperactive delirium, according to univariate analysis (Table 2). However, multivariable logistic regression showed that long-lived older people, PIMs, and high weighted deliriogenic load were independent variables (Table 2).

Thirty-five different medicines were identified as having an association with the occurrence of delirium, of which 21 have anticholinergic properties, 19 have deliriogenic properties, and 13 are PIMs for older people. The higher number observed after classification may be explained by the fact that a single medicine might have more than one property.

More than half of these medicines act on the nervous [40.0% (14/35)] and cardiovascular [20% (7/35)] systems (Table 3). They were prescribed 122 times, with the majority belonging to the following pharmacological classes: opioids [31.9% (39/122)]; benzodiazepines [18.8% (23/122)] and corticosteroids [10.6% (13/122)] (Table 3).

Discussion

Approximately one in six (50/286) hospitalizations of older people in the ED were associated with potential medication-induced hyperactive delirium. The independent risk factors identified were PIMs, high weighted deliriogenic load, and long-lived older people. Opioids, benzodiazepines, and

Table 2 Risk factors for the occurrence of potential medication-induced hyperactive delirium identified in the hospitalizations of older people in the internal medicine ward of an emergency department. Ribeirão Preto, São Paulo, 2018 (n = 286)

Variable	Hospitalization with potential medication-induced delirium		Univariate analysis		Logistic regression	
	Detected	Not Detected	OR (CI 95%)	*p* value	OR (CI 95%)	*p* value
Gender	N	N				
Male	20	122	1.60 (0.86–2.98)	0.133		
Female	30	114				
Age						
Young older people	33	195	2.45(1.25–4.8)	0.008*	2.7 (1.4- 5.6)	0.005*
Long-lived older people	17	41				
No. of comorbidities						
Mean ≤ 4	39	182	0.95 (0.46–1.9)	0.887		
Mean > 4	11	54				
Polypharmacy						
No (mean < 5 medicines)	4	33	1.87 (0.63–5.54)	0.252		
Yes (mean ≥ 5 medicines)	46	203				
PIM prescribed						
No	3	54	4.65 (1.2–15.53)	0.007*	4.0 (1.2–13.7)	0.025*
Yes	47	182				
Deliriogenic medicines prescribed						
No	1	36	8.82 (1.2–65.9)	0.011*		
Yes	49	200				
Weighted deliriogenic load						
Low (mean ≤ 1.0)	32	192	2.45 (1.3–4.8)	0.007*	2.4 (1.2- 4.8)	0.014*
High (mean > 1.0)	18	44				
Anticholinergic medicinesprescribed						
No	4	37	2.14 (0.7–6.3)	0.159		
Yes	46	199				
Anticholinergic load						
Low (mean < 2.0)	17	116	1.9 (1.0–3.5)	0.051		
High (mean ≥ 2.0)	33	120				
Medication Regimen Complexity						
Low and medium	9	68	2.3 (1.1–4.6)	0.018*		
High (mean ≥ 29.0)	41	168				
Quantitative	Mean (± SD)	Mean (± SD)				
Age	74.3 (8.0)	71.4 (7.8)	0.022*			
Days hospitalized	12.0 (5.9)	10.0 (7.5)	0.085			
Comorbidities	3.8 (2.2)	3.4 (1.8)	0.157			

PIM: potentially inappropriate medication, SD: standard deviation

*Significant value

corticosteroids were the most common pharmacological classes related to potential hyperactive delirium.

A systematic review study corroborated our findings since it suggested that opioids, benzodiazepines, dihydropyridines, and antihistamines increase in the risk of delirium [23]. In addition, medicines prescribed for psychiatric and neurological diseases, anti-infectives, and corticosteroids [8] also probably comprise the main pharmacological classes associated with neurocognitive disorders [8, 9, 12]. According to AGS Beers Criteria, most of them are considered PIMs for older people.

The association between delirium and opioids use is well described [24]. However, Daoust et al. [29] concluded that poorly controlled pain and paradoxically opioid pain

Table 3 Frequency of prescription of medicines that induced potential hyperactive delirium in the study population, according to the prescribed dose range and the frequency at which it was screened by the trigger-tools. Ribeirão Preto, São Paulo, 2018 (n = 122)

Medication	ATC Code	N	Dose interval (min–max)
Morphine	N02AA01	17	1.0 – 100.0 mg
Fentanyl	N02AB03	14	0.5 – 5.0 mg
Midazolam	N05CD08	13	15.0 – 800.0 mg
Prednisone	H02AB07	9	20.0 – 40.0 mg
Tramadol	N02AX02	8	100.0 – 300.0 mg
Ipratropium	R03BB01	7	40.0 – 160.0 drops
Acetylsalicylic acid	B01AC	5	100.0 mg
Clonazepam	N03AE01	5	0.4 – 4.0 mg
Sertraline	N06AB06	5	50.0 – 100.0 mg
Furosemide	C03CA01	3	120.0 – 160.0 mg
Dexamethasone	H02AB02	3	8.0 – 16.0 mg
Cefepime	J01DE01	3	4.0 mg
Zolpidem	N05CF02	3	10.0 mg
Butylscopolamine	A04AD01	2	20.0 – 60.0 mg
Bromopride	A03FA04	2	30.0 mg
Isosorbide	C01DA08	2	60.0 – 120.0 mg
Hydralazine	C02DB02	2	150.0 – 300.0 mg
Enalapril	C09AA02	2	10.0 – 20.0 mg
Warfarin	B01AA03	1	7.5 mg
Amiodarone	C01BD01	1	600.0 mg
Nitroglycerin	C01DA02	1	5.0 mg
Clonidine	C02AC01	1	300.0 mcg
Methylprednisolone	H02AB04	1	40.0 mg
Cyclobenzapyrine	M03BX08	1	5.0 mg
Haloperidol	N05AD01	1	2.5 mg
Diazepam	N05BA01	1	5.0 mg
Lorazepam	N05BA06	1	1.0 mg
Dexmedetomidine	N05CM18	1	800.0 mcg
Amitriptyline	N06AA09	1	25.0 mg
Mirtazapine	N06AX11	1	15.0 mg
Nicotine	N07BA01	1	21.0 mg
Terbutaline	R03AC03	1	1.5 mg
Formoterol	R03AC13	1	24.0 mcg
Tiotropium	R03BB04	1	5.0 mg
Dexchlorpheniramine	R06AB02	1	2.0 mg

ATC: Anatomical Therapeutic Chemical code

treatment have also been identified as triggers for delirium. Unmet health need is also considered a drug-related problem, as well as failure of treatment. Therefore, treating pain appropriately prevents the occurrence of delirium [29]. The selection of opioids relies on their pharmacokinetic characteristics, safety profile, clinical condition of the older person, and concomitant use with other medicines [30].

Gold-standard evidence considers the prescription of benzodiazepines potentially inappropriate for older people [19]. Nevertheless, their use in association with opioids has been increasing in the ED [31], which is highly contraindicated [30]. Older people exposed to benzodiazepines have a higher risk of developing delirium [31], and consequently, falls [32]. Furthermore, chronic use has been associated with impaired cognitive function [33] and the development of dementia [34]. These findings suggest the need to implement services that contribute to safe prescribing practices for older people in the ED, such as benzodiazepine stewardship [31] or deprescription protocols [35].

Although not fully understood, an association between the use of corticosteroids and disorders of mood, behavior, and cognition is reported [36]. Therefore, further studies are needed to elucidate the contributing factors related to the use of corticosteroids and the occurrence of delirium, as well as to improve the management of the neuropsychiatric symptoms that they cause [37]. Neuropsychiatric complications may occur with any corticosteroid, and the dose seems to be one of the most significant risk factors [37]. As this class has anticholinergic [18] and deliriogenic properties [17], the data from the present study suggest that the main factor related to delirium is the deliriogenic properties, since the calculation of the deliriogenic load considers the dose of the medicine, while the anticholinergic load does not. Therefore, increasing the dose culminates in increasing the deliriogenic load.

This fact is in line with the findings of studies conducted by Ahmed et al. [6], Silva et al. [7], Rawle et al. [13], and Clegg et al. [23]. The cohort study developed by Rawle et al. [13] showed that the anticholinergic load was not associated with the occurrence of delirium of any subtype in hospitalized older people. The meta-analysis conducted by Ahmed et al. [6] and Silva et al. [7], as well as the review conducted by Clegg et al. [23] did not show polypharmacy as a risk factor for delirium. These data strongly suggest that the deliriogenic load may have a greater contribution to the occurrence of the ADR in this population.

Nguyen et al. [22] evaluated the impact of gross and weighted deliriogenic loads on the occurrence of delirium and observed that both are considered risk factors when they are greater than two [OR = 1.29 (95% CI 1.16; 1.44)] and greater than one [OR = 1.60 (95% CI 1.24; 2.05)], respectively. These data corroborate the results of the present study, since the older people with weighted deliriogenic load prescription > 1.0 [OR = 2.3 (95% CI 1.1; 4.7) were twice as likely to have delirium. Thus, the exposure to low deliriogenic loads seems to be tolerated in the older people and these medicines can be used safely when their benefits outweigh the risks [22].

Despite the prevalence of PIMs being high among long-lived older people [38] and their use increasing odds of both hospital admissions and ED visits [39], a meta-analysis study did not find an association between them and the

occurrence of delirium during the hospitalizations in the ED [7]. Probably, the lack of evidence is related to the absence of subgroup analysis considering long-lived patients. This fact may explain why the present study identified PIMs as independent risk factors for development of hyperactive delirium. Multicomponent intervention has been applied for hospitalized older people to reduce the use of high-risk medications for delirium, such as PIMs [40]. Clinical pharmacists may develop an important role in multidisciplinary ED teams' early recognition and prevention of hyperactive delirium by conducting medication reviews [12].

Study limitations (bias)

Data collection was conducted in a single ED. Given this and the small sample size, the generalizability to other institutions may be limited. The prevalence of medication-induced delirium may also be underestimated due to the selected measurement instrument (AGS Beers criteria, which has not been validated for Brazilian market), and the causality assessments, which were conducted by using chart review and clinical judgment. This approach could hinder the identification of potential confounding variables that were not described in medical records, and results may change according to the complexity of the hospital, the judges who perform the causal association, and the design of the study (prospective or retrospective).

However, the study has strengths that are important for the evolution of the state of the art. The medication and chart review contributed to identifying the main characteristics of pharmacotherapy related to potential hyperactive delirium. Moreover, the study corroborated that long-lived older people may be more vulnerable to developing potential medication-induced hyperactive delirium. The risk factors detected can be considered in the development of algorithms for prioritizing patients eligible for pharmaceutical clinical services in an ED to prevent neurocognitive disorders associated with high weighted deliriogenic loads and prescription of PIMs for older people.

Conclusion

Approximately one in six (50/286) hospitalizations of older people in the ED were associated with potential medication-induced hyperactive delirium. Data suggest high weighted deliriogenic load and PIMs, rather than polypharmacy or anticholinergic burden, are considered the most important characteristics of pharmacotherapy associated with potential avoidable medication-induced hyperactive delirium among long-lived patients. The main pharmacological classes associated with the hyperactive delirium were opioids, benzodiazepines, and corticosteroids, which should be monitored to prevent the occurrence of avoidable harm in this age group. Therefore, clinical pharmacists may develop an important role in multidisciplinary ED teams' early recognition and prevention of hyperactive delirium by conducting medication reviews.

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Conflicts of interest The authors declare no conflicts of interest.

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