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Applicability of Anticholinergic Risk Scale in hospitalized elderly persons

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Abstract

Objective: to define the applicability of the Anticholinergic Risk Scale (ARS) as a risk indicator of delirium in hospitalized elderly persons. *Method:* the medical records of elderly patients hospitalized in the medical wards of a teaching hospital were analyzed with the ARS, translated and adapted for medicines used in Brazil. The version of the Confusion Assessment Method (CAM) for the clinical diagnosis of delirium translated and validated by Fabbri et al. was used. Individuals aged ≥60 years were included in the evaluation of drug use. The sample was divided by gender and age to analyze the effect of these variables on the use of anticholinergic drugs based on the ARS, and association with delirium. *Results:* 123 elderly persons, 47 men and 76 women, with a mean age of 72.7(±9.2) years were included. The average consumption of drugs not listed in the ARS (some with anticholinergic action as Ipratropium and Scopolamine) was 6.1(±3.0) and the average number of drugs used listed in the ARS (Metoclopramide, Ranitidine, Atropine, Haloperidol and Risperidone) was 0.9±0.6. Four elderly persons had a score ≥3 (3.3% of total cases). Delirium was observed in 27 patients (21.9% of the total), none of whom scored more than two ARS points. There was no statistical significance regarding gender, age and delirium. *Conclusion:* the average score of the ARS was low among this population, and did not correlate with delirium. The ARS does not cover all anticholinergics, meaning this study should be repeated in a geriatric ward for comparison.

Keywords: Elderly. Cholinergic Antagonists. Pharmaceutical Preparations. Iatrogenic Disease.

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INTRODUCTION

Anticholinergic drugs often have adverse effects on elderly persons[1-4]. However, they are part of the drug treatment of several situations and diseases, such as urinary incontinence and Parkinson's disease, which are common among this age group[3]. How should these drugs be prescribed to ensure a lower iatrogenic risk among the elderly?

Rudolph et al.[5] developed the Anticholinergic Risk Scale (ARS), which is based on publications about drugs and pharmacology during aging, with the aim of creating a simple tool to estimate the risk of the adverse effects of anticholinergics. The ARS is divided into four groups of drugs with scores of 0 to 3 (no or limited effect, moderate effect, strong effect, or very strong effect, respectively), with the risk being proportional to the sum of the points of the drugs used by the patient. A final sum greater or equal to 3 is considered a serious risk.

The ARS[5] methodology involved three independent reviews (one by a geriatrician and two by pharmacologists) of the 500 medications most prescribed by the Veterans Affairs Boston Health Care System, with the aim of identifying drugs with the known potential to produce adverse anticholinergic effects. Topical, ophthalmological, otological and breathing effects were excluded from the analysis. The inclusion of medications in the ARS and their anticholinergic risk score was based on three reviews: a) the KiBank data base 18 of the National Institute of Mental Health psychoactive drug search program: to determine the dissociation constant (pKi) for the cholinergic receptor; b) Microdex: evidence-based review of drugs registered with the Food and Drug Administration (FDA) to define rates of adverse anticholinergic events compared with a placebo; c) Medline: active search for literature related to adverse anticholinergic effects. The classification of the anticholinergic effect of drugs on a scale of 0 to 3 was based on the inclusion of the drug in the three analyzes and agreement between the researchers regarding the anticholinergic potential of each individual drug.

Therefore, the present study presents the question of whether the ARS is of practical use for the evaluation of elderly patients hospitalized in a medical ward in terms of the risk of drug iatrogenesis through anticholinergic agents and/or the association of this drug group with the clinical diagnosis of delirium, given the frequent association between this state of acute mental confusion and anticholinergic drugs.

The objective of this study was to evaluate the applicability of ARS, based on degree of anticholinergic risk, as an indicator of the risk of delirium among elderly persons hospitalized in the medical ward of a teaching hospital.

METHOD

The medical records of elderly patients hospitalized in the medical ward of a teaching hospital at the end of hospitalization were analyzed by the ARS[5] adapted for the Brazilian pharmacopoeia (Figure 1). The ARS was translated into Portuguese and adapted for medicines used in Brazil for the present study, the primary objective of which was to verify its practicality for use in Brazil. The drugs were grouped based on scores of 1 to 3 (moderate, strong and very strong, respectively). A final points total greater than or equal to 3 was considered a serious risk (Figure 1).

Patients who had used medication since the start of their hospitalization and who were 60 or older were included in the study. The clinical diagnosis of delirium was established using the Portuguese version of the Confusion Assessment Method (CAM) translated and validated by Fabbri et al.[12] and routinely used in Brazilian clinical practice since its publication in 2001. Positive cases were classified by motor subtypes of delirium[13]: a) hyperactive delirium: evidence in 24 hours prior to diagnosis of at least two of the following symptoms: quantitatively increased motor activity, loss of activity control, restlessness, perambulation; b) Hypoactive delirium: evidence in 24 hours prior to diagnosis of at least two of the following symptoms: significantly reduced activity, decreased movement speed, poor attention to surrounding environment, significantly reduced speech, decreased speech rate, indifference, reduced agility; c) Mixed delirium: evidence of two previous

Figure 1. Medications commercially available in Brazil and included in the Anticholinergic Risk Scale (Rudolph et al.5). São Paulo, 2012.

Medications with anticholinergic effect		
Very strong 3 points per drug	Strong 2 points per drug	Moderate 1 point per drug
Amitriptyline	Amantadine	Carbidopa-Levodopa
Atropine	Baclofen	Entacapone
Benztropine	Cetirizine	Haloperidol
Carisoprodol	Cimetidine	Metocarbamol
Ciproeptadine	Clozapine	Metoclopramide
Chlorpheniramine	Cyclobenzaprine	Mirtazapine
Chlorpromazine	Desipramine	Paroxetine
Dicyclomine	Loperamide	Pramipexole
Diphenhydramine	Nortriptyline	Quetiapine
Fluphenazine	Olanzapine	Ranitidine
Hydroxyzine	Prochlorperazine	Risperidone
Hyoscyamine	Pseudoephedrine	Selegiline
Imipramine	Tolterodine	Trazodone
Meclizine		Ziprasidone
Oxybutynin		
Perphenazine		
Promethazine		
Thioridazine		
Thiothixene		
Tizanidine		
Trifluoperazine		

Serious risk: final points total ≥3.

subtypes (hyper and hypoactive) in previous 24 hours; d) non-motor delirium: absence in the previous 24 hours of the symptoms listed in a and b to define the hyperactive and hypoactive subtypes.

As delirium is a syndrome of organic and multifactorial cause and not necessarily easy to etiologically determine, patients were not characterized in terms of severity, exacerbation or previous cognitive dysfunction. It was thus possible to use the syndromic diagnosis of delirium in a generic manner, to remain faithful to the basic proposal of this study, which is to determine the impact of the use of drugs with anticholinergic potential on patients with delirium diagnosed by the CAM[12].

The medical records and the patients in the present study (elderly patients hospitalized in the medical ward of a teaching hospital) were jointly analyzed by the two authors of this study (geriatricians) based on hospitalizations during the year 2011.

As the hospitalized elderly population is the group with the highest risk of drug iatrogenesis, the present study adopted a convenience sample. This decision was also based on greater accessibility to this group of patients, operational ease and low cost. As the present study is considered a pilot study in this line of research, risk was based on the lowest potential generalization of results based on this method of research, considering its practical utility in the institution where the study was carried out.

Statistical analysis was based on the Chi-squared Test (Corrected Yates Test or Fisher's exact test), dividing the study between men and women and age (< and 80 years) to allow analysis by gender and age in terms of the use of anticholinergic drugs

described by ARS and association with delirium. Considering the prescriptions of 120 elderly persons and ARS values 3 in between 5.0 and 2.5% of the studied population, it was estimated that a sample of between 105 and 109 inpatients would represent a significant value.

The present study was part of project n 418/08 approved by the Ethics Committee for Human Research of the Irmandade da Santa Casa de Misericórdia de São Paulo, the institution where the study was carried out.

RESULTS

The medical records of 123 elderly persons (47 men and 76 women), with a mean age of 72.7 (±9.2) years, were analyzed. A mean consumption of 6.1 (±3.0) drugs not listed in ARS[5] (some with an anticholinergic action, such as Ipratropium and Scopolamine)[14,15] and 0.9(±0.6) drugs listed in ARS were identified: 1) Metoclopramide: in 80 medical records, used symptomatically; 2) Ranitidine: in 21 records; 3) Atropine: in three records; 4) Haloperidol: in three records; 5) Risperidone: in one medical record.

Symptomatic drugs were taken at least once to be included in this list. The prescription of the two psychotropic drugs mentioned (Haloperidol and Risperidone) occurred after the clinical diagnosis of delirium.

A total of 31 patients had an ARS score of zero (25.2% of the total number of cases), 75 had a score of one (60,9%), 12 had a score of two (9.8%) and five elderly persons had a score 3 (4.1% of the total analyzed).

Delirium was observed in 27 patients (16 with hypoactive delirium, five with mixed delirium and six with hyperactive delirium), which represented 21.9% of the total sample. None of these individuals scored more than two ARS points. There was no statistical significance when ARS was individually related to age, gender or delirium.

DISCUSSION

Anticholinergic drugs have the potential to trigger serious adverse effects, particularly among the elderly, such as falls, cognitive dysfunction and delirium[1-11,14]. They also contribute to increased mortality in this age group[1,3,6,9].

Drugs with anticholinergic properties are cited in several lists and criteria of potentially inappropriate medications (PIM) for the elderly published between 2003 and 2012[15-19]. A PIM is defined as a drug that risks causing adverse effects that are greater than the benefits for the elderly.

These lists and criteria are useful in clinical practice, but merely cite and explain the reasons for the inclusion of the PIM, and do not quantify the degree of risk of adverse effects of each drug. Several anticholinergic drugs are cited, such as first-generation antihistamines[15,16,18,19], systemic[15,19] or urinary[16-19] antispasmodics, disopyramide[15,19], tricyclic antidepressants[15,16,18,19], first-generation antipsychotics[15,16,18], muscle relaxants[15,19], dimenhydrin[16], doxylamine[16,18] and diphenhydramine[16]. Some of these anticholinergic drugs are found in the ARS[5] adapted for the Brazilian pharmacopoeia, yet represent only approximately 40.0% of all drugs listed (19 out of 48). Such drugs are mainly in the list of drugs with three anticholinergic risk points (15 of the 21 drugs listed), or in other words, among those most likely to produce adverse effects.

The ARS fills a gap in the lists and criteria of PIM for the elderly, as it provides a more refined analysis of anticholinergic risk, detecting drugs with weaker anticholinergic action and allowing the risk of the total medication prescribed to be calculated. Some published studies[6-11] include findings that suggest limitations in the application of the scale in clinical practice.

Evaluations of samples from hospitals[6,9] have associated high ARS scores with a higher mortality risk among the elderly, a fact not observed in asylum institutions[11]. This discrepancy can be attributed to the low number of studies and the different dynamics of care and populations in hospitals and asylum institutions.

As was the case with the present study, Gouraud-Tanguy et al.[7] did not detect a greater number of central adverse effects, such as delirium, among hospitalized elderly persons. Both studies were

based on wards in teaching hospitals, with a care structure that allowed the early diagnosis of delirium and the non-prescription of anticholinergic drugs, facts that may explain this negative result.

Interestingly, while the present study and that of Vanier et al.[8] detected similar percentages of elderly individuals with scores ≥3, the findings for the number of individuals scoring one or two points differed, with approximately three times as many such individuals in the present study. However, it should be considered that the prescriptions of the present study presented a high percentage of symptomatic drugs, such as Metoclopramide and Ranitidine, a possible explanation for this discrepancy. The results of the present study were similar, in terms of ARS scores of two or three points, to a population of patients receiving outpatient care[11]. The prescription pattern of the medical records analyzed is closer to the American[11] than the French[8] model.

As a final observation, the ARS[5] adapted for the Brazilian pharmacopoeia does not include all the drugs with anticholinergic properties used in patients hospitalized in medical wards. Previously described examples such as Ipratropium[14] and Scopolamine[15] justify the extension of the present study by adding new drugs to the original ARS. In addition, repeating the study in a geriatric ward to compare cases of elderly people with different diagnostic and treatment dynamics would be worthwhile.

The present study should be refined by adding other variables, such as separating groups with or without previous cognitive dysfunction and/or based on the severity of the diseases that led to the hospitalization of the patients. This is a limiting factor for potential generalizations about the results of the present study. Considering the multifactorial etiology of delirium, it is also possible to further define ARS analysis based on the medication being used upon admission to the Emergency Department and the drugs prescribed in the medical ward.

CONCLUSION

The mean number of drugs in the Anticholinergic Risk Scale was low in the study population, and there was no correlation with cases of delirium. It was noted that the Anticholinergic Risk Scale does not include all anticholinergics, and so this study should be repeated in a geriatric ward for comparison.

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