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Short communication

# Reduction of anticholinergic burden in older patients admitted to a multidisciplinary geriatric acute care unit

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## 1. Introduction

Anticholinergic drugs form part of the standard treatment of various conditions such as incontinence, asthma, or psychiatric disorders in older adults. Between 20% and 50% of older patients are prescribed with anticholinergic drugs [1]. Constipation, dryness of the skin, mouth, and eyes are among their adverse effects (AEs) but also dizziness, cognitive impairment, confusion or delirium. Antihistaminics, muscle relaxants, tricyclic antidepressants, and antispasmodics typically produce AEs and are easily identified by prescribers, however, other drugs such as digoxin, warfarin or prednisolone also present anticholinergic properties, and often go unnoticed [2].

Anticholinergic-associated AEs affect between 8% and 27% of older adults. These are more frequent in older hospitalised patients (51%) [3]. Anticholinergic use in older patients is associated with impaired abilities in the basic activities of daily living and functional performance [4,5], such as confusion [3,6,7], cognitive impairment [4,5], falls [6], but also increased length of hospital stay [6,7], cardiovascular events and mortality [8]. Anticholinergics are included in many inappropriate medication lists, such as the STOPP/START [9], Beers [10] and PRISCUS criteria [11].

AEs appear due to the anticholinergic activity of the drug, which is determined by the drugs' affinity for the muscarinic receptor. This affinity is used as the main criteria to determine anticholinergic burden. In this sense, the Serum Anticholinergic Activity (SAA) is the gold standard to measure this affinity. This determination is expensive, can't be performed except in specialised laboratories, and presents some limitations [12,13]. In order to overcome these limitations, several anticholinergic-rating scales have been developed to predict the risk of anticholinergic-associated AEs. Medications are categorised according to their anticholinergic potential on a scale from 0 (no anticholinergic activity) to 3 (the greatest anticholinergic activity possible). In a systematic review, Salahudeen et al. [14] described clinically relevant anticholinergic scales and found that the Anticholinergic Cognitive Burden (ACB) scale [5] is the most validated scale, based on the number of studies that have investigated associations between AEs and ACB scores. The Anticholinergic Risk Scale (ARS) [6] and Anticholinergic Drug Scale (ADS) [13] are the second and third most validated scales [14]. Different authors have used these scales as benchmarks to reduce anticholinergic burden [14] in older patients, although only one scale was used in each study [15,16]. In fact, only low to moderate concordance has been found between these scales [17]. These differences affect their predictive validity, thus the role of these scales in clinical practice needs to be clarified [4,18]. The study of anticholinergic burden using these three scales may help to understand their differences in clinical

*Abbreviations:* ADS, Anticholinergic Drug Scale; ARS, Anticholinergic Risk Scale; ACB, Anticholinergic Burden Scale; AEs, Adverse Effects; SAA, Serum Anticholinergic Activity; MMSE, MiniMental Status Examination; FAC, Functional Ambulation Classification; GDS, Global Deterioration Scale; CI, Confidence interval; DM, Diabetes mellitus; CKD, Chronic kidney disease.

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practice and to determine if they can equally reduce this burden in a study with multidisciplinary collaboration between geriatricians and pharmacists.

Several studies have shown that admission to a geriatric hospital unit modifies drug prescriptions [19,20], but none show specificity on anticholinergic burden. The aim of this study was to determine, variations in anticholinergic burden of long-term medication in acute geriatric patients undergoing standard geriatric-pharmaceutical practice between admission and discharge.

## 2. Methods

### 2.1. Study design

The study included patients more than 80 years old who were admitted to the acute geriatric unit of a tertiary hospital. This unit has 10 beds and admitted 561 patients (mean age, 90 years) during 2014. The median length of stay was 6.5 days. Exclusion criteria were: readmission in less than 3 months, receiving palliative care before or during admission, and death within the hospitalization period. Data on sex, age, comorbidities, institutionalization, Barthel, Lawton, Functional Ambulation Classification (FAC), Global Deterioration Scale (GDS) and home medication were collected using emergency and primary care reports and interviews with the patients or relatives. Inhaled and ophthalmic medicines were included, but non-chronic medication (treatment for no more than 3 months) was excluded. Drugs used in combination were considered as separate drugs except for drug combinations specifically included in any of the scales (e.g., cabidopa-levodopa and salmeterol-fluticasone). All drugs were recorded at discharge except for those with a scheduled end date.

During hospitalization, the geriatric and pharmaceutical care of patients was performed according to standard clinical practice. Pharmacists collaborated in the clinical interview, performed medication reconciliation, reviewed data from the clinical history, validated the daily treatments based on the STOPP/START validation criteria [9] and recommended changes on patients' chronic treatments, which included deprescription, to geriatricians. All the members of the care team were blinded to the study, except for the pharmacist in charge of the data collection, which was not a member of the multidisciplinary team.

Anticholinergic burden was calculated according to the score assigned to each drug on the ADS, ARS, and ACB scales. Thus, the anticholinergic burden of each patient on admission and at discharge was determined using each of the three scales. The total number of drugs per patient on admission and at discharge was also recorded. Table 1 shows the prescribed anticholinergic drugs and their classification according to the three scales.

### 2.2. Statistics

Data analysis was performed using the STATA12® statistical software package. Continuous descriptive variables are expressed as means and confidence intervals and categorical variables as percentages. Correlations between continuous variables were assessed using the Wilcoxon or Mann-Whitney tests. Multivariate analysis was also performed using a logistic regression model in order to assess the differences found on univariate analysis.

## 3. Results

During the study period, 80 patients were screened. Five patients were excluded due to death and eight were excluded due to receiving palliative care before or during admission. Finally, sixty-seven patients met inclusion criteria. Table 2 shows the demographic characteristics of the patients.

**Table 1**
Anticholinergic drugs prescribed to the study patients and classification by scale.

| Active agent | ADS | ARS | ACB |
|---|---|---|---|
| Alprazolam | 1 | – | 1 |
| Amitriptyline | 3 | 3 | 3 |
| Atenolol | – | – | 1 |
| Carbamazepine | 2 | – | 2 |
| Carbidopa-levodopa | 0 | 1 | 0 |
| Cetirizine | – | 2 | – |
| Cyproheptadine | 2 | 3 | 2 |
| Clonazepam | 1 | – | – |
| Chlorthalidone | 1 | – | 1 |
| Codeine | 1 | – | 1 |
| Diazepam | 1 | – | 1 |
| Digoxin | 1 | – | 1 |
| Diltiazem | 1 | – | – |
| Fentanyl | 1 | – | 1 |
| Fluoxetine | 1 | – | – |
| Furosemide | 1 | – | 1 |
| Isosorbide | 1 | – | 1 |
| Lorazepam | 1 | – | – |
| Metoclopramide | – | 1 | – |
| Metoprolol | – | – | 1 |
| Mirtazapine | – | 1 | – |
| Nifedipine | 1 | – | 1 |
| Oxycodone | 1 | – | – |
| Paroxetine | 1 | 1 | 3 |
| Pramipexole | – | 1 | – |
| Prednisone | 1 | – | 1 |
| Quetiapine | – | 1 | 3 |
| Ranitidine | 2 | 1 | 1 |
| Risperidone | – | 1 | 1 |
| Salmeterol-fluticasone | 1 | – | – |
| Sertraline | 1 | – | – |
| Tramadol | 1 | – | – |
| Trazodone | – | 1 | 1 |
| Warfarin[a] | 1 | 0 | 1 |

ACB: Anticholinergic Cognitive Burden Scale; ADS: Anticholinergic Drug Scale; ARS: Anticholinergic Risk Scale.
[a] Acenocoumarol and warfarin were considered as different drugs.

At admission, 71.6%, 50.7%, and 79.1% of the study patients were treated with an anticholinergic drug listed on the ADS, ARS, and ACB scales, respectively. The most commonly used anticholinergic drugs at admission were furosemide (61.2% of patients; when considering ADS and ACB scales) and trazodone (28.4% of patients; when considering ARS scale).

There was a significant reduction in anticholinergic burden between admission and discharge according to the ARS ($P = 0.001$) and ACB ($P = 0.047$) scales, and a non-significant reduction in anticholinergic burden according to the ADS scale ($P = 0.087$) (Table 3). The anticholinergic burden was reduced in 32.8%, 34.3%, and 37.3% of the patients according to the ARS, ACB and ADS scales, respectively. Univariant analysis found significant differences in age (90.3 vs. 93.2; $P = 0.02$) and FAC (3.5 vs. 1.9; $P = 0.02$) between patients whose anticholinergic burden (ADS) got reduced and those who didn't. Nevertheless, multivariant analysis showed no differences between these groups. MNA was significantly different in patients with and without reduced ACB burden (9.4 vs. 5.4 respectively). No difference was found between patients whose anticholinergic burden measured by ARS was reduced and those who did not.

## 4. Discussion

A statistically significant reduction was found in anticholinergic burden in two (ARS and ACB) of the three scales used in the study. The greatest reduction was obtained on the ARS scale (44% reduction in total anticholinergic burden in 32.8% of the patients).

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