

# ABSTRACT

## Introduction

Anticholinergic (ACH) medications and medications with partial anticholinergic activity (AA) are prescribed in older patients particularly for the treatment of psychiatric, gastrointestinal, and genitourinary disorders, but also for other disease conditions. AA of combined drug regimens leads to ACH burden, which should be reduced as much as possible in seniors to avoid worsening of geriatric syndromes and other negative health outcomes. The aim of this diploma thesis was, in the first part, to summarize and review all currently published original and modified ACH drug scales, and to create a simple comprehensive tool for the assessment of ACH drug burden in older adults useful not only in clinical practice, but also in research. Furthermore, the focus of this diploma thesis was to describe the prevalence of use of ACH drug regimens and to document associations between administration of AA drug regimens and health problems in geriatric patients.

## Methods

In this study, the search was conducted in 4 different electronic databases: PubMed (N = 582), MEDLINE (N = 518), Scopus (N = 423), and Web of Science (N = 420) to identify all the ACH drug burden scales published between 2000-2022 and to compile a list of AA medication assessed by these scales. The search strategy was created by using Boolean operators AND/OR and key terms, that consisted of the group of free expressions and MeSH terms (Medical Subject Headings). Moreover, snowballing method was applied to search for additional sources in the bibliography of previously identified studies. A total of 12 validated scales were identified, listing a total of 732 drugs with an AA value of 0-3. This results list was used for further analyses.

Additionally, data of 2,865 community residing seniors (65+) assessed in 7 European countries as a part of the EuroAgeism H2020 project (2017-2022) were analysed: Croatia (N = 391), Estonia (N = 311), (the Czech Republic (N = 450), Bulgaria (N = 543), Spain (N = 260), Turkey (N = 450), and Serbia (N = 460). Seniors were prospectively assessed (Feb 2019-Mar 2020) using the standardized Comprehensive Geriatric Assessment (CGA) protocol. Descriptive statistics was used to describe the prevalence of use of ACH drug and ACH drug regimens. Logistic regression models (adjusted for country, gender, age, number of drugs and diseases) were applied to explore the associations between

cumulative ACH burden (calculated as a sum of AA of individual medications in drug regimen on average, obtained from all until now published and validated ACH drug scales) and the occurrence of at least 1 expected health problem caused by AA (e.g., vertigo; chronic constipation; falls in the last month; tachycardia; cognitive impairment etc.).

## Results

As a result, this study compiled a list of 27 studies and records including 15 original ACH scales and 9 modified ACH scales. 14 original scales were based on the opinion and consensus of experts who considered academic literature sources exploring the properties of the ACH medication. Chew scale (Chew et al., 2008) was developed based on the *in vitro* measurements of serum anticholinergic activity (SAA). Only 12 of 15 original scales were validated. Anticholinergic Drug Scale (Carnahan et al., 2006) assessed the largest set of medications from all scales (N = 534). However, the Anticholinergic Burden Score (Kiesel et al., 2018) contained the largest set of medications with AA (N = 151). In total, 868 various active substances assessed by scales were identified. Using the average of AA from the validated scales, AA was determined for 241 drugs: weak AA=1 (N =133), moderate AA=2 (N = 42), and strong AA=3 (N = 66).

When applying the compiled list of drugs with AA in the EuroAgeism H2020 project, there were 61,2 % women, and the mean age of participants was  $73,2 \pm 6,8$  SD (Standard Deviation) years. Polypharmacy (5-9 medications) and excessive polypharmacy (10+ medications) was documented in 40,9 % and 6,5 % of seniors. Total prevalence of use of at least one medication with AA was documented as 52,4 % (ranging from 37,6 % in Bulgaria to 67,2 % in Serbia). The prevalence of the Czech sample was 39,8 %. Combination of 2 and 3+ ACH medications were prescribed in 12,6 % and 7,0 % of older adults (with the highest prevalence in Spain 12,6 % and in Croatia 15,1 %, respectively). Patients from the researched sample used 114 drugs with AA 1-3. According to the ATC (Anatomical Therapeutic Chemical) classification system, the largest representation of prescribed drugs had drugs belonging to the group of antidepressants and antipsychotics (13,2 %; 12,3 %). The most commonly prescribed medications with various AA were metformin and furosemide (16,6 %, 6,0 % in the total sample; both with weak AA-1), paroxetine and solifenacin (0,9 %, 0,7 %; moderate AA-2), and hydroxyzine and amitriptyline (0,7%, 0,5%; strong AA-3). The adjusted odds ratio (OR) of experiencing at least one health problem that may directly or indirectly be associated with AA of drug

regimen was 3,47 times higher (95 % *CI* [Confidence Interval] 2.12-5.66,  $p < 0,001$ ) in seniors using drug regimen with 3 or more ACH drugs compared to nonusers of ACH drugs. Furthermore, the adjusted *OR* of experiencing of at least one health problem that may directly or indirectly be associated with AA drug regimen was 5,21 times higher (95 % *CI* 1.79-15.19,  $p = 0,003$ ) in seniors using drug regimen where cumulative score reached AA 5 and more compared to nonusers of ACH drugs.

## **Conclusion**

This study points out the wide range of existing available ACH scales used not only in the clinical conditions, but also in research. One of the drawbacks is that these scales tend to oversimplify the variability among individuals and complexity of the pharmacological mechanisms of ACH effects or drug complications. Available ACH drug scales vary greatly in the number of ACH medications they include. Nowadays, the prepared comprehensive tool represents one of the simplest ways to quantify ACH risk and to identify the ACH burden of drug regimens. Medication with AA are widely prescribed in community residing seniors in various drug combinations. Moreover, significant association between cumulative ACH burden and health problems/symptoms was also confirmed in our study in this population. ACH drug burden should be regularly checked and reduced as much as possible to improve individual health outcomes and health prognosis in older adults and thus prevent unwanted complications of pharmacotherapy.

## **Keywords**

rational geriatric pharmacotherapy, anticholinergic scoring scales, anticholinergic activity of medications

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