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Review

# Systematic review on the use of anticholinergic scales in poly pathological patients

Angela Mª Villalba-Moreno[a,*], Eva Rocío Alfaro-Lara[b], Mª Concepción Pérez-Guerrero[c], Mª Dolores Nieto-Martín[d], Bernardo Santos-Ramos[e]

[a] Pharmacy Service, University Hospital Virgen del Rocio, Seville, Spain
[b] Andalusian Agency for Health Technology Assessment, Seville, Spain
[c] Department of Pharmacology, Faculty of Pharmacy, Seville, Spain
[d] Internal Medicine Service, University Hospital Virgen del Rocio, Seville, Spain
[e] Pharmacy Service, University Hospital Virgen de Valme, Seville, Spain

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ABSTRACT

*Purpose:* Anticholinergic drugs may increase the risk of cognitive and functional disorders in older patients. There are anticholinergic scales on which said risk is estimated. The objectives of this study are: to identify the scales described in literature that are applicable to polypathological patients and analyze their clinical outcomes.

*Material and methods:* A systematic review was performed. Data sources were MEDLINE, EMBASE and Web of Science which were consulted until August 2014. Inclusion criteria: (1) studies that specify the list of drugs, describe the methodology for their elaboration and how they calibrate the anticholinergic potential and (2) studies that use the scales identified as a tool to measure exposure to anticholinergic drugs in polypathological patients or those with similar characteristics. The main differences between the scales and main results on cognitive, functional and mortality status were collected.

*Results:* 25 articles were included. 10 scales were identified. For their preparation, 8 were based on literature about drugs with anticholinergic activity and/or previously published scales as well as expert opinions. Exposure to anticholinergic drugs has been linked to cognitive disorders (basically measured with Anticholinergic Risk Scale (ARS), Anticholinergic Cognitive Burden Scale (ACB) and Drug Burden Index (DBI)) and functional scale (with ARS and DBI). However, there is no clear relationship with mortality. The Anticholinergic Drug Scale was the only one that obtained no association with any of the variables studied.

*Conclusions:* There is a great variety of scales published and applied to older patients. The clinical results are different depending on the scale used which is probably due to the different methodology in their elaboration.



**Contents**



## 1. Introduction

The concept of polypathological patients (PP) has been established as a subpopulation of patients with chronic diseases

* Corresponding author at: Pharmacy Service, University Hospital Virgen del Rocio, Semibasement floor, Avenue Manuel Siurot, s/n. 41013 Seville, Spain. Fax: +34 955 01 20 88.
*E-mail address:* angelavm_21@hotmail.com (A.M. Villalba-Moreno).

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and increasing frailty. It is characterized by old age, presenting several chronic diseases, being poly-medicated and suffering frequent exacerbations of underlying pathology, which create a constant demand for care in different medical areas (Ollero Baturone et al., 2007). It is a term that has been used for several years to define the "patient-centered care for older adults with multiple chronic conditions" when they have chronic diseases from two or more of the eight predefined categories (Bernabeu-Wittel et al., 2013). The PROFUND study, that included 1632 patients, was performed in 36 Spanish Hospitals and allowed us to characterize PP which is a homogeneous population, functionally impaired, with highly clinical complexity, vulnerability and dependence (Bernabeu-Wittel et al., 2011).

In primary care, the prevalence of PP was 1.38% in the general population with high levels of co-morbidity (up to 40% having three or more chronic diseases), cognitive (25% showed a significant deterioration) and functional (Ramírez-Duque et al., 2008) (34% on the Barthel index <60) disorders. Likewise, those with cognitive disorders took an average of 7.6 ± 3 drugs (Ramírez-Duque et al., 2008). These patients, as has recently been shown, take an average of 12.3 drugs/day in the hospital setting between those indicated by the clinician and those on sale (Alfaro-Lara et al., 2013). Approximately 50% of the older population takes at least one drug that has potential anticholinergic properties (Fox et al., 2011). Peripheral manifestations may occur such as urinary retention, constipation, decreased secretions, amongst others and central manifestations such as delirium, cognitive and functional disorders (Tune, 2001).

Older patients are more susceptible to these effects due to decreased renal and hepatic metabolism, as well as the increased permeability of the blood-brain barrier (Shi & Klotz, 2011). The prolonged and cumulative administration of these drugs makes them especially vulnerable to anticholinergic adverse effects because of the advanced age and frailty in PPs.

"Anticholinergic burden" is defined as the cumulative effect of taking one or more drugs that are capable of developing anticholinergic adverse effects (Tune, 2001). Recently, the design and development of tools has been increased to measure the anticholinergic burden a patient receives based on their pharmacotherapy. Generally, these are anticholinergic scales (AS) which are defined as medication lists that classify drugs according to their anticholinergic potential. Each drug receives a specific and growth score according to its anticholinergic activity. A patient's burden is the sum of the score for each drug included in the scale and its result allows us to estimate the greater or lesser risk of suffering anticholinergic adverse effects. The critical aspect in the use of these tools is that there are differences regarding the methodology used in their design and development and, consequently, there are variations in the drugs included in the scale and the score given to the drug according to its anticholinergic potential (Kersten & Wyller, 2014).

The main use of these scales is, therefore, to be able to estimate the risk of anticholinergic adverse effects in poly-medicated patients. Some studies have shown that some of them can act as predictors of cognitive and functional disorders in older people (Tune and Egeli, 1999; Hilmer et al., 2007a). Obtaining high scores after their application has been associated with an increased risk of suffering adverse events (falls, delirium, cognitive disorders, etc.) as well as their assessment provides the prescriber with the opportunity to reconsider the pharmacotherapy in order to optimize treatment (Durán et al., 2013). On the other hand, there are no specific scales for any specific population and they are generally used in older patients.

The aims of this paper are to identify all the AS described in literature that are applicable to PP and analyze the clinical results of studies that use these scales to measure the anticholinergic exposure in PP.

## 2. Material and methods

A systematic review was performed on literature published in the main databases (MEDLINE, EMBASE and Web of Science) up to August 31st, 2014. The search strategy is detailed in Table 1.

The references of the selected articles were reviewed as a complement.

PP was defined, according to the Integrated Assistance Process of the Andalusian Ministry of Health, as that which presents the coexistence of two or more chronic diseases that involve the appearance of exacerbations and inter-related pathologies, condition a special clinical frailty that exacerbates the patient with a progressive deterioration and a gradual decrease in their autonomy and functional capacity, and to generate a frequent demand for attention in different care settings (Ollero Baturone et al., 2007).

Systematic reviews, meta-analyses, experimental studies and observational studies were included.

Inclusion criteria were:

1. Studies on AS that specified the list of drugs included in the scales, the methodology used for the elaboration of the scale and how the anticholinergic potential of the drugs is classified.
2. Studies that use or validate the identified AS as a tool to measure exposure to anticholinergic drugs or the risk of suffering adverse or similar reactions to anticholinergic drugs in PP; which is understood as being over 60 years old and/or who had chronic diseases (with health problems requiring continuous treatment for years), co-morbidities (presence of secondary or associated pathologies with a disease or principal diagnosis), or being poly-medicated (taking 5 or more drugs).

Exclusion criteria were:

1. Languages in publications other than English or Spanish.
2. Studies in patients with Alzheimer's disease and severe senile dementia.
3. Studies in which the full text was not available.

**Table 1**
Search strategy in databases.

| MEDLINE |
|---|
| MeSH terms: (cholinergic antagonist OR muscarinics antagonists) AND (adverse effect) AND (aged)<br>Keywords: "anticholinergic cognitive burden", "anticholinergic loading scale", "anticholinergic risk scale", "drugs burden index", "aged", "aging", "older people", "scales", "index" and "burden" |
| EMBASE |
| Keywords: "anticholinergic cognitive burden"; "anticholinergic loading scale"; "anticholinergic risk scale"; "drugs burden index"; "aged"; "aging"; "older people"; "scales"; "index" and "burden" |
| WOS |
| Keywords: "cholinergic antagonist and adverse effects and aged" |

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