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REVIEW ARTICLE

# Effect of anticholinergic drugs on cognitive impairment in the elderly☆

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**KEYWORDS**
Anticholinergic drugs;
Serum anticholinergic activity;
Dementia;
Mild cognitive impairment;
Alzheimer's disease

**Abstract** The use of anticholinergic drugs is common in the elderly, even in people with cognitive impairment. A systematic search was conducted in PubMed (anticholinergic effects, anticholinergic and dementia) to define the effects of anticholinergic drugs in the elderly. We emphasised the search in patterns of use, the combined use with AChEIs, the measurement of the Serum Anticholinergic Activity, and the short-term and long-term cognitive effects. The conclusions are that the use of anticholinergic drugs is common in the elderly, even more so than the medical prescription of AChEIs in Alzheimer's disease. The use of anticholinergic drugs may result in cognitive impairment. In long-term use it may generate a worsening of cognitive functions. It can lead to a wrong diagnosis of mild cognitive impairment or dementia, and they can also initiate signs of dementia. Greater cognitive effects appear when there is a previous deficit, but cognitive effects from anticholinergic drugs disappear in severe dementia. The presence of ApoE-ε4 increases the vulnerability for cognitive impairment when these drugs are employed.


**PALABRAS CLAVE**
Fármacos anticolinérgicos;

**Efecto de los fármacos anticolinérgicos en el rendimiento cognitivo de las personas mayores**

**Resumen** El empleo de fármacos anticolinérgicos es frecuente en personas mayores, incluso con deterioro cognitivo. Se ha realizado una revisión bibliográfica en PubMed (*anticholinergic effects* y *anticholinergic and dementia*) acerca de los efectos de los fármacos anticolinérgicos

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Actividad anticolinérgica en suero;
Demencia;
Deterioro cognitivo leve;
Enfermedad de Alzheimer

en población anciana. Se ha enfatizado en determinar patrones de consumo, uso combinado con fármacos inhibidores de la acetilcolinesterasa (IACE), medida de la carga anticolinérgica y efectos cognitivos a corto y a largo plazo. Las conclusiones son que estos fármacos se emplean de forma habitual en población anciana, incluso tras la prescripción de IACE en la enfermedad de Alzheimer. Su empleo puede producir alteraciones cognitivas. Si el consumo es prolongado puede provocar un empeoramiento de la cognición a largo plazo originando falsos diagnósticos de deterioro, o incluso precipitando cuadros de demencia. Los efectos cognitivos son mayores ante un déficit preexistente, pero desaparecen en la demencia avanzada. La presencia de ApoE $\varepsilon$4 marca una vulnerabilidad a la afectación cognitiva por estos fármacos.


## Study objectives

The main objective of the study was to review the current literature on the effects of anticholinergic drugs on the elderly. Since there have been studies published about the very different effects of these drugs, we decided to focus this study on the cognitive effects. In this bibliographic review, the areas of interest were the following: the magnitude of the problem, methods for measuring anticholinergic action, short- and long-term cognitive effects, use of concomitant cholinergic drugs and the influence of the ApoE-$\varepsilon$4 allele on the cognitive effects of these drugs.

## Methodology

We performed a bibliographic revision about the cognitive effects of anticholinergic drugs. Given the lack of previous reviews in Spanish on this topic, to our knowledge, we decided not to limit the search to a certain period. Using the PubMed database, we carried out a search for articles with the key words ''anticholinergic effects'' in subjects older than 65 years of age. More than 5000 articles were found in the database. To refine the search, we used the search statements ''anticholinergic and dementia'' in subjects older than 65, and 439 articles published from 1973 to April 2012 were found. For this study, review articles and clinical trials were included. In a first stage, we selected those articles with English abstracts where the anticholinergic action on the cognitive function, psychological and behavioural symptoms and/or patient functionality were assessed, as well as articles that assess the prevalence of anticholinergic drug use, the concomitant use of acetylcholinesterase inhibitors (AChEI), methods for measuring anticholinergic action, and cognitive effects of these drugs regarding urinary incontinence. Fifty-seven articles were found. In a second stage, we specifically reviewed 25 articles that focused on prevalence, measurement of anticholinergic action, transversal and longitudinal cognitive effects, concomitant use of AChEI and the influence of ApoE-$\varepsilon$4 allele on cognitive status. The analysis of the bibliographic references of the selected articles enabled us to find 24 new articles which were used in this review, resulting in a total of 49 articles.

## Introduction

Drugs with anticholinergic action are widely used in current clinical practice for the treatment of a diverse range of conditions, such as urinary incontinence, peptic ulcer, spastic colon, depression, tremor or sedation. Despite their frequent use, their adverse effects are not insignificant.[1] The side effects of these drugs are related to its action on the cholinergic receptors:

- At the peripheral level, adverse effects include: reduced secretions, reduced bowel motion, blurred vision, increased heart rate, dry mouth, constipation, faecal impaction and urinary retention, among others.[2]
- At the central nervous system level, since the muscarinic receptors mediate attention, learning and short-term memory mechanisms,[3] the use of anticholinergic drugs may lead to cognitive function impairment and even precipitate the development of delirium.[2]

Cognitive adverse effects of anticholinergic drugs in these patients depend on the total anticholinergic burden, the underlying cognitive function and the individual pharmacokinetic and pharmacodynamic variability.[3,4] The metabolism and excretion of these drugs decrease with age. Moreover, the brain, as it ages, has less cholinergic activity; therefore, it is easier to exceed the symptomatic threshold for anticholinergic effect in old age.[5,6] Symptoms related to the anticholinergic effect include lack of concentration and loss of memory and, in subjects with cognitive deficit, exacerbation of the cognitive symptoms and functional impairment leading to a wrong diagnosis of dementia or mild cognitive impairment.[7] Therefore, the use of anticholinergic drugs is considered inadequate even in healthy elderly people.[4] It is estimated that between 2% and 12% of patients with suspected dementia do not have dementia syndrome and they actually have side effects of the drugs they take. This situation is more common if there is polypharmacy.[8] Table 1 shows the pharmacological groups with a higher risk of anticholinergic action. The lack of knowledge on the anticholinergic action of drugs may lead to iatrogenesis that goes unnoticed or has inexplicable alterations. Polypharmacy in turn increases the anticholinergic action.[5] It has been stated that in the elderly there is a risk of establishing a vicious circle consisting of the fact that the need for treatment causes side effects requiring the addition