

Commentary

## The Complexity of the Anticholinergic Burden in Frail Older Persons

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### ABSTRACT

The significant impact that some classes of drugs may have on older and frail people is nowadays an emerging issue. In particular, anticholinergics play a central role in this field. The systematic review and meta-analysis conducted by Stewart and colleagues, in accordance with the emerging literature on this topic, clearly demonstrate that an increased anticholinergic burden seems linked with low physical function and poor quality of life. This result underlines the well-established need of medication review, reconciliation, and a deprescribing activity during the clinical assessment of the older person.

**KEYWORDS:** anticholinergics; anticholinergic burden; polypharmacy; frailty

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Nowadays, a highly emerging issue in Geriatrics is represented by the significant impact that some classes of drugs may have on older people. In this field, a pivotal role is played by anticholinergics. The inhibition of acetylcholine seems to be connected with the occurrence of many side effects on the peripheral nervous system (e.g., urinary retention, constipation, tachycardia) and the central nervous system. Furthermore, it is always important to consider that older persons are particularly at risk of adverse drug reactions, mainly because of (1) the often present polypharmacy, and (2) modifications in pharmacokinetics and pharmacodynamics occurring with aging [1].

Emerging literature shows that anticholinergics may accelerate neurodegenerative processes, concurring at the onset of behavioral expressions of dementia, delirium, and cognitive decline [2,3]. The necessity to carefully monitor the effects of these medications has led to the development of ad hoc designed instruments, the so-called anticholinergic burden (ACB) scales, which are today commonly used in clinical practice. Several ACB scales are available, differing among them for the number of drugs considered and the scoring systems [1], making them non-interchangeable.

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The growing body of evidence urging cautiousness in the use of anticholinergics indeed required a comprehensive review. In particular, it was urgent to organize the existing literature about the effects of the ACB on those outcomes that are most relevant for the older person (i.e., quality of life and physical function). Such an additional step in the knowledge might further strengthen the available recommendations and provide a more straightforward standard in care.

The systematic review and meta-analysis conducted by Stewart and colleagues [4] goes in such direction. Their work retrieves and merges the results from thirteen studies conducted on persons aged 65 and older, coming from different clinical settings. As theoretically expected, authors demonstrate that an increased ACB burden seems linked with low physical function and poor quality of life. At the same time, consistently with the literature in the field [1], none of the many ACB instruments seemed superior to the others at detecting a particularly critical risk profile. The study thus reinforces the recommendations at conducting a strict control and accurate management of therapies in older persons, especially in the presence of frailty and polypharmacy.

It is well-established in geriatric literature for decades that living with multiple and often chronic conditions leads older patients to consult a larger number of specialists, each of them somehow “feeling compelled” to provide his own contribution to the therapy. The process results in an increased risk of polypharmacy, a major risk factor for negative outcomes (including adverse drug reactions!), independently of age [5]. This implies the need for always considering a medication review, reconciliation, and (potentially) a deprescribing activity during the clinical assessment of the older person [6]. In this context, the Comprehensive Geriatric Assessment, with its multidimensional, multidisciplinary, and dynamic approach, represents the gold standard for the optimisations of complex (pharmacological and non-pharmacological) interventions in frail older persons [7].

Several recommendations have been recently published for supporting physicians in the management of polypharmacy [8–10]. In particular, one of the critical aspects is the training to the principles of geriatric practice and the specific aspect of ACB consequences [11]. In this context, it might be important to train clinicians at reducing the ACB in older persons, but also avoiding these class of medications in younger individuals (to limit that their chronic use will end up to old age) [12]. After all, the use of anticholinergics in adults does not only expose them to potential adverse drug reactions, but can also contribute to the risk of developing dementia later in life [13].

Notwithstanding the importance of the results of the study, the fact that no “gold standard” instrument can be indicated to measure the ACB burden may remain an open issue. A recent review specifically considered different ACB scales, some of them also used in the study by Stewart and colleagues [4], to describe their rationale and characteristics, also in terms

of predictive capacity for adverse outcomes [14]. It emerged the substantial lack of a standardized approach, probably the main reason for the current difficulty at interpreting and comparing the results of studies conducted in this field. This problem might have potentially biased also the review by Stewart and colleagues [4]. They likely found themselves summarizing results from many tools depicting the same phenomenon from different perspectives. In fact, a metaanalysis of studies may pose several interpretative problems. Despite the attempt to limit biases and errors through the adoption of algorithms, the heterogeneity of the material may sometimes require a cautious reading of its results.

Finally, it is always important to keep in mind that the priority in the clinical management of a frail older person may not reside in the cure of the disease. Older persons may best value the maintenance of quality of life, physical and cognitive function, and independent living. It means that special attention should be posed to the prescription of potentially harmful medications, especially when administered following rigid therapeutic algorithms designed for someone else (see the evidence-based medicine issue in geriatric medicine) [15]. By changing objectives, it should also automatically lead to a change in the approach and methodology. It means shifting from a monodimensional observation of a standalone disease characterized by a well-defined pathophysiological process towards a comprehensive assessment of the biological, clinical, and social complexity of the individual [16]. Notably, such complexity (primarily based on the evaluation of functions) is not a static phenomenon but a highly dynamic one. In other words, the complexity faced by the clinician in real life is not only related to the intricate matter of (often aspecific) signs, symptoms, and conditions to disentangle. A longitudinal approach is needed to appreciate the functional and health trajectory the individual has been following over time [17]. Applying this necessity to the results of most of the available evidence, we can realize 1) how many confounders are potentially missed because of the limited and obsolete instruments we have, and 2) the need of growingly include novel technologies in the assessment, evaluation, and management of older persons [18].

In conclusion, although the connection between anticholinergics drugs and quality of life seems to be confirmed, we agree with the authors of the study about the need for further studies. A standardisation of the ACB measurements in the future together with the evidence that ACB represents a real issue during the process of drug prescription will lead physicians to a better optimisation of therapies. Also, the need for well-defined and randomized studies showing the bidirectional connections between ACB and the frailty of patients should be considered. Nevertheless, the results provided by Stewart and colleagues remain of great interest. They raise awareness among physicians about the importance of limiting inappropriate and unnecessary prescriptions in frail older persons.

## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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