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Commentary

Delirium due to Anticholinergic Drug Burden in Older Persons

Anna Soldati [1,*], Matteo Cesari [2,3]

[1] Geriatric Fellowship Program, University of Milan, Milan 20122, Italy
[2] Department of Clinical Sciences and Community Health, University of Milan, Milan 20122, Italy
[3] Geriatric Unit, IRCCS Istituti Clinici Scientifici Maugeri, Milan 20138, Italy
* Correspondence: Anna Soldati, Email: anna.soldati@unimi.it.

ABSTRACT

The cumulative effect of medications with anticholinergic activity (known as Anticholinergic Drug Burden, ADB) is associated with incident delirium and onset of adverse outcomes in older persons (e.g., cognitive and functional impairment). In a recent study by Egberts and colleagues, the association between delirium and ADB was demonstrated, mainly when assessed using the Anticholinergic Risk Scale (ARS). Although drugs with anticholinergic properties are often included in lists of potentially inappropriate medications, their prescription is still widespread. More efforts should be made to support deprescribing strategies and limit the prescription of potentially harmful medications.

KEYWORDS: anticholinergic drug burden; delirium; geriatrics; polypharmacy; deprescribing

Delirium is a common geriatric syndrome associated with the risk of poor clinical outcomes in older persons with frailty. The anticholinergic drug exposure is recognized as an important precipitating factor of delirium [1,2], with both central and peripheral side effects involved in its pathogenesis [3]. Despite drugs with anticholinergic properties being listed as potentially inappropriate medications in older persons [4], their use is still very common [5–7]. The need to measure the cumulative effect of taking multiple medicines with antimuscarinic activity (or the so-called Anticholinergic Drug Burden; ADB), with the overarching aim of limiting their use, has led clinicians to develop specific instruments to quantify the ADB [8].

In a recent systematic review considering almost 150,000 patients, Egberts and colleagues [9] have investigated the association between delirium and the ADB. The ADB was found to be heterogeneously measured, with six instruments most commonly used. The associations between the results obtained at the Anticholinergic Risk Scale (ARS) with

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both the prevalent and incident delirium were particularly evident. Inconsistent data were instead reported for the other scales/instruments.

The relationship between the ADB and clinical outcomes (e.g., cognitive and functional impairment, falls, all-cause mortality) in older persons is quite well-established [10–12]. However, to our knowledge, the study by Egberts and colleagues [9] is the first one demonstrating the superiority of one scale over the others in terms of predictive capacity for delirium. This work contributes to a debated field, where contradicting findings were published in the past [6,11].

The clinical relevance of this review can also be found in the identification of the ARS score, a very clinical friendly tool, as the possible best instrument to predict a critical geriatric condition as delirium. Over the years, many instruments were proposed to assess the relationship between ADB and delirium, but results were mixed. The measurement of serum anticholinergic activity to quantify the anticholinergic load in patients with delirium is also highly questionable [13] because of the problematic interpretation of its values [14]. In the current clinical practice, electronic medical charts can support the optimization of drug prescriptions. For example, the INTERcheck system [15] automatically allows the ADB measurement at the time of the hospital prescription. Nevertheless, the real capacity of these strategies to reduce the incidence of delirium is not yet demonstrated.

Another aspect to consider in the attempt to limit anticholinergic medications may reside in the adoption of a life-course preventive approach. Today, significant efforts are made to train physicians at deprescribing medications with anticholinergic effects at old age. Perhaps, it could be necessary to also train physicians at limiting their first prescription of these molecules. Furthermore, more attention should also be paid when first prescribing a potentially harmful drug, particularly by taking into account comorbidities. In other words, physicians should start considering the long-term effects of their therapeutical actions, and (1) choose safer medications for the aging populations, and/or (2) define more explicit temporal limits for their prescriptions.

Another limitation deserving to be highlighted is that cognitive impairment is not always adequately considered as a factor mediating the association between ADB and delirium. Indeed, cognitive impairment represents a crucial predisposing condition for the onset of delirium. At the same time, the latter is associated with an increased risk of incident dementia and accelerates cognitive decline. The anticholinergic load related to dementia and behavioral abnormalities treatment could be a major significant confounder that must not be underestimated.

Finally, we would like to point out how the study is implicitly showing the limitations of assessment tools. As in many fields of geriatric medicine, instruments remain instruments [16]. They are designed to make objective what is often difficult to quantify and frequently rely on arbitrary and or pragmatic assumptions. On the one hand, the study demonstrates the

superiority of the ARS over the other tested tools. However, on the other, it cannot be excluded that (1) different tools not considered in the review could work better than the ARS itself, and (2) the tools here showing a marginal relevance in the prediction of the delirium could be associated with other outcomes in a more robust way than what the ARS can do. Indeed, in geriatric medicine, finding a "gold standard" in a mono-dimensional tool is almost impossible. Common sense supported by objective data and careful evaluation of available evidence (i.e., "evidence-based medicine issue") should always drive decisions. Today, we are gathering the necessary data to have our discipline evolve and provide the foundations to build the evidence for tomorrow.

In conclusion, high ADB is associated with the onset of delirium, cognitive, and functional impairment. More decisive actions are needed to promote a regular medication review and improve the quality of our prescriptions, also through the use of tools (as the ARS scale). Deprescribing is essential, but prescribing better is undoubtedly preferable.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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