SHORT REPORT

A novel Artificial Intelligence-based tool to assess anticholinergic burden: a survey

Agostina Secchi¹, Hulkar Mamayusupova^{2,3}, Saber Sami⁴, Ian Maidment⁵, Simon Coulton⁶, Phyo Kyaw Myint⁷, Chris Fox⁸

Address correspondence: Chris Fox, University of Exeter, College of Medicine and Health St Luke's Campus, Heavitree Road, Exeter, EX I 2LU, UK. Email: Christopher.Fox@exeter.ac.uk

Abstract

Background: many medications possess anticholinergic activity. Their use is associated with a number of serious adverse effects including cognitive effects. The cumulative anticholinergic effect of medications as assessed by tools such as the anticholinergic burden scale (AchB) can identify people particularly at risk of anticholinergic side-effects. Currently, >20 tools are available for clinicians to use, but there is no consensus on the most appropriate tool.

Methods: a newly created online tool—International Anticholinergic Cognitive Burden Tool (IACT)—based on natural language processing and chemical structure analysis, was developed and made available for clinicians to test its functions. We carried out a survey (between 8th of February and 31st of March 2021) to assess the overall need for an assessment tool as well as the usability of the IACT.

Results: a total of 110 responses were received from different countries and practitioners' groups. The majority of the participants (86.11%) stated they would use a tool for AchB assessment if available and when they were asked to rate the IACT against other tools, amongst 34 responders, 20.59% rated it better and 8.82% rated it significantly better, 44.12% rated it neither better, nor worse, 14.71% rated it worse and 11.76% somewhat worse.

Conclusion: there is a need for an anticholinergic burden calculator to assess the anticholinergicity of medications. Tools such as the IACT potentially could meet this demand due to its ability to assign scores to current and new medications appearing on the market based both on their chemical structure and reported adverse pharmacological effects.

Keywords: anticholinergic, polypharmacy, adverse events, older people

Key Points

- A novel Artificial Intelligence-based anticholinergic tool can be used to assess anticholinergic burden.
- The absolute necessity to evaluate anticholinergic burden when prescribing.
- The International Anticholinergic Cognitive Burden Tool can be easily deployed.

Kent and Medway NHS and Social Care Partnership Trust

²AKFA University Medical School, Uzbekistan

³University of Essex, CO4 3SQ, UK

⁴University of East Anglia, Norwich, NR4 7TI, UK

⁵Aston University, Aston St, Birmingham B4 7ET, UK

⁶University of Kent, Giles Ln, Canterbury CT2 7NZ, UK

⁷Ageing Clinical & Experimental Research Team, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, Scotland, UK

⁸University of Exeter, College of Medicine and Health

Background and objectives

Global trends in use of medicines with anticholinergic activities are increasing [1–3]. In England, alone the use of anticholinergic medications or medications with anticholinergic activity has registered a significant increase between 1990 and 2001 (from 5.7 to 9.9%, respectively; [4]).

Anticholinergic activity is associated with a number of serious adverse events and it is often the result of prescribing multiple medications [5]. Reported adverse effects include dry mouth, nausea, constipation, blurred vision, urinary retention, cognitive impairment [6] and could increase risks of falls and may be associated with an increase in mortality [7–9]. Older people may be more susceptible to anticholinergic effects due to reduced renal and liver function, which affect the metabolism and elimination of the medications leading to increased exposure [10, 11]. There is also a linear relationship between anticholinergic burden and cardiovascular diseases or deaths [12].

Professionals should aim to reduce the overall anticholinergic burden (AchB) prescribed. Pharmacists might play an important role in deprescribing medications with anticholinergic activity [13]. To achieve this, an assessment of anticholinergic burden for individual medications is essential and it needs to be incorporated in routine clinical practice using a reliable scale.

Currently there are a number of scales available but National Institute for Health and Care [14] does not make recommendation of one over another and there is no gold standard scale [2]. Recent systematic reviews [15–17] could not recommend any particular tool. Lozano-Ortega *et al.* [18] identified 16 scales, 6 of which were suitable for quantification of anticholinergic exposure. However, the use of these scales and others currently in use [19] is limited, because they do not use an updating system, and there are differences in which medications are included and the impact of dose.

Against this background we developed a new method of measuring anticholinergic burden using machine learning technique—the International Anticholinergic Cognitive Burden (IACT) tool.

The novelty introduced with this tool is the use of a machine learning technique—a natural language processing—to develop an automated model available on a website portal. The anticholinergic burden is assessed by assigning a score based on reported adverse events and aligning closely with drug chemical structure, resulting in a more accurate and up-to-date scoring system.

The current report summarises the results of the survey we carried out with the view of testing the usability of this new calculator tool. The purpose was to better understand the benefits of usage as well as current limitations with the aim of future improved development.

Methods

We developed a questionnaire using Qualtrics software (Qualtrics, Provo, UT, USA). The survey was first piloted

among research team members with expertise in pharmacy, geriatric medicine, mental health and health service research who are involved in prescribing. After obtaining the ethical approval from University of East Anglia (reference: 2020/21-068) the survey was distributed via email and social media to various groups including NHS foundation trusts and pharmacies as well as internationally. Participants (doctors, non-medical prescribers, consultants, General Practitioners nurses and pharmacists) meeting the eligibility criteria, received the link to test the IACT and were invited to take part in the survey to evaluate the tool.

Participants were asked a mixture of closed and openended questions. Firstly, to gain more insight of their understanding of AChB calculation. Secondly, to ask an opinion on the usefulness of the IACT tool and possible suggestions for its improvement. The survey questions can be found in Appendix 2 (supplementary data are available in *Age and Ageing* online). More detailed explanation of the methods can be found in Appendix 4 (supplementary data are available in *Age and Ageing* online).

The feedback results were exported to Microsoft Excel and graphs plotted using Microsoft Excel (version 2020) and Origin (Pro) software (version 2021b, OriginLab Corporation, Northampton, MA, USA). The qualitative data extrapolated from the open-ended questions were analysed using a thematic analysis. This work was funded by EIRA (Enabling Innovation: Research to Application) at University of East Anglia and Research England and Eastern AHSN. Funders played no role in any parts of this work.

Results

One hundred and ten professionals participated in this survey (Appendix 1, Panel A, Supplementary data are available in *Age and Ageing* online). In total, 73% were aware of national guidelines on AchB assessment and risk of cognitive impairment (Appendix 1, Panel B, Supplementary data are available in *Age and Ageing* online). Participants' profession were 47.3% medical doctors (secondary and primary care), 38.2% pharmacists, 5.5% nurse prescribers and 9.1% other professions including physician associate, advance nurse practitioner and scientists (Appendix 1, Panel C, Supplementary data are available in *Age and Ageing* online).

When asked, the vast majority of 74.3% agreed that the prescriber should assess the AchB, whereas 20.2% responded as various professionals should be responsible and 5.5% were not sure (Appendix 1, Panel D, Supplementary data are available in *Age and Ageing* online).

The respondents were further asked whether they routinely assessed AchB and if yes which tools they frequently used. Around 54.13% answered affirmingly and the distribution of their tool usages is presented (Figure 1). Among those who used various tools, the majority (63.8%, total N=36) used the ACB scale or ACB calculator. When asked to rate the usefulness of the tools (if used) in a Likert scale from 1 least helpful and 5 most helpful, among the 58 respondents,

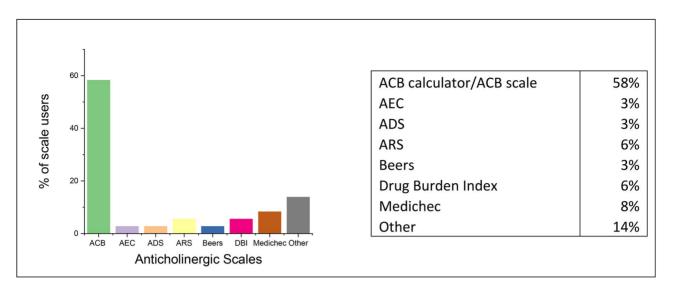


Figure 1. The usage of the different tools available to assess AchB. The total number of users N = 36. ACB, anticholinergic cognitive burden scale; AEC, anticholinergic effect on cognition scale; ADS, anticholinergic drug scale; ARS, anticholinergic risk scale; Beers, Beer's scale; DBI, Drug Burden Index scale; Medichec, online tool.

42.86% of them scored 4, 31.43% scored 5 (mean = 4.027, 95% CI [3.75, 4.30]).

Participants were also asked to rate the new IACT tool against the tool they routinely used (Q10 of the survey) and of 34 responders, 20.59% rated it better and 8.82% a lot better, 44.12% rated it as neither better nor worse, whereas 14.71% rated it worse and 11.76% somewhat worse indicating the need for more education on the use of the tool.

Indeed, lack of knowledge was reported as a major barrier to the use of IACT (Q12).

Other barriers were time required and the need to include more medications with known and unknown AchB scores. According to participants, suggestions for alternatives, consideration of doses and co-morbidities would greatly enhance the usage of the tool. One of the main reasons, which prevented participants from assessing AchB scores were the lack of incorporated tools into the healthcare electronic record systems, or the impracticability of using the scoring tools when prescribing off-site (patients' home).

Discussion

The purpose of the survey was to obtain feedback on usage and benefits of newly created IACT tool when prescribing medications with anticholinergic activity.

In line with a previous studies [20], the results show an understanding of the importance of calculating AchB and interest in using a tool to calculate AchB in the routine clinical practice. However, the use of the tools was perceived as time consuming and more than one-third of the participants admitted not using them, indicating that more work should be done to simplify their use. The ACB scale seemed to be the most popular tool used to calculate the anticholinergic burden as easily accessible, although its limitations were acknowledged.

The participants were asked to rate the ACB and the other tools against our tool, the IACT. The new AChB calculation system introduced with the IACT, was perceived useful as based on characteristics such as chemical structure, medication side-effects and textual information allowing to score newly added medications in the market, hence differentiating from other tools [19]. Minor issues highlighted were taken in consideration for amendment. For example, we acknowledged the limitation of using the tool when working without internet access; we recognised that the use of the tool was time consuming for many doctors (Appendix 3, Supplementary data are available in *Age and Ageing* online). To overcome these limitations, we decided to make the IACT available in a web application (APP) accessible when internet access is limited. To facilitate the use of the tool we considered incorporating it within the prescribing web programme used in the GP surgeries such as SystmOne (TPP) so that medications with high levels of AChB are flagged up immediately when prescribing and prescribers do not need to enter the name of the medications in two different web programmes. Although the participants indicated that a tool to calculate AChB should be used by prescribers, the participants valued tools to calculate AChB and following future development our tool, the IACT, has the potential to fulfill this need [21].

Strengths. The survey was completed by professionals coming from a varied background, which helped with creating a greater validity of the data collected.

Limitations. Due to time constraints we could not recruit more international professionals who would have enriched the data and contributed to assess the usability of the IACT tool.

Implication for practice. The aim of this survey was to identify issues on the use of the IACT in clinical practice. The IACT, once refined, will help practitioners to standardise

A. Secchi et al.

prescribing practice, it will help to improve medication monitoring and most importantly it will help to improve patients' health by preventing anticholinergic side-effects [8, 22–24].

In summary, we conclude that machine learning based systems could be developed to quantify anticholinergic burden with the view of improving patient outcomes. IACT tool has the potential to help clinicians in their clinical decision around prescribing by providing an easy to access to up-to-date scoring system.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Declaration of Conflicts of Interest: None declared.

Declaration of Sources of Funding: This work was funded by EIRA (Enabling Innovation: Research to Application) at UEA and Research England and Eastern AHSN.

References

- 1. Ruxton K, Woodman RJ, Mangoni AA. Drugs with anticholinergic effects and cognitive impairment, falls and allcause mortality in older adults: a systematic review and metaanalysis. Br J Clin Pharmacol 2015; 80: 209–20.
- 2. Salahudeen MS, Hilmer SN, Nishtala PS. Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people. J Am Geriatr Soc 2015; 63: 85–90.
- 3. Reinold J, Braitmaier M, Riedel O, Haug U. Anticholinergic burden: first comprehensive analysis using claims data shows large variation by age and sex. PLoS One 2021; 16: e0253336. https://doi.org/10.1371/journal.pone.0253336.
- 4. Grossi CM, Richardson K, Savva GM *et al.* Increasing prevalence of anticholinergic medication use in older people in England over 20 years: cognitive function and ageing study I and II. BMC Geriatr 2020; 20: 267. https://doi.org/10.1186/s12877-020-01657-x.
- **5.** Feinberg M. The problems of anticholinergic adverse effects in older patients. Drugs Aging 1993; 3: 335–48.
- **6.** Collamati A, Martone AM, Poscia A *et al.* Anticholinergic drugs and negative outcomes in the older population: from biological plausibility to clinical evidence. Aging Clin Exp Res 2016; 28: 25–35.
- 7. Fox C, Richardson K, Maidment ID *et al.* Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study. J Am Geriatr Soc 2011; 59: 1477–83.
- **8.** Fox C, Smith T, Maidment I *et al.* Effect of medications with anti-cholinergic properties on cognitive function, delirium, physical function and mortality: a systematic review. Age Ageing 2014; 43: 604–15.
- 9. Yrjana KR, Keevil VL, Soiza RL *et al.* Anticholinergic medication exposure predicts poor physical capability: findings from a large prospective cohort study in England. Maturitas 2020; 142: 55–63.

- **10.** Laatikainen O, Sneck S, Bloigu R, Lahtinen M, Lauri T, Turpeinen M. Hospitalizations due to adverse drug events in the elderly-a retrospective register study. Front Pharmacol 2016; 7: 358. https://doi.org/10.3389/fphar.2016.00358.
- **11.** Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. Br J Clin Pharmacol 2004; 57: 6–14.
- 12. Myint PK, Fox C, Kwok CS, Luben RN, Wareham NJ, Khaw KT. Total anticholinergic burden and risk of mortality and cardiovascular disease over 10 years in 21,636 middleaged and older men and women of EPIC-Norfolk prospective population study. Age Ageing 2015; 44: 219–25.
- **13.** Nakham A, Myint PK, Bond CM, Newlands R, Loke YK, Cruickshank M. Interventions to reduce anticholinergic burden in adults aged 65 and older: a systematic review. J Am Med Dir Assoc 2020; 21: 172–180.e5.
- 14. (NICE). NIfHaCE. Dementia: Assessment, Management and Support for People Living with Dementia and Their Carers. 2018 (NG97). Available at https://www.nice.org.uk/guidance/ng97 (19 August 2021, date last accessed).
- **15.** Stewart C, Yrjana K, Kishor M *et al.* Anticholinergic burden measures predict older people's physical function and quality of life: a systematic review. J Am Med Dir Assoc 2021; 22: 56–64.
- **16.** Taylor-Rowan M, Edwards S, Noel-Storr AH *et al.* Anticholinergic burden (prognostic factor) for prediction of dementia or cognitive decline in older adults with no known cognitive syndrome. Cochrane Database Syst Rev 2021; 2021: CD013540. https://doi.org/10.1002/14651858.CD013540. pub2.
- 17. Graves-Morris K, Stewart C, Soiza RL *et al.* The prognostic value of anticholinergic burden measures in relation to mortality in older individuals: a systematic review and meta-analysis. Front Pharmacol 2020; 11: 570. https://doi.org/10.3389/fphar.2020.00570.
- **18.** Lozano-Ortega G, Johnston KM, Cheung A *et al.* A review of published anticholinergic scales and measures and their applicability in database analyses. Arch Gerontol Geriatr 2020; 87: 103885. https://doi.org/10.1016/j.archger.2019.05.010.
- **19.** Okudur SK, Dokuzlar O, Aydin AE, Kocyigit SE, Soysal P, Isik AT. The evaluation of relationship between polypharmacy and anticholinergic burden scales. North Clin Istanb 2021; 8: 139_44
- **20.** Kouladjian O'Donnell L, Gnjidic D, Nahas R, Bell JS, Hilmer SN. Anticholinergic burden: considerations for older adults. J Pharm Pract Res 2017; 47: 67–77.
- 21. Ghossein N, Kang M, Lakhkar AD. Anticholinergic Medications. Treasure Island (FL): StatPearls, 2022.
- **22.** Cardwell K, Hughes CM, Ryan C. The association between anticholinergic medication burden and health related outcomes in the 'oldest old': a systematic review of the literature. Drugs Aging 2015; 32: 835–48.
- **23.** Cancelli I, Beltrame M, Gigli GL, Valente M. Drugs with anticholinergic properties: cognitive and neurophsychiatric side-effects in elderly patients. Neurol Sci 2009; 30: 87–92.
- **24.** Jamsen KM, Gnjidic D, Hilmer SN *et al.* Drug burden index and change in cognition over time in community-dwelling older men: the CHAMP study. Ann Med 2017; 49: 157–64.

Received 15 February 2022; editorial decision 1 July 2022