Maturitas 168 (2023) 92–93

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Editorial

Lifetime perspectives on dementia prevention: The role of 'preventive' polypharmacy

ARTICLE INFO

Keywords
Aging
Dementia
Polypharmacy
Cognition
Prevention
Epidemiology

Within the new reality of multimorbidity, co-occurrence of chronic diseases necessitates frequent and simultaneous use of multiple medications. These combinations of medications easily lead to the simultaneous use of 5 or more drugs ('polypharmacy'). Contrary to widespread belief, it has been shown that preventive cardiovascular medications form the backbone of polypharmacy among adults, present in up to 90 % of all occurrences of polypharmacy on a population-level [1]. Is this a sign of preventive health or are these preventive drugs part of inappropriate polypharmacy that could potentially harm cognitive health?

Polypharmacy does not necessarily imply overtreatment, as co-occurring diseases may warrant treatment by multiple drugs. It does, though, relate to adverse health outcomes, drug-drug interactions and frequent hospitalizations – partly driven by confounding by indication due to co-existing diseases [2]. The question of whether the potential harms of polypharmacy outweigh its benefits for cognitive health is therefore complex, particularly against the backdrop of evidence that suggests beneficial effects of stringent cardiovascular prevention against dementia [3].

Theoretically, prescribing multiple cardiovascular preventive drugs seems a promising strategy to battle the multifactorial nature of late-life dementia. The pathological substrate of late-life dementia in the general population is a conglomerate of vascular pathologies, amyloid and lipid deposits and hippocampal sclerosis. In clinical practice, however, the shape of this preventive polypharmacy strategy and its potential for dementia prevention will largely be determined by the age of the patient.

For middle-aged individuals (40–70 years), initiation of medication to lower both blood pressure and lipid levels specifically to reduce the long-term risk of dementia seems far away. However, advances in the field of cardiology – shifting the preventive treatment window to younger ages – provide a longer time to benefit. These lifetime perspectives on disease risk reduction also take out the significant contribution of advancing age in estimates of risk prediction that determine treatment qualification. For example, young adults with very adverse risk profiles are at very high risk of developing disease in their remaining lifetime and now increasingly qualify for cardiovascular preventive treatment guided by lifetime risk prediction models. Although initiation of preventive medication should be preceded by lifestyle advice, sustainable changes in lifestyle are challenging - especially for adults - who have built up behavioral daily routines. Given that the majority of (middle-aged) individuals at risk for cardiovascular disease are also at an increased risk of developing late-life dementia in their lifetime, there is a unique opportunity to jointly target and prevent both late-life dementia as well as cardiovascular disease.

In older adults (≥70 years), a first step to reduce potential harms of (inappropriate) polypharmacy to cognitive health is to limit use of anticholinergic drugs, opioids and benzodiazepines whenever possible. A more complex challenge is whether older adults with sustained use of cardiovascular preventive medication are better off without these drugs to reduce the harms of polypharmacy to their cognitive health, such as drug-drug interactions or orthostatic hypotension. This seems reasonable, since absolute risk reductions among the elderly are relatively small and the preventive window of opportunity has largely passed. In fact, a large proportion of older adults most likely already qualifies for pharmaceutical preventive control based on their 10-year cardiovascular risk, regardless of their risk for late-life dementia. This questions whether the consideration of dementia risk as an additional indication for preventive treatment will result in different clinical decision making. It perhaps does provide new incentives for people to adhere to their existing treatment regimens, to jointly reduce risks of dementia and cardiovascular disease. Lipid-lowering treatment remains worthwhile for primary cardiovascular prevention among the very old [4], but 'time-to-benefit', that is, to potentially contribute to the prevention or postponement of dementia, may be too limited for these patients.

Benefits and harms of (preventive) polypharmacy among older adults at risk for dementia thus balance on a thin line, with many questions that remain unanswered. So far, studies among older adults have been restricted to investigations of the net benefit of discontinuing

https://doi.org/10.1016/j.maturitas.2022.06.003
Received 30 May 2022; Accepted 2 June 2022
Available online 9 June 2022

a single preventive drug in selected populations of older adults or terminally ill patients (<3 months' life expectancy) [5]. Very little is known about the harms and benefits of simultaneously prescribed preventive cardiovascular drugs at old age in the contemporary, multimorbid population at the highest risk of disease and frailty. At younger ages, key questions remain unresolved regarding long-term benefits of cardiovascular preventive medication for dementia risk reduction later in life. A lifetime perspective on dementia risk reduction does provide new insights to identify persons at risk for cognitive decline who currently remain untargeted. The time seems right to at least assess the potential of lifetime perspectives on dementia risk reduction. Then, perhaps in a not so distant future, we may determine cardiovascular preventive medication initiation as well as discontinuation based on personalized lifetime risk calculators that also take the risk of late-life dementia into account.

Contributors

Silvan Licher is the sole author of this editorial.

Funding

No funding from an external source was received for the preparation of this editorial.

Provenance and peer review

This article was commissioned and was not externally peer reviewed.

Declaration of competing interest

The author declares that they have no competing interest.

References

[1] S. Licher, et al., Epidemiology of polypharmacy in the general population: 27-year prospective cohort study, J. Am. Med. Dir. Assoc. 21 (8) (2020) 1177–1179.
[2] D. Mangin, et al., International Group for Reducing Inappropriate Medication Use & Polypharmacy (IGRIMUP): position statement and 10 recommendations for action, Drugs Aging 35 (7) (2018) 575–587.
[3] SPRINT MIND Investigators for the SPRINT Research Group, Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial, JAMA 321 (6) (2019) 553–561.
[4] M.B. Mortensen, B.G. Nordestgaard, Elevated LDL cholesterol and increased risk of myocardial infarction and atherosclerotic cardiovascular disease in individuals aged 70–100 years: a contemporary primary prevention cohort, Lancet 396 (10263) (2020) 1644–1652.
[5] M.A. van der Ploeg, et al., Recommendations for (discontinuation of) statin treatment in older adults: review of guidelines, J. Am. Geriatr. Soc. 68 (2) (2020) 417–425.

Silvan Licher
Department of Epidemiology, Erasmus MC – University Medical Center Rotterdam, Rotterdam, the Netherlands
E-mail address: s.licher@erasmusmc.nl.