Letters to the Editor

Potentially Inadequate Medications in the Elderly: PRISCUS 2.0

First Update of the PRISCUS List

by Nina-Kristin Mann, Prof. Dr. rer. medic. Tim Mathes, Prof. Dr. med. Andreas Sönnichsen, Prof. Dr. rer. medic. Dawid Pieper, Elisabeth Klager, M.Sc., Dr. med. Mahmoud Moussa, and Prof. Dr. med. Petra A. Thürmann in issue 1–2/2023

Evaluations Are in Part Implausible and Not Reasonable

We read the publication by Mann et al. regarding the PRISCUS List 2.0 with great interest (1). Adapting pharmacotherapy to the special requirements of elderly persons is without argument justified, but the dichotomization created by the Delphi procedure into "potentially inadequate medication" (PIM) or non-PIM has resulted in recommendations that lack a scientific evidence base and deviate from the clinical expert consensus of the international Parkinson specialist societies. The following evaluations of anti-Parkinson medications are partly implausible and misleading:

All MAO-B inhibitors are classified as PIM and recommended as an alternative to the dopamine agonist ropinirole (and in the detailed PRISCUS LIST rotigotine), although dopamine agonists were identified as clearly having more adverse effects in a large "real world" comparison study (2).

Ropinirole (and rotigotine) are listed as an alternative to two non-ergot-dopamine agonists that were classified as PIM: piribedil and pramipexole. As regards geriatric adverse effects, differences between these dopamine agonists can't be concluded for hallucinations/delirium nor for orthostasis (3).

Amantadine should in fact be used restrictively on older persons and current guidelines recommend it only in case of dopaminergic induced hyperkinesia as the medication of choice. In this indication the use of levodopa or dopamine agonists as recommended in the PRISCUS List is counterproductive.

In sum, the recommendation concluded from the PRISCUS List to use preferentially dopamine agonists as alternatives to MAO-B inhibitors or amantadine in older persons is misleading and even dangerous in geriatric patients because of the particularly high risk of adverse effects of dopamine agonists. We advise a revision of the recommendations of the PRISCUS List for anti-Parkinson treatment with support and input from neurologists.

DOI: 10.3238/arztebl.m2023.0083

References

1. Mann NK, Mathes T, Sönnichsen A, et al.: Potentially inadequate medications in the elderly: PRISCUS 2.0—first update of the PRISCUS list. Dtsch Arztebl Int 2023; 120: 3–10.
2. Med Collaborative Group et al.: Long-term effectiveness of dopamine agonists and monoamine oxidase B inhibitors compared with levodopa as initial treatment for Parkinson's disease (PD MED): a large, open-label, pragmatic randomised trial. Lancet 2014; 384: 1196–205.
3. Claus X, Warnecke Die Parkinson-Therapie beim älteren Menschen. Internistische praxis 2022; 66, 117–26.

Prof. Dr. med. Georg Ebersbach
Neurologisches Fachkrankenhaus für Bewegungsstörungen/Parkinson
Beelitz-Heilstätten
ebersbach@kliniken-beelitz.de

Prof. Dr. med. Tobias Warnecke
Klinik für Neurologie und Neurologische Frührehabilitation
Schwerpunkt Parkinson-Syndrome und andere Bewegungsstörungen
Osnabrück

Conflict of interest statement

GE received payments from AbbVie, Esteve, Stada, BIAL, and Desitin for participating in advisory boards. He was paid lecture fees by AbbVieBial,, Esteve, Stada, und Zambon.

TW received advisory fees from AbbVie, Zambon, Biall, and Kyowa. He was paid lecture fees by AbbVie, Bial, Desitin, Zambon, Stada, and Esteve.

"Consensus Based" Alternative Recommendations Are Disconcerting

The PRISCUS List is a very important instrument for the evaluation of medications for elderly people (1). Such lists have an enormous standardizing effect—non-adherence will have to be supported by sound reasons in case of a dispute. This is especially so for drugs that were unequivocally categorized as "potentially inadequate medication" (PIM). We were involved in the development process of the list—and we still have concerns regarding the substances named as alternatives to the PIM. The consensus process does not always allow for sufficient discussion. The following examples of "consented" alternative recommendations, however, seem disconcerting to us:

- Melatonin is a largely ineffective substance that is barely prescribable, which is suggested as an alternative to levomepromazine and promethazine in sleep disorders. The potential for harm caused by those two substances is undisputed—pharmacological measures should not have been recommended as an alternative.
- DPP4 inhibitors are suggested as alternatives for sulfonylureas. Their potentially most severe adverse effect—hypoglycemia—is well known. Instead of suggesting a largely ineffective substance (2), the guideline conform alternative is aiming for higher targets for glycated hemoglobin in older persons.
- Potential adverse effects of tricyclic antidepressants are a problem. The suggested alternative, however—citalopram—is just as poorly tolerated (3).
- Memantine is named as an alternative to pentoxifylline and naftidrofuryl, pyritinol and piracetam,

as well as ginkgo, nicergoline, and nimodipine. Memantine is licensed with restrictions only for moderate to severe dementia—and was withdrawn from the market in France because of its lack of effectiveness (4).

We worry that healthcare provision for older people will not improve if prescribing behavior changes as a result of the PRISCUS List without satisfactory proof of benefit for the suggested alternatives.

DOI: 10.3238/arztebl.m2023.0084

References

1. Mann NK, Mathes T, Sönnichsen A, et al.: Potentially inadequate medications in the elderly: PRISCUS 2.0—first update of the PRISCUS list. Dtsch Arztebl Int 2023; 120: 3–10.
2. Palmer S, Mavridis D, Nicolucci A, et al.: Comparison of clinical outcomes and adverse events associated with glucose-lowering drugs in patients with type 2 diabetes. A meta-analysis. JAMA 2016; 316: 313–24.
3. Coupland C, Dhiman P, Morriss P, Arthur A, Hippisley-Cox J: Antidepressant use and risk of adverse outcomes in older people: population based cohort study. BMJ 2011; 343: d4551.
4. Ministère de la Santé et de la Prevention: Arrêt de prise en charge par l'Assurance maladie des médicaments dans la maladie d'Alzheimer. www.sante.gouv.fr/soins-et-maladies/medicaments/article/arret-de-prise-en-charge-par-l-assurance-maladie-des-medicaments-dans-la (last accessed on 23 January 2022).

Dr. med. Günther Egidi, Bremen, guenther.egidi@posteo.de
Prof. Dr. med. Wilhelm Niebling, Titisee-Neustadt
PD Dr. med. Guido Schmiemann, Bremen
Dr. med. Hans Wille, Bremen
Prof. Dr. med. Stefan Wilm, Düsseldorf

Conflict of interest statement
The authors declare that no conflict of interest exists.

In Reply:

Ebersbach and Warnecke point out the classification of MAO-B inhibitors as "potentially inadequate medication" (PIM) and the naming of ropinirole as an alternative. The cited study included patients with newly diagnosed Parkinson syndrome and investigated the efficacy and tolerability of levodopa, a dopamine agonist, or a MAO-B inhibitor as initial medication (1). Treatment cessation was rarest in patients treated with levodopa (2%), highly significantly less than in those treated with a dopamine agonist (28%) or a MAO-B inhibitor (23%); the difference between the latter two did not reach significance.

The FORTA classification also prefers ropinirole and rotigotine (patch) as label B(eneficial) treatment) for elderly patients over rasagiline (C-areful) and selegiline (D-on't) (2).

When comparing the adverse effect profile of ropinirole (and rotigotine) with piribedil or pramipexole we wish to mention the explanation of adverse effects in the prescribing information or Micromedex®. Piribedil and pramipexole were also labeled by experts as C in the FORTA List.

As regards amantadine in the named restricted indication we agree with our colleagues' assessment; the suggested alternatives apply for more general use and it goes without saying that they require critical evaluation in the individual case.

As regards the comments by Egidi et al, we have to clarify that in the consensus process it was unfortunately not possible to coordinate all comments and alternative suggestions. The focus was on considering potential harms, less on weighing up benefits against harms, which obviously has to be undertaken in the individual case.

We agree with our correspondents that non-pharmacological measures have to be consistently listed as alternatives for all sedatives—this is included in the longer online version of the article.

As regards the effectiveness of DPP-4 inhibitors in elderly patients, the evidence is really limited. When emphasizing their safety, the study data are actually supportive of DPP-4 inhibitors (3). The cited systematic review and resulting GRADE tables were available to the experts.

The German National Disease Management Guideline on Unipolar Depression (NDGM) also mentions the anticholinergic potential of tricyclic antidepressants as an argument for exercising restraint in elderly patients. The US Beers List classifies tricyclics because of the anticholinergic characteristics generally as "to be avoided" (4). Tricyclics and selective serotonin reuptake inhibitors similarly increase the risk of suicide, and when selecting the antidepressant the risk of falls has to be balanced against other adverse effects. Further alternatives are listed in the long version.

We understand the point in recommending memantine. Memantine as well as cholinesterase inhibitors are named in the long online version.

DOI: 10.3238/arztebl.m2023.0085

References

1. Gray R, Ives N, Rick C, et al.: Long-term effectiveness of dopamine agonists and monoamine oxidase B inhibitors compared with levodopa as initial treatment for Parkinson's disease (PD MED): a large, open-label, pragmatic randomised trial. Lancet (London, England) 2014; 384: 1196–205.
2. Pazan F, Weiss C, Wehling M: The FORTA (Fit for The Aged) list 2021: Fourth version of a validated clinical aid for improved pharmacotherapy in older adults. Drugs Aging 2022; 39: 245–7.
3. Schott G, Martinez YV, Ediriweera de Silva RE, et al.: Effectiveness and safety of dipeptidyl peptidase 4 inhibitors in the management of type 2 diabetes in older adults: a systematic review and development of recommendations to reduce inappropriate prescribing. BMC geriatrics 2017; 17: 226.
4. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel: American Geriatrics Society 2019 updated AGS Beers Criteria(R) for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2019; 67: 674–94.
5. Mann NK, Mathes T, Sönnichsen A, et al.: Potentially inadequate medications in the elderly: PRISCUS 2.0—first update of the PRISCUS list. Dtsch Arztebl Int 2023; 120: 3–10.

On behalf of the authors
Prof. Dr. med. Petra A. Thürmann
Lehrstuhl für Klinische Pharmakologie
Department für Humanmedizin
Fakultät für Gesundheit
Universität Witten/Herdecke
petra.thuermann@uni-wh.de

Conflict of interest statement
The author declares that no conflict of interest exists.