COMMENT ON SAMARA ET AL.

Metformin Use Is Associated With Slowed Cognitive Decline and Reduced Incident Dementia in Older Adults With Type 2 Diabetes: The Sydney Memory and Ageing Study. Diabetes Care 2020;43:2691–2701

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We have read with great interest the article published by Samaras et al. (1); the authors found an association of metformin use with slowed cognitive decline and lower risk of incident dementia in older adults with type 2 diabetes. In this work, the authors reported an impressive 81% risk reduction in the incidence of dementia between patients with diabetes and metformin (DM+MF) compared with the group with diabetes without metformin (DM-noMF).

We found some aspects of the study worth further discussion. First, there is high contrast in the number of medications required in the DM+MF and DM-noMF groups. In the metformin group, 50% of the subjects were taking at least one additional antidiabetic drug added to metformin. In contrast, in the DM-noMF group, 60% of the subjects were on a diet-only regimen.

Most international guidelines have metformin as foundational drug therapy in patients with type 2 diabetes (2). Why is metformin not the treatment for all of these subjects? Several reasons could explain these findings, e.g., good glycemic control with nonpharmacological therapy, poor tolerability to metformin, or contraindications to its use, such as renal impairment.

It came to our attention that renal impairment markers like microalbuminuria and estimated glomerular filtration rate (eGFR) were not evaluated, even though several works describe the relation between renal impairment and risk of dementia (3,4). Orkaby et al. (4) analyzed the data of a retrospective cohort of patients aged ≥65 years with type 2 diabetes in treatment with metformin or sulfonylureas for the last 2 years. They reported a reduction in the risk of dementia, with a difference in risk of 11% between groups, and they used eGFR as a variable in a subgroup analysis to calculate the risk of dementia and found an association between a reduced risk of dementia with an eGFR ≥60 mL/min/1.73 m^2.

Finally, we consider the findings a significant step toward in discovering possible treatments to prevent dementia and reduce the cognitive decline rate. In future works with a prospective study design, it would be interesting to add renal function markers like eGFR in the risk of dementia evaluation; this would help to lower the survival bias risk, thus improving the quality of evidence that will help the medical community to better understand this enigmatic disease.

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