https://doi.org/10.1590/1806-9282.20221037

Comment on "Alemtuzumab improves cognitive processing speed in active multiple sclerosis – a longitudinal observational study"

Elnaz Asadollahzade[1], Fereshteh Ghadiri[1], Zahra Ebadi[1], Abdorreza Naser Moghadasi[1*]

Dear Editor,

An interesting article was recently read about the effect of alemtuzumab on cognitive impairment (CI) in multiple sclerosis (MS)[1]. This brings up the question whether other highly efficacious treatments can impact CI? If the answer is positive, is it permissible to select an escalation approach?

MS is a debilitating disease of central nervous system (CNS), which is common among young adults with noticeable economic consequences on the government[2]. Due to widespread distribution of lesions, MS manifests a broad range of the symptoms. CI is one of the most critical symptoms, with prevalence rate ranging from 43 to 70%[3], embracing all types of clinical courses and disease stages[4]. The evidence suggests that neuropsychological scores are better in relapsing-remitting (RR) patients compared to secondary-progressive (SP) and primary-progressive (PP) cases[5]. Cognitive impairment is more severe in SP patients than in PP patients[6]. Unfortunately, the effect of disease-modifying therapy (DMTs) on cognition is not well known. There is less evidence that DMTs are beneficial to improve the cognition[1]. However, there is still no clear answer to this question: Do high potent DMTs significantly impact CI by slowing and stabilizing the course compared with low potent drugs? Clarification of this issue seems to make a significant change in treating MS patients.

Studies showed a link between CI and brain atrophy. Brain atrophy can be seen in the early stages of MS, which is associated with a decrease in brain volume and function. It was found that the higher the severity of cognition impairment in the patients, the higher the severity of brain atrophy[7,8]. Previously, the prevention of relapses was an important goal for treating MS patients[9]. However, this approach has changed, and improving the patients' clinical condition and remission was considered a goal in advancements of the treatments and using new drugs. Therefore, in MS, as in many diseases, such as cancer and rheumatoid arthritis, the term "no evidence of disease activity" (NEDA) is used. NEDA is used as a criterion to assess the clinical outcome of DMT[10]. Brain atrophy is known as NEDA-4 diagnostic benchmark, which can be used to diagnose better and understand the disease's activity and progression. Brain atrophy can manifest itself as CI[11]. CI can affect patients' lifestyles and social activities[12]. It seems that DMTs could alter the CI course[13].

Two approaches (escalation and induction) were used to treat MS patients[14]. In recent years, it has been shown that the induction approach to patients with high performance drugs can reduce the survival of patients in terms of side effects of the drugs because drugs with a higher risk profile are used from the beginning[15]. In contrast, an escalation is an approach that starts treating patients with low-risk, moderately effective drugs. If the patient poorly responds to this treatment, more aggressive treatments are used to reduce the risk of complications[15]. Also, the advantage of escalation approaches is to allow many patients to have a satisfying control of the disease, while receiving relatively safe drugs and never escalating to more aggressive therapy[16].

The diagnosis of MS with high accuracy along with the predictive feature is very useful because it can determine the initiation of early treatment. CI can be considered a prognostic factor for MS. Consequently, the CI value considered as a measure of exacerbation is a question that needs to be answered in future studies.

AUTHORS' CONTRIBUTIONS

EA: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, validation, visualization, writing – original draft, writing – review & editing. **FG:** Funding acquisition, methodology, writing – original draft, writing – review & editing. **ZE:** Conceptualization, data curation, formal analysis, investigation, project administration, resources, software, supervision, validation, visualization, writing – original draft. **ANM:** Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing – review & editing.

[1]Tehran University of Medical Sciences, Neuroscience Institute, Multiple Sclerosis Research Center – Tehran, Iran.
*Corresponding author: abdorrezamoghadasi@gmail.com

Conflicts of interest: the authors declare there is no conflict of interest. Funding: none.
Received on August 01, 2022. Accepted on August 25, 2022.

REFERENCES

1. Riepl E, Pfeuffer S, Ruck T, Lohmann H, Wiendl H, Meuth SG, et al. Alemtuzumab improves cognitive processing speed in active multiple sclerosis – a longitudinal observational study. Front Neurol. 2018;8:730. https://doi.org/10.3389/fneur.2017.00730
2. Barten LJ, Allington DR, Procacci KA, Rivey MP. New approaches in the management of multiple sclerosis. Drug Des Devel Ther. 2010;4:343-66. https://doi.org/10.2147/DDDT.S9331
3. Benedict RH, Cookfair D, Gavett R, Gunther M, Munschauer F, Garg N, et al., Validity of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS). J Int Neuropsychol Soc. 2006;12(4):549-58. https://doi.org/10.1017/s1355617706060723
4. Piras MR, Magnano I, Canu EDG, Paulus KS, Satta WM, Soddu A, et al. Longitudinal study of cognitive dysfunction in multiple sclerosis: neuropsychological, neuroradiological, and neurophysiological findings. J Neurol Neurosurg Psychiatry. 2003;74(7):878-85. https://doi.org/10.1136/jnnp.74.7.878
5. Huijbregts S, Kalkers NF, Sonneville LMJ, Groot V, Reuling IEW, Polman CH. Differences in cognitive impairment of relapsing remitting, secondary, and primary progressive MS. Neurology. 2004;63(2):335-39. https://doi.org/10.1212/01.wnl.0000129828.03714.90
6. Foong J, Rozewicz L, Chong WK, Thompson AJ, Miller DH, Ron MA. A comparison of neuropsychological deficits in primary and secondary progressive multiple sclerosis. J Neurol. 2000;247(2):97-101. https://doi.org/10.1007/pl00007804
7. Benedict RH, Carone DA, Bakshi R. Correlating brain atrophy with cognitive dysfunction, mood disturbances, and personality disorder in multiple sclerosis. J Neuroimaging. 2004;14(3 Supll):36S-45S. https://doi.org/10.1177/1051228404266267
8. Bonnan M, Marasescu R, Demasles S, Krim E, Barroso B. No evidence of disease activity (NEDA) in MS should include CSF biology – towards a 'disease-free status score'. Mult Scler Relat Disord. 2017;11:51-5. https://doi.org/10.1016/j.msard.2016.12.001
9. Mayssam EN, Eid C, Khoury SJ, Hannoun S. "No evidence of disease activity": is it an aspirational therapeutic goal in multiple sclerosis? Mult Scler Relat Disord. 2020;40:101935. https://doi.org/10.1016/j.msard.2020.101935
10. Pandit L. No evidence of disease activity (NEDA) in multiple sclerosis-Shifting the goal posts. Ann Indian Acad Neurol. 2019;22(3):261-3. https://doi.org/10.4103/aian.AIAN_159_19
11. Fenu G, Lorefice L, Frau F, Coghe GC, Marrosu MG, Cocco E. Induction and escalation therapies in multiple sclerosis. Antiinflamm Antiallergy Agents Med Chem. 2015;14(1):26-34. https://doi.org/10.2174/1871523014666150504122220
12. Freedman MS, Devonshire V, Duquette P, Giacomini PS, Giuliani F, Levin MC, et al. Treatment optimization in multiple sclerosis: Canadian MS Working Group recommendations. Can J Neurol Sci. 2020;47(4):437-55. https://doi.org/10.1017/cjn.2020.66
13. Landmeyer NC, Bürkner PC, Wiendl H, Ruck T, Hartung HP, Holling H, et al., Disease-modifying treatments and cognition in relapsing-remitting multiple sclerosis: a meta-analysis. Neurology. 2020;94(22):e2373-e2383. https://doi.org/10.1212/WNL.0000000000009522
14. Sumowski JF, Benedict R, Enzinger C, Filippi M, Geurts JJ, Hamalainen P, et al., Cognition in multiple sclerosis: state of the field and priorities for the future. Neurology. 2018;90(6):278-88. https://doi.org/10.1212/WNL.0000000000004977
15. Harding K, Williams O, Willis M, Hrastelj J, Rimmer A, Joseph F, et al. Clinical outcomes of escalation vs early intensive disease-modifying therapy in patients with multiple sclerosis. JAMA Neurol. 2019;76(5):536-41. https://doi.org/10.1001/jamaneurol.2018.4905
16. Le Page E, Edan G. Induction or escalation therapy for patients with multiple sclerosis? Rev Neurol (Paris). 2018;174(6):449-57. https://doi.org/10.1016/j.neurol.2018.04.004