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Letter to the Editor

Aducanumab: A Novel Drug for Alzheimer's Disease; Future Challenges in Treatment

Running Title: Aducanumab: A Novel Drug for Alzheimer's Disease

Reza Bidaki[1], Yekta Rameshi[2], Farahnaz Hoseinzade[3], Fatemeh Saghafi[4*]

[1]Professor, Research Center of Addiction and Behavioral Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[2]Student Research Committee, School of Pharmacy, Shahid Sadoughi University of Medical Science, Yazd, Iran.
[3]Student Research Committee, School of Pharmacy, Isfahan University of Medical Science, Yazd, Iran.
[4]Assistant Professor of Pharmacotherapy, Department of Clinical Pharmacy, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

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Corresponding author
Shahid Sadoughi University of Medical Sciences, Department of Clinical Pharmacy, Faculty of Pharmacy, Shohadaye gomnam Blvd., Yazd Province, Yazd, Iran.
Tel: +98- 9132733898
E-mail
saghafi.fa@gmail.com,
f.saghafi@ssu.ac.ir

Dear Editor

Alzheimer's disease (AD) is a common frustrating disease among older adults. It imposes a high economic and medical burden on society and families. Although Alzheimer's disease is a progressively disabling psychiatric-neurological disorder, and there is no effective drug stopping or delaying the disease process over the last decade, lots of research has been done on some antibodies against amyloid plaques, which are the main etiology of this disease (1). By June 2021, Aducanumab (Aduhelm®) was approved by the Food and Drug Administration (FDA); it was demonstrated that this drug could be an effective intervention to prevent and remove the formation of amyloid plaques (2). Because of the lack of extensive research on this drug, many physicians and patients are concerned about its efficacy and side effects. However, many Alzheimer's specialists are satisfied with the approval of this drug.

Keywords: Alzheimer's disease, Aducanumab, Amyloid-β

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Amyloid-β has a crucial role in the pathogenesis of Alzheimer's disease. Various studies based on genetics and biomarkers showed that amyloid-β is involved in either familial (early-onset) or sporadic (late-onset) Alzheimer's (3). Acute and chronic exposure to the amyloid-β can cause neurotoxicity leading to neurodegeneration; this is because of the formation of soluble amyloid oligomers, and amyloid-β misfolding monomers that can be aggregate (3-5).

Aducanumab is a monoclonal antibody that binds to the amyloid-β complex with a high affinity and causes the receptor-mediated phagocytosis Fc (fragment crystallizable) region to be removed; while it has less affinity to monomers (6, 7).

Based on physician prescription, Aducanumab is administered intravenously every four weeks to an Alzheimer's patient. However the question is whether accurate indications for the patients should be considered. This is important that this drug can not be injected to every Alzheimer's patient. Aducanumab was approved in collaboration with the American company (Biogen) and a Japanese company (Eisai) (8).

In the early stages of AD, it can be effective. Due to concern about adverse effects such as bleeding and brain edema, Aducanumab is not recommended in moderate to severe Alzheimer's disease. It is given as an intravenous (IV) infusion every four weeks for at least 21 days in the patients with mild cognitive impairment or mild dementia (9). Mild adverse effects such as headache, dizziness, and nausea have also been reported. Patients have to be injected intravenously every four weeks over the lifelong, but the cost of treatment seems to be high. It should be noted that the current ineffective drugs that are administered for Alzheimer's disease are also very costly.

Assessing the challenges of aducanumab treatment is as followed:

1. Is this drug accessible and affordable to everyone?
2. given that aducanumab is a new antibody-based drug, could it have serious adverse effects?
3. Do patients benefit enough from this drug? Are the people experiencing the early stages of AD and have not reached the end stages benefit?
4. What are the indications for prescribing it?
5. Could a better drug be designed and marketed?
6. Can the patients with other forms of dementia rather than AD (vascular dementia, traumatic dementia, parkinsonism) benefit from this drug?
7. Should treatment be continued with conventional Alzheimer's drugs (cholinesterase inhibitors)?
8. Is it necessary to change the dose?
9. How about interactions?

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