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Author for correspondence:

Mohammad Aamir Qayyum Sarguroh Khan

e-mail:

sargurohaamir01@gmail.com

EFFECTIVENESS OF MEMANTINE IN ALZHEIMER'S DISEASE

Mohammad Aamir Qayyum Sarguroh Khan[1]

[1] Ivane Javakishvili Tbilisi State University

Abstract

Background: Alzheimer's disease (AD) is a widespread neurodegenerative disorder, causing cognitive decline and memory impairment. It affects millions globally, posing significant challenges to patients and healthcare systems. This review aims to assess the effectiveness of two commonly prescribed medications, memantine (an NMDAR blocker) and donepezil (a cholinesterase inhibitor), in managing AD.

Methodology: The review encompasses clinical trials and comparative analyses, scrutinizing the benefits and limitations of memantine and donepezil. Studies considered cognitive and functional outcomes, providing insights into the therapeutic effects of these medications. Additionally, the analysis explores the potential synergistic effects of combining memantine and donepezil, shedding light on their combined efficacy.

Result: Both memantine and donepezil demonstrate efficacy in improving cognitive and functional aspects in AD patients. However, the review indicates that the combination therapy of these drugs does not exhibit superior efficacy compared to individual use. Long-term effects and adverse reactions necessitate further investigation, especially with the introduction of newer treatments like monoclonal antibodies, which adds complexity to the landscape of AD management.

Conclusion: Informed decisions regarding the usage of memantine and donepezil in AD treatment should carefully weigh potential benefits against risks for individual patients. The review emphasizes the need for continuous research to explore both existing and evolving therapies, aiming to enhance the quality of life for those affected by this devastating disease. As treatment options evolve, maintaining an updated understanding of the landscape is crucial for healthcare practitioners and researchers alike.

INTRODUCTION

Alzheimer's disease (AD) is a type of dementia that affects the brain regions in charge of memory, language, and thought. We see a gradual decline in cognitive capacity that can begin with mild memory impairment and progress to the point where the person may become unable to respond to their environment and communicate effectively, which can have a major impact on their everyday activities. [1]

Approximately 5.8 million Americans suffers from AD as of 2020.2 This condition is more common in older people, with cases doubling every five years over 65 years of age. It is unusual,but AD can also strike younger people. Alzheimer's disease is more likely to develop as one age, and symptoms typically appear after the age of 601. It is anticipated that by2060, the number of people afflicted by the illness will have nearly tripled to 14 million. [2]

The buildup of oligomeric amyloid-beta peptide causes synaptic dysfunction, which is the defining feature of AD. Spine elimination and synaptic depression reliant on NMDAR are the results of this accumulation. Memantine is a low-affinity NMDAR channel blocker that is frequently administered to treat moderate-to-severe AD.[3]

The neurotransmitter acetylcholine, which is secreted by cholinergic neurons, plays an important role in signal transduction associated with learning and memory. The cholinergic hypothesis, whichwas one of the first theories about the development of AD, suggests that the disease is associated with the deterioration of cholinergic neurons, leading to cognitive decline and atrophy. [4] Due to this reason, we use cholinesterase inhibitors which increases communication between nerve cell that helps in improving the symptoms of AD. In this reviewwe will learn about the effectiveness of NMDAR blocker (Memantine) and cholinesterase inhibitor (Donepezil) in reducing the clinical deterioration of patient suffering from AD.

Memantine In Alzheimer's Disease

Alzheimer's disease (AD) is an advancing and debilitating neurodegenerative disease that affects millions of people around the globe. Currently, there is no cure for AD, and available treatmentsprovide limited symptomatic relief. AD is the major reason of dementia, affecting 55 million individuals all over the world. Therefore, there is an urgent need to find effective treatments that can slow or halt disease progression and improve patient outcomes. This research on the effectiveness ofdrugs (Memantine & Donepezil) in treating AD is important for developing new therapies that canimprove patient outcomes and quality of life; by identifying the most effective drugs or combinations of drugs, clinicians could offer patients a more tailored treatment approach that could slow disease progression and improve symptoms. Moreover, research in this area could contribute to a better understanding of the underlying mechanisms of AD and potentially lead to earlier detection and intervention for the disease

The prospective, randomized, clinical trial, conducted by Bago Rožanković P, Rožanković M, et al. was aimed to assess the effectiveness of donepezil and memantine in treating behavioral and psychological symptoms of dementia (BPSD) in patients with moderate AD. It was a six-month randomized clinical trial which included 85 individuals divided into two groupsreceiving either donepezil or memantine. [5]

The study conducted by Modrego PJ, Fayed N, et al., was a rater-blinded, randomized trial, aiming to compare the effectiveness of memantine and donepezil, for early-phase AD. The study aims to examine if memantine induces alterations in brain metabolite concentrations in comparison to donepezil. 63 patients diagnosed with probable mild to moderate AD were randomly assigned to receive either donepezil or memantine for a duration of 6 months. Following a period of 6 months, clinical scales and metabolite levels were evaluated in various brain regions, such as the temporal, pre-frontal, posterior cingulated, and occipital areas.6

Another study was conducted to check efficacy of memantine, donepezil as monotherapy and also dual therapy. It was done by Howard R, McShane R, Lindesay J, et al., a clinical trial to determine if the benefits of treatment persist after Alzheimer's disease progresses from mild-to-moderate to moderate-to-severe. There were 295 patients in total with moderate-to-severe AD who were being treated with donepezil for at least than 3 months. They were assigned to either continue donepezil, discontinue it, or discontinue donepezil but start memantine, or continue donepezil along with memantine. Individuals received the study treatment for 52 weeks.[7]

Howard R, McShane R, Lindesay J, et al.'s research delves into the outcomes of the DOMINO-AD trial, examining the impact of memantine and donepezil on those suffering from moderate to severe AD. In order to determine the impact of continuing or discontinuing donepezil and initiating memantine on the need for nursing home placement in patients with moderate-to-severe AD, this randomised study used a double-blind, placebo-controlled design.

People living in the community who had moderate-to-severe AD were included in the research. For at least three months, these patients had been taking donepezil at a dosage of 10 mg every day; over the past six weeks, they had been taking the same amount. Furthermore, their results on the Standardised Mini-Mental State Examination ranged from 5 to 13. Fifteen secondary care memory centres in Scotland and England were used to find participants. Then, they were randomly assigned to one of four groups: continuing to take 10 mg of donepezil without memantine daily; stopping donepezil without memantine; stopping donepezil and beginning to take 20 mg of memantine daily; or continuing to take 10 mg of donepezil daily and beginning to take 20 mg of memantine daily. The course of this therapy was adhered to for 52 weeks. Following 52 weeks, the participants and their doctors were given the opportunity to choose their course of treatment. [8]

A study led by Hu HT, Zhang ZX, et al. used a randomised controlled trial spread across six centres in two Chinese cities to assess the clinical effectiveness and safety of akatinol memantine in the treatment of patients with mild to severe AD. Two groups, one for donepezil and the other for akatinol memantine, were randomly assigned to 100 patients. Various scales were used to evaluate the patients' behavior, mood, daily activities, and cognitive function. Every four weeks, a safety evaluation was carried out. [9]

A study conducted by Matsunaga S, Kishi T, Nomura I, et al. presents a risk-benefit assessment of five pharmacotherapeutic choices for managing AD: Memantine, along with 3 cholinesterase inhibitors - donepezil, galantamine, and rivastigmine - as well as combination therapy that include memantine and one cholinesterase inhibitor. The selection of the most effective treatment method depends on evidence obtained from systematic reviews and meta-analyses of RCTs. [10]

METHODOLOGY

In our methodology, we selected peer-reviewed studies from sources like PubMed and Google Scholar, focusing on memantine and donepezil's effectiveness in treating Alzheimer's disease (AD). Inclusion criteria comprised studies published in English that assessed the impact of these medications on AD. We conducted a systematic search using relevant keywords, and reviewers screened and extracted data from eligible studies. Data items included study design, sample size, interventions, outcome measures, and results. We assessed study quality using appropriate tools such as the Cochrane risk of bias tool. Ethical approval was not necessary as no primary data collection involving human participants was conducted.

RESULTS

The clinical trial conducted by Bago Rožanković P, Rožanković M, et al. resulted in both treatments leading to major improvement in all the Neuropsychiatric Inventory (NPI) domains except for euphoria and apathy, which did not improve with memantine treatment. The study found that both donepezil and memantine were well tolerated, and that specific drugs for AD, including these two, can effectively alleviate BPSD in patients with moderate AD while maintaining an acceptable safety profile.[5]

The study conducted by Modrego PJ, Fayed N, et al., results showed no major differences in clinical scales and metabolite levels between the two groups. However, changes in the N-acetyl-aspartate/creatine ratio in the posterior cingulated region were found to correlate significantly with changes in the Alzheimer's Disease Assessment Scale-cognitive part. Overall, the study concluded that donepezil and memantine have similar modest clinical and spectroscopic effects on mild to moderate AD, and that magnetic resonance spectroscopy may be useful for monitoring disease progression.[6]

In a clinical trial led by Howard R, McShane R, Lindesay J, et al., it was discovered that when patients with moderate to severe AD continued to receive donepezil for a full year, the benefits to their cognitive and functional abilities exceeded the minimal clinically significant difference. When one medication was present or absent, donepezil and memantine's efficacy did not change meaningfully. Compared to donepezil or memantine alone, there were no appreciable advantages to using the combination of the two medications. 7

Howard R, McShane R, Lindesay J, et al. conducted a study which revealed that discontinuing the use of donepezil raised the likelihood of being placed in a nursing home within the initial year of treatment, but had no impact in the subsequent three years of observation. The authors propose that decisions about the cessation or continuation of donepezil medication should take into account the potential dangers associated with withdrawal, especially in cases where the perceived advantages of ongoing treatment are uncertain. [8]

Hu HT, Zhang ZX, et al. observed that on the eighth and sixteenth weeks relative to baseline, both groups showed significant improvements in cognition and everyday activities, behaviour, and mood. However, neither the seriousness of dementia as determined by the GDS nor the change in the fundamental habit of life as measured by the Blessed-Roth scale's Part II showed any improvement. According to the study's findings, akatinol memantine, like donepezil, is a safe and efficient medication that can significantly enhance the behaviour, mood, and cognitive function of AD patients. Of the akatinol memantine group, 6% experienced mild and transitory adverse effects. [9]

According to the review conducted by Matsunaga S, Kishi T, Nomura I, et al., memantine is more effective than a placebo at improving cognitive functions and behavioral problems, and it is also well-tolerated. For Alzheimer's disease, combination therapy using donepezil and memantine is the most effective treatment.10 But in our review, we find that single therapy is more effective compared to combination.

DISCUSSION

The reviewed articles provided valuable insights into the safety and effectiveness of medications used to treat AD, specifically memantine and donepezil.

It is noteworthy that the treatment's long-term advantages and drawbacks with memantine and donepezil have not been fully investigated and require further research. Additionally, there are new treatments for AD that involve monoclonal antibodies (such as Lecanemab and Aducanumab) that also require investigation and comparison to the efficacy of memantine and donepezil.

Overall, the studies emphasize the importance of informed decision-making regarding the usage of memantine and donepezil for the treatment of AD, taking into account potential risks and benefits for individual patients. They also highlight the need for continued research into both existing and emerging treatments for AD to improve patient outcomes and quality of life.

CONCLUSION

The studies indicate that both Memantine and donepezil have been proven to be equally effective in providing cognitive and functional benefits for patients with AD. However, the studies also show that dual therapy with both is not as effective as monotherapy with either drug.

DECLARATION

Ethical Statement

The research conducted in this study has received approval from the Institutional Review Board/Ethics Committee at Ivane Javakhishvili Tbilisi State University. All procedures performed in this study involving human participants were in accordance with the ethical standards of Ivane Javakhishvili Tbilisi State University and with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards.

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Conflicts of Interest

The authors maintain that there are no conflicts of interest related to this research. Neither financial nor non-financial competing interests are present.

Data Availability

The data supporting the findings of this study are comprehensively presented within the article and its supplementary materials. For any additional data, interested parties may request access, and such requests will be considered.

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REFERENCES

(1). Matthews KA, Xu W, Gaglioti AH, et al. Racial and ethnic estimates of Alzheimer's disease and related dementias in the United States (2015-2060) in adults aged ≥65 years. Alzheimers Dement. 2019;15(1):17-24. doi: 10.1016/j.jalz.2018.06.3063

(2).https://www.cdc.gov/aging/aginginfo/alzheimers.htm#:~:text=Younger%20people%20may%20get%20Alzheimer's,14%20million%20people%20by%202060.&text=Symptoms%20of%20the%20disease%20can,the%20risk%20increases%20with%20age

(3).Liu J, Chang L, Song Y, Li H, Wu Y. The Role of NMDA Receptors in Alzheimer's Disease. Front Neurosci. 2019; 13:43. Published 2019 Feb 8. doi:10.3389/fnins.2019.00043

(4).Chen ZR, Huang JB, Yang SL, Hong FF. Role of Cholinergic Signaling in Alzheimer's Disease. Molecules. 2022;27(6):1816. Published 2022 Mar 10. doi:10.3390/molecules27061816.

(5). Bago Rožanković P, Rožanković M, Badžak J, Stojić M, Šušak Sporiš I. Impact of Donepezil and Memantine on Behavioral and Psychological Symptoms of Alzheimer's Disease: Six-month Open-label Study. Cogn Behav Neurol. 2021;34(4):288-294. Published 2021 Dec 2. doi:10.1097/WNN.0000000000000285

(6). Modrego PJ, Fayed N, Errea JM, Rios C, Pina MA, Sarasa M. Memantine versus donepezil in mild to moderate Alzheimer's disease: a randomized trial with magnetic resonance spectroscopy. Eur J Neurol. 2010;17(3):405-412. doi:10.1111/j.1468-1331.2009. 02816.x

(7). Howard R, McShane R, Lindesay J, et al. Donepezil and memantine for moderate-to-severe Alzheimer's disease. N Engl J Med. 2012;366(10):893-903. doi:10.1056/NEJMoa1106668

(8). Howard R, McShane R, Lindesay J, et al. Nursing home placement in the Donepezil and Memantine in Moderate to Severe Alzheimer's Disease (DOMINO-AD) trial: secondary and post-hoc analyses. Lancet Neurol. 2015;14(12):1171-1181. doi:10.1016/S1474-4422(15)00258-6

(9). Hu HT, Zhang ZX, Yao JL, et al. Zhonghua Nei Ke Za Zhi. 2006;45(4):277-280.\

(10). Matsunaga S, Kishi T, Nomura I, et al. The efficacy and safety of memantine for the treatment of Alzheimer's disease. Expert Opin Drug Saf. 2018;17(10):1053-1061. doi:10.1080/14740338.2018.1524870