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Effect of Combination Therapies on Alzheimer's Disease

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Abstract

Background:

Alzheimer's disease (AD) is a gradually advancing form of dementia that impacts 24 million individuals globally. Recent research has identified numerous novel multi-target medications aimed at improving Alzheimer's disease symptoms to enhance patients' quality of life. This study aims to investigate the effect of combination therapies on Alzheimer's disease.

Method

A retrospective observational study analyzed the impacts of combination therapy vs standard therapy in patients with mild-to-moderate Alzheimer's disease. The patients were categorized into three groups: a control group receiving standard Cholinesterase inhibitors (ChEIs), a drug-drug combination group receiving ChEIs with Memantine, and a drug-lifestyle intervention group receiving ChEIs alongside lifestyle adjustments. The study comprised 67 patients diagnosed with AD, extracted from medical information from January 2023 to January 2024.

Results

Quality of life markers diminished in the control group by 1% to 3%, whereas the second and third groups had an increase. The MIMNI Mental Scale B index declined by 1% to 3% in the control group, whereas the Katz ADL Scale B index diminished by 2% to 5% in the second group, and the Barthel Index fell by 3% to 5% in the control group. The Dementia Behavior Scale declined by 2% to 5% in the control group, whereas the second and third groups experienced an increase. The control group experienced a decline in medical examinations by 1% to 4%, but the second and third groups observed an increase.

Conclusion

Combination therapy either in drug-drug group or drug-lifestyle group showed significant improvement in the scores of each used scale indicating that combination therapy is more effective than single therapy in management of AD. Drug-lifestyle group showed significant improvement over the drug-drug group.

Keywords: *Dementia, Alzheimer's disease, drug-drug combination therapy, drug-lifestyle combination treatment.*

Introduction

Alzheimer's disease (AD) is a slowly progressing dementia that is known to affect 24 million people

in the world (Tahami et al., 2022). In AD patients, depositions known as amyloid plaques, formed by an aggregation of β-amyloid peptides and hyperphosphorylation of tau proteins, contribute to neurodegeneration starting from the hippocampus and involving surrounding cortical regions in the advanced stages of the disease (Parhizkar & Holtzman, 2022) Correlating progression in histopathological findings, AD patients begin with mild cognitive impairment (MCI), continue with diverse clinical symptoms during the intermediate stage, and finally end up losing their lives. (Porsteinsson et al., 2021). Current clinical treatments are developed as anti-acetylcholinesterase inhibitors, N-methyl-D-aspartate receptor competitive antagonists, tau aggregation suppressors, or multi-target acting drugs (Martins et al., 2020). These drugs provide essentially palliation rather than prevention of AD symptoms, along with several side effects that enforce discontinuation of the treatments (Sexton et al., 2021).

The underlying weakness of single-target acting therapies leads AD researchers to combination treatments by using compounds acting at various targets (Albertini et al., 2021). Recent studies have discovered many new potential multi-target acting drugs for better ameliorating AD symptoms in order to enhance patients' quality of life (Cheong et al., 2022). The common point of the selected compounds is their potential to interfere in either AD's amyloid or tau cascades and also in the co-occurrences/metabolic pathways of these (Perluigi et al., 2024). However, searching by these methods, the possible synergetic toxic effects of the combinations are not evaluable (Ianevski et al., 2022). On the other hand, AD patients' senescence condition brings along secondary diseases, metabolic defects, and comorbidity issues (Ostolaza et al., 2021).

Over the past few years, researchers claimed that Alzheimer's disease will trigger social and economic disaster if breakthrough therapies against the disease cannot be developed. The only relief for patients and caregivers is early detection if there is no possibility of a cure (Karlawish, 2021). So far, no drugs have been shown to stop or delay its progression. Only a few drugs have been proven to slow down its progression but lose their effectiveness within months (Shi et al., 2022). Therefore, efficient therapeutic and preventive approaches to the disease are desperately necessary (Low et al., 2020). These drugs reduce not only Aβ but also other Aβ assemblies like oligomers (Du et al., 2021). A significant increase in Aβ oligomers correlates with an earlier onset of Alzheimer's disease. Moreover, a visible decrease in oligomers over time is a hallmark of compounds with therapeutic potential (Hector & Brouillette, 2021).

The NMDA receptor, a subtype of the glutamate receptor, has been the topic of intensive research in connection to the treatment of AD (Babaei, 2021). It is thought to be involved in memory processes. There are differences in the effects of NMDA receptor antagonists: one may cause similar side effects to those of another; conversely, another antagonist may mediate cognition with an improved cognitive profile (Rogasch et al., 2020). Mediation occurring via the glycine co-agonistic site may also have clinical effects. NMDA receptor antagonists act as anesthetics; extracellular-release inhibitors and non-selective ion channel blockers. (Boullerne et al.2020) They can also act as neuroprotective agents against damage by over-excitation of glutamate. (Albrakati, 2023) NMDA receptor antagonists can also block long-term potentiation and are believed to be important in the disruption of memory seen in schizophrenia and high doses of another substance (Kikuchi, 2020). This role in long-term potentiation forms much of the foundation for the NMDA receptor's role in the pathophysiology and treatment of AD (Yang et al., 2023).

The impetus for combination therapies comes from the multifactorial nature of Alzheimer's disease (Kabir et al., 2020). In addition to the peptide aggregates such as insoluble amyloid line deposits,

soluble oligomeric intermediates and increased soluble secreted amyloid precursor protein fragments appear to contribute to the disease (Hector & Brouillette, 2021). Several other components, including oxidative stress, inflammation and excitotoxicity as well as altered cellular processes mediated by GSK3β, are likely to be involved (Kandezi et al., 2020). In addition, genetic risk factors and feedback inhibition mechanisms from cleavage of amyloid precursor protein to amyloid formations further complicate the disease (Hampel et al., 2021). In light of this complexity, it is unlikely that a single monotherapeutic agent will be sufficient to treat the disease, especially in the later stages. The widespread marketing of Alzheimer's disease was also hindered by recent failures in large clinical trials of monotherapy using the single target approach for drugs already in existence (Pardo-Moreno et al., 2022).

Material and method

Study design

Retrospective observational study was conducted to compare the effect of two types of combined therapy with the traditional therapy. The study groups were divided to 3 groups as follow:

- The first group was “Control group” in which the patients were on the traditional Cholinesterase inhibitors (ChEIs) (Marucci, G., et al., 2021).
- The second group was” Drug-Drug” combination group” in which the patients were on a combination of ChEI with Memantine. This combination is often used as a main treatment for moderate to severe Alzheimer's disease. It combines the benefits of both medications (Knorz, A. L., & Quante, A., 2022).
- The third group was “Drug-lifestyle interventions” in which patients were on the combination of drug (ChEIs) and life style. The life style modification adopted was regular program of physical activity (Iso-Markku, P., et al., 2022), healthy diet rich with whole grains, healthy fats, fruits and vegetables (Kępka, A., et al., 2022). In addition, to involving patients in cognitive activities (Xiang, C., & Zhang, Y. (2024) to maintain cognitive function such as puzzles, games, and learning new skills. Finally involving patients in social engagement.

Patients

The study population will consist of 67 patients diagnosed with mild-to-moderate Alzheimer's disease (AD) according to the “National Institute on Aging-Alzheimer's Association” (NIA-AA) criteria. Patients were selected from the medical records of KFU (polyclinic complex)over the period from January 2023 to January 2024 according to the following inclusion and exclusion criteria:

Inclusion Criteria:

- Patients diagnosed with mild-to-moderate Alzheimer's disease (AD) by the (NIA-AA) criteria
- Individuals aged 65 years or older.
- Patients with a recorded history of undergoing combination therapy, encompassing drug-drug or drug-lifestyle interventions.
- Comprehensive medical records, encompassing complete information on pharmacological treatments, lifestyle alterations, and clinical evaluations.

Exclusion criteria

- Individuals with advanced Alzheimer's disease who cannot engage in clinical evaluations or furnish dependable information.

- Individuals diagnosed with alternative neurodegenerative conditions, including Parkinson's disease or frontotemporal dementia.
- Patients have substantial medical comorbidities that may obscure the study outcomes (e.g., serious cardiovascular disease, uncontrolled diabetes).
- Individuals have a background of substance misuse that may disrupt cognitive function or compliance with therapy.
- Patients possessing incomplete or absent medical records that hinder precise data extraction.

Patient information were gathered from electronic health records and medical charts, encompassing demographic details, clinical traits, treatment backgrounds, and lifestyle changes. The demographic information encompassed age, gender, educational background, AD diagnosis, the extent of cognitive impairment, existing health conditions, treatment history, and any dietary modifications. The treatment history encompassed details about medication. Lifestyle changes was gathered from medical records, conversations with patients.

Outcomes

The following scales were used to assess the outcomes of each intervention based on the available data in the medical records. Medical examinations, Daily Activities Performance Scale%, MIMN Mental Scale%, Quality of Life Scale%.

Data analysis

Descriptive statistics were used to outline the study population, focusing on aspects such as average age, gender distribution, and initial cognitive abilities. The relationship between combination therapy and clinical outcomes will be evaluated using suitable statistical methods.

Results:

Table (1) delineates the demographic characteristics of the three groups: the control group comprised 20 members, the second group included 25 members, and the third group consisted of 22 members, totaling 67 individuals, with less than 60% of the first group's ages represented. Fifteen In the second group, the percentage was 20%, while in the third group, it was 22% and 73%. The proportion of individuals aged 60 to 70 years in the first group was 75%, whereas in the second group, it was 56%. The third group recorded a percentage of 68%. In the initial group, individuals aged above 70 years were included. Ten percent. The above data indicates that females constitute 45% and males comprise 55% of the entire patient population, which amounts to 67 individuals.

Table1: Demographic characteristics of the three groups.

All participants	***n (67)***					
Demographic characteristics	***control group (N=20)***	***%***	***Drug-drug combinations (N=25)***	***%***	***Drug-lifestyle interventions (N=22)***	***%***
gender						
male	***11***	***55.00%***	***13***	***52.00%***	***12***	***54.55%***

female	***9***	***45.00%***	***12***	***48.00%***	***10***	***45.45%***
age						
less than < 60 years	***3***	***15.00%***	***5***	***20.00%***	***5***	***22.73%***
between 60:70 years	***15***	***75%***	***14***	***56%***	***15***	***68%***
more than >70	***2***	***10.00%***	***6***	***24.00%***	***2***	***9.09%***

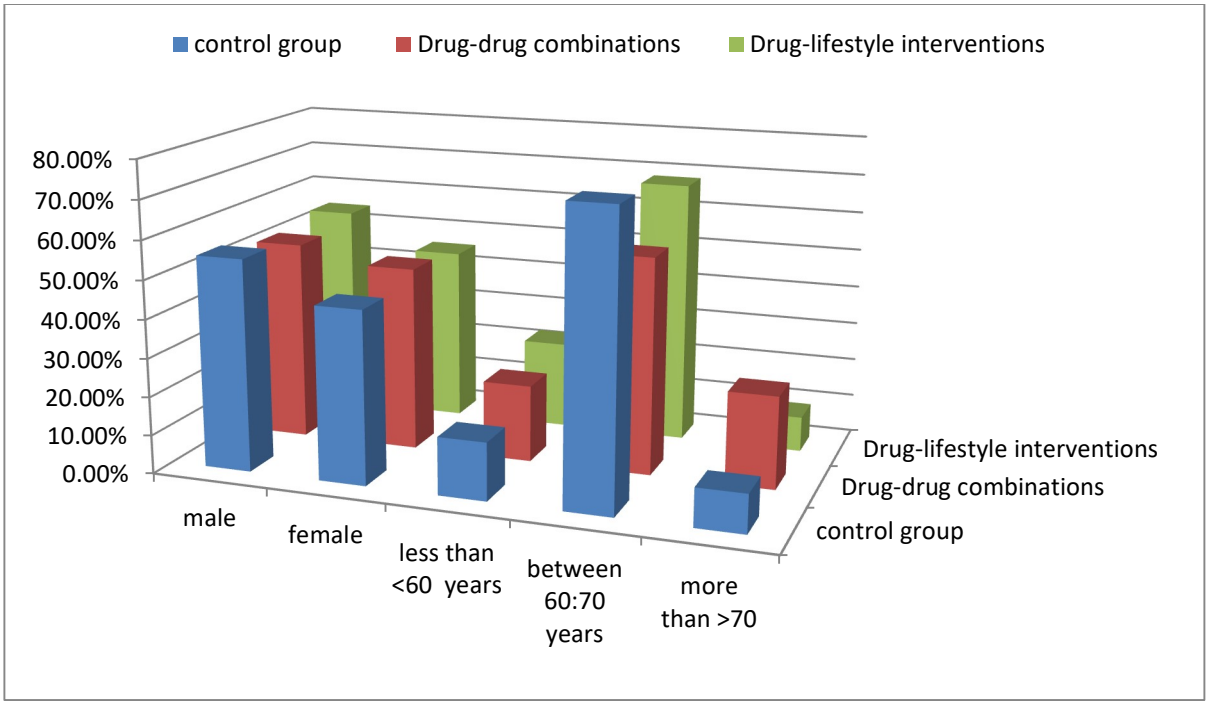

Figure 1: Comparison of the three groups in terms of demographic characteristics.

Figure 1, presented earlier, illustrates a comparison of the demographic characteristics among the control group, the second group, and the third group. The data indicates that the proportion of patients aged 60 to 70 years was 70% in the first group, 56% in the second group, and 68% in the third group, signifying that this age demographic constitutes the largest segment across all three groups, totaling approximately 72% of the overall patient population. The figure clearly indicates that the proportion of males in the three groups exceeds that of females, with the first group having a male percentage 10% higher than that of females, the second group 4% higher, and the third group 11% higher.

Table 2: Basic characteristics and indicators of the three groups.

	Characteristics	***control group (N=20)***	***GROUP-Drug-drug Combinations (N=25)***	***Drug-lifestyle Interventions (N=22)***	***f***	****P -value***
PRE	***Demographic characteristics***					
	age (year)	*66.6± 5.8*	*67.3 ± 6.1*	*68.9 ±6.6*	*14.3*	*0.02*
	male %	*55%*	*52%*	*56%*	*15.2*	*0.0025*
	female%	*45%*	*48%*	*44%*	*23.3*	*0.001*
	Medical examinations					
	MRI%	*61.1± 6.1*	*59.2 ± 5.8*	*60.3 ±6.3*	*24.2*	*<0.001*
	brain damage	*54.2 ± 6.2*	*49.3 ± 6.1*	*54.2 ±6.6*	*23.6*	*<0.001*
	PET	*52.12 ±6.2*	*50.4 ± 6.1*	*48.9 ±4.6*	*33.2*	*<0.001*
	Dementia Behaviour Scale%					
	THB	*58.0 ± 5.7*	*60.0 ± 5.8*	*52.8 ± 3.9*	*23.5*	*<0.001*
	IBE	*60.35 ± 6.5*	*60.95 ± 5.5*	*60.3± 3.5*	*12.5*	*0.02*
	Response	*54.2 ±9.2*	*60.2±5.4*	*50.02 ±4.65*	*22.5*	*<0.001*
	Difficult situations	*91.1±6.1*	*66.3 ±4.8*	*66.4 ±4.88*	*31.2*	*<0.001*
	Daily Activities Performance Scale%					
	Katz ADL Scale)	*80 ±5.1*	*70.2 ±4.8*	*67.7 ±3.88*	*33.2*	*<0.001*
	(Barthel Shows the ratio of females to males overall. Index).	*81 ± 4.2*	*83.3 ±4.78*	*83.5 ± 4.33*	*24.8*	*<0.001*
	MIMN Mental Scale%					
	Temporal and spatial orientation	*30.1 ± 4.9*	*28.2± 4.8*	*26.8 ± 2.9*	*33.2*	*<0.001*
	Short-term memory	*34.1 ± 4.5*	*32.8 ± 4.5*	*29.8± 3.5*	*21.3*	*0.02*
	Attention and concentration	*33.2 ±3.9*	*31.5±4.68*	*29.8 ±3.65*	*24.6*	*<0.001*

	Arithmetic	*31.1 ±3.88*	*30 ±3.88*	*28.8±3.88*	*23.3*	*<0.001*
	Language	*39.1 ± 3.24*	*37.6 ± 3.6*	*35.8 ± 3.33*	*23.5*	*<0.001*
	Quality of Life Scale%					
	Visuospatial ability:	*31.1 ± 3.9*	*52.2 ± 3.8*	*58.8 ± 3.9*	*26.2*	*<0.001*
	SF-36	*54.02 ± 4.5*	*66.4 ± 3.5*	*66.6± 4.5*	*11.3*	*0.02*
	CIBIC-Plus	*60.1±4.92*	*66±3.68*	*60.02 ±3.65*	*31.1*	*<0.001*
	uroQol-5D	*54.2 ±4.88*	*52.2 ±3.88*	*50.02 ±3.88*	*22.2*	*<0.001*
	Katz ADL Scale	*66± 5.3*	*66.6 ± 4.6*	*66.6 ± 4.33*	*24.3*	*<0.001*
POST	***Medical examinations***					
	MRI%	*62.2± 6.1*	*63.3 ± 4.3*	*66.5 ±5.38*	*24.2*	*<0.001*
	brain damage	*55.2 ± 6.2*	*55.3 ± 5.1*	*60.2 ±5.6*	*23.6*	*<0.001*
	PET	*53.12 ±6.3*	*54.4 ± 5.51*	*55.8 ±4.62*	*33.2*	*<0.001*
	Dementia Behaviour Scale%					
	THB	*58.0 ± 5.7*	*63.0 ± 4.6*	*60.8 ± 4.1*	*23.5*	*<0.001*
	IBE	*60.35 ± 6.5*	*66.95 ± 5.1*	*63.3± 36*	*12.5*	*0.02*
	Response	*55.2 ±8.2*	*64.2±5.02*	*56.02 ±4.36*	*22.5*	*<0.001*
	Difficult situations	*92.1±5..88*	*69.3 ±4.25*	*69.4 ±4.3*	*31.2*	*<0.001*
	Daily Activities Performance Scale%					
	Katz ADL Scale)	*76.2 ±6.1*	*76.2.2 ±4.8*	*75.7 ±3.16*	*33.2*	*<0.001*
	(Barthel Index).	*75.8 ± 6.2*	*86.3 ±4.25*	*86.5 ± 4.43*	*24.8*	*<0.001*
	MIMNI Mental Scale%					
	Temporal and spatial orientation	*30.1 ± 4.9*	*32.1± 4.8*	*31.0 ± 3.1*	*33.2*	*<0.001*
	Short-term memory	*35.1 ± 4.6*	*36.8 ± 4.2*	*35.5± 3.5*	*21.3*	*0.02*
	Attention and concentration	*33.6 ±4.6*	*33.3±4.04*	*31.1 ±3.65*	*24.6*	*<0.001*
	Arithmetic	*31.8±3.6*	*32.2 ±3.80*	*32.8±2.88*	*23.3*	*<0.001*
	Language	*38.1 ± 3.24*	*39.6 ± 3.6*	*40.8 ± 4.33*	*23.5*	*<0.001*
	Quality of Life Scale%					
	Visuospatial ability:	*30.1 ± 3.6*	*54.3 ± 2.9*	*58.8 ± 3.9*	*26.2*	*<0.001*
	SF-36	*52.02 ± 4.5*	*67.4 ± 3.6*	*67.6± 4.54*	*11.3*	*0.02*

	CIBIC-Plus	*59.5*	*66.6±4.62*	*63.2.02 ±3.65*	*31.1*	*<0.001*
	uroQol-5D	*52.23 ±4.82*	*55.2 ±3.85*	*53.02 ±3.62*	*22.2*	*<0.001*
	Katz ADL Scale	*60± 5.24*	*67.6 ± 4.2*	*68.6 ± 4.65*	*24.3*	*<0.001*

The preceding table indicates that quality of life markers diminished in the control group by 1% to 3%, whereas the second group had a rise of 1% to 3%, and the third group saw an increase ranging from 1% to 3.2%.

The MIMNI Mental Scale B index diminished in the control group by 1% to 3%, but the index augmented in the second group by 1% to 3%. In the third category, the index rose at a rate between 1% and 3.2%.

The MIMNI Mental Scale index diminished in the control group by 1% to 3%, but it augmented in the second group by 1% to 3%. In the third category, the index rose at a rate between 1% and 4%.

The Katz ADL Scale B index diminished in the control group by 2% to 5%, whereas it augmented in the second group by 3% to 6%, and in the third group, the index rose by 2% to 6%.

The Barthel Index declined in the control group by 3% to 5%, while it rose in the second group by 2% to 6%, and in the third group, it increased by 2% to 8%.

Regarding the Dementia Behavior Scale indications The control group had a reduction of 2% to 5%, whereas the second group saw an increase of 1% to 6%, and the third group exhibited an increase of 1% to 7%.

Regarding indicators, medical examinations The control group saw a decline of 1% to 4%, but the second group exhibited a rise of 2% to 6%. In the third group, the index rose at a rate between 3% and 6%.

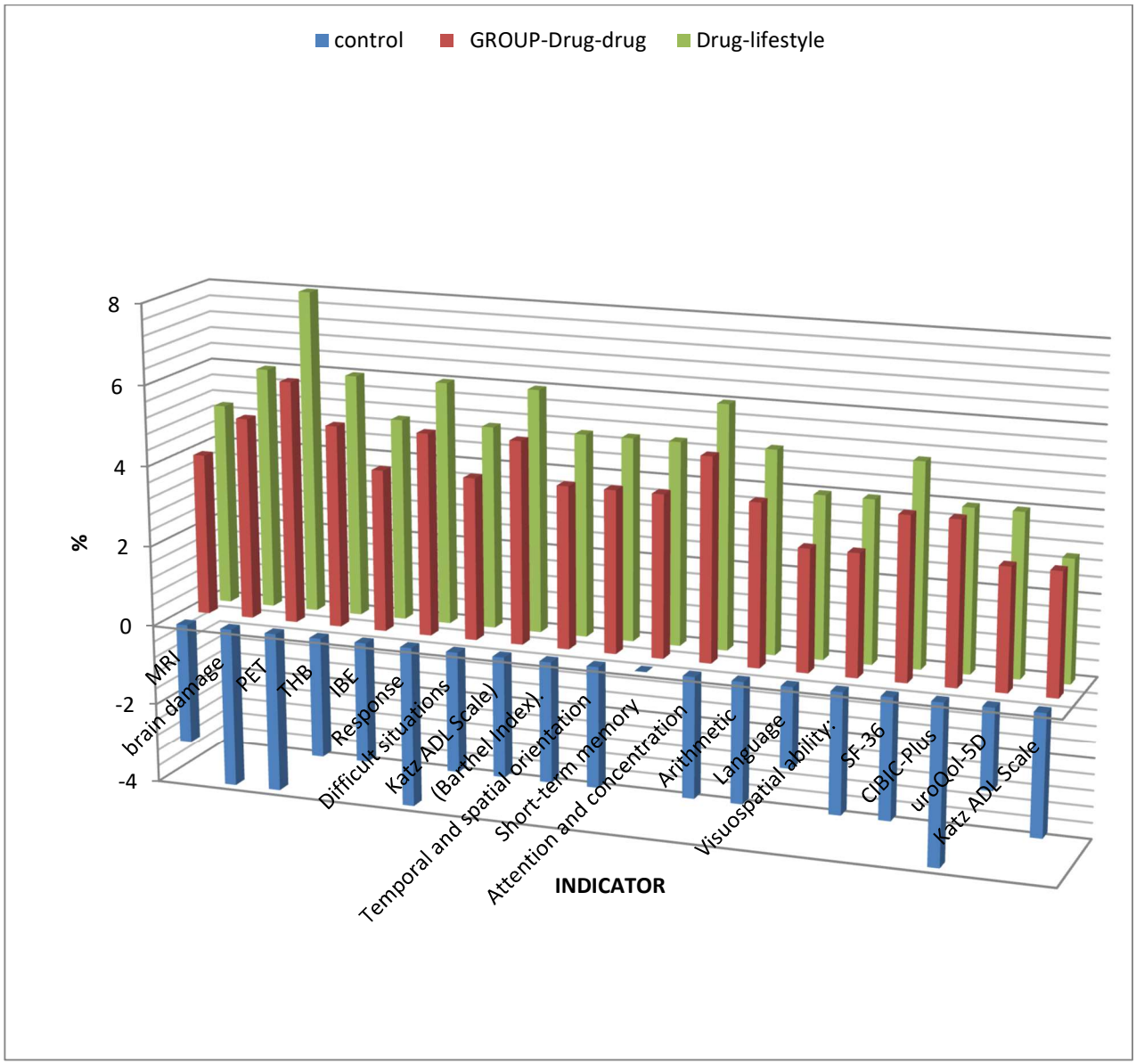

Figure 3: indicators of the three groups.

The preceding chart indicates a decrease in the metrics of the first group, the control group, by a margin of 1% to 5%. The indicators of the second group exhibited a rise in combination. The drug-drug interaction rate ranges from 1% to 7%, whereas the indications for the third category are concurrent. Drug-lifestyle treatments have risen at a pace between 1% and 8%. While it is impossible to ascertain which of the two methods is superior, the third group method, which involves adherence to specific life programs regarding nutrition and exercise, may yield results that surpass those of the second group by a margin of 1 to 2%. It is important to acknowledge that these findings may vary according on the type of the sickness. Integrated therapies or the characteristics of therapeutic interactions, along with the lifestyle and environmental factors affecting other patients in other locations.

Discussion

Alzheimer's disease is a condition that gradually worsens over time, impacting a person's

memory, cognitive abilities, and behavior. This condition is the leading cause of dementia, representing around 60-80% of all dementia cases worldwide (Kumar A, Sidhu J, Lui F, et al. 2024). This study aims to investigate the effect of combination therapies on Alzheimer's disease.

The study revealed that 75% of the control group fell within the age range of 60 to 70, while 10% were over the age of 70. The age distribution for both experimental groups was quite similar, with 68% and 56% of participants falling within the 60 to 70 age range, respectively. A smaller percentage, specifically 22% and 20%, was below the age of 60. The gender distribution was quite balanced, featuring 45% females and 55% males, which offered a more accurate reflection of the target population.

Gustavsson, A., et al., 2023 in his study revealed that It is estimated that there are 32 million individuals with AD dementia, 69 million with prodromal AD, and 315 million with preclinical AD worldwide. They made up 416 million across the AD continuum, representing 22% of all individuals aged 50 and older.

Alzheimer's disease mainly impacts older individuals, particularly those aged 65 and above (Tran, J., et al., 2024). The age distribution of individuals with Alzheimer's is as follows: 26% are in the 65-74 age group, 39% are in the 75-84 age group, and 37% are in the 85 and older age range. Nonetheless, the condition can impact younger individuals as well, with one in three people experiencing young-onset dementia being diagnosed with Alzheimer's disease. This emphasizes that although age plays a crucial role, Alzheimer's can also impact individuals who are younger.

The decline in quality of life indicators in the control group, between 1% and 3%, indicates that standard care treatment by itself might not be enough to sustain or enhance the quality of life for those living with AD. This decrease is probably a result of the ongoing development of the condition.

ChEIs are often given to individuals with AD to help alleviate symptoms and enhance their overall well-being (Birks J., 2006). ChEIs have demonstrated slight enhancements in cognitive abilities, which can beneficially affect the quality of life for certain individuals. They can improve everyday activities and lessen disruptive behaviors, leading to a more positive experience for everyone involved. Research indicates a difference in quality of life assessments between patients and their caregivers, with patients frequently expressing a higher quality of life than what their caregivers recognize. Moreover, ChEIs can come with side effects such as nausea, diarrhea, and muscle cramps, which might impact the overall quality of life and could result in some individuals choosing to stop treatment.

In accordance, Meziou, L., & Haubrick, K. (2024) in his systematic review which included 45 carefully chosen articles, shows strong evidence that AChEI is effective in enhancing cognitive outcomes in Alzheimer's disease. Although higher doses of AChE inhibitors may lead to more significant cognitive enhancements, they also increase the likelihood of negative side effects.

Yaghmaei, E., et al., 2024 in his study reported that the combined use of Donepezil and Memantine significantly elevates the probability of five-year survival. In particular, their combined use increases the probability of five-year survival by 0.050 (0.021, 0.078) (6.4%), 0.049 (0.012, 0.085), (6.3%), 0.065 (0.035, 0.095) (8.3%) compared to no drug treatment. These findings align with ours.

MIMNI Mental Scale index decreased in the control group by a rate ranging from 1% to 3%, while the index increased in the second group by a rate of 1% to 3%. In the third group, the index increased by a rate ranging from 1% to 4%.

The MMSE is a commonly utilized tool for evaluating cognitive function, especially among older individuals. The assessment looks at different areas of thinking, such as awareness, memory, focus, and communication, with scores from 0 to 30, where lower scores suggest more significant challenges in cognitive function (Myrberg, K., et al., 2020).

Kabir, M. T., et al., 2020 in his study reveled that research indicated that combination therapy can positively impact cognitive function measured by MMSE in people experiencing moderate-to-severe AD. Memantine and ChEIs have demonstrated enhancements in cognitive function, revealing a notable distinction between the control and memantine groups.

The Katz ADL index assesses self-care activities, including washing, dressing, toileting, transferring to and from a chair, maintaining continence, and feeding. Responses are provided in a binary format - affirmative or negative for each task. The scores reflect the degrees of functional impairments: a total score of 6 signifies complete function, 3 to 5 indicates moderate functional impairment, and a score of 2 or less denotes severe functional impairment (Rathnayake, N., et al., 2023).

Our results revealed that Memantine and ChEIs combination therapy have proved its efficacy in decreasing Katz ADL Scale B index. The same findings were obtained by Conti, A., et al., 2024 who found that Lifestyle and drug therapies that include physical, dietary, and psychological elements have shown successful in the general older population.

There is also a universal consensus that patients can improve their quality of life with lifestyle interventions such as a structured daily routine, proper nutrition, social engagement, and physical and intellectual activities (Belkacem et al., 2020). The patient seems to benefit from brain-healthy lifestyle interventions, especially as adjuvant treatment. Diet, social engagement, brain-stimulating activities, structured daily routines, emotional wellness, physical exercise, and reducing the risk of and treatment for cardiovascular and cerebrovascular diseases are also recommended (Ding et al., 2023).

Regular physical activity is associated with improvements in mood and cognitive function, likely reducing behavioral and psychological symptoms of dementia and slowing disease progression (Dominguez et al., 2021). The nutritional status of the patient is essential for overall health, but there is a shortage of evidence on its contribution to the disease's progression. (James et al., 2021).

Concerning dietary patterns, certain diets have shown some potential in aiding cognitive health or reducing dementia risk. Social inclusion seems beneficial to cognitive function in patients (Zheng et al., 2021). Engaging in meaningful social activities and community participation can improve quality of life and reduce the risk of dementia. Social engagement may slow cognitive decline, even in subjects with previous low social participation (Tanaka et al., 2021).

Bhatti, G. K., et al., 2020 reported that nutrient-dense foods, abundant in antioxidants and anti-inflammatory qualities, can modulate the immune system and perhaps impede cognitive loss and the advancement of Alzheimer's disease. Nutraceuticals and dietary patterns, encompassing omega-3 fatty acids, minerals, micronutrients, and vitamins, have been examined for their contributions to health and disease. These therapies can enhance the pathophysiology of diabetes, obesity, cardiovascular diseases, and cancer. Dietary treatments can influence molecular pathways in age-related neurodegenerative illnesses, such as Aβ production, tau hyperphosphorylation, oxidative stress, and epigenetic regulation.

Conclusion

This retrospective observational study offers important insights into the possible advantages of

combination therapies for managing AD. Although there are limitations in the study design and sample size, the results indicate that integrating medication with lifestyle changes could provide a more holistic strategy for treating AD.

Conflict of interest

None

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