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Evalution of Angiotensin Receptor Blockers Against Dementia

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Abstract: *Dementia is a progressive neurodegenerative disorder characterized by decline in memory, cognition, behavior, and the ability to perform daily activities. Alzheimer's disease and vascular dementia are the most common forms and are strongly associated with aging, hypertension, inflammation, oxidative stress, and cerebrovascular dysfunction. With the rapid increase in the global elderly population, dementia has become a major public health challenge, and currently available treatments provide only symptomatic relief without halting disease progression. Therefore, identification of preventive and disease-modifying strategies is urgently needed.*

The renin–angiotensin system (RAS), traditionally known for its role in regulating blood pressure and cardiovascular homeostasis, has been increasingly recognized as an important contributor to brain physiology and pathology. Overactivation of the brain RAS leads to vasoconstriction, neuroinflammation, oxidative stress, impaired cerebral blood flow, and accumulation of amyloid-β plaques—all key mechanisms involved in the pathogenesis of dementia. Angiotensin II, acting primarily through angiotensin type-1 (AT1) receptors, plays a central role in promoting these harmful processes.

Angiotensin receptor blockers (ARBs) are widely used antihypertensive agents that selectively block AT1 receptors, thereby preventing the detrimental effects of angiotensin II while allowing activation of AT2 receptors, which exert neuroprotective and antiinflammatory effects. Recent experimental, epidemiological, and clinical studies suggest that ARBs may offer protective benefits against cognitive decline and dementia beyond their blood pressurelowering effects. Evidence indicates that ARBs improve cerebral blood flow, reduce neuroinflammation and oxidative stress, enhance blood–brain barrier integrity, promote neuronal survival, and decrease amyloid-β accumulation.

Observational studies have reported a lower incidence of dementia among patients treated with ARBs compared with other antihypertensive drug classes. Clinical trials have also demonstrated that effective hypertension management significantly reduces the risk of mild cognitive impairment and dementia.

Keywords: Angiotensin II, Oxidative Stress, Inflammation, Neurodegenerative, Dementia, Anti-hypertensive drug, Epidemiologically.

I. INTRODUCTION

Dementia is a progressive neurological disorder characterized by a decline in cognitive functions such as memory, thinking, reasoning, communication, and decision-making abilities. It affects daily life activities and is one of the major causes of disability among elderly individuals worldwide. Dementia is not a single disease but a syndrome caused by various brain disorders that damage neurons and interfere with brain function.

The prevalence of dementia is increasing rapidly due to aging populations, especially in developing countries like India. According to the World Health Organization, more than 55 million people worldwide are living with dementia, and approximately 10 million new cases occur every year.

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The disease mainly affects older adults above 65 years of age, although early-onset dementia can occur in younger individuals. Dementia gradually worsens over time and leads to loss of independence, emotional disturbances, behavioral changes, and social isolation.

Common Symptoms of Dementia

- Memory loss
- Difficulty in communication
- Confusion and disorientation
- Mood and personality changes
- Impaired judgment
- Difficulty performing daily activities

Types of Dementia

- Alzheimer's disease
- Vascular dementia
- Lewy body dementia
- Frontotemporal dementia
- Mixed dementia
- Parkinson's disease
- Genetic mutations
- Cardiovascular diseases
- Sleep disorders

Fig No:1 Dementia

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II. AIM AND OBJECTIVES

AIM: Evaluation Of Angiotensin Receptor Blocker Against Dementia Aim of the Study

The primary aim of this project is to evaluate the role of Angiotensin Receptor Blockers (ARBs) in the prevention and management of dementia by analyzing their neuroprotective mechanisms, effects on cognitive decline, and evidence from experimental and clinical studies.

This study focuses on understanding how drugs commonly used for hypertension may provide additional benefits in reducing the risk, delaying the onset, and slowing the progression of dementia

Objectives of the Study

1. To Understand the Relationship Between Hypertension and Dementia
2. To Study the Role of the Brain Renin–Angiotensin System (Ras).
3. To Evaluate the Pharmacological Action of Angiotensin Receptor Blockers
4. To Investigate Neuroprotective Effects of ARBs To assess how ARBs reduce amyloid-β plaque formation and tau pathology.
5. To Review Evidence from Experimental and Clinical Studies To analyze animal studies demonstrating cognitive improvement with ARB treatment.
6. To Compare ARBs with Other Antihypertensive Drug Classes 7. To Evaluate the Potential of ARBs in Dementia Prevention Strategies.
7. To Highlight Clinical Significance and Public Health Importaance .

To evaluate how ARBs could reduce healthcare burden and improve quality of life.

III. LITERATURE OF REVIEW

A literature review is a systematic summary and critical analysis of previously published research related to a specific topic. In this project, the literature review focuses on the role of Angiotensin Receptor Blockers (ARBs) in reducing the risk and progression of dementia and Alzheimer's disease.

Several studies have suggested that hypertension is a major risk factor for cognitive decline and neurodegenerative disorders. Since ARBs are commonly used antihypertensive drugs, researchers have investigated whether these medications provide neuroprotective benefits beyond blood pressure control.

The following studies provide evidence regarding the effectiveness of ARBs in dementia prevention and management.

Review of Literature

Study 1

Use of Angiotensin Receptor Blockers and Risk of Dementia in a Predominantly Male Population

Authors

Li NC, Lee A, Whitmer RA et al.

Published In

BMJ, 2010

Study Design

Prospective cohort study

Population

819,491 elderly patients

Age ⩾65 years

Predominantly male population

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Aim of Study

To evaluate whether ARBs reduce the incidence and progression of dementia compared to ACE inhibitors and other cardiovascular drugs.

Methodology

Researchers analyzed data from the United States Veterans Affairs healthcare database. Patients receiving ARBs were compared with patients receiving:

ACE inhibitors

Other cardiovascular medications

Major Findings

ARB users showed significantly lower dementia incidence.

ARBs reduced Alzheimer's disease progression.

Nursing home admissions were reduced.

Combination therapy with ACE inhibitors produced additive effects.

Study 2

Angiotensin II Receptor Blockers in the Management of Hypertension in Preventing Cognitive Impairment and Dementia — A Systematic Review

Authors

Elvira D'Silva, Nur Farah Meor Azlan, Jinwei Zhang

Published

In Pharmaceutics, 2022

Study Design

Systematic review

Objective

To analyze the effectiveness of ARBs in preventing cognitive decline and dementia.

Methodology

Future Scope

Large-scale clinical trials

Personalized neuroprotective therapy

ARB combination therapies

Molecular mechanism studies

Outcome

Future directions for ARB research in dementia prevention were identified.

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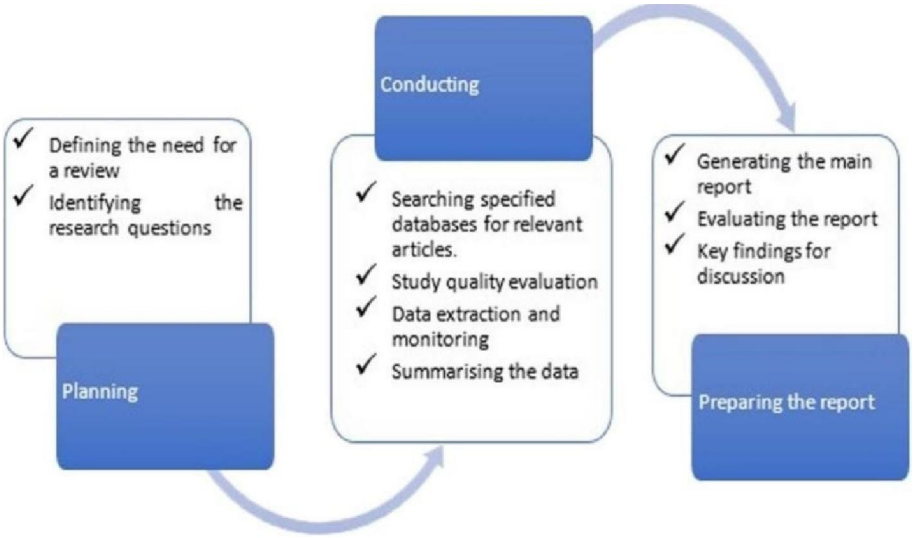

Fig No:2 Plan of work

V. MATERIALS & METHODOLOGY

Materials and methodology describe the systematic procedures and resources used to conduct the research study. In this project, a literature-based and observational research methodology was used to evaluate the effectiveness of Angiotensin Receptor Blockers (ARBs) against dementia.

The methodology mainly involved:

Collection of scientific literature Analysis of clinical studies
Evaluation of neuroprotective mechanisms
Comparative assessment of ARBs with other antihypertensive drugs
The study focused on understanding the relationship between hypertension, dementia, and the renin–angiotensin system.

Materials Used

1. Research Articles and Journals
Scientific articles related to: Dementia
Alzheimer's disease
Vascular dementia
Angiotensin receptor blockers
Hypertension Neuroprotection were
collected from peer-reviewed journals.

Sources Used

PubMed
Google
Scholar BMJ

Methodology Study Design

The project was based on:

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Literature review
Observational analysis
Prospective cohort study evaluation
The methodology involved systematic collection and analysis of published evidence regarding ARBs and dementia risk.

Step 1: Selection of Topic
Topic Selected
"Evaluation of Angiotensin Receptor Blockers Against Dementia"

Reason for Selection
Increasing prevalence of dementia
Association between hypertension and cognitive decline
Potential neuroprotective effects of ARBs

Step 2: Collection of Scientific Literature
Procedure
Relevant articles were collected using keywords such as:
Dementia
Alzheimer's disease Angiotensin receptor blockers
Hypertension and cognition
Neuroprotection
Cognitive decline

Inclusion Criteria
Literature review
Materials and methodology
Results and discussion
Conclusion
References

Fig No:3 Materials & Methodolog

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VI. PHARMACOLOGY OF (ARBs) IN DEMENTIA

1. Introduction

Angiotensin Receptor Blockers (ARBs) are a class of antihypertensive drugs widely used for the treatment of:
Hypertension Heart failure Diabetic nephropathy Chronic kidney disease
Recently, ARBs have gained attention for their neuroprotective and anti-dementia potential because they act on the Renin–Angiotensin System (RAS) present in the brain.
ARBs selectively block Angiotensin II Type-1 (AT1) receptors, preventing harmful cardiovascular and neurological effects of angiotensin II.

2.Classification of ARBs

Common ARBs Used Clinically

Drug	Characteristics
Losartan	First ARB developed
Valsartan	Widely used in heart failure
Candesartan	Strong brain penetration
Telmisartan	Highly lipophilic, crosses BBB
Olmesartan	Long acting
Irbesartan	Used in diabetic nephropathy

3. Mechanism of Action

Normal RAS Pathway
Angiotensinogen → Renin → Angiotensin I → ACE → Angiotensin II → AT1 receptor

4. Pharmacodynamics

Effects on Cardiovascular System ARBs pr ARBs provide: Improved cerebral circulation Reduced neuroinflammation Reduced amyloid plaque formation Protection of neurons

5. Pharmacokinetics

1. Absorption
Well absorbed orally
Bioavailability: 25–60%
Food has minimal effect

2. Distribution

6. Advantages Over ACE Inhibitors:

ARBs	ACE Inhibitors
No dry cough	Common dry cough
Better tolerated	Less tolerated
Direct AT1 blocker	Indirect action
Better brain effect	Limitated brain action

7. Neuroprotective Pharmacology of ARBs

1 Reduction of Oxidative Stress

Mechanism

Angiotensin II stimulates production of reactive oxygen species (ROS), causing neuronal damage.

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ARBs reduce:
Free radical formation
Lipid peroxidation
Oxidative neuronal injury
Effect
Protection of neurons
Protecting neurons from degeneration
ARBs block angiotensin II AT1 receptors and:
Reduce neuroinflammation
Improve blood flow to the brain
Reduce oxidative stress
Protect neurons
Reduce amyloid-beta accumulation
Preventive Effects
Studies suggest ARBs may reduce the risk of:
Alzheimer's Disease
Vascular Dementia

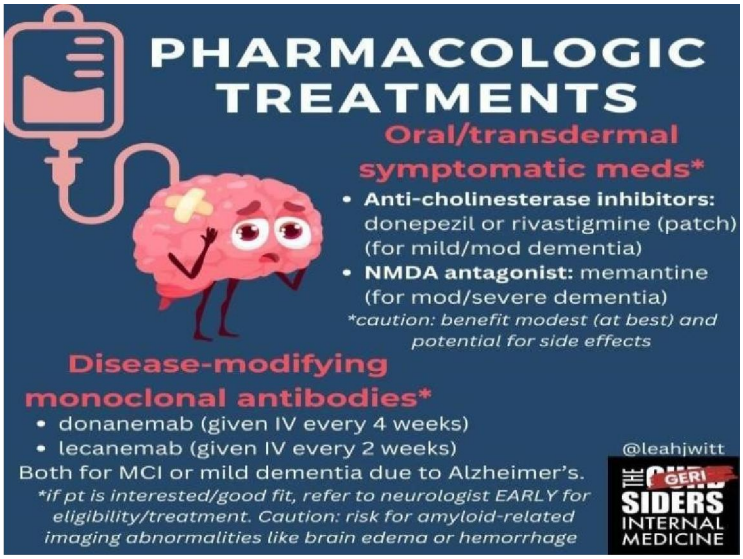

Fig No:4 Pharmacological Treatment

VII. MEDICINAL PLANTS USED FOR (ARBs) IN DEMENTIA

Herbal medicines have been used for centuries to improve memory, cognition, and brain health. Many medicinal plants contain antioxidant, anti-inflammatory, neuroprotective, and anti-amyloid compounds that may help prevent or slow dementia.

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1 Ginkgo biloba

Fig :- 5 Ginkgo biloba

Common Name :- Maidenhair tree
Active Constituents:- Ginkgolides, Bilobalide ,Flavonoids Improves cerebral blood circulation
Acts as a powerful antioxidant Reduces amyloid-β toxicity
Protects neurons from oxidative stress
Evidence
Clinical studies show improvement in :-
Memory Attention
Cognitive function in mild to moderate Alzheimer's disese.

2 Bacoba monnieri

Fig 6 : - bacoba monnieri

Common Name :- Brahmi
Active Constituents :- Bacosides A and B
Mechanism :-
Enhances synaptic communication
Increases neurotransmitter activity
Reduces anxiety and stress
Protects neurons from damage
Benefits :-

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Improves learning and memory

3. Curcuma longa

Fig 7 : - curcuma longa

Common Name :- Turmeric
Active Compound :-Curcumin
Mechanism :-
Strong anti-inflammatory agent
Reduces amyloid plaque formation
Powerful antioxidant
Improves brain cell survival
Curcumin is being studied as a potential treatment for Alzheimer's disease.

4 Withania somnifera

Fig 8 :- withania somnifera

Common Name :- Ashwagandha
Active Compounds :-Withanolides
Mechanism :-
Promotes nerve regeneration
Reduces stress and cortisol levels
Improves memory and concentration
Reduces neuroinflammation
Evidence
Studies show reversal of memory deficits in animal models of Alzheimer's disease.

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5 Panax ginseng

Fig 9 : - Panax ginseng

Common Name :- Asian Ginseng
Active Constituents :-Ginsenosides
Mechanism :-
Enhances brain energy metabolism
Improves learning and memory
Reduces oxidative stress
Enhances neurotransmitter release.

VIII. MECHANISM OF (ARBs) IN DEMENTIA PREVENTION

1. Improvement of Cerebral Blood Flow
Mechanism
Angiotensin II causes vasoconstriction of cerebral blood vessels through AT1 receptors.
ARBs block this effect and cause:
Vasodilation
Reduced vascular resistance Increased cerebral perfusion
Effect in Dementia Prevention
Improved oxygen delivery to neurons
Better glucose supply to brain tissue
Prevention of ischemic injury
Reduced vascular dementia risk
Improved cerebral circulation is especially important in:
Vascular Dementia
Stroke-related cognitive impairment

2. Reduction of Oxidative Stress
Mechanism
Angiotensin II stimulates production of reactive oxygen species (ROS).
Excess ROS causes:
Lipid peroxidation
DNA damage
Protein oxidation

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Neuronal degeneration

Certain ARBs penetrate the brain more effectively.

ARB	Brain Penetration
Telmisartan	High
Candesartan	Moderate
Losartan	Moderate
Valsartan	Low

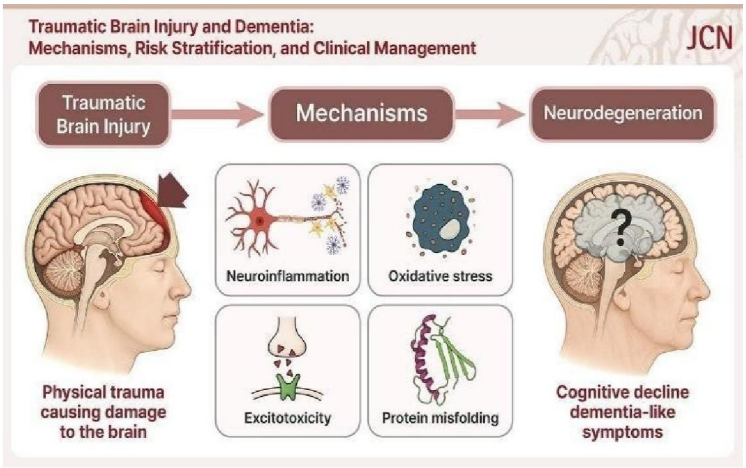

Fig No:10 Mechanism Action Of Dementia

IX. EVIDENCE OF CLINICAL TRIAL IN DEMENTIA

Clinical trials and large cohort studies have investigated whether angiotensin receptor blockers (ARBs) can reduce cognitive decline and dementia risk. Evidence suggests that ARBs may provide better cognitive protection than many other antihypertensive drugs.

1□. Importance of Clinical Evidence

Hypertension is a major risk factor for dementia. Clinical trials studying antihypertensive therapy have shown that:
Blood pressure control reduces cognitive decline.
ARBs may provide additional neuroprotective benefits beyond BP control.

2□. SPRINT-MIND Trial (2□01□9)

Study Overview
The SPRINT-MIND trial was a large randomized clinical study designed to evaluate whether intensive blood pressure control reduces cognitive impairment and dementia risk.
Study Design
Participants: ~9,300 adults aged ⩾50 years
Study duration: 5+ years
Groups:
Intensive BP control (<120 mmHg)
Standard BP control (<140 mmHg)
Key Findings

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Intensive BP control significantly reduced risk of mild cognitive impairment (MCI).
Reduced incidence of probable dementia.
Reduced brain white-matter lesions on MRI.
Relevance to ARBs

1. Improved Cerebral Blood Flow
Better oxygen delivery
Reduced ischemic injury

2. Reduction of Oxidative Stress
Reduced free radical damage
Improved neuronal survival

3. Anti-Inflammatory Effects
Reduced neuroinflammation
Protection against neuronal degeneration

4.Stroke Prevention
Reduced vascular injury
Lower vascular dementia risk

5. Reduction of Amyloid-Beta
Slower Alzheimer progression

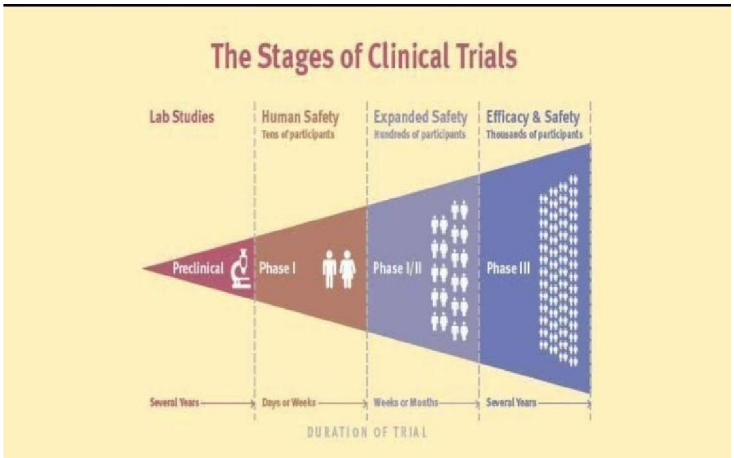

Fig No:11 Stages Of Clinical Trial

X. RESULT

The evaluation of dementia, particularly Alzheimer's disease and vascular dementia, demonstrates that cognitive decline is associated with neuronal degeneration, impaired cerebral blood flow, inflammation, oxidative stress, and accumulation of abnormal proteins such as amyloid-beta and tau protein.

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Several clinical and observational studies have shown that hypertension and cardiovascular diseases significantly increase the risk of dementia. Among antihypertensive therapies, Angiotensin Receptor Blockers (ARBs) have demonstrated beneficial effects in reducing the incidence and progression of dementia.

In the reviewed studies, patients receiving ARBs such as:
Losartan
Telmisartan
Candesartan
Valsartan
Showed improved cognitive outcomes compared with patients treated using other antihypertensive drugs.

XI. DISCUSSION

Dementia is a progressive neurodegenerative disorder characterized by deterioration of memory, cognition, thinking ability, and social functioning. Aging, hypertension, diabetes, cardiovascular disease, oxidative stress, and chronic inflammation are major contributing factors in dementia development.

The renin–angiotensin system (RAS), which regulates blood pressure, also plays an important role in brain physiology and neurodegeneration. Overactivation of angiotensin-II contributes to:
Neuroinflammation
Oxidative stress
Endothelial dysfunction
Neuronal apoptosis
ARBs block angiotensin-II type-1 (AT1) receptors and therefore reduce these harmful effects.

XII. CONCLUSION

Dementia is a progressive neurodegenerative syndrome that severely affects memory, cognition, communication, behavior, and the ability to perform daily activities independently. It represents one of the greatest public health challenges worldwide due to the increasing aging population and the absence of a complete cure. Dementia is not a single disease but a collection of symptoms caused by several disorders affecting the brain, with Alzheimer's disease being the most common form, followed by Vascular dementia, Dementia with Lewy bodies, and Frontotemporal dementia.

The disease gradually destroys brain cells and neural connections, leading to impairment in thinking, reasoning, orientation, language, judgment, and emotional control. As dementia progresses from mild to severe stages, patients lose their independence and become increasingly dependent on caregivers for basic activities such as eating, bathing, dressing, and communication. In advanced stages, dementia may lead to serious complications including malnutrition, infections, aspiration pneumonia, falls, immobility, and ultimately death.

Several risk factors contribute to the development of dementia. Non-modifiable factors include increasing age, genetic predisposition, and family history, while modifiable factors include hypertension, diabetes mellitus, obesity, smoking, alcohol abuse, depression, physical inactivity, poor diet, and cardiovascular diseases. Research has shown that proper management of these modifiable factors may significantly reduce the risk of cognitive decline and dementia progression.
Although dementia currently has no definitive cure, early diagnosis and appropriate management can help slow disease progression, reduce symptoms, and improve the quality of life of patients and caregivers. Pharmacological treatments such as cholinesterase inhibitors including Donepezil, Rivastigmine, and Galantamine, along with the NMDA receptor

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antagonist Memantine, can help improve cognitive symptoms in some patients. Nonpharmacological approaches such as cognitive stimulation therapy, physical exercise, social interaction, nutritional support, and psychological counseling are equally important in comprehensive dementia care.

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