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BRIEF REVIEW ON DEMENTIA

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ABSTRACT

The burden of dementia continues to increase as the population ages, with no disease-modifying treatments available. However, dementia risk appears to be decreasing, and progress has been made in understanding with different factors Dementia is a clinical diagnosis requiring new functional dependence on the basis of progressive cognitive decline. It is estimated that 1.3% of the entire UK population, or 7.1% of those aged 65 or over, have dementia. Applying these to 2013 population estimates gives an estimated number of 19,765 people living with dementia in Northern Ireland. The clinical syndrome of dementia can be due to a variety of underlying pathophysiological processes. The most common of these is Alzheimer's disease (50-75%) followed by vascular dementia (20%), dementia with Lewy bodies (5%) and frontotemporal lobar dementia (5%). The clinical symptoms and pathophysiological processes of these diseases overlap significantly. Biomarkers to aid diagnosis and prognosis are emerging.

Acetylcholinesterase inhibitors and memantine are the only medications currentlylicensed for the treatment of dementia. The nature of symptoms mean people with dementia are more dependent and vulnerable, both socially and in terms of physical and mental health, presenting evolving challenges to society and to our healthcare system.

Keywords: Dementia, Causes, Treatment, Alzheimer Disease, Cholinesterase Inhibitor, Fontanel Dementia, Vascular Dementia, Treatment Diagnosis, Cognition, Neuropathology, Biomarkers, Epidemiology, Neuro congestive Disorder, Instability.

I. INTRODUCTION

Dementia is an acquired loss of cognition in multiple cognitive domains sufficiently severe to affect social or occupational function[1] .Dementia describes a chronic and progressive clinical syndrome characterized by cognitive impairment (particularly memory loss), inability to perform activities of daily living, and neuropsychiatric features (psychiatric symptoms and behavioural disturbances, also known as behavioural and psychological symptoms of dementiaor BPSD). It affects an estimated 800 000 people in the UK and four million in the USA.

Alzheimer's disease (AD) is the most common cause of dementia (60%), [2]. it is a syndrome characterized by acquired cognitive decline, with a chronic and progressive nature, that compromises several brain functions, including memory, thinking and orientation. There is primary and secondary dementia, and both have increased in importance due to the higher lifeexpectancy.[3]

Physiological and behavioural symptoms ofdementia

More than 50% of people with dementia have BPSD, and these symptoms affect both patients and their relatives.[4] symptoms that probably consisting in the dementia is of disturbed perception, nervousness, inability to recognize the common things thought content, mood, and behaviour frequently occurring in patients with dementia' by consensus among clinicians in 1996[5,6] The core symptoms of different dementia subtypes are the behavioral and psychological symptoms of dementia (BPSD) and its neuropsychiatric symptoms (NPS). BPSD symptoms may occur at any stage in the case of dementia due to Alzheimer's disease (AD), [7]. Depression is inextricably linked to cognitive disorders and dementia. Over the years, there hasbeen a discussion about the relationship between depression and dementia [8].

Most psychotic symptoms that occure in dementia are hallucination thus the patient needed antipsychotic treatment. Alzheimer's disease is characterized by an irregular sleep-wake rhythm, sundowning, wandering, and obstructive sleep apnea. PDD is characterized by REM sleep behavior disorder, sleep maintance insomnia, hypersomnia, restless leg syndrome/periodic limb movements in sleep, while DLB patients demonstrate REM sleep behavior disorder, hypersomnia, periodic limb movements in sleep, and irregular sleep-wake rhythms.

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[9]

Causes and pattern of dementia

The main causes of the dementia is alzhiemer disease m AD has been used to describe both the neuropathologicalentity as well as the prototypical clinical syndrome of memory loss and other cognitive problems. Over the following quarter-century, problems with this conceptualization emerged. First, evidence increasingly indicated that persons with mild cognitive impairment (MCI), and indeed without any cognitive impairment, could meet pathologic criteria for AD [10,11]]

Although AD is the most common pathologic cause of dementia in old age, a number of other common pathologies are known to contribute as well. Just as the burden of AD pathology increases markedly with age, several other brain diseases that affect cognition accumulate as well, including cerebrovascular disease manifesting as infarctions, atherosclerosis, arteriolosclerosis, and white matter changes, as well as neocortical Lewy body disease (LBD) and increasingly recognized roles for TAR DNA-binding protein 43 (tdp43) and hippocampal sclerosis [12]

Some of the common causes of dementia are

- Alzheimer's disease. This is the most common cause of dementia.
- Vascular dementia. This may occur in people who have long-term high blood pressure,severe hardening of the arteries, or several small strokes. Strokes are the second mostcommon cause of dementia.
- Parkinson's disease. Dementia is common in people with this condition.
- Dementia with Lewy bodies. It can cause short-term memory loss.
- Frontotemporal dementia. This is a group of diseases that includes Pick's disease.
- Severe head injury.[13]

II. TYPES OF DEMENTIA

Types of dementia include:

- **Alzheimer's disease**- the most common dementia diagnosis among older adults. It is caused by changes in the brain, including abnormal buildups of proteins known as amyloid plaques and tau tangles. Alzheimer's disease (AD) (named after the German psychiatric Alois Alzheimer) is the most common type of dementia and can be defined as a slowly progressive neurodegenerative disease characterized by neuritic plaques and neurofibrillary tangles (Figure as a result of amyloid-beta peptide's (Aβ) accumulation inthe most affected area of the brain, the medial temporal lobe and neocortical structures [14]. Alois Alzheimer noticed a presence of amyloid plaques and a massive loss of neurons while examining the brain of his first patient that suffered from memory loss and change of personality before dying and described the condition as a serious disease of the cerebral cortex. Emil Kraepelin named this medical condition Alzheimer's disease for the first time in his 8th edition psychiatry handbook [14,15]. Progressive loss of cognitive functions can be caused by cerebral disorder like Alzheimer's disease (AD) or other factors such as intoxications, infections, abnormality in the pulmonary and circulatory systems, which causes a reduction in the oxygen supply to the brain, nutritional deficiency, vitamin B12 deficiency, tumors, and others [16,17]. Alzheimer's Disease Diagnostic Criteria -A patient suspected to have AD should undergo several tests, including neurological examination, magnetic resonance imaging (MRI) for neurons, laboratory examinations such as vitamin B12, and other tests besides the medical and family history of the patients[18] . Vitamin (vit.) B12 deficiency has been long known for its association with neurologic problems and increasing risks of AD, according to some studies. A special marker of vit. B12 deficiency is elevated homocysteine levels, which can cause brain damage by oxidative stress, increasing calcium influx and apoptosis. Diagnoses of vit. B12 deficiency can be done by measuring serum vit. B12 level alongside complete blood count and serum homocysteine levels tests [19].

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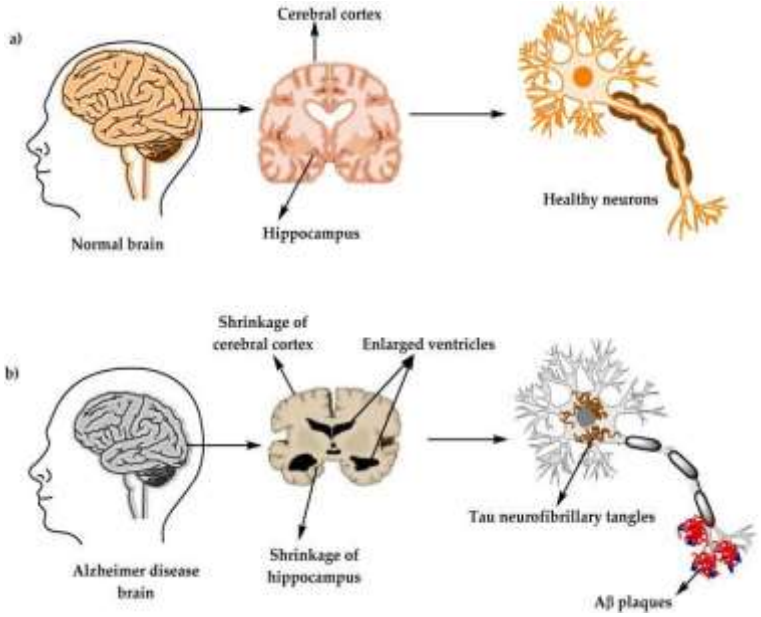

Fig 1: Alziemer disease

Frontotemporal dementia - a rare form of dementia that tends to occur in people younger than It is associated with abnormal amounts or forms of the proteins tau and TDP-43. Lewy body dementia, a form of dementia caused by abnormal deposits of the protein alpha- synuclein, called Lewy bodies. Frontotemporal dementia (FTD) is a term used to describe a group of neurocognitive disorders that encompass progressive dysfunction in executive functioning, behavior, and language. It is considered the third most common form of dementia following Alzheimer's disease (AD) and dementia with Lewy bodies[22] . As per its namesake, it is a cluster of syndromes that result from degeneration of the frontal and temporal lobes, and is subdivided into two categories that are unique in respect to their predominating presentations; namely, the behavioral subtype that accounts for about half of FTD cases, and the language subtype[23]. As the population of geriatric patients grow and neurocognitive disorders become more prevalent, there will be an increased need for physicians with an expert understanding of the diverse clinical findings that define the heterogeneous FTD subtypes. This review will focus on the most recent findings concerning FTD neurobiology, current classification and assessment systems, and the most up-to-date expert consensus on the treatment of this unique collection of syndrome [24].

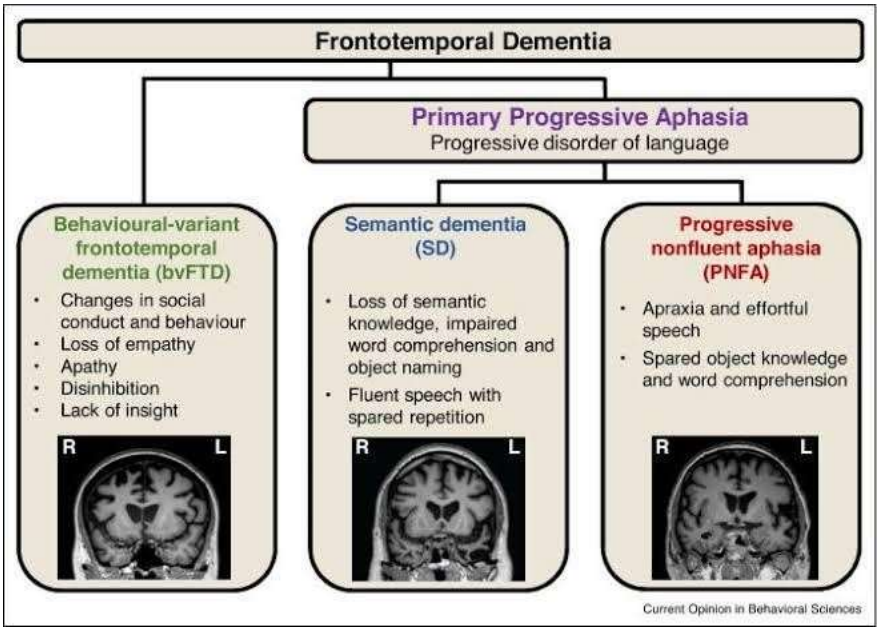

Fig 2: Frontonal dementia

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Vascular dementia- a form of dementia caused by conditions that damage blood vessels in the brain or interrupt the flow of blood and oxygen to the brain. Vascular dementia (VaD)1 is a neurocognitive disorder that represents clinically significant cognitive impairment directly related to vascular injury to the brain [25] .with a number of potential contributing factors recognized (Fig). Of note, from a mechanistic standpoint, the development of vascular- mediated cognitive impairment reflects specific areas of cognitive domain involvement. The resultant clinical picture can result from either localized larger vascular territory injury orcumulative cerebral small vessel disease (SVD). VaD is generally viewed as the second most common cause of age-related dementia. The pathogenesis is attributed to vascular causes in the absence of other pathologies.2 It accounts for roughly 20% of all dementia with the prevalence tending to parallel stroke risk. Reflective of evolving concepts in the dementia realm, the Fifth Edition of the Diagnostic and Statistical Manual (DSM-V) criteria has replaced the term "vascular dementia" with "vascular neurocognitive disorder".[26,27] Various terminologies have evolved in recognition of the various mechanisms of VaD including both large vessel and small vessel (Table 1).

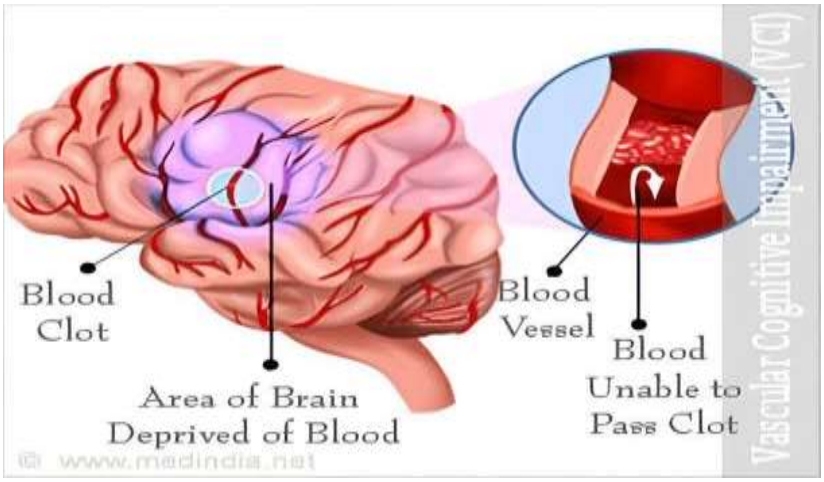

Fig 3: Vascular dentia

Otto Binswanger, for example, described a subcortical arteriosclerotic encephalopathy, which became known as Binswanger's disease,12 and presumably translates into what now may be referred to as subcortical microvascular ischemia, cerebral small vessel disease (SVD), ischemic demyelination, leukoaraiosis or the "lacunar state". 11 To reflect greater inclusiveness of the various mechanisms, including hemorrhagic stroke, the term Vascular Cognitive Impairment (VCI) has been proposed13 as has Post-Stroke Dementia (PSD).14 [28,29]. The pathophysiology of VaD was the subject of a comprehensive review by Kalaria.11 It is generally noted that the pathology and clinical features of VaD is dependent on the mechanism of the stroke, degree of tissue loss, impact on connectivity of neural pathways, impact on exquisite regions of the brain vital for interaction with the environment40,45,46 as well as remote effects including what has been termed diaschisis.47 The potential molecular [30] mechanisms contributing to the pathogenesis of cerebral infarction is illustrated in Fig. 2. As noted in the Fig., there has been increasing attention paid to the potential for inflammation to contribute to both atherosclerosis48 as well as to cerebral SVD.49 Due to this heterogeneity of pathophysiologic mechanism, a consensus on defined pathogenesis has not been established.45 The pathogenesis of VaD can originate from primary central nervous system vascular insult such as in situ thrombosis related to atherosclerosis, fibrinoid necrosis or lipohyalinosis which can overlap with some of the mechanisms related tohypertensive ICH [31,32]

Mixed dementia

A combination of two or more types of dementia. For example, through autopsy studies involving older adults who had dementia, researchers have identified that many people had a combination of brain changes associated with different forms of dementia. Mixed dementia is the coexistence of Alzheimer's disease and cerebrovascular disease (CVD) in the same demented patient. Currently, its diagnosis and treatment remains a challenge for practitioners. To provide an overview of the epidemiology, pathogenesis, natural history, diagnosis, and therapy of Mixed Vascular-Alzheimer Dementia (MVAD). The literature was reviewed for articles

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published between 1990-2016 by using the keywords linked to MVAD. Neuropathological studies indicate that MVAD is a very common pathological finding in the elderly with a prevalence about of 22%. The distinction between Alzheimer's dementia and vascular dementia (VD) is complex because their clinical presentation can overlap. There are international criteria for the MVAD diagnosis. The pharmacologic therapy shows modest clinical benefits that are similar among all drugs used in patients with Alzheimer's dementia and VD. The non-pharmacologic therapy includes the rigorous management of cardiovascular risk factors (especially hypertension) and the promotion of a healthy diet[33] . The diagnosis and treatment of MVAD cannot be improved without further studies. Currently available medications provide only modest clinical benefits once a patient has developed MVAD. In subjects at risk, the antihypertensive therapy and healthy diet should be recommend for preventing or slowing the progression of MVAD. According to the American Heart Association/American Stroke Association (AHA/ASA), the vascular and neurodegenerative disorders are common in the elderly and it could coexist in the same patient. These processes underlying dementia are mutually potentiated for developing cognitive impairment and dementia, generating overlapped clinical phenotypes and neuroimaging.[34]. Thus, the mixed dementia occurs in patients with a neurodegenerative disorder (such as Alzheimer's disease (AD), Lewy body disease, or Pick body disease) and, additionally, a cerebrovascular disease (CVD). [35]. The MVAD, as well as other dementias, starts several years before the symptoms display, which allow their diagnosis. The pathogenesis of Alzheimer's dementia is unclear.

However, there are two theories that attempt to explain their origin: amyloid theory and vascular theory. Taking into account the theme of this review, we consider pertinent to discuss the last theory.According to vascular theory, the chronic non-communicable diseases hypertension, diabetes mellitus, dyslipidemia, obesity, and cardiac disease) and the sedentary lifestyle produce several vascular changes such as the thickening of the capillary basal membrane and the accumulation of collagen in the vascular endothelium, which both generate vascular atrophy of the vascular terminations, as well as a decrease in the number of terminal blood vessels. These changes affect the cerebral microvasculature and reduces the cerebral blood flow, which especially observed in untreated hypertensive patients and those treated irregularly or insufficient [36]

Diagnosis of dementia-

Neuropsychology contributes greatly to the diagnosis of dementia. Cognitive deficits can be detected several years before the clinical diagnosis of dementia. The neuropsychological profile may indicate the underlying neuropathology. Neuropsychological assessment at an early stage of dementia has two goals: (a) to determine a memory disorder, not always associated with a memory complaint, and (b) to characterize the memory disorder in light of the cognitive neuropsychology and to assess other cognitive (and noncognitive) functions toward integrating the memory disorder in a syndrome. We review the global tools, the memory tests that describe the memory profile and indicate the underlying pathology, the assessment of other cognitive functions, and the neuropsychological patterns of typical Alzheimer’s disease, frontotemporal dementia, primary progressive aphasia, semantic dementia, Lewy body dementia, subcortical dementia, and vascular dementia. These patterns must be interpreted in the light of the history, rate of progression, imaging results, and nature of existing behavioral disturbances. Moreover, there may be overlap between two or more pathologies, which complicates the diagnostic process. Follow-up of patients is necessary to improve diagnostic accuracy. Neuropsychology contributes greatly to the diagnosis of dementia: it documents significant cognitive decline and reveals patterns of cognitive dysfunction that suggest the cause of the dementia. Cognitive deficits can be detected several years before the clinical diagnosis of dementia . Establishing the neuropsychological profile often indicates the underlying neuropathology. Although Alzheimer's disease (AD) is the most frequent disorder, it is not the only cause of dementia in adults. Therefore carrying out the neuropsychological assessment at an early stage of dementia has two goals: (a) revealing memory disorders, which are not always associated with memory complaints (memory impairment is a core feature of dementia, while [37]. memory complaints are not always due to a memory disorder, e.g., in anxiety disorders), and (b) characterizing the memory disorder in the context of cognitive neuropsychology, thus allowing other cognitive (and noncognitive) functions to be integrated with the memory disorder into a broader syndrome. Here we concentrate on the conditions in which dementia is relatively isolated, in the absence of major motor symptoms. [38]. In diagnosing the cause of dementia it is important to distinguish between failures of (a) storage (or retention),

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associated with damage to limbic and especially hippocampal structures, (b) retrieval associated with frontal-subcortical dysfunctions, and (c) short-term memory associated with temporo-parietal lesions: – Storage disorders are characterized on testing by deficits in both recall and recognition and rapid loss of information at delayed recall. The patient shows little benefit from cues and provision of multiple choice alternatives. – Retrieval disorders are characterized by a difficulty in accessing information. Free recall is low, perhaps because of lack of active or efficient search strategies, but cues and multiple-choice alternatives enhance performance. Recognition is better than recall, and delayed recall is not impaired. – Short-term memory disorders are characterized on testing by reduced memory span and rapid loss of information measured by the Brown-Peterson paradigm [68]. The Wechsler Memory Scale-Revised (WMS-R), contains nine subtests and has excellent age norms. It may distinguish amnesic from demented patients [39], but it was not designed for this purpose, and the overall score submerges potential differences in reasons for failure. Moreover, it does not assess specifically the various components of memory. The best instrument for assessing memory disorders in early dementia is probably the Free and Cued Selective Reminding Test (FCSRT) .

Unlike most clinical memory tests which do not control cognitive processing, this test includes a study procedure in which subjects search for items (e.g., grapes) in response to cues (e.g., fruit) that are later used to elicit recall of items not retrieved by free recall. Including a study procedure is particularly important for identifying early dementia. Other pathological or physiological conditions which limit learning when study conditions are not controlled are otherwise confused with dementia-associated memory impairment in preclinical and early stage disease. Furthermore, cued recall is considered the most useful test among a large neuropsychological battery in making diagnosis decision by neuropsychologists.

III. TREATMENT OF DEMENTIA

Although they are not a cure, ChEIs currently offer the best hope in treating AD. Initially the availability in the UK of ChEIs for the treatment of AD depended on where patients lived rather than their clinical need, so called ‘‘post code prescribing’. The National Institute for Health and Clinical Excellence (NICE) 2001 guidelines for the treatment of AD with ChEIs8 recommended their use [41]. The future use of ChEIs in the UK for National Health Service (NHS) patients is, however, again in doubt following the publication of NICE’s new draft guidance.9 They have maintained their position from 2001 that the medications have an effect and are safe in the treatment of AD, but have now concluded that the drugs are not cost effective and should not be reimbursed by the NHS. NICE received over 4000 responses, their largest ever, during the initial consultation period of the new guidelines. NICE reported that since the publication of its original guidelines the clinical evidence base for ChEIs has matured and that it demonstrates a consistent gain on cognitive and global scales compared to placebo in mild to moderate AD.9 They were concerned that the effects are small and there is little positive randomised evidence available on the long term gain of ChEIs. [42] Despite these concerns, NICE concluded that ChEIs were effective but were not cost effective and therefore would no longer be recommended. It has been felt by many that NICE’s appraisal had several shortcomings which influenced their conclusions regarding cost effectiveness. They had underestimated the cost of full-time institutional care and had not fully considered the full benefits for carers. It has been estimated that ChEI treatment costs £2.50 a day and yet there is evidence to suggest that treatment can reduce carer input by half an hour a day.10 For a professional carer this would constitute a saving of at least £2.50 a day: the price of ChEI for one day.[43]

INITIATING TREATMENT WITH CHOLINESTERASE INHIBITORS

Once a diagnosis of AD has been made it is important to discuss in detail with the patient and their relative/carer what treatment will entail. For most the diagnosis of a dementia can be devastating and understandably they may have high expectations, sometimes unrealistic, of any treatments offered. It is therefore important to be clear from the outset on several key points: c The medications are not a cure.[44] c The medications do not work for everyone. The rule of thirds in medicine applies approximately: one third get better, one third do not deteriorate further, and in one third it makes no difference and the patient deteriorates at the rate as if untreated. c The medication will be discontinued if the patient does not respond to it.The NICE guidance8 (table 1) published in 2001 provided a structure which includes systematic monitoring which, although under review, provides a sensible template for the prescription of the drugs. It has been suggested that the primary aim of the guidelines is to contain prescribing and control drug costs.11 The guidance certainly lacks some practical

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elements. It is, for example, important for patients to have an electrocardiogram (ECG) before starting a cholinesterase inhibitor, as bundle branch block is a relative contraindication to their prescription. A set of practical guidelines for initiating treatment with cholinesterase inhibitors is set out in [45].

Medicines to treat dementia

Most of the medicines available are used to treat Alzheimer's disease as this is the most common form of dementia. They can help to temporarily reduce symptoms.

Some of the main medicines are used to treatment for dementia

Acetylcholinesterase inhibitors -

These medicines prevent an **enzyme** from breaking down a substance called acetylcholine in the brain, which helps nerve cells communicate with each other.

Donepezil (also known as Aricept), rivastigmine (Exelon) and galantamine (Reminyl) are used to treat the symptoms of mild to moderate Alzheimer's disease. Donepezil is also used to treat more severe Alzheimer's disease.

There's evidence that these medicines can also help treat dementia with Lewy bodies and Parkinson's disease dementia, as well as people who have a mixed dementia diagnosis of Alzheimer's disease with vascular dementia.

There's little difference in how effective these medicines are. However, rivastigmine may be preferred if hallucinations are one of the main symptoms.

Side effects can include nausea and loss of appetite. These usually get better after 2 weeks of taking the medicine.

Memantine

This medicine (also known as Namenda) is given to people with moderate or severe Alzheimer's disease, dementia with Lewy bodies and those with a combination of Alzheimer's disease and vascular dementia.

Memantine is suitable for those who cannot take or are unable to tolerate acetylcholinesterase inhibitors. It works by blocking the effects of an excessive amount of a chemical in the brain called glutamate.

Side effects can include headaches, dizziness and constipation, but these are usually only temporary. Their isn't specific treatment is available for the treatment of dementia but we can improve the abillity of the patient with different drug interactions with their therapeutic yield .different medication and therapies are suggested to that perticular patient who is suffering from the dementia thus above mentioned drugs having high therapeutic values

Drug name	Mechanism	Daily dosage	Side effects
Donepezil	AChE inhibitor	5–10 mg	Nausea, vomiting, diarrhea, vivid dreams, leg cramps
Rivastigmine	AChE inhibitor	3–12 mg	Nausea, vomiting, diarrhea, weight loss, anorexia
Galantamine	AChE inhibitor	8–12 mg	Nausea, vomiting, diarrhea, weight loss, anorexia
Memantine	NMDA receptor antagonist	10–20 mg	Hallucinations, confusion

Abbreviations: AChE, acetylcholinesterase; NMDA, *N*-methyl-D-aspartic acid.

Fig 4: Different drugs with their mechanism, dose and along with their side effect

IV. CONCLUSION

Dementia is a term used to describe a decline in cognitive function that affects a person's ability to think, remember, and reason. There are many different types of dementia, but the most common is Alzheimer's disease. Other types of dementia include vascular dementia, Lewy body dementia, and frontotemporal

dementia. The symptoms of dementia can vary widely, but generally include memory loss, difficulty communicating, confusion, disorientation, and changes in mood and behavior. There is no cure for dementia, but there are treatments available that can help manage symptoms and improve quality of life. These treatments may include medications, therapy, and lifestyle changes. It's important to seek medical advice if you or a loved one are experiencing symptoms of dementia.

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