Systematic review: Systematic review of neurological problems and stress in Alzheimer's patients with drug tips

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ABSTRACT

Introduction: Alzheimer's disease is a brain disorder that causes the brain to shrink and eventually die brain cells. The present study systematically reviewed neurological problems and stress in Alzheimer's patients with drug tips.

Materials and methods: An extensive search strategy was developed for literatures by 50 article. To obtain scientific evidence related to the prevalence of old age sufferings in the elderly in Iran from articles published in interior and foreign databases such as Scientific Information Database (SID), Magiran, Web of Science, Psyc INFO, PubMed, Scopus, and Google Scholar search engine were used. All articles, regardless of the time period, were searched in the databases until September 2024. PRISMA 2020 checklist was used in order to screen articles, extract data and brief related findings.

Results: The most common symptoms of Alzheimer's are forgetting recent events or conversations and difficulty remembering newly learned information. Over time, memory problems become more severe and the person eventually loses the ability to perform daily tasks. After a while, patients usually have difficulty finding the right words to express their thoughts and will need more time to complete routine daily tasks. Some brain imaging tests can detect protein deposits called amyloid in the brain, allowing treatment before the onset of major symptoms.

Conclusion: Dementia also affects other body systems, such as breathing. For example, as the gray matter of the brain deteriorates and the person loses the ability to perform certain voluntary actions, such as moving the diaphragm, the patient becomes susceptible to diseases such as pneumonia, which shortens their lifespan. Therefore, it is not possible to make a definitive judgment about the lifespan of a person with Alzheimer's.

Introduction

Alzheimer's disease is the most common cause of dementia and is associated with high mortality in the elderly. Today, 47 million people worldwide are affected by the disease, affecting 13% of people over 65 and 45% of people over 85. It is predicted that by 2050, one person will be diagnosed with the disease every 33 seconds, with a total of one million new cases per year [1-3].

Although the cause of Alzheimer's disease is still not fully understood, the amyloid cascade

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hypothesis seems to be the main cause of the disease. It is thought that an imbalance between the production and clearance of amyloid beta proteins in the brain, resulting in impaired synaptic function and neuronal degeneration, is the main cause of the progressive and irreversible impairment of memory, affecting speech, personality and cognition [4].

Amyloid plaques are formed by the accumulation of amyloid beta proteins, which are themselves derived from a parent protein called amyloid precursor protein. Three types of secretase enzymes (alpha, beta, and gamma) break down the amyloid precursor protein into soluble components [5-7]. If this protein is not properly broken down by the beta and gamma secretase enzymes, insoluble beta amyloid proteins are formed, which accumulate in the brain and lead to the formation of amyloid plaques, neurotoxicity, and cell death. Intraneuronal tangles are composed of filaments containing the phosphorylated form of tau proteins. Tau proteins naturally contain phosphate molecules [8].

In Alzheimer's disease, these proteins become excessively phosphorylated, which causes them to coil around each other and form insoluble tangles, resulting in the presence of macrophages and mononuclear cells in the cerebral cortex and the activation of microglia in the parenchyma, dementia, and atrophy of the frontotemporal cortex [9].

Although neuropathologists believe that amyloid plaques and intraneuronal tangles are the most important cause of Alzheimer's disease, there are other predisposing factors that will be discussed in general below. In some families, genetic mechanisms for the development of this disease have been identified, including the e-4 allele of Apo lipoprotein E [10]. Apo lipoprotein E plays an important role in the breakdown and clearance of the amyloid precursor protein, and it seems that carriers of the e-4 allele do not have the necessary ability to clear the breakdown products of this main protein, and as a result, the production and accumulation of beta proteins in the individual's body increases. Neuroinflammation is an important factor as a cause of the disease and also as a result of the development of the disease [11].

The production of plaques and tangles probably occurs in part in connection with the inflammatory process caused by aging. The production of plaques and tangles themselves causes inflammation and accelerates the formation of subsequent plaques and cognitive decline [12].

Materials and methods

An extensive search strategy was developed for literatures by 50 article. To obtain scientific evidence related to the prevalence of old age sufferings in the elderly in Iran from articles published in interior and foreign databases such as Scientific Information Database (SID), Magiran, Web of Science, Psyc INFO, PubMed, Scopus, and Google Scholar search engine were used. All articles, regardless of the time period, were searched in the databases until September 2024. PRISMA 2020 checklist was used in order to screen articles, extract data and brief related findings.

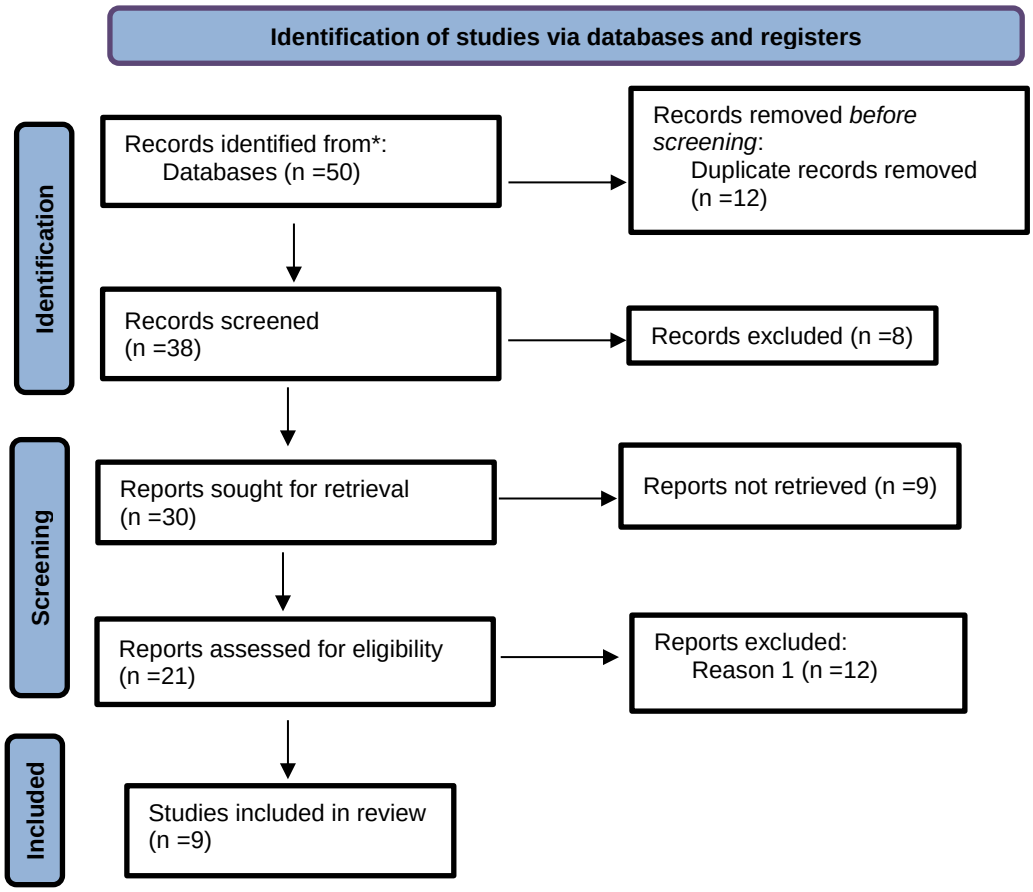

Figure 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

Acquired risk factors

In a statistical analysis, factors such as diabetes, high blood pressure, obesity, physical inactivity, depression, smoking, and low education level have been reported as modifiable risk factors that predispose a person to developing Alzheimer's disease in one third of known cases of the disease [13].

Various polygenic and acquired factors can increase the risk of developing Alzheimer's disease, including lipid disorders, cerebrovascular disease, altered glucose metabolism, and brain trauma. Many of these risk factors are more associated with the development of Alzheimer's disease if they occur in middle age [14-16]. Strict management of vascular factors in middle age is a key strategy to reduce the risk, progression, and severity of Alzheimer's disease and other forms of dementia.

High blood pressure

In cross-sectional studies and long-term cohort studies, high blood pressure in midlife has been consistently associated with an increased risk of Alzheimer's disease and dementia [17]. This risk is mediated by cerebrovascular disease and the long-term effects of high blood pressure, and is increased by diabetes and smoking. This association is stronger in women than in men, although this is not universally true [18]. Arterial stiffness and blood pressure variability play important roles in the association between blood pressure and Alzheimer's disease risk. Arterial stiffness increases with age and with levels of blood pressure, diabetes, and smoking.

In one cohort study, arterial stiffness was directly associated with the deposition of amyloid beta plaques [19].

While observational studies suggest that treating high blood pressure reduces the risk of dementia, clinical trials of high blood pressure treatment do not consistently report a reduction in this risk, but it is noteworthy that most of these trials have examined short-term outcomes and that long-term treatment of high blood pressure may alter the risk of Alzheimer's disease in later life [20].

Lipid disorders

Although some epidemiological studies have suggested an association between total cholesterol and low-density lipoprotein cholesterol and the risk of Alzheimer's disease, these studies are difficult to interpret. Peripheral low-density lipoprotein cholesterol is unable to cross the blood-brain barrier unless the barrier is damaged by factors such as vascular disease. Most of the cholesterol in the brain is made by stellate cells and neurons and delivered to brain cells by high-density lipoprotein and low-density lipoprotein cholesterol is either negligible or absent in the brain. However, observational data support an association between total cholesterol and low-density lipoprotein cholesterol levels and the risk of Alzheimer's disease [21].

In a long-term cohort study, a threefold increased risk of developing Alzheimer's disease was reported in patients with high total cholesterol levels in midlife with a mean age of approximately 50 years, independent of Apo lipoprotein E genotype, education level, smoking, and alcohol consumption [22].

There is conflicting data on the association between total cholesterol levels in old age and the risk of Alzheimer's disease, with some studies reporting a direct association, some studies reporting an inverse association between the two variables, and some studies reporting no clear association [23].

In addition, in patients with Alzheimer's disease, increased levels of total cholesterol and low-density lipoprotein cholesterol have been associated with more cognitive impairment. It is thought that brain cholesterol increases the risk of Alzheimer's disease by increasing the formation or deposition of amyloid beta proteins or by affecting other non-amyloid factors such as cerebrovascular problems, local inflammation, and tau protein metabolism [24].

Based on these data, research has focused on the use of cholesterol-lowering drugs for the prevention of Alzheimer's disease. Randomized trials have failed to demonstrate a protective effect of statin drugs on cognition in cardiovascular patients or in individuals at high risk of cardiovascular disease. Oral statin drugs have not been shown to slow cognitive decline in patients with mild to moderate Alzheimer's disease [25].

Cerebrovascular disease

This group of diseases is associated with Alzheimer's disease, and the simultaneous presence of Alzheimer's disease and vascular problems is called mixed dementia. Cerebrovascular disease is more common in older age and is associated with factors such as high blood pressure, diabetes, smoking, obesity, low physical activity, and lipid disorders. Reduced blood flow has been shown to precede the deposition of amyloid beta protein in mouse models of Alzheimer's disease, and human studies support the accumulation of amyloid proteins as a result of impaired clearance [26].

A case-control study showed that reduced cerebral blood flow and white matter abnormalities were associated with an increased risk of Alzheimer's disease. In autopsies performed on patients with Alzheimer's disease, vascular pathology is found in 35 to 50% of patients with Alzheimer's

disease. On the other hand, one-third of patients with a definite diagnosis of vascular dementia show abnormalities consistent with Alzheimer's disease at autopsy [27-29].

If the pathological findings are not consistent with Alzheimer's disease, the presence of large infarcts and lacunae may be more likely to confirm the diagnosis. The e-4 Apo lipoprotein E genotype is associated with an increased risk of Alzheimer's disease and cardiovascular disease. In one study, the severity of coronary artery disease was clearly associated with increased density of neuropathological findings of Alzheimer's disease in carriers of the e-4 Apo lipoprotein E allele. In another study, the e-4 Apo lipoprotein E allele was associated with capillary changes in the subcortical area of Alzheimer's disease patients, but these changes were not in favor of extensive cerebrovascular damage. Cerebrovascular disease is associated with worse cognitive function in patients with Alzheimer's disease, and clinic pathological studies suggest that these diseases lower the threshold for dementia in patients diagnosed with Alzheimer's disease [30-32].

Medications

Many studies have confirmed the association between the use of different drug classes such as benzodiazepines, drugs with anticholinergic effects or side effects, antihistamines, and opioids and the occurrence of cognitive impairment in the elderly, but in most cases it has been noted that these effects have been transient and reversible. Long-term exposure to these drugs has been associated with an increased risk of Alzheimer's disease and other types of dementia in many studies. These studies also suggest that the cognitive effects caused by the drugs may not be reversible in some patients or that this long-term exposure may cause Alzheimer's disease to progress from an asymptomatic or early symptomatic stage to a symptomatic stage [33-35].

Results

There are currently four drug treatments for Alzheimer's disease, all of which have received approval from the US Food and Drug Administration over the past decade. Of these four drugs, the first-line treatment is acetylcholinesterase inhibitors [36], including donepezil, rivastigmine, and galantamine. By inhibiting this enzyme, these drugs increase the concentration of acetylcholine, a neurotransmitter responsible for cognitive function and memory, in the brain. Since this class of drugs slows the progression of cognitive impairment, they have been approved for the treatment of dementia in patients with Alzheimer's disease. The effectiveness of these three drugs has been studied in Alzheimer's disease of different severity [37-39].

The severity of the disease can be classified according to the score obtained from various tests in Error! Reference source not found. The results of a recent study showed that the use of related drugs is very effective in slowing the progression of the disease. In this regard, the following drugs can be mentioned:

1- Benzodiazepine drugs: There is conflicting data regarding the relationship between the use of this class of drugs and the risk of dementia. In a case-control study of 2000 elderly individuals, after adjusting for multiple confounding variables such as anxiety, depression, and insomnia, taking benzodiazepines for more than 180 days was associated with a 1.5-fold increased risk of developing Alzheimer's disease. On the other hand, a dose-response relationship was also reported, with an increase in the incidence of complications with increasing duration of drug use and an increase in the incidence of complications with increasing half-life of the drug [40].

It is possible that benzodiazepines were used to treat the early symptoms of Alzheimer's disease. Therefore, the researchers included individuals who had been prescribed this class of drugs for

at least 5 years before their diagnosis of Alzheimer's disease. Other large studies have failed to show an association between long-term use of benzodiazepines and the occurrence of dementia [41].

2- Medications with anticholinergic effects or side effects: In a prospective study of more than 3400 elderly patients who were not dementia-free at baseline, high cumulative doses of anticholinergic medications were associated with an increased risk of dementia. The most common anticholinergic medications used by patients included tricyclic antidepressants, first-generation antihistamines, and antimuscarinics that act on the bladder [42].

3- Proton pump inhibitors: As with benzodiazepines, there is conflicting data regarding the association between the use of this class of medications and the risk of dementia. At least two studies have reported a clear association between the use of this class of medications and the occurrence of dementia. In a prospective cohort study of 73,000 patients aged 75 years or older who were not at baseline with dementia, regular use of proton pump inhibitors was associated with an increased risk of dementia, which remained significant after adjustment for confounding variables including age, sex, depression, stroke, heart disease, and concomitant medication. In contrast, two other observational studies, including a large case-control study of more than 70,000 Alzheimer's disease cases matched for age, sex, and geographic location, reported no association between use of this class of drugs and increased risk of Alzheimer's disease or evidence of a dose-response relationship. Limited preclinical data suggest an interaction between these agents and beta- and tau proteins. Malabsorption of vitamin B12 and other nutrients due to long-term use of proton pump inhibitors may play a role in this association [43].

Mild to moderate dementia

Although the effectiveness of acetylcholinesterase inhibitors in these patients has varied according to different studies, from no significant effectiveness in 30-50% of patients to above-average effectiveness in 20% of patients, in general, their usefulness is evaluated as a slight improvement in cognition, neuropsychiatric disorders, and daily activities.

Severe dementia

The relative effects of acetylcholinesterase inhibitors in patients with severe symptoms at diagnosis have been reported to be similar to those in the previous group. It should be noted that more limited studies have been conducted in this group than in patients with mild to moderate symptoms [44].

In the early stages of moderate to severe dementia in homebound patients who have not received previous treatment and patients who are cared for at home under the supervision of a nurse, the two drugs donepezil and galantamine have been found to be slightly beneficial in improving some of the cognitive and functional symptoms of patients [45].

There is no significant difference in effectiveness between the drugs in this group. Donepezil is often prescribed because it is better tolerated, but any of the drugs in this class may be used to initiate treatment. All patients should be evaluated for cognitive impairment, weight loss, and gastrointestinal problems. In 2015, the American Geriatrics Society warned against the use of this class of drugs due to the risk of low heart rate and postural hypotension in patients with a history of syncope [46].

The fourth drug, meantime, is also approved by the US Food and Drug Administration for the treatment of dementia in patients with Alzheimer's disease. Meantime is an N-methyl-d-aspartate receptor inhibitor and prevents the binding of glutamate, an excitatory neurotransmitter in the central nervous system,

to its corresponding receptor. This prevents the death of nerve cells due to excessive glutamate stimulation and subsequently prevents the progression of Alzheimer's disease. In advanced stages of Alzheimer's disease, meantime is prescribed in combination with an acetylcholinesterase inhibitor. Today, a commercial combination of meantime and donepezil is available in the world's markets. Notes on the four drugs used in Alzheimer's disease are given in the tables below. All drugs used in Alzheimer's disease slow the progression of the disease and delay the time of development of symptoms, but none significantly improve cognitive function or cure the disease. It is believed that these drugs are only marginally effective and the clinical significance of their effectiveness is questionable. This point is important for two reasons:

- ✓ The patient and his family members must be fully informed, so as to avoid having unrealistic expectations of drug therapy [47].
- ✓ If the patient does not respond adequately to drug therapy or if drug side effects occur, there is no need to continue the drug for life and its administration should be stopped.

Table 2. Acetylcholinesterase inhibitors

Rivastigmine	Galant amine	Donepezil	Drug
Nausea, vomiting, diarrhea, dizziness, headache, weight loss.			Side effects
Capsules: Initially 5.1 mg twice daily, then increase by 3 mg daily every two weeks to a maximum dose of 6 mg twice daily. Skin patch: Initially 6.4 mg patch/24 hours daily, after at least 4 weeks increase to 5.9 mg patch/24 hours daily.	Immediate-release solution or tablet: Initially 4 mg twice daily, then increase to 8 mg twice daily after 4 weeks. Maximum daily dose: 24 mg. Sustained-release capsule: Initially 8 mg daily, then increase to 16 mg daily after 4 weeks. Maximum daily dose: 24 mg.	Immediate-release tablets: Initially 5 mg daily, then increase to 10 mg daily after 4-6 weeks. 23 mg tablets: In moderate to severe cases, 23 mg once daily. If the patient has had a good response to 10 mg daily for 3 months and has not experienced side effects.	Dose

Skin patch: Remove the current patch at the designated time each day and apply a new patch to clean, dry, intact skin on the back, chest, or upper arm. The new patch should be applied to a new location and should not be applied to the same location for less than 14 days. The patch should be removed from the skin before an MRI. While using the patch, avoid tanning, sunbathing, using electric blankets, saunas, and hot baths.	Solution: Must be mixed with 120 ml of water or non-alcoholic beverage before drinking. Sustained-release capsule: This dosage form should be swallowed whole and not chewed, broken or crushed.	The drug should be taken at bedtime. Gastrointestinal side effects are expected to resolve within one to three weeks. 23 mg tablet: Swallow whole. Do not chew, break, or crush. Or dispersible tablets: Do not remove the tablet from the container before taking it and do not touch it with wet or damp hands. The tablet should be placed on the tongue and allowed to dissolve. After the tablet has dissolved, the patient should drink a glass of water. Swallowing the tablet whole should be avoided.	Method of prescribing
Take with food to reduce gastrointestinal side effects. If you miss a dose for several days in a row, consult your doctor. You may need to restart the medication at a lower dose and then gradually increase it to the current dose.			Advice to the patient

Table 3. N-methyl-d-aspartate receptor inhibitors

Memantine	Drug
Dizziness, lightheadedness, headache, diarrhea, constipation, increased blood pressure.	**Side Effect**
Immediate-release dosage form: Initially 5 mg daily, then increase by 5 mg per week for three weeks, aiming for a dose of 10 mg twice daily by the fourth week. Doses greater than 5 mg per day should be administered in two divided doses.	**Dose**
Oral solution: The oral solution should be prepared using a measuring device, drawn up, and placed in the side of the patient's mouth. This solution should not be mixed with other liquids. **Immediate-release tablet:** This dosage form should be taken whole with water. **Sustained-release capsule:** Swallow whole or regurgitate and the contents mixed with applesauce and taken immediately by the patient.	**Direction of Administration**
If you miss a dose for several days in a row, consult your doctor. You may need to start the medication again at the lowest dose and then gradually increase it to the current dose.	**Patient Advice**

Approach to managing side effects of acetylcholinesterase inhibitors

Since the effects of this class of drugs are relative, the physician should ensure that the patient benefits from this drug treatment before prescribing, to avoid prescribing consecutive drugs to overcome the side effects of the drugs prescribed initially.

1- Nausea and diarrhea: The most common side effects of drugs in this class are gastrointestinal side effects, including nausea, vomiting, and diarrhea. These side effects are dose-dependent and in most cases improve with time or dose reduction. In the case of oral rivastigmine, administering the drug in lower doses and with higher frequency or changing it to a skin patch form may be helpful. Both rivastigmine and galantamine should be taken with food. Since the likelihood of gastrointestinal side effects with donepezil is lower than with the other two drugs in this class, changing them to donepezil seems logical in case of intolerance to rivastigmine or galantamine.

2- Anorexia and weight loss: This complication occurs more frequently with drugs in this class than with placebo, but since dementia is also associated with weight loss, it is difficult to determine the clinical significance of this complication in the patient. Patients treated with this class of drugs who experience weight loss should be counseled about nutrition before discontinuing the medication. Alzheimer's disease is often accompanied by a loss of the sense of smell, which results in a decrease in the patient's sense of taste. Enhancing the taste of food by using spices, sweet and sour flavors, or soy sauce may increase the patient's appetite. In patients who also have depression in addition to Alzheimer's disease, the antidepressant mirtazapine may be a good option due to the possibility of increased appetite.

3- Decreased heart rate and blood pressure: Decreased heart rate, heart block, and syncope can occur as a result of increased vagal tone. In patients with symptomatic hypotension and heart rate reduction without other known causes, such as concomitant antihypertensive medications, cholinergic therapy should be discontinued. Acetylcholinesterase inhibitors are contraindicated in patients with low baseline heart rate or known cardiac conduction system disease.

4- Sleep disorders: Insomnia, vivid dreams, and other sleep disorders are more common with donepezil than with the other two drugs in this class. If nightmares occur, changing the time of administration to the morning or using an alternative drug is recommended.

Multidrug regimens

Due to the changing medication needs of the elderly with Alzheimer's disease due to cognitive decline and associated psychiatric and behavioral symptoms, prescribing medications for these individuals is challenging. In addition, a greater number of medications are needed to manage comorbidities in the elderly population. Although sometimes prescribing this number of drugs is necessary for some people, this is a concern for the community, especially in the elderly. It increases the incidence of medication errors, patient non-compliance, and drug interactions. Since people with Alzheimer's disease gradually lose their decision-making power and as a result, their ability to express drug side effects decreases, more cautious care is necessary in this particular group of people. Epidemiological studies indicate that receiving a large number of drugs is associated with unnecessary and inappropriate use. The Beers criteria include a list of drugs that should not be prescribed in the elderly population due to the high side effects or that their administration increases unnecessary hospitalization of elderly

patients. In most cases, multidrug studies have focused on the elderly population without dementia or people with dementia living in nursing homes, and little information is available on the use of prescription drugs in the community. Since a large percentage of these individuals are on the verge of being admitted to care facilities, it is essential to review their medication regimen to prevent future problems.

Discussion

The increasing understanding of the pathophysiology of Alzheimer's disease has led to an expansion of research into new compounds with the aim of finding a cure for the disease. In the Alzheimer's drug development process in 2018, 112 compounds were being investigated in phases I, II, and III trials, of which 63% were in the category of disease-modifying compounds with the aim of improving the disease. A quarter of the drugs under investigation were tested for improving cognition, which can lead to improvements in memory, language, thinking, and judgment.

Approximately 10% of the drugs may reduce behavioral disorders such as restlessness, apathy, and sleep disorders. Most disease-modifying drugs target amyloid beta or tau proteins. Inhibition of the enzyme secretase, which is involved in the production of amyloid beta protein from amyloid precursor protein, is the primary mechanism of action of many of the new compounds.

Beta-secretase inhibitors target this enzyme, which is involved in the first step of amyloid precursor protein breakdown, while gamma-secretase inhibitors target the second step of amyloid precursor protein breakdown. Many beta-secretase inhibitors have shown the ability to reduce the production of beta-amyloid plaques, but they have not been effective in clearing existing plaques and improving cognition. In addition, these compounds must be administered early in the disease process to be effective, when the disease is usually not diagnosed.

Because beta-secretase breaks down many vital proteins in the brain in addition to amyloid precursor protein, researchers are seeking ways to inhibit beta-amyloid production with minimal side effects. An increasing focus of disease-modifying drugs is targeting tau proteins. Although early studies in this area have not yielded promising results, the research has raised new questions that have led to the investigation of new approaches, including immunotherapy, in phase I and II clinical trials. Many drugs have been studied to alleviate the behavioral symptoms of Alzheimer's disease that were previously approved for the treatment of other diseases. Sometimes these compounds can move from the preclinical phase to phase II clinical trials, accelerating the research process. Some drugs with potential modulatory effects include citalopram and mirtazapine, carbamazepine and levetiracetam, lithium and methylphenidate.

Despite extensive research, the definitive underlying cause of this complex disease remains unknown. Combination therapies are likely needed, but studies have focused on single-drug therapies. New treatments tested in animal models often lack predictive value in humans, and many drugs tested in human models have been ineffective or have unacceptable side effects.

Recruiting and retaining volunteers for the long process of clinical trials is difficult, and bringing a selected drug to market is expensive. Due to the complexity of Alzheimer's disease, current treatments only help control clinical symptoms and delay disease progression. New clinical studies are changing the treatment of Alzheimer's disease by shifting the focus to disease modification, but more information is needed before these products can enter the pharmaceutical market.

The pharmacist is ideally placed not only to ensure the safe and effective use of the drug by the patient, but also to introduce up-to-date treatments. As one of the most accessible members of the healthcare team, the pharmacist can also communicate with the patient's family to clarify realistic expectations of treatment. With over 100 compounds under investigation, the role of pharmacology in the management of Alzheimer's disease is expanding. In a study by Estevez et al., the effect of cerium oxide nanoparticles on animal models of stroke was investigated.

In treated mice, nanoparticles were found to play a significant role in reducing stroke-induced damage by inhibiting peroxynitrite. In this study, neuronal cell death was also assessed by lactate dehydrogenase release, and it was observed that neuronal cell death caused by excess glutamate was reduced by treatment with these nanoparticles. Nanomaterials can also be used as gene delivery vehicles to intervene in neurological diseases. Although viral gene delivery has been successful in promoting and maintaining brain cells, the use of some nanoparticles for gene delivery is suggested due to safety, high biocompatibility, effective penetration into the cell and its nucleus, and precise targeting.

Research has shown that the use of nanoparticles inhibits neutrophils that cause immune responses and prevents severe brain damage in brain models. It has been shown that increased levels of the protein Nestin are effective in repair mechanisms after injury. This protein is also highly expressed during the early stages of development of the peripheral and central nervous systems. Researchers showed an increase in the number of Nestin-expressing cells as a result of treatment with silver nanoparticles in mouse models of stroke, indicating the effectiveness of these nanoparticles in neurogenesis [48].

Conclusion

Alzheimer's disease is the most common age-related disease characterized by extracellular accumulation of amyloid beta (Ab) plaques and intracellular tangles of hyper phosphorylated tau neurofibrils. Since Ab is a key molecule in the pathogenesis of Alzheimer's disease, it interferes with many aspects of mitochondrial function, including energy metabolism dysfunction, reactive oxygen species (ROS) production, and pore formation. Recent studies have shown that Ab gradually accumulates in the mitochondrial matrix and is directly related to mitochondrial toxicity. Compelling evidence suggests that mitochondria are a crucial organelle in ROS production and that oxidative stress is linked to neuronal death and neuronal dysfunction, suggesting a key pathogenic role of oxidative stress in Alzheimer's disease. Alzheimer's disease (AD) is the most common cause of age-related neurodegeneration and cognitive impairment, and currently there is no effective treatment. The underlying pathogenesis is complex, but a growing body of evidence suggests that mitochondrial dysfunction is a common path mechanism involved in many of the hallmark features of the Alzheimer's disease brain, including the formation of amyloid beta (Aβ) aggregates (amyloid plaques), neurofibrillary tangles, dysfunction of the cholinergic system, impaired synaptic transmission and plasticity, oxidative stress, and neuroinflammation, leading to neurodegeneration and cognitive dysfunction. In fact, mitochondrial dysfunction, along with the progressive accumulation of mitochondria in Alzheimer's disease, is an early event in the pathogenesis of AD. Healthy mitochondria are critical for providing adequate energy to maintain endogenous neuroprotective and repair mechanisms, whereas abnormalities in mitochondrial function, motility, fission, and fusion lead to impaired neuronal function and degeneration associated with excessive

production of free radicals and decreased intracellular calcium buffering. Neurological diseases such as stroke, movement disorders, and Parkinson's disease are more common among the elderly. These problems can be managed well by providing adequate care and creating a controlled environment for the affected person. Early diagnosis of these diseases is very important to start treatment and care as soon as possible. After knowing the types, symptoms, and treatment, necessary measures should be taken.

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