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THE DARK SIDE OF MEDICATIONS: HOW CERTAIN DRUGS CAN CAUSE DEMENTIA

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ABSTRACT
Dementia is a devastating neurodegenerative disorder affecting millions worldwide. While age, genetics and lifestyle factors contribute to dementia risk; certain medications have been implicated in its development. This review aims to summarize the current evidence on drug-induced dementia, highlighting the most commonly implicated medications and their mechanisms of action. Anticholinergic medications, benzodiazepines and antipsychotics were consistently associated with increased dementia risk. Additionally, certain antidepressants, antihistamines and cardiovascular medications were also implicated. Epidemiological study also clearly states that worldwide nearly 50 million people suffering from dementia and nearly 10 million new cases diagnosed each year. The underlying mechanism of drug-induced dementia are complex and multifaceted, involving neurotransmitter dysregulation, oxidative stress, and inflammation. Our findings highlight the need for healthcare providers to carefully consider the potential risk and benefits of medications.

KEYWORDS: Dementia, Alzheimer s, anticholinergic, antidepressants, antipsychotics, mixed dementia.

INTRODUCTION

Dementia is a chronic and irreversible condition that effects memory, language, problem solving abilities, emotional, cognitive and behavioral symptoms which occurs due to inadequate supply of blood and oxygen to brain and also shows many symptoms and brain disorders including Alzheimer's disease. The main symptoms of dementia are agnosia, aphasia, apraxia and disorientation. Dementia is caused by many ways they are due to progressive death of brain cells and neurons. Dementia is also cause due to head injuries, strokes, brain tumors and so on. There are 4 types of dementia they are Alzheimer's disease, vascular dementia, Lewy body dementia (which may occur with Parkinson's disease), frontotemporal dementia, mixed dementia.[1] Alzheimer occurs due to accumulation of toll and amyloid protein in frontal and temporal cortex which leads to formation of neurofibrillary tangles and amyloid plaques. It approximately causes 75% of all dementia. It causes memory loss, word finding difficulties, language difficulties etc. Vascular dementia is caused due to inadequate blood supply to brain and also due to small strokes. It is also known as multi infract dementia. It shows neurological signs like hypertension, diabetes mellites, smoking, arterial disease. Lewy body dementia is caused due to the presence of Lewy bodies and abnormal crumps in the brain including cerebral cortex. Approximately 10-15% of dementia. It causes recurrent fall, visual hallucinations, disturbance in sleep and marked fluctuations in conscious. Frontotemporal dementia affects the both frontal and temporal lobes of the brain. It occurs approximately 2-3% of dementia. It is also known as picks disease. it occurs mostly in young age. It shows symptoms like apathy, decreased motivation, socially inappropriate behavior. Mixed dementia in this more than one type of dementia is involved, mostly Alzheimer's and vascular dementia is involved. This type of dementia is common in aged people beyond 80.[2] Dementia is also cause due to excessive use of drugs.

COMMON CLASSES OF DRUGS THAT CAUSES DEMENTIA

- [2]Anticholinergics
- Antidepressants
- Antipsychotics
- Benzodiazepines
- Antiepileptic drugs
- Anti histamines
- Incontinence drugs
- Chemotherapy drugs
- Corticosteroids
- Antimuscarinics
- High blood pressure drugs

- Statins
- Motion sickness drugs

EPIDEMOLOGY OF DEMENTIA

Dementia is a major public health that effecting millions of people world widely. The epidemiology of dementia is complex and influenced by various factors including age, sex, education and lifestyle. according to the world health organization (WHO), nearly 50 million people were suffering from dementia and nearly 10 million new cases diagnosed each year.

[3]AGE-SPECIFIC PREVALENCE

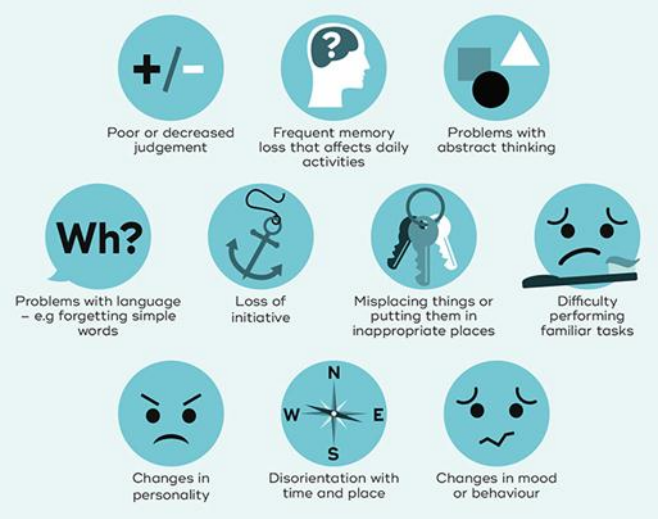
- 1% of people aged 60-64yrs
- 3% of people aged 65-69yrs
- 6% of people aged 70-74yrs
- 12% of people aged 75-79yrs
- 24% of people aged 80-84yrs
- 37% of people aged 85yrs and older

SEX SPECIFIC PREVALANCE: Women are mostly affected by dementia than men particularly after the age of 80 yrs. According to the systematic review and meta-analysis, the pooled prevalence of dementia was 12.6% for women and 9.4% for men.

GEOGRAPHIC VARIATION: According to a systemic review and meta-analysis, the highest prevalence of dementia is found in western Europe (12.3%) and north America (11.4%), the lowest prevalence was found in south Asia (2.4%) and sub-Saharan Africa (2.1%).

INCIDENCE OF DEMENTIA: The incidence of dementia ranges from 1.4 to 5.4 per 1,000-person year.

MORTALITY AND MORBIDITY: According to WHO, dementia is the fifth leading cause of death in world widely, accounting for 2.4 million deaths in 2019.



MECHANISMS INVOLVED IN MEDICATION-INDUCED DEMENTIA

Excessive use of drugs like anticholinergic, antipsychotic, statins, opioids etc., causes changes that is neurotransmitter imbalance, inflammation in brain, oxidative stress.

Anticholinergic drugs block the acetylcholine and histamine receptors which is a neurotransmitter important for cognitive function.

Benzodiazepines modulates the activity of GABA which is involved in learning and memory and antipsychotic blocks the action of dopamine. Blockade of acetylcholine, GABA and dopamine imbalance of neurotransmitter release and affects the cognitive function.

Antihistamines play a crucial in many physiological processes, cognitive function, attention and memory. The various mechanism of antihistamines that leads to dementia are inhibits the release of acetylcholine which helps in cognitive function, modulates the glutamate and GABA which is involved in learning and memory, histamines used for inflammation and oxidative stress which leads to damage of brain cells and also excessive use of histamines can cross the blood brain barrier then the toxins and inflammatory molecules enter into the brain then it leads to dementia.

Opioids induce dementia by several mechanisms, opioids activate the μ-opioids receptors which leads to increase in production of reactive oxygen species (ROS) and also causes inflammation in brain. It also crosses the blood brain barrier and allows toxins and inflammatory molecules in to brain and causes neurodegeneration. Opioids induce apoptosis in neurons and increase the inflammation and oxidative stress which leads to decrease in cognitive function and neurodegeneration. And it also modulates the activity of neurotransmitters such as dopamine, serotonin and acetylcholine that involved in cognitive function.

RISK FACTORS FOR DRUG-INDUCED DEMENTIA

- Age old age people have high risk of developing dementia due to their excessive medicines related to their disease. In adults there is a moderate chance of causing drug induced dementia.
- Taking of multiple medication for long period of time can cause dementia. This is known as polypharmacy which causes inappropriate prescribing, adverse drug events, increased mortality and unplanned hospitalization.
- Patients with pre-existing cognitive impairment are at higher risk of causing dementia.
- Based on higher dose and longer duration of medications use cause dementia.
- Genetic predisposition: family history of dementia.
- It may occur in patients with comorbidities such as diabetes, hypertension, cardiovascular diseases.
- Due to decrease in medication clearance in renal impairment patient there is risk of developing drug induced dementia.

MANAGEMENT FOR DRUG INDUCED DEMENTIA

NON-PHARMACOLOGICAL INTERVENTIONS

- [5]Regular review of medications to minimize the risk of dementia.
- We should go for alternative medication which not leads to dementia.
- Provide cognitive stimulation such as cognitive training and cognitive therapy to improve cognitive function.
- Modifications should be done in their environment like reducing noise pollution, reduce stress and improve cognitive function.
- Regular cognitive assessment should be done to decrease the risk of dementia.

PHARMACOLOGICAL INTERVENTIONS

- Discontinue the offending medication to prevent further cognitive decline.
- Use cholinesterase inhibitors such as donepezil, rivastigmine for improving cognitive decline.
- Memantine is used to slow down cognitive decline.

DISCUSSION

The association between medications and the onset of dementia has emerged as a crucial topic in modern healthcare. As highlighted in this review, various classes of medications, including anticholinergics, antidepressants, antipsychotics, and benzodiazepines, have been implicated in cognitive decline and the development of dementia. This phenomenon underscores the importance of understanding the mechanisms by which these drugs influence brain function. One of the primary mechanisms involves neurotransmitter imbalances caused by these medications. For instance, anticholinergics inhibit acetylcholine, a neurotransmitter vital for memory and cognitive processes, while benzodiazepines alter GABAergic activity, affecting learning and memory. The cumulative impact of these disruptions contributes to cognitive impairment, particularly in vulnerable populations such as the elderly. Additionally, drugs like antihistamines and opioids exacerbate oxidative stress and neuroinflammation, further accelerating neuronal damage and cognitive decline. The epidemiological data presented in this review provide a broader context for understanding the prevalence and impact of dementia. It is evident that age and sex play significant roles, with older adults and women being disproportionately affected. Furthermore, the geographic variations in dementia prevalence point to the interplay between environmental, genetic, and lifestyle factors in shaping dementia risk.

The findings also emphasize the importance of addressing risk factors such as polypharmacy, comorbid conditions, and genetic predispositions. Older adults, in particular, face increased susceptibility due to physiological changes that affect drug metabolism and clearance. This underscores the necessity of personalized medicine approaches and regular medication reviews to mitigate risks. Management strategies for drug-induced dementia are multifaceted, involving both non-pharmacological and pharmacological interventions. Cognitive stimulation and environmental modifications have proven beneficial in preserving cognitive function, while medications like cholinesterase inhibitors and memantine offer pharmacological avenues to slow cognitive decline. Discontinuing or substituting offending drugs remains a cornerstone of prevention and treatment.

CONCLUSION

Dementia is a multifaceted and challenging condition that not only arises from natural neurological deterioration but can also be exacerbated by certain medications. Drugs such as anticholinergics, antipsychotics, benzodiazepines, and opioids have been identified as contributors to cognitive decline due to their interference with neurotransmitters, induction of oxidative stress, and promotion of neuroinflammation. The epidemiology of dementia highlights its significant impact worldwide, with women and older populations being disproportionately affected.

Management strategies for drug-induced dementia emphasize the importance of regular medication reviews, non-pharmacological interventions such as cognitive stimulation and environmental modifications, and the use of specific medications like cholinesterase inhibitors and memantine to mitigate cognitive decline. By raising awareness and implementing preventive measures, it is possible to reduce the risk and impact of medication-induced dementia, thus improving patient outcomes and quality of life.

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