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DRUG INDUCED DELIRIUM IN GERIATRIC PATIENTS: AN OVERVIEW

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ABSTRACT

Drug induced delirium is one of the most common psychological problem in Geriatric patient's, this is mainly due to polypharmacy. In addition to polypharmacy, altered pharmacokinetics and pharmacodynamics seen with aging and associated co-morbidities have a crucial role with drugs in causing delirium. About 12-39% of all case of delirium is due to drugs, mainly due to drugs that act on the brain including narcotics, painkillers, sedatives (particularly benzodizepines) stimulants, anti depressants, Parkinson's disease medication and antipsycotics. The aim of the article to provide an idea about how to control drug induced delirium in geriatric patients by early recognization and provide proper pharmacological and non pharmacological management for drug induced delirium,it also reviews about the mechanism of action of the condition and discuss about the age related changes that result in altered pharmacological effect and the pharmacist intervention of drug induced delirium are discussed.

KEYWORDS: Drug induced delirium, geriatric Patients, Polypharmacy, Pharmacist intervention.

INTRODUCTION

Aging is a physiological factor and delirium is more common in elderly due to various etiology, drugs have been widely associated with the development of delirium in elderly and

it is reversible.[1] Medications with anti cholinergic properties, analgesics and narcotics are common cause of drug induced delirium.[2]

Delirium is common in the United States. In a systematic review of 42 cohorts in 42 studies 10-31% of new hospital admission, and the mortality rate are 10-26%.[3] Delirium is a cognitive disorder result in disturbance of memory, intellect and behaviour, most common symptoms are restlessness, agitation,rapid mood changes or hallucinations.[4] Delirium was also considered as a point between wakefulness and coma and it is described as "clouding of consciousness."[5] Hypoactive delirium, may include inactivity or reduced motor activity, abnormal drowsiness and lethargy. Hyperactive form in which patients are agitated have increased arousal or are very vigilant. it is mainly treated by using antipsychotic drugs(to treat agitation and hallucinations)which may Includes Risperidone, Halloperidol, Olanzepine and Quetiapine etc.[6]

The mechanism of drug induced delirium are not well defined. Delirium can result from an imbalance in brain chemical (neurotransmitter) which are crucial molecules that relay signals between nerves such as acetylcholine. The mechanism of drug induced delirium are not well defined.[7] Reversible cause of delirium are, drugs including any new medication, increased dosages, drug Interactions, OTC drugs, alcohol etc and Lack of drugs such as when long term sedatives (including sleeping pills) or pain killers are stopped.[8]

Creatinine clearance should be measured routinely in the elderly and dosage should be adjusted for medications that are more prone to cause delirium, if possible medications with anti cholinergic properties should be avoided or doses of necessary medications should be minimized.[9]

Anti cholinergic delirium is best managed by physostigmine, a cholinestrase inhibitor, Donepezil also a cholinestrase inhibitor, is an effective choice in the management of drug induced delirium.[10] Effective management of drug induced delirium Involves recognition, cessation or dose reduction of the causative drugs and supportive medical care, special antidotes are appropriate in only a few limited cases.[11] Since many older People take multiple medications or polypharmacy which may interact in harmful ways, result in drug interactions, so pharmacist intervention are needed to provide proper information about every prescription and non prescription medication being taken.[12]

Drugs Causing Delirium (Deliriants)

Many groups of drugs can cause delirium mainly drugs with anticholinergic properties various class of drugs includes cardiovascular drugs, pulmonary drugs, centrally acting drugs include sedatives and hypnotics, anti parkinsonian drugs, etc, psychotropic drugs analgesics, anti histamines and gastrointestinal agents.[13]

Class	Drugs	Effect
CARDIOVASCULAR AGENTS i) Anti arrhythmic drugs	Disopyramide	Have strong anti cholinergic effect and can induce delirium because of decreased renal clearance.
ii) Antihypertensive drugs	Digoxin	Normal dose of digoxin can accumulate and cause toxicity and delirium.
	Propanolol	Beta blockers cause delirium, diuretics can induce delirium by dehydration.
PULMONARY DRUGS	Theophylline	In high dose of this drug contribute to delirium these are used in patients with poor oxygenation which itself can increase risk of delirium.
CNS DRUGS i) sedatives and hypnotics	Benzodiazepines	Which are lipid soluble having prolonged half life in elderly due to accumulation of lipid tissue due to increased duration of action and sensitivity to sedatives hypnotics in elderly can cause delirium.
II) Anti Parkinson's agents	Levodopa	Dopamine agonist can contribute to delirium in dose related manner,it may result in confusion in elderly.
	Trihexyphenidyl	In which delirium occurs in the end stage of Parkinson's disease due to high dose of the drug.[14]
PSYCHOTROPIC AGENTS i) Trycyclic anti depressants	Nortriptaline	Have an anti cholinergic effect and can induce delirium.
II) SSRI	Paroxetine	Having greater affinity for muscarnic receptor.
III) Anti manic drugs	Lithium	Can cause delirium even at therapeutic serum levels.[15]
ANALGESICS		

I) Narcotics	Meperidine	Narcotics is also also a risk factor of delirium Is often avoided in elderly due to decreased renal function meperidine is converted to anti cholinergic metabolites that Can cross BBB and lead to delirium.
I) NSAIDs	-	It also induce delirium in which some NSAIDs can cross BBB.[16]
ANTI HISTAMINES	Diphenhydramine Chlorpheniramine	Have potent anti cholinergic effect and are associated with delirium.[17]
GASTROINTESTINAL AGENT		
H2 blokers	Cimetidine Ranitidine Famotidine	In which cimetidine mainly cause delirium.
Anti spasmodic	-	Used for gastrointestinal motility or bladder urgency have some anti cholinergic effect which can cause increased risk of delirium.[14]

Factors That Contributes To Drug Induced Delirium

There are many factors that cause drug induced delirium which includes physiological changes due to aging, polypharmacy, medical condition morbidities and altered pharmacokinetic and pharmacodynamic changes.[18]

1) Polypharmacy

Polypharmacy is the major risk factor of drug induced delirium,elderly patients using large number of medication having a significant number of co morbidities It's may be due to pharmacokinetic and dynamic drug interactions. But we can't avoid polypharmacy so, careful prescribing and pharmacist intervention are needed in older persons.[19] For that expert knowledge in prescribing psychotropic medication is essential which includes mechanism of action, side effect, various drug interactions and also importance of thorough history of the patients.[18]

2) Physiological Changes Due To Aging

In geriatric patients response to drugs may be modified by age related changes, which may have a role in inducing delirium are an increase in total body fat, decreased in lean body mass and water, decrease in albumin and GFR.

3) Co-Morbidities

Elderly patients with multiple Co morbidities who take many medication are at an elevated risk for delirium, In heart failure patients have reduced metabolism due to hepatic congestion and reduced elimination of drugs due to renal insufficiency result in renal failure may increase free concentration of certain drugs and increase the risk of delirium. In stoke and dementia there is impaired integrity blood brain barrier, reduced integrity of BBB function is strongly associated with susceptibility to delirium.

4) Altered Pharmacokinetics and Pharmacodynamics Changes

It is important to review medications in the elderly for both pharmacokinetics and pharmacodynamics effect as drug-drug or drug-disease interactions can contribute to delirium. Pharmacokinetics parameters that changes with age include an extension of half life due to reduced metabolic capacity or decreased volume of distribution and renal elimination.In elderly patients with decreased muscle mass the digoxin reaches much higher level because of volume of distribution is smaller. Reduced renal function can contribute to extended high levels of medication, renal elimination is decreased due to reduce renal blood flow. Plasma protein particularly albumin is altered with aging, in delirium albumin is decreased thus by changing the amount of free drug available,protein binding drug interactions may affect mental status. So high level of albumin bonded medications in conservative dose can given during delirium.

Drug may interact pharmacodynamically leading to an enhanced toxic effect for eg:multiple anti cholinergic medications can lead to toxic effect can trigger delirium. Knowledge of these interactions can help pharmacists to predict drugs that pharmacodynamically interact to increase the delirium.[20]

Anti cholinergic medication appears to have adverse effect secondary to receptor site changes. Decreased drug sensitivity to anti cholinergic, sedative medications can lead to delirium, in the elderly changes in receptor function occur across organ.[21]

Mechanism of Drug Induced Delirium

The mechanism of drug induced delirium Is not well defined, In benzodiazepines withdrawal there is decline on GABAergic function may precipitate delirium. GABA receptor Inhibits the release of dopamine, excess of dopamine is Implicated in the etiology of delirium, so speaking blocker are helpful in providing symptomatic relief of delirium. Delirium can result

from an imbalance of neurotransmitters which are crucial molecules that relay signals between nerves such as acetylcholine, GABA etc.[20]

Early Recognition of Drug Induced Delirium

Early diagnosis of delirium is crucial to improve the prognosis of elderly patients. The diagnosis of delirium require not only careful mental status but also thorough history from the patient's family and also by applying confusion assessment method criteria.[18] increased awareness of clinical staff and routine screening of cognitive function with standardized instrument are needed, and also any acute change in patients mental status presenting as the early sign of delirium.

Drugs are the main cause of delirium, so healthcare professional should be aware about medication mainly which have anti cholinergic effect. A record should be given to the delirogenic drugs to identify the anti cholinergic load of these medication and to check possible drug interactions,any addition of new drugs or increased dose should be also verified.[22]

Management of Drug Induced Delirium

Effective management of drug induced delirium involves recognition,dosage reduction of the causative drugs and initiation of reorientation strategies and supportive medical care.[11]

Pharmacological management

Drug review is one of the method to identify the precipitating cause of delirium, avoid non essential drugs and drugs with significant anti cholinergic properties.Creatinine clearance is also measured routinely in hospitalized geriatric patients and dosage should be adjusted for medication that are more prone to cause delirium.[9] A drug with low anti cholinergic potency should be prescribed for eg: tricyclic antidepressant and that is secondary amine such as desipramine, nortriptaline Instead of tertiary anime Amitriptaline.[23]

Also drug treatment aimed at sedation should be introduced for specific indications such as aggression, hallucinations, patient distress and compliance with therapy, certain haloperidol and benzodiazepines (diazepam, lorazepam, midazolam) is useful in benzodiazepines withdrawal and seizures, may be most appropriate choice in this circumstance.[24] While antipsychotics are not labelled for the use in delirium,that they may reduce agitation and combativeness.[25]

Non Pharmacological Management

Multi Component intervention targeting specific risk factors for delirium has been developed through training and educational programs of health care staff, non pharmacological intervention protocols and improvement of the environment of the patient and promoting daily activities. Also requires high quality nursing care are effective in reducing the incidences, severity and duration of delirium.[26]

PHARMACIST'S INTERVENTIONS

- Pharmacist can play a key role in the recognition and prevention of delirium and can promote safe and effective treatment.[27]
- Interviewing the patient and family which are helpful method to obtain accurate history,[28]

Role of Clinical Pharmacist In Drug Induced Delirium

- Pharmacists can promote the avoidance of drugs that are associated with delirium and can choose the alternative drugs for the therapy. In addition, appropriate dosing of certain drugs and it's effect should be ensured.[29]
- Pharmacist can evaluate drug related cause of delirium

a) Checking the patient is taking an appropriate dose.
b) whether electrolyte supplement is needed or requires adjustment.
c) Appropriateness of glucose control regimen.
d) Appropriateness of antibiotic regimen.[30]

- Clinical pharmacists can also play major role in interactions, can identify drug -drug and drug - disease interactions and can recommend interventions and proper patient counselling for the drugs and disease.[31]
- Pharmacists can form an interdisciplinary team including (Physicians,nurses and other health care professional) their activities includes

a) Provide educational sessions explaining about the risk factors for delirium recognition etc.
b) Provide delirium education to family members, reorient patient and encourage family involvement.
c) Maintain the patient's mobility and self care ability like physical and occupational therapy.

d) Promote nutrition and hydration and promotes normal sleep habits are essential.[30]

CONCLUSION

Drug induced delirium is one of the serious condition in geriatric patients, it's mainly effect patients with cognitive impairment or dementia. Proper care should be taken for patients with delirium, clinical recognition and appropriate management of drug induced delirium is important. Minimizing polypharmacy and use non delirogenic drugs, if drugs with known risk of inducing delirium is used close observation and monitoring is essential. Non pharmacological management like history collection is also helpful.

Clinical pharmacist can play a major role in creating awareness about the drugs and disease about the major interactions in drug induced delirium and can recommend proper interventions.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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