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DRUG CASCADES IN ELDERLY CARE, CLINICAL RECOGNITION AND MANAGEMENT

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Abstract

Prescribing cascades happen when side effects from one medication in older adults get mistaken for a new health problem, leading to more prescriptions that pile on complications and make polypharmacy worse. This narrative review covers the background, underlying mechanisms, risk factors, and ways to spot them clinically, their impacts, management approaches, prevention steps, and the roles of healthcare teams, based on real-world hospital studies of multimorbid elderly patients taking several medications. Everyday examples include swelling from calcium channel blockers treated with water pills, or raised blood pressure from NSAIDs managed with blood pressure drugs-issues made worse by aging bodies that process medicines differently and multiple health conditions. These cascades often lead to more hospital stays, loss of daily function, and higher death risks tied to too many drugs. Effective management relies on pharmacists guiding medication reviews and safely stopping unneeded drugs to break the cycle, while prevention draws on tools like Beers Criteria, STOP/START guidelines, and educating patients. Teams of doctors, pharmacists, and nurses working together cut down adverse reactions. In busy hospital settings with limited resources, these practical steps can make medications safer and help older adults live better.

Keywords: *Drug cascades, Prescribing cascades, Polypharmacy, Adverse drug reactions, Deprescribing strategies, Management, Prescribing guidelines.*

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INTRODUCTION

Drug cascades are also known as prescribing cascades they occur when a drug is prescribed to manage side effects of an another drug, usually when a side effect is assumed as a new condition [1]. Drug cascades commonly occur when signs and symptoms of a patient are assumed as an adverse drug reaction and misinterpreted as a new condition which results in prescribing a new drug and lead to polypharmacy, especially in case of elderly people. This polypharmacy increases the risk adverse effects which lead to hospitalizations [2].

Polypharmacy is described as usage of multiple medications which leads unnecessary side effects, which are most commonly observed in elder patients. Elderly patients usually contains multiple comorbidities and receive five or more medicines (polypharmacy), making them particularly open to adverse drug reactions and cascades. Age-related pharmacokinetic and pharmacodynamic changes, along with overlapping symptoms such as dizziness, edema, urinary incontinence, or cognitive changes, make it easy to mislabel drug toxicity as a new disease [3]. Studies report that drug cascades in 15 to 40 percent of elderly patients with multiple illnesses who use five or more medicines in Indian tertiary care hospitals, more than half of older patients receive several drugs at the same time each new symptom risks being treated as a new disease which adds more medicines and raises harm [4].

Common examples of drug cascades in the elderly patients include:

1) ACE inhibitors → Chronic cough → Cough suppressant/ Codeine →Constipation →Laxative.

2) NSAIDs → HTN → Antihypertensive drugs.

3) CCBs → Edema → Diuretics.

The drug cascades starts when an drug A is prescribed for actual illness and the causes an adverse effect ADR where clinicians interpreted as a new symptom and prescribe drug B for the adverse event which actually caused by drug A.[2] For example, Amlodipine prescribed for hypertension causes pedal edema and it is considered as a new symptom clinician prescribes drug belongs to the class of diuretics which results in increase of medication

unnecessarily to the patient increases burden and risk adverse events.

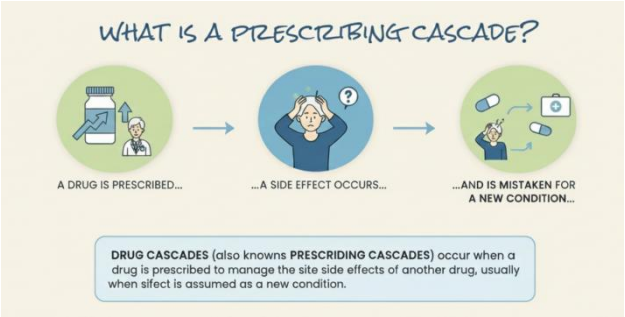

Fig 01: What is a prescribing cascade

Pathophysiology and mechanism for drug cascades

The Pathophysiology of the drug cascades depends on pharmacological actions and age-related body changes and combination of one or more diseases rather than a single disease.

Physiologic decline

After certain age there is a progressive decrease in the function and working of the body organs related to age which makes elder people to experience like anxiety, depression.

Diagnostic oversight

In elder people most common thing is misidentification it occurs most commonly due to symptoms or conditions presented to the patient symptoms like confusion, fatigue get noted as age related things instead of concluding them as signs of disease. As a result, the real problem gets untreated or treatment may be delayed. Patient present with multiple morbidities rather than a single disease in relation to age and clinical assessments, rather than a single illness [5].

PHARMACOKINETIC CHANGES

Elder people experiences reduced organ function and ability includes decreased GFR (glomerular filtration rate), hepatic blood flow, metabolism, where body takes longer time to eliminate the drugs present in the body (prolonged half-lives) which elevates the drug serum levels in the blood stream. For example, A standard dose of medication like diazepam accumulates in the body and cause excessive sleep or sedation which increases the risk these conditions are similar in case of low blood-pressure and misinterpreted and treated with more medication which worsens the condition. Usage of multiple medications leads to complications like drug-drug interactions like, drug interaction between amiodarone and warfarin results in bleeding which might be misdiagnosed as a stomach issue and it is treated with an another unnecessary drug PPI (proton-pump inhibitor) leads to polypharmacy.

PHARMACODYNAMIC CHANGES

According to age elder people and their body receptor sensitivity changes which makes them more susceptible to side effects or ADR. Most common medications like beta-blockers used for heart conditions causes symptoms like bradycardia and fatigue and it is misinterpreted as depression in elder people and treated with anti-depressants. Another class of drugs like CCB's like amlodipine used to manage blood pressure causes peripheral edema (swelling in the lower extremities) which is assumed as a new condition and treated with drugs belonging to the class of diuretics like furosemide.

MECHANISM OF CASCADE FORMATION

Step by step mechanism of cascade formation

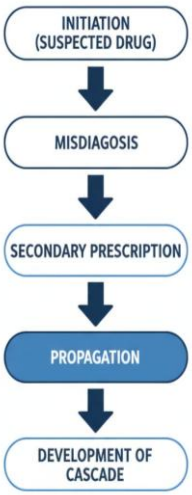

Fig 02: Mechanism of cascade formation

Cascade Pair	Index Drug Effect	Misinterpreted As	Secondary Drug	Potential Downstream Harm
Calcium channel blocker → Loop diuretic	Peripheral edema	Heart failure	Furosemide	Electrolyte imbalance, incontinence
NSAID → Antihypertensive	Hypertension/edema	Essential HTN	ACE inhibitor	Renal impairment, cough
Antipsychotic → Dopaminergic	Parkinsonism	PD	Levodopa	Dyskinesia, hallucinations
Benzodiazepine → Antivertigo	Dizziness/falls	Vertigo	Betahistine	Sedation, dependency
Opioid → Laxative	Constipation	IBS	Polyethylene glycol	Overflow diarrhea, dehydration

Risk factors related to drug cascades

Risk factors related to drug cascades or prescribing cascades in elder patients involves patient characteristics, underlying diseases and prescribing system related factors and misinterpretation of ADR's as new conditions.

- **Patient-related factors**
- **Disease related factors**
- **Prescribing system related factors**

Patient related factors

Elder people with age greater than 60 years face a high risk of ADR related to multiple medications, prolonged usage of multiple medications, reduced creatinine clearance, decreased drug elimination from the body. Altered pharamacokinetic activity, Low body weight, Polypharmacy (medications ≥ 5) Renal or hepatic impairment causes major risks [6].

Disease related factors

Patients with multimorbidities include cardiovascular diseases, Neuropsychiatric diseases, Chronic arthritis, Pain, Diabetes milletus, Chronic kidney disease, require multiple medications to treat the conditions so it causes usage of multiple medication leads to polypharmacy results in risk to patient.

Clinical recognition of drug cascades in elder adults:-

Drug cascades occur when an adverse drug reaction is misinterpreted as new condition where a new drug or second drug is added & risk occurs, Early recognition helps patients to prevent polypharmacy decreases hospital stay and death.

Drug classes which frequently involved in drug cascades or prescribing cascades include:

- Central nervous system;
  - Benzodiazepines
  - Anti-psychotics
  - Anti-depressants
  - Anti-epileptics
- Cardiovascular drugs :
  - CCB's (Calcium channel blockers)
  - Beta blockers
  - Diuretics
  - ACE inhibitors
- Analgesics and anti-inflammatory drugs :
  - NSAIDs
  - Opiods
- Urogenital drugs :
  - Anti-muscarnics
- Gastro intestinal drugs :
  - PPI's (Proton Pump Inhibitors)
  - Laxatives
- Endocrine and Metabolic drugs :
  - Corticosteroids
  - Hypoglycemics

CLINICAL SIGNS

Recognising a drug cascade is often knowing patient new symptoms and their recent prescriptions and noticing any new symptoms arising after any drug intiation or discontinuation. Temporary signals like any new condition arising after a week or within a week of starting a medication and any worsening condition after increase in the dose and patient feels relaxed after an symptomatic treatment.

Specific symptom patterns that often signal a cascade, including sudden confusion, frequent falls, unexplained swelling (edema), or new tremors and rigidity. These are frequently misidentified as getting older rather than drug-induced which are symptomatic clues. Treatment signals include rise in the count of prescribing drugs and addition of new drugs without stopping older ones and lack of diagnostic confirmation and the risk is high for the patients, particularly those are managing multiple chronic conditions, those taking five or more medications, or anyone who has recently shifted home from a hospital stay.

DIAGNOSTIC CHALLENGES IN GERIATRIC POPULATIONS

Diagnosing problems in older adults is often difficult because illness and medicine side effects look alike. Many adverse drug reactions show up as tiredness, falls, or confusion, symptoms that are common in old age and easily dismissed as part of aging. When patients live with several chronic diseases, as the same symptom can point to a disease, a drug effect, or both. Getting an accurate history is also challenging. Memory problems limit what patients can report, and caregivers may not clearly remember when medicines were started or changed. Care is often uneven, with multiple doctors prescribing drugs, poor medication understanding, and discharge summaries that miss key details. Busy clinics leave little time for careful review, so treatment focuses on controlling symptoms rather than questioning existing medicines. As a result, common and predictable drug reactions are often missed and attention is directed toward unusual causes.

Tools and criteria for identifying drug cascades

There are several tools for identifying drug cascades which improves drug cascade detection when used consistently they are of following.

- Medication history interview
- Beers criteria
- STOPP and START criteria
- Naranjo casuality scale
- Geriatric assessment tools
- Medication chart review

CLINICAL CONSEQUENCES

Drug cascades in elderly patients creates severe clinical consequences by developing (ADR's) adverse drug reactions by polypharmacy which leads to geriatric

syndromes, hospitalizations & mortality. 15-40% of elderly patients with multimorbidity (multiple chronic illness) are consuming five or more medications simultaneously leads to chain reaction people instead of removing problem causing drugs takes more medication leads to side effects and further hospitalizations or even death [7].

Direct clinical consequences

- Geriatric syndromes: Falls caused due to benzodiazepine sedation treated with anti vertigo agents increases risk.
- Prolonged symptoms: Pedal edema occurred due to amlodipine managed with furosemide causes persistent fatigue and hypokalemia.
- Functional decline: Parkinsonism caused due to antipsychotics managed with levodopa effects on mobility and dyskinesia.
- Hospitalization and mortality: Hyperpolypharmacy (medications greater than or equal to 10) correlates with 20-30 % mortality [9].

Link to Adverse drug reactions (ADR's)

- ADR Prevalence: General ADR risk increases 5-10 % per an additional drug in drug cascades add 2-3 unnecessary agents multiplied by 3-5 times more.
- Predictable toxicity chains : In general NSAIDs trigger hypertension (ADR incidence 15-20 %) → ACE inhibitors → cough → opiods (cause constipation ADR 40-80 %) → laxatives (cause diarrhea)
- Renal or Hepatic strain : Cascades related to diuretics speed up declining of eGFR by 5-10 ml/min/year.
- Scale related to anticholinergics >3 from cascades causes central toxicity like cognitive impairment [8].

Impact on morbidity and mortality

Drug cascades increases morbidity and mortality in elder people by ADR's and polypharmacy the study shows that 15-40 % prevalence among patients with multiple illness hospitalized patients and these chains contribute further risks [10].

- Increased morbidity: 30-50 % falls caused due to benzodiazepine sedation treated with anti vertigo agents increases risk and Parkinsonism caused due to antipsychotics managed with levodopa effects on mobility and dyskinesia leads to morbidity.
- Mortality risk: Hyperpolypharmacy (≥10 medications) associates with 1.5 – 2 times more mortality hazard [11].

Hospital admissions and health care burden

Drug cascades place a heavy burden on hospitals and healthcare systems. They contribute to about 10 to 20 percent of preventable hospital admissions, increasing pressure on inpatient services. Adverse drug reaction–related admissions occur in roughly 2.9 to 8.7 percent of patients, but this risk rises two to three times when a cascade develops, such as complications following treatment for ACE inhibitor–induced cough. Older adults with multiple illnesses who experience drug cascades tend to stay in hospital longer, often by three to five additional days [15]. Evidence from Irish hospital wards shows a 39 percent prevalence of cascades, associated with a 15 percent increase in length of stay. Readmissions are also more frequent, as discharge-related cascades double the risk of 30-day readmission to around 25 to 35 percent, with combinations like benzodiazepines and antipsychotics commonly involved [12].

Management strategies of drug cascades

Management drug cascades majorly follows certain steps they are as follows:

1. Recognition
2. Evaluation of drug cascades
3. Deprescribing strategies
4. Monitoring of outcomes

RECOGNITION

Drug cascades occurs when a person suffering with adverse effects of a drug and physician prescribe the medication to the symptom this leads to prescribing cascades and polypharmacy, the primary goal is to recognize the effect of a drug. Managing the drug cascades prevent harm which reduce harmful out outcomes and helps to improve patient outcomes. Management begins with a total review of patients medication list of past and present which helps to adjust the drug dose and physicians should monitor the symptoms whether it is an adverse effect or a new medical condition [13].

Evaluation of drug cascades:

Once the drug cascade is confirmed then the medication should be evaluated whether the medicines have any new symptoms (adverse effects) this type of evaluation helps to identify the additional drugs which helpful to reduce symptoms or further drugs should be added to reduce adverse effects [14].

DEPRESCRIBING STRATEGIES

Deprescribing is the key component to manage the drug cascades the drugs which are unnecessary should be discontinued. Unnecessary drugs are nothing but the drugs which added to treat the adverse effects . Meanwhile the drugs which is a reasons for the adverse effect should be reduced ,frequency dose should adjusted the drugs should be replaced with alternative or the drug should be discontinued [16].

MONITORING OF OUTCOMES

Monitoring and follow up is the most important step after the medication changes the drugs which have adverse effects should be documented [18]. Documentation of drug profile helps to prescribe the correct medication , helps to reduce the future drug cascades. Management of drugs cascades helps to reduce the symptoms and leads to use safer medication and reduces the treatment expenses; remove the unnecessary medication in the medication char [17].

Patient education also plays a major role helps to notify the new symptom which is caused by the drugs, patient should know the medication which is given to them and they have to understand the drug cascade by educating the patient the future cascades can be reduced which helps to prevent the new symptoms which may occur by drugs .Patient education helps to report the symptoms caused by the drugs and which drug is responsible for the new symptoms and patient should understand the purpose of all drugs used in their medication list [19].

PREVENTION OF DRUG CASCADES

Drug cascades or prescribing cascades can be prevented by developing positive strategies highlighting the rational prescribing, guideline adherence, and stakeholder engagement, reducing incidence by 20-40% in high-risk polypharmacy cases.

Rational prescribing is nothing but the correct medication ,correct dose for the right person at low risk and low cost in older patients the special care is needed because they have decreased renal and liver function, increased drug sensitivity, multiple co morbidities, poly pharmacy to manage chronic illness, higher ADR risk. There are few principles for rational prescribing they are as followed:

1. start low , go slow :
    a. Start with low effective dose
    b. Closely monitor the things
2. Avoid poly pharmacy :
    a. Monitor all the medications regularly
    b. Try to stop unnecessary drugs
    c. Stop duplicate therapy
3. Choose safer alternatives :
    a. Choose correct drugs for treatment
    b. Avoid drugs which causes risk for treatment
4. Adjust dose for renal treatment:
    a. Calculate creatinine clearance (crcl) of the patient
    b. Adjust or reduce dose
    c. Increase or decrease the dosing interval
5. Monitor for ADR's and drug cascades to prevent harm and risk to the patient and avoid addition of unnecessary drugs.
6. Simplify the drug regimen and adjust the dosing.
7. Consider non pharmacological therapy like diet, exercise, counselling, hygiene for better outcomes and preventing the risk.
8. Educate the patient and care giver about the use and potential side effects of the drugs [20].

ROLE OF GUIDELINES AND PRESCRIBING CRITERIA

Guidelines and prescribing criteria are evidence based tools that are useful for clinicians:

a) Select the correct medication
b) Avoid unnecessary medications
c) Try to decrease the ADR's
d) Helps to improve patient safety and outcomes of elder patients

Major prescribing guidelines / criteria:

1. Beers criteria (American geriatrics society):

This criteria helps to identify the correct medications and reduce errors in older patient includes:

- Which drugs are avoided in specific disease
- Drugs which are avoided in specific disease
- Drug drug interactions
- Reduction of data in renal impairment

2. START-STOPP criteria (Europe /widely used globally): (STOPP) – (screening tool of older person's prescription): helps to identify the potentially of unnecessary medications.
    - Examples: Duplicate drug classes, Long term usage benzodiazepines, NSAIDS in case of heart failure.
    - (START)- (screening tool to alert to right treatment) : helps to recognise missing beneficial treatment.
    - Examples: no statin in diabetic with risk, no calcium /vitamin d in osteoporosis, any ACE inhibitors in heart failure.
3. WHO guides to good prescribing : Helps to provide step wise rational prescribing approach
    a. Patients problem is defined
    b. Therapeutic objective is specified
    c. Helps to choose suitable drug
    d. Correct prescription is identified
    e. Patient instructions are given and monitor the treatment
4. National /hospital treatment guidelines :

Therapy is standardised, irrational variations are reduced, cost effectiveness is improved.

Examples : HTN, DM , etc. [21].

PATIENT CARE GIVER INVOLVEMENT

Caregiver involvement in older adults improves medication management like care giver helps the patients when there are more medications for intake, helps to understand prescription in a correct manner, they also helps the elder patients to take medication at correct time [22]. Caregiver support is key factor to elder patients for safe medication use and coordination safe medication is necessary for elderly patients it happen only when the caregiver is supported and safe medication is particularly difficult among the elder patients [23].

The caregiver helps to manage the errors and polypharmacy by communicating with healthcare providers to reduce errors and organize the medication and pillbox with hand written list caregiver assistance is associated with improved management behavior like the medication is assisted by the caregiver and helps to monitor the medication-taking behavior to ensure the safety of the patient [24].

ROLE OF HEALTHCARE PROFESSIONALS

Healthcare professionals play key roles in drug cascade detection, management, and prevention, with joint efforts reducing polypharmacy harm by 25-40% in geriatric care settings. Physicians lead clinically, pharmacists provide expertise, and teams integrate for comprehensive care. [27]

Physician-Led Interventions

Physicians mainly focus on the diagnosis, decision making and clinical judgement which includes ADR vigilance, deprescribing intiation, guideline adherence and education. [26]

Clinical Pharmacist Contributions

Pharmacist involves in reviewing, optimisation and detecting the drug cascades like medication reconciliation, screening of cascades, intervention and ADR counselling [25].

Multidisciplinary team approach involves physicians, pharmacists, nurses, patients, and other health care professionals work together for patient well being which decreases huddles and improve patient health.

CONCLUSION

Drug cascades or prescribing cascades characterize a threat to geriatric pharmacotherapy, where ADRs trigger the inappropriate prescriptions, increasing polypharmacy and geriatric vulnerability. This review has demonstrated their background, pathophysiology, risk factors, recognition, consequences, management, prevention, and professional roles for clinical improvement. Breaking a drug cascade starts with careful attention, teamwork, and the willingness to stop medicines when they do more harm than good. When you identify and interrupt a cascade, patients often regain function and avoid further complications. More importantly, you protect older adults from preventable harm and putting patient safety first.

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CONFLICT OF INTEREST

None

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Yes

ETHICAL STATEMENT

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AUTHOR CONTRIBUTION

All are contributed equally.

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