Adverse Drug Events in the Older Adult Population

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Dane County

BeSafe!

2-1-1
Get Connected. Get Answers.

Safe Communities
Objectives

1) Assess the impact of adverse drug events on the older adult population
2) Recite the most common adverse drug events leading to ER visits and hospitalizations
3) Recognize drug-induced geriatric syndromes
4) List the most commonly involved drugs associated with adverse drug events
5) Describe the key risk factors associated with adverse drug events
6) Identify the most common causes of adverse drug events in older adults
7) Select the tools that can be used to reduce adverse drug event risk
Adverse Drug Event (ADE)

Definition: An unintended effect from a drug that produces symptoms sufficient to cause a person to seek medical attention

OR

0 Produces symptoms sufficient to affect function or quality of life
Impact of ADEs

- Older adults are 4 to 7 times more likely to experience an ADE
- 13 to 30% of hospital admissions due to ADEs versus 3-6% of the population
- 2/3rd of hospital discharges associated with adverse medical events are ADEs
Impact of ADEs

• ADEs now 4\textsuperscript{th} or 5\textsuperscript{th} leading cause of death by disease

• Rate of increase in reported ADE fatalities to FDA from 2000 to 2010 was 451\%
Cost of ADEs

- Ambulatory care: $1300
- Hospital: $7000-$10,000
  - Increased length of hospital stay
Most Common ADEs

ADEs most commonly leading to ER visit or hospitalization:

- Gastrointestinal bleeding
- Electrolyte imbalance
- Hypoglycemia
- Internal bleeding
- Falls
- Delirium
- Drug toxicity
- Renal failure
Commonly Associated Drugs

Drugs most commonly implicated in ER visits and hospitalization:

- Warfarin (Anti-coagulants)
- Insulin
- Oral anti-diabetic agents
- Anti-platelets
- ACEIs/ARBs
- Diuretics
- NSAIDs
- Opiates
Commonly Associated Drugs

Drugs most commonly implicated in ER visits and hospitalization:

- Antibiotics
- Antineoplastics
Drug-Induced Geriatric Syndromes

The “Soft ADEs”

- Falls
- Memory loss
- Delirium
- Urinary Incontinence
- Pain
- Depression
- Insomnia
Geriatric Syndromes

Functional Decline Syndrome

- Loss of one or more ADLs
  - Increased morbidity
  - Increased mortality
- Any ADR reduces function
What don’t’ we know?

“You see only what you look for and recognize only what you know”-
Dr. M. Chisner
Real but Unrecognized ADEs

- Hypomagnesemia from PPIs
- Memory loss from statins
- Renal failure from PPIs
- Neuropathy from statins
- Pain from bisphosphonates
- Urinary incontinence from cholinesterase inhibitors
Risk Factors

Number of drugs

- 30% used >= 5 drugs = 4% risk of serious drug-drug interactions
- 2-4 drugs = baseline comparator
  - 4-fold increase 5-7 drugs
  - 8-fold increase 8-10 drugs
  - 13-fold increase 11-13 drugs
Risk Factors

• Number of co-morbid conditions
• Care Transitions
  • Age
  • Renal impairment
  • Gender
  • Use of PIMs
  • Use of “narrow therapeutic index” drugs
ADE Causation

- Lack of monitoring 40-60%
- Drug-drug interactions 13-26%
- Adverse drug reaction from new drug
- Increased drug burden causing delirium or falls
- Changes in adherence patterns
Lack of Monitoring

- Electrolytes
- Blood glucose
- Drug levels
- Vital signs (BP and orthostatics)
- INR
- Patient symptoms
Drug-Drug Interactions

- 13-26% of all ADEs
- Pharmacist must screen and alert prescriber and nurse
Drug-Drug Interactions: Attempts to Classify Relevance

• 2005: consensus panel developed list of 25 serious DDI’s in older adults
  • “Which one’s matter?” – J. Hanlon
  • Frequently narrow therapeutic index drugs
Top drug-drug interactions: 20 years ago

- Procainamide – Amiodarone
- Procainamide – Cimetidine
- Procainamide – Trimethoprim
- Cimetidine – Quinidine
- Cimetidine - Theophyline
- Cimetidine – Disopyramide
- Cimetidine - Quinidine
- Carbamazepine – Diltiazem
- Phenytoin – Cimetidine
- Phenytoin – Fluoxetine
- Phenytoin – Warfarin
- Phenytoin – Theophylline
- Phenytoin – Amiodarone
- Digoxin – Amiodarone
- Digoxin – Quinidine
- Digoxin – Verapamil
- Lithium – ACE Inhibitors
- Lithium – NSAIDs
- Lithium - Diuretics
- Theophylline – Erythromycin
- Warfarin – Amiodarone
- Warfarin – Sulfamethoxazole
- Warfarin – Quinolones
- Warfarin – Macrolildes
- Quinidine – Fluvoxamine
Top drug-drug interactions: 20 years ago

- Procainamide – Amiodarone
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- Cimetidine – Quinidine
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- Cimetidine – Quinidine
- Cimetidine - Quinidine
- Carbamazepine – Diltiazem
- Phenytoin – Cimetidine
- Phenytoin – Fluoxetine
- Phenytoin – Warfarin
- Phenytoin – Theophylline
- Phenytoin – Amiodarone
- Digoxin – Amiodarone
- Digoxin – Quinidine
- Digoxin – Verapamil
- Lithium – ACE Inhibitors
- Lithium – NSAIDs
- Lithium - Diuretics
- Theophylline – Erythromycin
- Warfarin – Amiodarone
- Warfarin – Sulfamethoxazole
- Warfarin – Quinolones
- Warfarin – Macrolides
- Quinidine – Fluvoxamine
Top drug-drug interactions

- ACEIs – potassium-sparing diuretics
- ACEI’s - potassium supplements
- Anti-hypertensives – NSAIDs
- NSAIDs - corticosteroids
- Diuretics – NSAIDs
- Verapamil – Beta-blockers
- Digoxin – Macrolides
- Warfarin – Aspirin
- Warfarin – Antiplatelets
- Warfarin – NSAIDs

- ARBs potassium-sparing diuretics
- ARBs – potassium supplements
- SSRI’s- Opiates
- SSRI’s – NSAIDs
- SSRI’s - Aspirin
- Sulfonylureas – Sulfamethoxazole
- Trimethoprim – ACEIs
- Trimethoprim - ARBs
Observational Studies: Where the data are strongest

• Population-based studies

• Nested case control
  • Nested case crossover
Drug Interactions that Matter Most

- ACEIs + K+-sparing diuretic
  - Risk for hospitalization for hyperkalemia OR = 20.3
  - After receiving a K+ sparing diuretic within previous 7 days
Drug Interactions that Matter Most

• Overall risk for hip fracture from benzodiazepine (BZD) use  OR 1.2
• BZDs + interacting drugs
  • Risk for hospital admission d/t hip fracture  OR 1.5 – 2.1
Drug Interactions that Matter Most

- Calcium channel blockers (CCBs) + macrolides (erythromycin, clarithromycin)
  - Risk for hospital admission d/t hypotension/shock = OR 3.7–5.8
  - After addition of macrolide within 7 days
  - Does NOT include azithromycin
Drug Interactions that Matter Most

- Digoxin + macrolides
  - Risk for hospital admission d/t digoxin toxicity = OR 11.7
  - Clarithromycin 14.83, azithromycin 3.71, erythromycin 3.69
  - After addition of macrolide within 7 days
Drug Interactions that Matter Most

- Glyburide + SMX/TMP
  - Risk for hospital admission d/t hypoglycemia = OR 6.6
  - After addition of SMX/TMP within 7 days
Drug Interactions that Matter Most

- Warfarin + SMX/TMP (sulfa)
  - Risk of hospitalization d/t GI bleeding = OR 2.04 – 3.84
  - After addition of SMX/TMP within 14 days
  - Many antibiotics showed increased ORs; SMX/TMP most pronounced
Drug Interactions that Matter Most

- Warfarin + NSAIDs
  - Risk of hospitalization d/t GI bleeding = OR 3.58
  - For those with NSAID use in prior 90 days
  - NSAIDs = ibuprofen, naproxen, meloxicam, nabumetone, celecoxib
Observational Studies: Where the data are strongest

- Warfarin + aspirin
  - Warfarin + aspirin are overused with little evidence benefit in 800,000
  - Estimates suggest 800-1200 unnecessary deaths each year
  - Reserve for high-risk groups
SSRIs plus NSAIDs or Aspirin

- Increased risk for GI bleeding
- Adjusted risk for SSRI use alone = 2.6 (CI 1.7-3.8)
- Adjusted risk for NSAIDs alone = 3.7 (CI 3.2-4.4)
- Adjusted risk for SSRIs + NSAIDs = 15.6 (CI 6.6-36.6)
- Adjusted risk for SSRIs + aspirin = 7.2 (CI 3.1-17.1)
Drug Interaction Intervention Strategies

- Discontinue precipitant drug
- Change precipitant drug
- Alter dose of either drug
- Initiate target monitoring
  - Patient education of key symptoms to monitor
ADE Detection

- **Temporal association**
  - Any new symptom should be considered an ADE

  “Assume the drug is responsible until proven otherwise”

- **Surrogate markers eg. Serum K+**
Temporal Association

Association of time with the onset of a known adverse effect after starting a drug or increasing the dose

- Discontinuation of drug and abatement of symptoms supports suspected ADE
- Re-challenge further increases likelihood drug was responsible
Naranjo Scale

- Are there previous *conclusive* reports of this reaction?
- Was the reaction more severe when the dose was increased or less severe when the dose was decreased?
- Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure?
Self-Reporting

Self-reporting of ADEs

- Reliable
- 0.70 sensitivity, 0.85 specificity
- 1/3rd not reported to MD
- 1/3rd of those reported not acted upon by MD
- No action led to increased severity of ADEs
Prescribing Cascades

Definition:

The addition of a drug that is used to treat a side-effect from an existing drug assuming the side-effect is a new medical condition
Prescribing Cascades

- NSAIDs → HTN → Anti-HTN
- HCTZ → Gout → Allopurinol
- Amlodipine → Edema → Diuretic
- BisPO4 → Pain → Analgesic
- Aricept → Incontinence → Detrol
Prescribing Cascades

- Statin → Neuropathy → Gabapentin
- Statin → Memory loss → Aricept
ADE Prevention

26-95% preventable
  50-55% in most references
O Increase monitoring
O Avoid serious drug-drug interactions
O Adjust drug doses based on renal function
O Managing care transitions
O Medication minimization
Screening Tools (explicit criteria)

- Beer’s
- AGS updated Beer’s criteria 2012
- STOPP
- ARS and Drug Burden Index
### Anticholinergic Risk Scale

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<th>3 Points</th>
<th>2 Points</th>
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<td>Amitriptyline</td>
<td>Amantadine</td>
<td>Carbidopa-levodopa</td>
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<tr>
<td>Atropine products</td>
<td>Baclofen</td>
<td>Entacapone</td>
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<td>Benztropine</td>
<td>Cetirizine</td>
<td>Haloperidol</td>
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<td>Carisoprodol</td>
<td>Cimetidine</td>
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<tr>
<td>Trifluoperazine</td>
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ADE Prevention in Care Transitions

Care transitions associated with high risk for ADEs

50% of ADEs will have occurred by 14th day post-discharge

- New medications
- Lack of monitoring
- Changes in adherence patterns
- Poor patient education
ADE Prevention in Care Transitions

Create a Medication Action Plan

- Pharmacists: Use screening tools to identify risk and create MAP for nursing to follow up
- Nursing: Use MAP to incorporate monitoring for ADEs and learn! Build your working knowledge-base
Medication Minimization

Doron Garfinkel, MD

- Community-based older adults average age 82 y/o
- Protocol for medication discontinuation
- 58% of drugs recommended for discontinuation
  - 88% acceptance rate (4.2 drugs per patient)
    - 2% restarted due to re-emergence of condition
  - 81% overall success rate
    - No adverse medical events or deaths
  - 88% reported global improvement in health
  - 56 out of 64 had measured improvement in cognition
    - MMSE scores went from 14 to 24; 14 to 23; 14 to 30
Medication Minimization

Doron Garfinkel, MD

- LTC residents (N=119)
  - Average age approx. 82 y/o
  - Discontinued 2.8 drugs per resident
    - 18% failure rate
  - 1-year mortality in control group = 45%
    - 21% in study group
  - Hospitalization rate in control group = 30%
    - 11.8% in study group
Summary

• ADEs are more common in older adults
• ADEs can cause serious harm or death
• ADEs can lead to decline in function and quality of life
• Many ADEs can be prevented through:
  • Improving monitoring
  • Avoiding serious drug-drug interactions
  • Provider and patient education
Summary

• Self-reporting of ADEs is a valid tool in their detection and our ability to mitigate their effects
• Medication minimization may improve function and quality of life
• Medication minimization may reduce the incidence of ADEs
• United Way of Dane County: 608-246-4350
Abbreviations

• ACEI = ACE inhibitor- enalapril, lisinopril, captopril, fosinopril
• ARB = angiotensin receptor blocker
• SMX/TMP = Bactrim DS, Septra DS (sulfa drug or sulfonamide)
• Sulfonylurea = glyburide, glipizide, glimepiride (OHA or oral hypoglycemia agent)
• NSAID = non-steroidal anti-inflammatory drug (ibuprofen, naproxen, nabumetone, or Motrin, Aleve, Celebrex)
• CCB = calcium channel blocker (verapamil, amlodipine, diltiazem, nifedipine)
• OR = odds ratio: Any OR over 1.0 is significant, but >2.0 is most significant. The higher the OR, the greater the chance of an ADE.
• CI = confidence interval: Statistical measure when narrow means data are more reliable.
• ARS = anti-cholinergic risk scale
• DBI = drug burden index
References


Rochon RA, Schmader KE, Sokol HN. Drug Prescribing for Older Adults. *UpToDate* September 2010.


References


References


