Adverse Drug Events and Patient Burden

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Disclosures

- No relevant disclosures
Definitions: Drug Related Harm

• Harm Occurred
  – Adverse Event
    • Harm in a patient given drug but not necessarily caused by drug
  – Adverse drug reaction
    • Harm caused by drug at normal doses
  – Adverse drug event
    • Harm caused by drug or inappropriate use of

• Harm may have occurred
  – Medication error
    • Inappropriate use of drug that may or may not result in harm
  – Side effect
    • Predictable or dose-dependent

• Harm did not occur
  – Potential adverse drug event
    • Could result in harm but did not harm
ADE Statistics

• Inpatient
  – Account for 1 in 3 of all hospital adverse events
  – 2 million hospital stays per year
  – Prolongs hospital stays by 1.7 to 4.6 days

• Outpatient
  – Over 3.5 million office visits
  – About 1 million ER visits
  – Approximately 125,000 hospital admission

Health.gov
Pharmacogenetics

• Linkage between individual’s genotype and their ability to metabolize a foreign compound

• Enzyme inhibition and induction
  – Wide variations in individuals

• Polymorphism
  – Specific gene mutation or deletions are maintained in a population
    • Extensive metabolism
    • Poor metabolism
    • Ultra-extensive metabolism
  – ADEs as well as incidence of exposure linked cancer
Enzymes and Metabolism

• Phase 1 (Oxidative)
  – Cytochrome P-450
    • CYP2C19 and CYP2D6 are highly polymorphic
      – Amitriptyline >> demethylation >> nortriptyline >> hydroxylation
      – Identification of patients with low risk of ADRs

• Phase 2 (Conjugative)

Steimer et al
Are migraineurs at increased risk of adverse drug response? (meta analysis)

• RCTs of topiramate for epilepsy or migraines
• Outcomes: adverse effects, adverse drug reaction, related drop outs, serious adverse events
• Migraine trial: older, more females and slower titration
• Equivalent dose of topiramate was associated with different ADRs and higher drop off in migraineurs

Luykx et al
Using a graphical risk tool to examine willingness to take migraine prophylactic medications

- <30% migraine patients with chronic migraine adhere to meds at 6 months
- What is the degree of benefit (decreased headache frequency) that would lead to patients willingness to take medications?
  - Divalproex, venlafaxine, gabapentin, propranolol, topiramate
- Results: <60% pts willing to take meds even if 50% reduction in frequency

Turner et al.
Living With Medicines Questionnaire

• Developed to measure overall medicine burden
• Multidimensional
  – Includes psychosocial issues, daily living, patient doctor communication, patient pharmacist communication
• More positive experience with those using <8 medications
• Further work needed

Krska et al.
National Action Plan for ADE Prevention

- Federal Steering committee
  - Greatest number of measurable harm
  - Can be effectively measured
  - Considered largely preventable

- Anticoagulants, Diabetes, Opioids (overall morbidity and mortality)
  - Surveillance
  - Prevention
  - Research

- Advocate for other classes
Conclusion

• ADE documenting and reporting is important

• Pharmacogenetics may serve as an important tool

• Better studies needed to fully estimate the multidimensional burden of ADEs