Side Effects to Psychiatric Medication
Has the Solution Become the Problem?

A. Wilson MD
Aug 19, 2010

“... a surgeon who uses the wrong side of the scalpel cuts his own fingers and not the patient; if the same applied to drugs they would have been investigated very carefully a long time ago”

Rudolph Bucheim  1849

Objectives

• What is a side effect (S/E)?
• Concept of risk/benefit ratio
• Groups at higher risk for side effects
• Side effects common to many psychotropic meds
• Some important side effects to specific meds
• How caregivers can help in managing side effects
What is a Side Effect (S/E)?

- Undesirable secondary effect of a drug or therapy
- A person with a drug side effect has a symptom or illness that is caused by a medication.
- In most cases, a side effect is undesirable.
- Almost all drugs are capable of causing side effects.
- What is the difference between an adverse event and an adverse drug reaction (side effect)?

Some Issues in Dual Diagnosis

- Not all health problems nor all psychiatric problems have a pharmacological answer
- Medication is not the universal solution to challenging behaviour
- Caregivers must have an awareness of S/E because many persons with intellectual disability have difficulty in communicating about possible S/E they may be experiencing

Common Meds in Dual Diagnosis

**Antidepressants**
- Tricyclics (numerous but uncommonly used)
  - Amitriptyline (Elavil)
  - Imipramine (Tofranil) etc.
- SSRI
  - Escitalopram (Cipralex)
  - Citalopram (Celexa)
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)
  - Fluvoxamine (Luvox)
- Other
  - Venlafaxine (Effexor)
  - Mirtazapine (Remeron)
  - Bupropion (Wellbutrin)
  - Duloxetine (Cymbalta)
  - Trazadone (Desyrel)

**Antipsychotics**
- Typical (numerous)
  - Chlorpromazine (Largactil)
  - Methotrimeprazine (Nozinan)
  - Haloperidol (Haldol)
  - Fluphenazine (Moderate)
  - Perphenazine (Trilafon)
  - Flupenthixol (Fluxaneo)
  - Zuclopenthixol (Clieptax) etc.
- Atypical
  - Risperidone (Risperdal)
  - Olanzapine (Zyprexa)
  - Quetiapine (Seroquel)
  - Aripiprazole (Abilify)
  - Ziprasidone (Zeldox)
  - Clozapine (Cogentin)
- Anti-Parkinsonian
  - Benztropine (Cogentin) etc.
Common Meds in Dual Diagnosis

• Mood Stabilizers (* = also anticonvulsants)
  – Lithium
  – Divalproex (Epival) *
  – Carbamazepine (Tegretol) *
  – Lamotrigine (Lamictal) *

• Anti-anxiety medications
  – Benzodiazepines [numerous]
    – Lorazepam (Ativan)
    – Clonazepam (Rivotril)
    – Oxazepam (Serax)
    – Alprazolam (Xanax)
    – Diazepam (Valium) etc.
    – Buspirone (BuSpar)

• Sleeping Pills
  – Temazepam (Restoril)
  – Flurazepam (Dalmane)
  – Zopiclone (Imovane)

• Medication for ADHD
  – Methylphenidate (Ritalin, Concerta, Biphentin etc.)
  – Amphetamines
    – Dexmethylphenidate (Dexedrine)
    – Mixed amphetamine salts (Adderall XR)
  – Non-stimulants
    – Atomoxetine (Strattera)

• Medication for Alzheimers
  – Donepezil (Aricept)
  – Galantamine (Reminyl)
  – Rivastigmine (Exelon)
  – Memantine (Ebixa)

• Miscellaneous
  – Propranolol (Inderal)
  – Clonidine (Catapres)

Risk / Benefit Analysis

the consideration of whether a medical or surgical procedure, particularly a radical approach, is worth the risk to the patient as compared with possible benefits if the procedure is successful.


Risk / Benefit Analysis

• Chances for a positive response to the medication
• What outcome is likely if no treatment undertaken
• Alternate treatments for this disorder?
  – Pharmacological
  – Non-pharmacological
• Possible S/E and how likely are they to occur?
• How serious or troublesome are the S/E?
• What additional factors could contribute to S/E developing? (age, health, drug interactions etc.)
• Remember that not all symptoms that coincide with use of meds are S/E
Special Groups at Higher S/E Risk

- Children
- The elderly
- Persons with liver or kidney disease
- Personal idiosyncrasy
- Persons with intellectual disability?

“There is no good-quality evidence to either support or refute concerns that people with ID may be at greater risk of the adverse effects of medication than people from the general population who do not have ID”

International guide to prescribing psychiatric medication for the management of problem behaviours in adults with intellectual disabilities; Deb et al; World Psychiatry 2009

Issues Related to Intellectual Disability Which May Contribute to Higher Risk for S/E

- Cerebral insults causing intellectual disability may also affect how a medication acts on the brain
- Syndromes of intellectual disability may have medical co-morbidities which can affect how the body reacts to meds
- Poor compliance / unintended excessive use of meds
- “Brown Bag” issues in intellectual disability may lead to drug interactions
- “To chew or not to chew”
- Unrecognized S/E

S/E Common to Many Meds

- Nausea / indigestion
- Diarrhoea
- Constipation
- Headache
- Dizziness / light-headedness
- Sedation & lethargy
- Insomnia
- Tremor
- Dry mouth
- Weight gain
- Sexual dysfunction
Antidepressant Side Effects

- **Tricyclic Antidepressants**
  - Can have numerous unpleasant S/E
  - Anticholinergic (dry mouth, blurred vision, constipation, urinary retention)
  - Sedation
  - Light-headedness
  - High risk in overdose

- **SSRIs**
  - Most of the S/E common to many meds may be seen with SSRIs to varying degrees
  - Discontinuation Syndrome

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### Citalopram
- Nausea
- Insomnia
- Headache
- Constipation

### Escitalopram
- Nausea
- Insomnia
- Headache

### Fluoxetine
- Nausea
- Headache
- Insomnia
- Drowsiness
- Sexual

### Paroxetine
- Nausea
- Headache
- Insomnia
- Diarrhoea
- Sexual

### Sertralin
- Nausea
- Headache
- Insomnia
- Diarrhoea

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### Citalopram
- Tremor
- Sexual
- Fatigue
- Anxiety

### Escitalopram
- Sexual
- Dry mouth
- Headache
- Insomnia

### Fluoxetine
- Dizziness
- Weakness
- Sexual

### Paroxetine
- Tremor
- Constipation
- Decreased appetite

### Sertralin
- Tremor
- Sexual
- Headache

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Antidepressant Side Effects

- **SNRIs**
  - Most of the S/E common to many meds may be seen with SNRIs to varying degrees
  - Some people may develop heavy perspiration

- **Mirtazapine**
  - Sedation & weight gain are commonest S/E

- **Bupropion**
  - Higher risk of lower seizure threshold than other antidepressants & should not be used in persons with a current seizure disorder
  - Fewer sexual S/E than any other antidepressant
Mood Stabilizers (Lithium)

- Polyuria (urinary frequency) & thirst may be seen in up to 30% of persons on Lithium
- Nausea (30%) – don’t give it on an empty stomach;
- Hypothyroidism (30%)
  – need to check thyroid function at least once a year
- Weight gain (up to 30% of persons on lithium)
- Cognitive blunting (short term memory problems, taking longer to process information (10%)
- Tremor (sometimes a low dose of propranolol helps)
- Worsening of psoriasis
- Hair thinning (10%)

Lithium Toxicity
Easy to Identify
Potentially Fatal to Ignore

- Vomiting
- Worsening diarrhoea
- Pronounced weakness/lethargy
- Severe tremor or muscle twitching
- Difficulty walking
- Unsteadiness
- Lack of coordination
- Slurred speech
- Confusion

See a doctor immediately!

Causes of Lithium Toxicity

- Overdose
  – Suicide
  – Medication Error
- Dehydration
  – Overheating and poor fluid intake
  – Concurrent illness (influenza, gastroenteritis etc.)
- Drug interactions
  – NSAIDS (naproxen, Celebrex, Meloxicam, ibuprofen)
  – ACE inhibitors (Ramipril)
  – Diuretics (diazide)
<table>
<thead>
<tr>
<th><strong>Divalproex</strong></th>
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<tr>
<td>• Risk of congenital anomalies if taken in pregnancy</td>
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<td>• Tremor</td>
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<td>• Weight gain</td>
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<tr>
<td>• Reduced platelets – usually benign</td>
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<tr>
<td>• Polycystic ovary</td>
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<td>• Hair thinning</td>
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<td>• Many of the “common” S/E</td>
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<th><strong>Lamotrigine</strong></th>
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<tr>
<td>• Stevens Johnson Syndrome</td>
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<tr>
<td>— Potentially fatal but fortunately rare</td>
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<td>— ~ 1/2000; benign rash in 7 %</td>
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<tr>
<td>— Any rash should be assessed by a physician</td>
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<tr>
<td>• Sedation</td>
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<tr>
<td>• Headache</td>
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<td>• Unsteadiness</td>
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<th><strong>STEVENS JOHNSON SYNDROME</strong></th>
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Antipsychotics - Conventional

- Many of the “common” S/E
- Acute Motor S/E
  - Parkinsonism (tremor, ‘cog-wheeling’, stiffness, masked face, little arm swing, shuffles)
  - Dystonia (sustained often painful involuntary muscle contraction)
  - Akathisia (distressing inner restlessness pacing, rocking, shifting back & forth, fidgeting)
- Chronic Motor S/E
  - Tardive dyskinesia, tardive dystonia, tardive akathisia
  - May be irreversible

Antipsychotics - Conventional

- Neuroleptic Malignant Syndrome (NMS)
  - Rare but potentially life threatening
    - Risk ↑ with extreme heat, dehydration, exhaustion
    - Pronounced muscular rigidity, fever, rapid pulse, sweating, unstable blood pressure, respiratory dysfunction

Atypical Antipsychotics

- Has the move to atypicals simply exchanged one problematic S/E for another with even greater risk potential?
  - Highest weight gain: olanzapine & clozapine
  - Ziprasidone & aripiprazole: weight neutral
- Stroke risk in the elderly (in both atypical and conventional antipsychotics)
  - Small but statistically significant
Cardiometabolic Changes with Atypical Antipsychotics

Anti-anxiety Medications

- Benzodiazepines (the “pams”)
  - Sedation
  - Effect on cognition
  - Effect on motor coordination
  - Risk of dependence

- Buspirone
  - Usually well tolerated

Medication for ADHD

- Stimulants (methylphenidate & amphetamines)
  - Overall well tolerated
  - May worsen tic disorders
  - May cause fast heart rate or increased blood pressure
    - Avoid if significant cardiac risks present
  - Hyperactive rebound between doses with short acting forms
  - Precipitate mania in untreated bipolar??
  - Street value! (especially short acting formulations)

- Non-stimulant (atomoxetine)
  - Headache, dry mouth runny nose
  - Avoid if significant cardiac risk
Clonidine

- Generally well tolerated
- Potential for low blood pressure
  - Start low, go slow
- Sedation
- Headache
- Dizziness

Medication for Alzheimer’s

- Donepezil, rivastigmine, galantamine, memantine
- Most common S/E are nausea, loss of appetite, bowel changes
- Start low & go slow

Psychiatric S/E to Medical Drugs

- Any medication can cause S/E & any S/E may be associated with change in behaviour or challenging behaviour
- Phenytoin toxicity
- Phenobarbital / Primidone
  - Hyperactivity & irritability
- Levetiracetam
  - Psychosis, depression, anger & aggression
- Steroids
  - Depression & mania
- Levodopa / carbidopa
  - Depression, hallucinations
Drug Interactions

• Too many to remember
• Many theoretical or minor but some are serious
• Drug interaction profile when new meds added
• SSRIs can inhibit metabolism of numerous other meds
• Carbamazepine can increase metabolism of other meds, rendering them inactive
• Grapefruit juice & herbal products

How Can Caregivers Minimize Impact of Side Effects

• Read patient information brochures for each medication a person is on
• Careful observation after implementation of a medication or a dose change
• Minor S/E will often subside and can be mentioned at next physician visit – pharmacists may have suggestions for managing these
• Physician should be notified about serious S/E
• Don’t be shy to inquire about possible drug interactions

Strategies for Common S/E

• Dry Mouth
  — Frequent sips of water / ice chips
  — Avoid candies & liquids with high sugar content
  — Frequent brushing teeth
• Nausea
  — Avoid meds on empty stomach
  — Take meds with full glass of fluid
  — Plenty of water or ginger ale
  — Pepto Bismol
  — Dose change to bedtime?
• Dizziness
  — Lying & Standing BP
  — Encourage avoidance of sudden changes in posture
  — Drink lots of fluids
Strategies for Common S/E

- **Constipation** (can become a very serious often unrecognized problem)
  - At least 8 glasses of fluids per day
  - High fibre foods
  - Daily exercise
  - Speak with physician re stool softener or psyllium or need for investigation depending on severity

- **Diarrhoea**
  - Clear liquids when pronounced
  - Bananas, rice, apples, toast, smooth peanut butter when loose
  - Avoid caffeine, fatty, spicy & dairy foods

- **Sedation**
  - 1-2 short naps per day
  - Encourage regular exercise
  - Discuss with physician change in administration schedule

- **Perspiration / heat intolerance / sun sensitivity**
  - Extra fluids in hot weather
  - Light loose clothing / fans
  - Avoid strenuous exercise
  - Limit sun exposure, long sleeves, liberal sun screen

- **Rash**
  - Notify physician especially if person on lamotrigine or carbamazepine

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**Weight Gain**

- Weigh persons on meds with a potential for weight gain – initially every 1-2 weeks and then monthly as long as on the medication
- If weight begins to increase, implement guidance around diet & exercise ASAP
- Watch portion size at meals
- Increase availability of healthy but tasty food choices for snacks
- Consider requesting consultation from dietician / nutritionist
Lithium Induced Urinary Volume

- Do not try to control urinary frequency by restricting fluids
  - High urinary volume is not caused by too much fluid intake, but by lithium causing reduced capacity of the kidney to concentrate urine
  - Fluid restriction causes dehydration b/c high urine volume will continue even if fluids are restricted
  - this can increase risk of lithium toxicity
- Provide at least 8 glasses of water / day to replenish fluid lost in the urine

Resources

- Compendium of Pharmaceuticals & Specialities - CPS (the "Big Blue Book")
- Clinical Handbook of Psychotropic Drugs; Virani et al; Pub by Hogrefe & Huber 2009

Summary

- When taking any medication consider the Risk/Benefit Ratio
  - Most S/E are minor, often transient and may be managed symptomatically
  - More serious or more unpleasant S/E may require dose adjustment or even med discontinuation
- Persons with intellectual disability may sometimes be at higher risk for S/E or of having S/E go unnoticed
- Specific S/E discussed today were selective & do not represent a comprehensive review of potential S/E to psychiatric medication
DUAL DIAGNOSIS – learn online

COURSE DESCRIPTION:

- first four chapters of NADD Ontario text *Dual Diagnosis: An introduction to the mental health needs of persons with developmental disabilities.*
  - basic introduction to developmental disabilities
  - recognizing and understanding the mental health needs of persons with developmental disabilities within a biopsychosocial model, and implications and strategies for optimizing supports
  - criteria used by health care professionals to recognize and differentiate various psychiatric conditions.