Management of Antidepressant- and Lithium-Induced Side Effects

Mark H. Pollack, M.D.
Massachusetts General Hospital
Nicholas Ward, M.D.
University of Washington

Pre-Lecture Exam Question 1

1. **Which of the following is a rationale for managing antidepressant side effects?**

A. To improve compliance with treatment
B. To permit dosing at adequate levels
C. To prevent patients from prematurely stopping treatment
D. All of the above

Question 2

2. All of the following are potential risks of employing "drug holidays" to manage antidepressant induced side effects, *except*

A. Withdrawal effects
B. Relapse of the disorder
C. Increased sexual dysfunction
D. Encouragement of non-compliance

Question 3

3. All of the following may be used to treat antidepressant induce tremor *except*

A. Decrease caffeine intake
B. Adjunctive gabapentin
C. Adjunctive benzodiazepine
D. Adjunctive antiparkinsonian agents
E. Adjunctive beta blockers

Question 4

4. Which of the following may be used to minimize lithium induced gastrointestinal distress?

A. Dose prior to meals
B. Divide doses
C. Hydrochlorothiazide
D. Vitamin E
E. Beta blocker

Question 5

5. Which skin condition should always be managed in consultation with a dermatologist for patients on lithium?

A. Psoriasis
B. Acne
C. Atopic dermatitis
D. Tinea versicolor

MANAGEMENT OF SIDE EFFECTS

- Enhances compliance
- Permits adequate dosing
- Prevents premature abandonment of therapy

GENERAL PRINCIPLES OF SIDE EFFECT MANAGEMENT

- Drug selection
- Anticipate probable side effects
- ? lowest effective dose
- Buy time
  - tolerance
  - treatment of underlying disorder

ANTIDEPRESSANT-INDUCED SIDE EFFECTS

Sexual Dysfunction

- Libido
- Arousal
  - genital sensation
  - female swelling and lubrication
  - male erection
- Orgasm
  - male ejaculation

MANAGEMENT OF SEXUAL DYSFUNCTION

- Minimize adrenergic/cholinergic blockage
- Sildefanil (Viagra)
  - 50-100 mg prn
- Dopaminergic agonists
  - amantadine 100 mg bid–tid
  - bupropion 75–150 mg/d (usual dose)
  - methylphenidate 5–10 mg qd–qid
- Ginkgo biloba extract 60 mg bid to tid
- Yohimbine (Yocon®) 2.5–15 mg/d
  - equally effective in men & women
  - risks anxiety & insomnia
- Buspirone (5–20 mg bid–tid)

MANAGEMENT OF SEXUAL DYSFUNCTION

- Serotonergic antagonists (cyproheptadine 2–16 mg/d)
  - risks sedation or loss of antidepressant effect
- Adrenergic agonist (pseudoephedrine 30–90 mg)
- Cholinergic agonists (bethanechol 5–30 mg/d)
  - best in men with impotence secondary to TCA

MANAGEMENT OF SEXUAL DYSFUNCTION

Changing Administration of SSRI

If Adjunctive Strategies Fail:

- First consider temporary dose reduction or shift of dose to after intercourse
- Try “drug holiday” by stopping medication 1 or 2 days a week
  - works better with shorter-acting agents sertraline, paroxetine, fluvoxamine > fluoxetine)
  - risks withdrawal side effects, relapse, encouragement of medication noncompliance

CNS EFFECTS
Jitteriness

- Panic or anxious patients at increased risk
- Dosing: “start low, go slow”
- Benzodiazepines
- Beta-blockers

CNS EFFECTS
Tremor

- Assess and treat anxiety
- Decrease caffeine intake
- Beta-blockers
- Benzodiazepines
- Antiparkinson agents usually not effective

CNS EFFECTS
Disturbed Sleep

- AM dosing of stimulating agent
- PM dosing with stimulating med (fluoxetine, sertraline, sometimes paroxetine) in a minority of patients that have very delayed (ε8 hours) stimulating effect
- Benzodiazepines
- Gabapentin (Neurontin) 300-1800 mg qhs
- Nefazodone (Serzone) 100-300mg hs
- Mirtazapine (Remeron) 12-45 qhs
- Trazodone (25–500 mg)
  - beware of priapism in men (1:1000–1:8000)

CNS EFFECTS
Periodic Limb Movement Disorder (nocturnal myoclonus)

- TCA or levodopa can cause or worsen
- Clonazepam 0.5 mg
- Other benzodiazepines
- Trazodone 25–500 mg
- All Rx treatments improve sleep but not leg movements

CNS EFFECTS
Bruxism

- Imipramine 25–50 mg qhs
- Buspar 5–10 mg qhs
- Diazepam 0.5–2.0 mg qhs

CNS EFFECTS
Paresthesias

- ? MAOI-induced pyridoxine deficiency
- Pyridoxine 50–150 mg qd

CNS EFFECTS
Fatigue/Sedation

- Switch to bedtime dosing
- Lower dose/“drug holiday”
- Caffeine
- Add more stimulating AD (e.g., DMI)
- Dopaminergic agonists
- Stimulants
  - methylphenidate 5–10 mg qd–qid
  - pemoline 18.75–37.5 mg qd–tid
- Thyroid supplementation

CNS EFFECTS
Suicidality

- Drug *vs* disorder
- Rare
- Not unique to any agent
- Minimize early agitation/anxiety
- ? relationship to limbic dysrhythmia, bipolar, personality
- Frequent contact early in treatment

GASTROINTESTINAL DISTRESS

- Dose after meals
- Divided doses
- Antacids (calcium preferred)
- Bismuth subsalicylate (Pepto-Bismol®)

GASTROINTESTINAL DISTRESS

- H2 blockers
  - nizatidine (Axid®) 15–300 mg qd
  - famotidine (Pepcid®) 20–40 mg qd
- For diarrhea
  - loperamide (Immodium®)
  - diphenoxylate HCl (Lomotil®)
  - acidophilus (1 capsule/meal)
  - cyproheptadine (Periactin®) 2 mg qd–tid
  - psyllium fiber (Metamucil®)
    - also good for constipation
    - risks lower levels of lipophilic drugs

GASTROINTESTINAL DISTRESS For Nausea

- Metoclopramide (Reglan®) (5–10 mg qd–bid) has phenothiazine side effects, as do promethazine & prochlorperazine
- Ondansetron (5HT3 blocker)
  - short half-life (3 hours)
  - expensive
- ? mirtazapine (Remeron®)
  - 5HT3 blocker
  - antidepressant

AVOIDING WEIGHT GAIN

- Use antidepressants without significant weight gain
- All new (post-TCA) antidepressants have minimal weight gain (except mirtazapine)
- All with minimal antihistaminic (H_1) effects
  - SSRIs (fluoxetine, paroxetine, sertraline, fluvoxamine)
  - bupropion
  - venlafaxine
  - trazodone
  - nefazodone
  - desipramine
  - protriptyline
  - tranylcypromine

WEIGHT GAIN
Low-Risk Antidepressants

Antidepressant		Affinity*
Desipramine	Norpramin, Pertofrane	0.91
Trazodone	Desyrel	0.29
Fluoxetine	Prozac	0.016
Bupropion	Wellbutrin	0.015
Paroxetine	Paxil	0.0045
Nefazodone	Serzone	0.0044
Sertraline	Zoloft	0.0041
Fluvoxamine	Luvox	0.00092
Venlafaxine	Effexor	0.00002
Citalopram	Celexa	0.000019

10^{-7} X 1/Kd where Kd = equilibrium dissociation constant in molarity

WEIGHT GAIN
Antidepressants That Risk Weight Gain

Antidepressant		Affinity*
Doxepin	Adapin, Senequan	420
Trimipramine	Surmontil	370
Amitriptyline	Elavil, Endep	91
Maprotiline	Ludiomil	50
Nortriptyline	Pamelor	10
Imipramine	Tofranil	9.1
Protriptyline	Vivactil	4.0
Amoxapine	Asendin	4.0
Clomipramine	Anafranil	3.2

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Weight Gain by Other Mechanism

Mirtazapine	Remeron	5HT2 blocker
Phenelzine	Nardil	MAOI

ANTICHOLINERGIC EFFECTS
Urinary Retention

- Bethanechol (avoid with enlarged prostate)

SWEATING

- Alpha-1 adrenergic antagonists
  - terazosin (Hytrin®) 1 mg qhs
  - doxazosin (Cardura®) 1–2 mg qhs
- Hyosyamine (Levsin®) 1–2 mg qhs
- Ditropan 5 mg bid

SWEATING

- Beta-blocker can help with adrenergic TCA (e.g., desipramine)
- Clonidine
- Aluminum chloride in anhydrous ethyl alcohol, topical
  - used locally (e.g., armpits, palms)
  - duration of action 1–7 days

OTHER EFFECTS
Hair Loss

- Selenium/zinc supplementation
  - Centrum Silver®
- Selsun Blue® shampoo
  - contains selenium
- Minoxidil (Rogaine®)

LITHIUM-INDUCED SIDE EFFECTS
Nausea

- Give with meals
- Try slow release preparations
  - watch for diarrhea
- In some patients, lithium citrate may have increased risk of nausea

LITHIUM-INDUCED SIDE EFFECTS
Gastrointestinal Distress

- Dose after meals
- Divided doses
- Antacids (calcium preferred)
- Bismuth subsalicylate (Pepto-Bismol®)

LITHIUM-INDUCED SIDE EFFECTS
Gastrointestinal Distress

- H2 blockers
  - nizatidine (Axid®) 15–300 mg qd
  - famotidine (Pepcid®) 20–40 mg qd
- For diarrhea
  - loperamide (Immodium®)
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LITHIUM-INDUCED SIDE EFFECTS
Polyuria

- QD dosing
  - mixed results
- Hydrochlorothiazide 50–10 mg qd
  - risks lithium level increase
- Amiloride (Midamor®) 5–10 mg qd–tid
  - does not increase lithium level
- Furosemide
  - does not usually increase lithium level

LITHIUM-INDUCED SIDE EFFECTS
Tremor

- Reduce dose
- Decrease caffeine
- Beta-blocker

LITHIUM-INDUCED SIDE EFFECTS
Dermatologic Disturbance

- Acne
  - benzoyl peroxide (5% topical qd–bid)
  - tetracycline (500–1500 mg qd)
  - topical retinoic acid
- Psoriasis
  - dermatology consultation
  - alternative mood stabilizer

Post Lecture Exam Question 1

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Answers to Pre & Post Competency Exams

1. D
2. C
3. D
4. B
5. A