Management of SSRI Induced Sexual Dysfunction

John J. Miller, M.D.
Medical Director,
Center for Health and Well-Being
Exeter, NH

Serotonin Reuptake Inhibitors*

- fluoxetine (Prozac)
- clomipramine (Anafranil, a TCA)
- sertraline (Zoloft)
- paroxetine (Paxil, Paxil CR)
- fluvoxamine (Luvox)
- venlafaxine (Effexor, IR XR)
- citalopram (Celexa, Lexapro)
- duloxetine (Cymbalta)

*In order of U.S.A. market entry.

Email: jjmiller@pol.net

Adapted from Table 2: "Incidence of Sexual Dysfunction With Antidepressants Assessed by the Psychotropic-Related Sexual Dysfunction Questionnaire" (N=1022)

Drug	N	Mg mean dose	# with SD	% with SD
Citalopram	66	28.7	48	72.7
Paroxetine	208	23.4	147	70.7
Venlafaxine	55	159.5	37	67.3
Sertraline	159	90.4	100	62.9
Fluvoxamine	77	115.7	48	62.3
Fluoxetine	279	24.5	161	57.7

Montejo, A., et. al.; J Clin Psychiatry; 62 (suppl 3), pages 10-21 (2001)

COMMON SEXUAL SIDE EFFECTS OF ANTIDEPRESSANTS

- **Decreased Libido**
- **Decreased Arousal/Excitation**
  - Decreased penile engorgement
  - Decreased clitoral engorgement
  - Decreased vaginal lubrication
  - Genital numbing (decreased sensitivity)
- **Orgasmic/Ejaculation Dysfunction**
  - Difficulty with orgasm
  - Anorgasmia
  - Delayed ejaculation
  - Inability to ejaculate

Unusual Sexual Side Effects Of Antidepressants

- Penile Priapism
- Clitoral Priapism
- Painful Ejaculation
- Retrograde ejaculation
- Increased Libido
- Spontaneous Orgasm With Yawning

Putative Etiology of SSRI Induced Sexual Dysfunction

- Central elevation of serotonin
- Spinal cord elevation of serotonin
- Anticholinergic side effect
  - paroxetine
- Nitric Oxide Synthase inhibition
  - paroxetine
- Prolactin elevation
  - fluoxetine, paroxetine, fluvoxamine, citalopram
- Other

Email: jjmiller@pol.net

Potency of Antidepressants for Blocking Monoamine Transporters

Drug	NE Transporter	5-HT Transporter	DA Transporter
Amitriptyline	+++	++++	-
Citalopram	-	+++++	0
Clomipramine	+++	++++++	-
Desipramine	+++++	+++	-
Doxepin	+++	+++	0
Duloxetine	++++	++++++	+
Fluoxetine	++	+++++	-
Imipramine	+++	+++++	-
Paroxetine	+++	++++++	+
Sertraline	+	++++++	+++
Venlafaxine	+	++++	-

Richelson, E; J Clin Psychiatry; 2003; 64 (suppl 13); page 6.

Protein Binding and Urinary Excretion of SRIs

Drug	% Protein Bound	% Urinary Excretion	Half-Life
fluoxetine	94	<2.5	14 days
S-sertraline	98	<1	26 hours
R-paroxetine	95	<2	21 hours
fluvoxamine	77	<5	15 hours
venlafaxine	27	4.6	5 hours
D-M-venlafaxine	30	29	11 hours
citalopram	80	10.5	35 hours
S-citalopram	56	18*	29 hours

The Pharmacological Basis of Therapeutics; Goodman & Gilman; 10th Edition; 2001
*From Physician's Desk Reference; 2004; page 1302.

Serotonin Discontinuation Syndrome

- Somatic symptoms
  - Disequilibrium, dizziness, unsteadiness, vertigo
  - Feeling "spacey", confusion, memory dysfunction
  - Flu-like symptoms (myalgia, chills, fatigue, nausea)
  - Sensations of electric shocks, paresthesia, tremor
  - Insomnia, overactivity, vivid dreams
- Psychological symptoms
  - Agitation, anxiety, irritability
  - Mood lability, crying spells
  - Cognitive fog

"Don't Ask/Don't Tell" Approach is Countertherapeutic and Can Create More Dysfunction

- An informed patient is more likely to remain medication compliant
- Onset of uninformed sexual dysfunction can create:
  - Relationship stress with significant other
  - Self-judgment and increased depression
  - Confusion as to source of sexual dysfunction
- Can compromise the therapeutic alliance
- Awareness of availability of "antidotes" enhances compliance

Treatment Strategies For The Sexual Side Effects Of Antidepressants

- Decrease the dose
- Switch antidepressants
- Wait for a decrease or disappearance of the side effect
- Augment treatment with a second agent
- Add an " antidote" for prn use
- Avoid drug holidays

"Antidotes" to Serotonin-Induced Sexual Dysfunction

"Antidotes" For The Sexual Dysfunction Side Effects Of Antidepressant Medications

ANTIDOTE	COMMONLY EFFECTIVE DOSE
Amantadine	100-200 mg prn
Bupropion SR	300-400mg/day (given BID)
Buspirone	15-60 mg/day (given BID)
Cyproheptadine	4-16 mg prn
Dextroamphetamine	10-20 mg prn
Ginkgo Biloba	80mg TID
Methylphenidate	10-20 mg prn
Nefazodone	100-400mg qhs
Pramipexole	0.125-1.5mg/day prn
Sildenafil	25-100mg qd prn
Yohimbine	2.7-16.2 mg prn or 5.4 mg TID

Amantadine

- Effective dosage range 100-200 mg prn
- Putative mechanism:
  - Release dopamine and norepinephrine??
  - Inhibit reuptake of dopamine and norepinephrine??
- One placebo controlled study showed improvement no greater than placebo

Bupropion SR

- Effective dosage range 300-400mg/day
  - Give BID, 200mg/dose max, 6-8 hours apart
- Useful in augmentation of depression:
  - Improves energy, decreases hypersomnia, improves cognition and motivation
- May be used as primary "antidote"
- Mechanism of action:
  - dopamine and norepinephrine reuptake inhibitor
- Contraindicated in patients with seizure hx

Buspirone

- Effective dosage range 15-60 mg/day
  - Give BID
- Mechanism of action
  - Serotonin 5HT-1A partial agonist
- One placebo controlled study showed improvement no greater than placebo
- Seems to work better in women than men

Psychostimulant Dopamine Agonists

- Dextroamphetamine 10-20 mg/day or prn
- Methylphenidate 10-20 mg/day or prn
- Contraindicated in substance abusers
- Side effects include:
  - insomnia, anxiety
- Mechanism of action:
  - dopamine reuptake inhibition
  - presynaptic dopamine and norepinephrine release

Anti-Parkinsonian Dopamine Agonists

- Mirapex (pramipexole) 0.125-1.5mg/day prn
- Requip (ropinirole) 0.25-3mg qd prn
- Mechanism of action:
  - Dopamine agonist D3>D2
- Very little clinical experience to date
- Await more peer reviewed research literature

Cyproheptadine

- Effective dose 4-16 mg qd prn
- Mechanism of action
  - Serotonin receptor antagonist
  - Likely action at spinal cord
- Antihistaminic sedation
- DO NOT use daily – will reverse SSRI effect
- May reverse antidepressant effect of SSRIs
- RARE incidence of retroperitoneal fibrosis

Ginkgo Biloba

- Effective dose 80mg TID
- Onset of action delayed up to 14 days
- Sold as a food supplement/herbal remedy
- No accountability re quality control
- Putative mechanism of action is vasodilation
- Increases blood flow to genitals and brain
- Double benefit:
  - Improves sexual functioning
  - Remember they had sex the next day

Nefazodone

- Effective dose 100-400mg qhs
- New black box warning re liver disease
- Baseline LFTs, and follow closely first 6 months
- Mechanism of action 5HT-2A antagonist
- Will also treat residual anxiety and insomnia
- Antihistaminic sedation
- Weight neutral
- Drug interactions at Cytochrome P450-3A4

Yohimbine

- Effective dose 2.7-16.2 mg prn or 5.4 mg TID
- Anxiety, panic attacks and agitation are common side effects
- Available prior to 1938
- natural Yohimbe is a tree bark which contains yohimbine
  - Sold OTC as a dietary supplement for body building and "enchanced male performance" ; reports of renal failure, seizures and death.
- Mechanism of action
  - Central alpha-2-receptor antagonist
  - Increase in sympathetic drive secondary to an increase in norepinephrine release

Sildenafil (Viagra)
The "Gold Standard"

- Effective dose 25-100mg qd prn
- Effective in men and women
- Contraindications in women same as in men with addition of pregnancy & breast feeding
- Take one hour before sexual activity
- True kamikaze effect – does the job and leaves in four hours
- cyclicGMP Phosphodiesterase Type 5 inhibitor