POST-SSRI’S SEXUAL DISORDERS (PSSD)

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SSRI’s: Indications & Use

- Depressive disorder
- Anxiety disorder
- OCD
- Panic attacks
- PTSD
- PE

- Prevalence: up to 7% of US population
- SSRI’s are the 3rd most often prescribed medication in US
- In NL: 3% of population use SSRI

Ekhart CG, Tijd Psychiatry 2014
Mojtabai R, Health Aff 2011
SSRI’s: Sexual Side-Effects

- Decreased libido
- Erectile dysfunction/decreased lubrication
- Ejaculatory disorders (Delayed)
- Delayed/Anorgasmia
- Anesthesia of genitals
- PGAS

- Depression or SSRI?
- SSRI side-effect

Clayton A, Postgrad Med 2014; Dutch Pharmacovigilance Center Lareb 2012
Leiblum SR. J Sex Marital Ther 2008
• Prevalence up to 70%

• Due to activation of the 5-HT$_{2A}$ receptors

• Endure for the duration of treatment, assume to be resolved upon discontinuation
Desire, Arousal & Depression

- **Depression** - *Decreased* desire in
  - 40% of men
  - 50% of women (variability up to 70%)

- **Depression** – *Increased* desire in
  - 23% of men
  - 9% of women

- **Increased risk of**
  - OR-3.4 for erectile dysfunction
  - OR-2.3 for vaginal dryness

- Nocturnal penile tumescence is decreased in 40% of men with depression

Ejaculation, Orgasm & Depression

• 15-25% increased risk of premature or delayed ejaculation
• 40 % of women report orgasmic problems
• Large variability in studies

The Effect of Psychopharmaca on Sexual Function

- **Unspecific:**
  - Overweight, tiredness

- **Specific effect on CNS neurotransmitters:**
  - Serotonin, noradrenaline, dopamine, NO, cholinergic system

- **Direct hormonal effect:**
  - Prolactin

- **Indirect hormonal effect**
  - SHBG & metabolic syndrome

Segraves 1989
Corona G. Eur Endocrin 2008
Central Effects of Neurotransmitters & Hormones on Sexual Functioning

- Estrogen
- Testosterone
- Oxytocin
- Melanocortins
- Dopamine
- Prolactin
- Opioids
- Progesterone
- Norepinephrine
- 5-HT$_{2+3}$ (serotonin)
- Desire
- Subjective excitement
- Orgasm

Clayton A. JSM 2007;4260-268
Peripheral Effects of Neurotransmitters & Hormones on Sexual Functioning

- **Testosterone**
- **Estrogens**
- **Cholinergic stimulation**
- **Blood flow**
- **Erectile tissue**
- **Sensation**

**Blood flow:**
- + Testosterone
- + Estrogens

**Erectile tissue:**
- + Testosterone
- + Estrogens

**Sensation:**
- - 5-HT$_{2+3}$ (serotonin)
- - NO

**Cholinergic stimulation:**
- + Testosterone
- + Estrogens

**Noradrenaline:**
- - Testosterone
- - Estrogens

Clayton A. JSM 2007;4260-268
More about Anti-depressant & Sexual Dysfunction

• Sexual dysfunction, sleeping problems and weight gain are major reason for stopping anti-depressant treatment (60-75% of patients)

• 90% of patients stop prematurely with the medication

• Side effects early in treatment can decline, decrease or persist – but it will rarely disappear

• Sex is important for patients
Treatment Of Medication Induced SD

- Wait for tolerance (10%)
- Dose-reduction
- Change of drug / Drug with less side effects
- ”Drugholiday”
- Change sexual habits
- Pharmacological treatment of SD
  - PDE5-inhibitors
  - Antidote treatment
- Information/ couple therapy
ANTIDOTES

- Bupropion (Zyban®) dopamin & noradrenalin agonist 
- Buspiron (Buspar®) 5-HT₁₅ partiel agonist 
- Mirtazapin (Remeron®) adrenerg antagonist & 5HT₃ & 5HT₂₅ antagonist 
- Sildenafil (Viagra®) PDE5 inhibitor 
- Granisetron (Kytril®) 5HT₃ antagonist 
- Apomorfin SL dopaminagonist 
- Cyproheptadine serotonin antagonist 
- Yohimbin adrenerg α₂ antagonist 
- Neostigmin cholinerg agonist 
- Amantadine dopamin agonist 
- Dextroamfetamin dopamin agonist
Emerging evidence that in some patients these SD side-effects persist after cessation of SSRi’s >> PSSD

No-one know what withdrawal syndrome and PSSD actually are !!!

What is the treatment / How to manage ???
PSSD

- Difficult to diagnose
- Difficult to treat
- Difficult to cure

Frustration for patient & physician
What Is The Evidence

• Lareb database¹:
  • 140,000 registrations, 44,000 about SSRI
  • 19 reports of PSSD
  • 13 ♂: 6 ♀
  • Mean age 30 years (20-59)
  • Paroxetine, Sertraline, Venlafaxine, Citalopram, Fluoxetine, Fluvoxine, Esitalopram
  • DE, Libido decrease, ED, Orgasmic disorders, reduced sensitivity

  • SSRI use: 9 days – 10 years
  • PSSD: 2 months – 2 years

• Csoka²:
  • 3 males (20, 28 and 44 years old)
  • After use of SSIR’s for different period (4-24 months)
  • Libido loss, ED, genital anesthesia
Csoka & Shapro³:
- 2♂ & 1♀
- 24 – 30 years
- Libido loss, ED, numbness

Bolton⁴:
- 26 years ♂
- Genital anesthesia, libido loss and orgasmic dysfunction
- 6 years after Sertraline

Kaufman⁵
- 32 years ♀
- Genital anesthesia and anorgasmia persist 1 year after Citalopram

- No relationship problems or Sexual complains prior to SSRI
- SD after start medication
- Depression in remission, no CVD risk factors
- Normal Serum T, LH, FSH, Cortisol, ACTH, Estrogen & Serotonin

Diminished Physical Capacity to Experience Sexual Pleasure

1 Dutch Pharmacovigilance database 2012
2 CSoka AB, J Sex Med 2008
3 Csoka AB Psychoth Psycchosom 2006
4 Bolton JM, J Sex Mart Therp 2006
5 Kaufmann
Possible Theories

- Serotonin increase in hypothalamus - down regulation receptors - Testosterone decrease
- Epigenetics: Serotonin transmission: single Nucleotide Polymorphism (SNP)
- Sodium channels changes – decrease in Oxytocine release
- Transient Receptor Potentia Channels (TLPR)
- Change in brain structures with SSRI (Amygdala)
- Endocrine: SSRI & OAC more side effects, decreased Dopamine

Markman 2016
Bishop JR 2006
Yamada 2005
Scala 1987
Baird AD 2004
Rosen RC 1999
Contributing Factors

• Psychological
• Concomitant medical disorders
• Medications
WHAT WE SHOULD DO?

- Registration and longer follow-up
- Informed consent before treatment
- When possible - avoid SSRI's
- Assess Sexual function before, during and after treatment
- When side effect:
  - Drug holiday
  - Reduce doses
  - Change to drug with less Sexual side effects (Bupropion, Mirtazapine, Nefazodone)*

*Clayton A, 2007 & 2012
Ben-Sheetrit 2015
• Multidisciplinary approach
  • Other contributing factors/ Psycho-pathology
• History and Physical examination
• Routine Laboratory and Hormones (TSH, LH, FSH, Testo, PRL, Estrogen)
• Support & addressing the fear of permanent problem

• Sleep, Nutrition, Physical activity, Routine
• Avoiding of Alcohol & Drugs
Anecdotal evidence

- Fenylethylamine (Wine, Chocolate, Cheese) & Sofran
  - Reduction of symptoms severity
- Imipramine & Amineptine
  - Increase dopamine transmission. Improvement of ejaculation
- Pramipexol (Dopamine agonist)
- Methylphenidole (Ritalin) –
  - Increase dopamine transmission
- Trazodone (5HT2 antagonist)
  - Reduction of SD severity
- Low-power laser irradiation for genital anesthesia

Montejo 1999
Stacey J 2009
Waldinger 2015
Kahani 2013
Thank you
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