

# Psychopharmacological Treatment of Sexual Dysfunction

R T Segraves, MD

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# Teaching Points

- 1. Sexual problems have a high prevalence in the general population
- 2. Sexual dysfunction has a high prevalence in a number of psychiatric disorders
- 3. Some sexual dysfunctions respond to psychopharmacological interventions

# Outline

- Prevalence
- Treatment erectile dysfunction
- Treatment of rapid ejaculation
- Treatment of female arousal disorder
- Treatment of hypoactive sexual desire disorder

# Pre-Lecture Exam

## Question 1

- The most common male sexual concern is:
  - 1.rapid ejaculation
  - 2.low sexual desire
  - 3.erectile dysfunction
  - 4. difficulty reaching orgasm

# Question 2

- The most common female sexual concern is:
  - 1. low sexual desire
  - 2. difficulty with vaginal lubrication
  - 3. difficulty reaching orgasm
  - 4. pain with coitus

# Question 3

- Which drug is most effective in the treatment of rapid ejaculation?
  - 1. paroxetine
  - 2. sertraline
  - 3. fluvoxamine
  - 4. citalopram

# Question 4

- Which drug has been shown to be effective in the delay of ejaculation when used on a PRN basis?
  - 1. citalopram
  - 2. fluoxetine
  - 3. fluvoxamine
  - 4. clomipramine

# Question 5

- Low sexual desire is common in both men and women with major depressive disorder.
- True
- False



# Prevalence:US population study

- Probability sample of US population aged 18 to 59
- 1410 men
- 1749 women
- Percentage indicating problem in past 12 months

# Sexual problems, US men reporting

- Rapid ejaculation 28.5%
- Lack of interest 15.8%
- Erectile dysfunction 10.4 %
- Inability to orgasm 8.3%

# Sexual problems, US women reporting

- Lack of interest 33.4%
- Difficulty with orgasm 24.1%
- Trouble lubricating 18.8%

# Global Study

- Sample of 27,500 people ages 40-80 from 29 countries
- Same questionnaire
- Different sampling and administration in different countries
- In Europe, used random digit dialing
- Response rate 16% for telephone

# Frequency of sexual activity

- 80% of men and 65% of women had sex in previous year
- 44% men and 37% women had sex at least 5 times a month

# Northern European, men reporting

- Orgasm too quickly 20.6 %
- Erectile dysfunction 12.7 %
- Lack of interest 12.1 %
- Inability to orgasm 8.4 %

# Southern Europe, men reporting

- Orgasm too quickly 21.2 %
- Lack of interest 13.2 %
- Erectile dysfunction 13 %
- Inability to orgasm 12.2 %

# Northern Europe, women reporting

- Lack of interest 25.3 %
- Lack of lubrication 17.7 %
- Inability to orgasm 23.8%



# Southern Europe, women reporting

- Lack of interest 29.6 %
- Inability to orgasm 23.8 %
- Lack lubrication 15.5%

# Correlates

- Depression related to increased risk of low desire and erectile dysfunction in men and to low desire in women
- Age correlated with increased risk of erectile dysfunction and trouble with lubrication

# Sexual problems, US women reporting

- Lack of interest 33.4%
- Lack of orgasm 24.1%
- Lack of lubrication 18.8%

# Prevalence of Sexual Disorders

- One must use caution when interpreting the clinical significance of the finding of a high prevalence of sexual concerns in the general population

# Differences between sexual concerns and sexual dysfunction

- Many sexual problems are related to life stress and relationship issues
- These often are transient and resolve without medical intervention
- Sexual problems should be differentiated from sexual disorders which tend to be more severe and persistent and to require medical intervention

# Other Issues Using Epidemiological Data

- Many individuals with alterations in sexual function
- Many alterations in sexual function are of brief duration and resolve without clinical intervention
- Surveys often do not distinguish between sexual disorders and expected variations in sexual behavior with vicissitudes of life

# Sexual Disorders in DSM IV TR

- Diagnostic criteria in DSM IV TR are imprecise and do not have clear duration and severity criteria

# Prevalence of Sexual Disorders

- Prevalence of severe, persistent problems unclear
- Severe sexual problems are less common than less severe problems
- Transient sexual problems are much more common than persistent problems



# Epidemiology of Rapid Ejaculation

- Probability sample of men in the Netherlands, Turkey, Spain, United Kingdom, United States
- Intravaginal ejaculatory latency measured by stop watch
- Median latency 5.4 minutes
- Range . 55 to 44 minutes

Waldinger et al, J Sex Med, 2005

# Proposed Definition of Premature Ejaculation

- Use of .0.5 percentile standard of disease definition
- Intravaginal ejaculatory latency of less than 60 seconds proposed as definition of premature ejaculation

Waldinger, J Men's Health Gender, 2005

# Sexual Co-Morbidity

- Major depressive disorder
- Obsessive compulsive disorder
- Post traumatic stress disorder
- Anorexia nervosa
- Schizophrenia
- Social phobia
- Panic disorder

Lindal & Steffanson, SPPE, 1993; Wiederman et al, IJEP, 1996; Kennedy et al, JAP,1999, Kockett et al, JAD,1999; Minnen & Kampman, SRT,2000; Kivela & Palhala, IJSP,1988  
Aisenberg et al, JCP, 1995; Aversa et al, IJA,1995; Bodinger et al, JCP,2002  
Arsaray et al, JSMT,2001; Figueira et al, ASB. 2001

# Sexual dysfunction in Depression

- Numerous studies have found decreased libido and erectile problems to be common in depression

Mathews & Weinnan , ASB, 1982

# Proposal

- It has been proposed that the relationship between depression and erectile dysfunction is bidirectional
- An increased prevalence of erectile dysfunction in depressive illness has been established
- An improvement in depression has been observed in depressed men successfully treated for erectile dysfunction

Makhlouf et al, Urol CI NA 2007

# Sexual dysfunction and depression

- 134 patients with untreated depression
  - 40-50% decreased libido
  - 40-50% decreased arousal
  - 15-20% delayed orgasm

Kennedy et al, JAD, 1999

# Treatment of Erectile Dysfunction

- Phosphodiesterase Inhibitors
  - Sildenafil ( Viagra)
  - Tadalafil ( Cialis)
  - Vardenafil (Levitra)

Wylie & Mac Innes, 2005

# PDE-5 Inhibitors

- Cyclic guanosine mono-phosphate (cGMP) determines the extent of corporeal smooth muscle relaxation
- PDE-5 inhibitors block the breakdown of cGMP



# PDE-5 Inhibitors

- The three available PDE-5 inhibitors have similar efficacy and side effects
- Tadalafil has a half-life of 17.5 hours whereas sildenafil and vardenafil have half-lives of around 4 hours

# Common side effects

- Facial flushing
- Headache
- Dyspepsia
- Rhinitis
- Transient visual disturbances

# Cautions

- PDE-5 inhibitors contraindicated if taking nitrates
- Use with caution in patients on multiple anti-hypertensive agents
- Rare risk priapism
- Unclear if increased risk of blindness

# Cabergoline

- Cabergoline has been reported to be effective in men with erectile disorder who are not responsive to phosphodiesterase inhibitors
- Cabergoline has also been shown to be effective in psychogenic erectile dysfunction

Safarinejad, Int J Impot Res , 2006; Nickel et al, Int J Impot Res, 2007

# Alternatives

- Intracavernosal alprostadil
- ( Prostaglandin E-1)
- Intraurethral alprostadil
- Vacuum constriction devices

# Treatment of Premature Ejaculation

Paroxetine*	20-40 mg daily
Clomipramine	10-50mg daily
Sertraline	50-100mg daily
Fluoxetine	20-40mg daily

\*Strongest effect

# Dapoxetine( Priligy) and Topical Ointments

- Short-acting SSRI approved in Europe for treatment of premature ejaculation
- Anesthetic topical ointments have been demonstrated to be effective in double blind trials
- No drug in US approved for this indication

# On Demand Treatment

- Clomipramine 10-50mg 4-6 hours prior to coitus
- Data concerning on demand use paroxetine inconsistent



# Treatment Female Sexual Dysfunction

- Alpha-blockers, topical alprostadil, oral phosphodiesterase inhibitors all increase peripheral vasocongestion but have no effect on reversing sexual dysfunction in women

Segraves, Exp Opin Emerging Drugs, 2003

# Testosterone

- Numerous double-blind multi-site controlled studies have found that high dose testosterone therapy increases libido in postmenopausal women
- Long term safety of testosterone therapy is unknown

# Testosterone

- Food and Drug Administration did not approve transdermal testosterone for females
- Concern about absence of data concerning long term safety
- However, it was approved by European Union for treatment of low sexual desire in post menopausal women

# Androgen Insufficiency Syndrome

- Androgen levels drop precipitously after oophorectomy
- Androgen therapy increases libido in women post-oophorectomy
- Hypothesis that an androgen insufficiency syndrome may explain HSDD

# Androgen Insufficiency Syndrome

- Limitations of androgen assays in females
- Much biologically active androgen in women is formed by intracellular conversion which is not detected by serum assays
- No measure of androgen is predictive of female sexual dysfunction

# Menopausal Transition

- Large Australian prospective epidemiological study found that age, relationship duration, and menopausal transition all had independent contributions to decreased sexual function
- Decreased sexual function after menopause related to decreased estradiol levels

Dennerstein et al, Fert Ster 2005

# Predictor Postmenopausal Sexual Function

- Strongest predictors of sexual function after menopause were
- Relationship satisfaction and prior sexual function

Dennersten et al, Fert Ster 2005

# Sexual Function and Menopause

- Greater decrease in sexual function after surgical menopause than natural menopause



# Bupropion

- One double-blind multi-site study of women with HSDD found that 4-6 weeks of bupropion 300-450mg per day increased orgasm completion and sexual satisfaction
- The clinical effect was modest although statistically significant

Segraves, J Sex Med 2003

# Investigational Agents

- Flibanserin-a 5HT 2a antagonist and 5HT1a agonist has been found to be effective in the treatment of HSD in pre-menopausal women

Melanocortin analogues are being studied for their effects on libido

Morris LN 2003; Borsini CNS DRUG Rev 2002

# Conclusions

- A variety of psychopharmacological interventions are available to treat sexual disorders
- Numerous interventions are being investigated

# Post Lecture Exam

## Question 1

- The most common male sexual dysfunction is:
  - 1.premature ejaculation
  - 2.hypoactive sexual desire disorder
  - 3.erectile dysfunction
  - 4.male orgasmic disorder

# Question 2

- The most common female sexual dysfunction is:
  - 1.hypoactive sexual desire disorder
  - 2. female sexual arousal disorder
  - 3. female orgasmic disorder
  - 4.dyspareunia

# Question 3

- Which drug is most effective in the treatment of rapid ejaculation?
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# Question 5

- Low sexual desire is common in both men and women with major depressive disorder.
- True
- False



# Answers to Pre & Post Lecture Exams

1. 1
2. 1
3. 1
4. 4
5. True