Male Sexual Dysfunction: Assessment and Management Post Cancer Treatment

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Historical Background

• American Cancer Society’s 2008 estimates of leading four cancer sites among men:
  1. **Prostate**
  2. Lung and Bronchus
  3. **Colon/Rectum**
  4. **Urinary Bladder**

• Increased attention to quality of life post cancer treatment by patients and national credentialing centers
Male Sexual Dysfunction Post Cancer Care

- Erectile Dysfunction
  - Organic
  - Psychogenic
  - Mixed
- Ejaculation/Orgasm disorders
  - Anejaculation/decreased volume
  - Dysorgasmia
  - Retrograde ejaculation
  - Retarded orgasm
- Incontinence
- Infertility
- Hypogonadism
Assessment of Sexual Dysfunction

- Medical History
- Surgical History
- Social History
  - Relationship status
  - Alcohol, recreational drugs, tobacco use
- Physical Examination
- Tests:
  - Laboratory (blood, urine)
  - Biothesiometry
  - Duplex sonogram (DUS)
  - Dynamic Infusion Cavernosometry (DIC)
Erectile Dysfunction (ED) is...

• ... the consistent inability to achieve or maintain a penile erection sufficient for “adequate” sexual relations.

• The effects of ED interfere with¹:
  – Man’s self-esteem
  – Interpersonal relationships
  – Sense of well-being

Method to Evaluate ED

International Index of Erectile Dysfunction (IIEF)$^1$
Questoinnaire-based, reliable self-administered symptom scales
Maxium score = 30

5 domains: (15 questions, rating 0 or 1 – 5)
• Erectile function (6 questions)
• Orgasmic function (2 questions)
• Sexual desire (2 questions)
• Intercourse satifaction (3 questions)
• Overall satifaction (2 questions)

Results:
• < 10 = severe
• 11 – 17 = moderate
• 18 – 25 = Mild
• > 26 = normal

1 Rosen RC et al 1997
Sample Questions on IIEF

• Q1: How often were you able to get an erection during sexual activity?

• Q2: When you had erections with sexual stimulation, how often were the erections firm enough for penetration?

• Q3: When you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?

• Q4: During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?

• Q5: During sexual intercourse, how difficult was it to maintain your erection to complete intercourse?

• 0 = No Sexual Activity
• 1 = Almost never/never
• 2 = A few times (much less than half the time)
• 3 = Sometimes (about half the time)
• 4 = Most times (much more than half the time)
• 5 = Almost always/always

• 0 = Did not attempt intercourse
• 1 = Almost never/never
• 2 = A few times (much less than half the time)
• 3 = Sometimes (about half the time)
• 4 = Most times (much more than half the time)
• 5 = Almost always/always

• 0 = Did not attempt intercourse
• 1 = Extremely difficult
• 2 = Very difficult
• 3 = Difficult
• 4 = Slightly difficult
• 5 = Not difficult
Likely Post Treatment Causes of ED

- Arteriogenic (accessory pudendal artery injury)
- Venogenic (erectile tissue damage)
- Neurogenic (cavernous nerve injury)
- Psychogenic (confidence erosion)
- Androgen Deprivation
Accessory Pudendal Arteries

• Some men have APA as a major source of cavernosal inflow

• Most authorities believe injury to these arteries (surgery and/or radiation) plays some role in erectile dysfunction.

Flaccid

P0₂ = 35-40 mmHg

- Increased TGF-β₁ Secretion
- Collagen Production
- Fibrosis and venous leak

Erect

P0₂ = 70-100 mmHg

- Increased PGE Secretion
- Decreased Collagen Production
- Preserved erectile tissue integrity
Venous Leak

- Three crucial steps to achieve erection
  - Relaxation of trabecular smooth muscle
  - Arterial dilation
  - Venous compression

- When venous compression fails = venous leak
Mechanism of Penile Erection

Tunica albuginea

Subtunical Venule

Smooth muscle
Cavernous Nerves
Evolution Of ED Therapy

1960’S
Sex therapy

1970’s
Penile Prosthetics

1980’s
Penile injection therapy

1997
MUSE™

1998
Viagra™

PDE5I Transdermal Tx Injection Tx
# Management of ED

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PDE5 Inhibitors

- Nitric oxide dependent mechanism

- Success in patients depends on
  - Time of trial
  - Degree of neuron sparing (surgery/radiation)
  - Responsiveness of CCSM

- Post-RP evolution of response
  20% @ 3 months
  50% @ 12 months
  Slightly higher @ 18 months

Correct PDE5 Inhibitor Use

- Take one hour prior to sexual activity
- Take on empty stomach
- Avoid taking when tired or under stress
- Must be engaged in sexual activity (partner or masturbatory)

Contraindicated:
- Unstable angina requiring nitroglycerine use (Nitrolingual®, Imdur®)
- History of hypotension
- History retinitis pigmentosa
Vacuum Erectile Device (VED)

- Mechanical or battery operated
- Placed over penis
- Vacuum created drawing venous blood into penis
- Tension ring placed at base of penis to hold in the blood
Intracavernosal Injection (ICI) Therapy

• Involves direct injection of papaverine, phentolamine, and alprostadil separately or in combination into the corpus cavernosum

• Utilized when oral agents not effective

• Results in inhibition of PDE5, leading to increased cAMP and cGMP in penile erectile tissue.
Medications

• Papaverine

• Phentolamine

• Alprostadil (Caverject®, Edex®)

• Compounded multi-agent mixtures (Bimix, Trimix, Super Trimix)
Papaverine

• Vasodilator

• Smooth muscle spasmolytic producing a generalized smooth muscle relaxation

• Muscle relaxation occurs due to inhibition of phosphodiesterases in a non-specific fashion increasing cAMP
Phentolamine

• Non-selective $\alpha$-adrenoceptor blocker

• Completely blocks $\alpha$-adrenergic receptors to produce brief antagonism of circulating epinephrine and norepinephrine

• Used in combination with papaverine or papaverine and alprostadil
Alprostadil (PGE1)

• Prostaglandin E1

• Causes vasodilation by means of direct effect on vascular smooth muscle

• Relaxes trabecular smooth muscle by dilation of cavernosal arteries promoting arterial flow and blood entrapment within the lacunar spaces of the penis
MSKCC Compounded Mixtures

- **Bimix**
  - Papaverine 30mg/ml
  - Phentolamine 1mg/ml

- **Trimix**
  - Papaverine 30mg/ml
  - Phentolamine 1mg/ml
  - PGE1 10mcg/ml

- **Super Trimix**
  - Papaverine 30mg/ml
  - Phentolamine 2mg/ml *(check this)*
  - PGE1 20mcg/ml
Contraindications

• Obese abdomen
• History vaso-vagal response
• Dexterity problems
• Uncontrolled hypertension
• Concurrent use of MAO Inhibitors
Contraindications

- Predisposition to priapism due to hematologic disorders (e.g., sickle cell anemia, multiple myeloma, leukemia)

- Penile prosthesis

- Sexual activity is inadvisable or contraindicated
Training

• Scheduled for two sessions

• Provided verbal and written instructions

• First session: injected with Trimix 5 units to assess response (i.e., rigidity & duration)

• Second session: self-injection taught (dose adjusted according to response at first session)
Training

• Injection supplies:
  – Vial of medication
  – Syringe (29 gauge, ½” needle, 50 unit/0.5cc)
  – Alcohol swabs
  – Sharps container

• Instructed on drawing medication from multi-dose vial

• Taught to rotate injection sites
Training

• Preparation of penis and choice of injection site

• Divide penis into two parts:
  – Area proximal to mid-point of shaft
  – Area distal to mid-point of shaft

• Anatomical landmarks reviewed
Training

- Patient grasps glans with less dominant hand (must retract foreskin if uncircumcised) and gently stretches penis

- Area to be injected located and swabbed with alcohol wipe

- Holding needle as dart or pen position toward area to be injected
Training

• Instructed to angle needle at 10 o’clock or 2 o’clock position on shaft directly behind midline
Responses

• Patient informed may experience warm sensation within 3-5 minutes followed by “stretching”, “tight”, or “heavy” non-painful sensation along shaft

• Rigidity should occur within 10-20 minutes with minimal stimulation
Responses

• Erection scale used to grade response

  0 = no erection
  6 = erection just firm enough for penetration
  8-10 = Satisfactory for sexual intercourse
  10 = 100% erect
Complications

• Poor or no response:
  – Majority due to technique leading to subcutaneous or intra-tunical injection
    • Plunger pressed as needle inserted
    • Needle pulled out as plunger pressed
    • Accidental release of penis as injecting
    • Needle rolls against tunica when inserting
    • Injected at base of penis
  – Vial of medication exposed to heat or light
Complications

• Adverse Reactions:
  – Priapism
  – Penile pain (Lane, et al., 2005)
  – Hematoma or ecchymosis at injection site
  – Penile rash or edema
  – Fibrosis
• Instructed to take 4 tablets of pseudophedrine (Sudafed®) 30mg if erection 6 or firmer > two hours

• Erection remains ≥ 6/10 at third hour after pseudophedrine, patient contacts office

• By fourth hour, at Emergency Department for intracavernosal injection of phenylephrine (Neo-Synephrine®)

• If unresponsive to phenylephrine will need to aspirate blood
Monitoring

- Contacts office reporting result after first home injection for titration instructions
- Injects 2-3x/week regardless of sexual activity
- If poor or no response cannot repeat for 24 hrs
- No PDE5 Inhibitor within 18-24 hours of ICI
Monitoring

• May take 3-4 weeks injecting 2-3x/week to reach appropriate dose

• Continues nightly low dose PDE5 Inhibitor on nights when not injecting for first year post surgery or RT

• Follow-up scheduled four months or sooner for additional teaching session if required
Patient Drop-out

• 30-80% at 3-5 yrs

• Realistic expectations

• Patient/partner education

• Reasons:
  – Cost
  – Failure
  – Needle-phobia
  – Adverse effects
  – Change in patient goals
  – Partner issues

Althof et al. J Sex Mar Ther, 15:121-129;
Sundaram et al, Urology. 49: 932, 1997;
Mulhall et al, J Urol. 158: 1752, 1999
Auto-injectors

- Experience in other conditions supports use (e.g., Epipen®, diabetes)
- Primary purpose to reduce anxiety
- Absence of evidence-based analyses
- Use based on personal preference
- Needle-less injectors
Penile Prosthesis

- Utilized in patients who have failed drug therapy or patient burn-out with therapies
- Advantages:
  - Generates a 100% rigid erection
  - 5-15 seconds to generate erection
- Disadvantages:
  - Invasive surgical procedure
  - Risk of infection (2-3%)
  - Mechanical breakdown (15% first 10 years)
- Implant types:
  - Mechanical
  - Inflatable
    - Two piece
    - Three piece
Penile Prosthesis 2-Piece Implant
Penile Prosthesis 3-Piece Implant
Ejaculation Disorders

• Anejaculation or decreased volume
• Dysorgasmia (painful erections)
  – Tamsulosin HCL (0.4mg)
  – Alfuzosin (10mg)
  – Patient education regarding side effects of $\alpha$-blockers
• Retrograde ejaculation
• Retarded orgasm
  – Neuropathy (chemotherapy/radiation)
Incontinence

• Common after radical pelvic surgery
• Fear of urine loss with foreplay/intercourse
• Patient and partner distress
• Treatments:
  – Kegel exercises
  – Condoms
  – Penile constriction loop
  – Artificial urinary sphincter
Infertility

• Effects of chemotherapy, radiation, and/or surgery
• Counsel patients regarding sperm preservation
  – Sperm banking
  – Electro-ejaculation
• Interventions post-treatment
  – Testicular tissue extraction
  – Androgen replacement
Hypogonadism

• Testosterone
  – Major sex hormone in adult male
  – Produced predominantly by testicles (small amount by adrenal glands)
• Failure of testicles to produce testosterone
• Failure of pituitary to secrete enough LH to stimulate cells in testicles
• Surgery (Orchiectomy)
• Chemotherapy, total body irradiation (bone marrow and stem cell transplants)
Hypogonadism

- Reduction in general well-being
- Decrease in sexual drive (libido)
- Increased fatigability
- Loss of energy
- Depression
- Erectile problems
- Osteopenia/osteoporosis
  - Axial Bone Densitometry Scan
  - Androgen replacement
Hypogonadism

• Androgen Replacement
  – Testosterone
    • Patches
    • Topical Gels
    • Intramuscular injections
  – Clomiphene citrate (25mg QOD)

• Laboratory blood work

• Repeat Axial DEXA Scan
Summary

• Important to counsel patients pre and post cancer treatment
• Early intervention and initiative to assess and manage patient can be key to post treatment satisfaction
• Refer to the Male Sexual and Reproductive Medicine Program

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