Intracavernosal Injection Therapy in the Management of ED

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Outline

- Introduction to ICI
- ICI and Color Penile Doppler Ultrasound in Diagnosis of ED
- ICI Therapy in the Treatment ED
- ICI for Penile Rehabilitation After Radical Prostatectomy (RP)
ICI and Erectile Dysfunction

- Prior to ICI, psychosexual Rx, surgery, VED for ED patients
- Opened door for pharmacological Rx
- ICI first described by Virag in 1982\(^2\)
  - 80mg *papaverine* injection improved blood flow to cavernous tissue
- Advent of PDE-5 inhibitors supplanted ICI as first-line therapy

“I had been wondering why he was wearing sweatpants. Suddenly I knew. It was a big penis, and he just walked around the stage, showing it off.” A. Melman

Vasculogenic ED and ICI

- Vasculogenic ED: arterial insufficiency and/or corporeal venous occlusive dysfunction (CVOD)
- Color penile Doppler ultrasound (CPDU) in conjunction with ICI
  - Correlated with abnormalities on pelvic arteriography and cavernosometry\(^1\)
  - Help detect vascular abnormalities and differentiate between vasculogenic ED\(^1\)

CPDU Parameters

- Normal peak systolic velocity (PSV) >30 cm/s
- PSV <25 cm/s indicates arterial insufficiency
- End diastolic velocity (EDV) ≥6 cm/s indicates venous leak
- PSV <25 cm/s and EDV >6 cm/s indicative of mixed arterial and venous dysfunction

ICI and CPDU

- Alprostadil has a higher response rate and lower incidence of priapism than papaverine or bimix\(^1\)
  - Starting dose is around 10 mcg
- Trimix is used in non-responders to alprostadil\(^2\)
  - Useful to diagnose VOD in young patients to prevent poor response due to anxiety\(^2\)

ICI for Treatment of ED

- ICI therapy remains an important second-line treatment for ED
- Most patients are able to obtain erection satisfactory for penetration with ICI after failing sildenafil¹
  - Also noted improved sexual penetration and maintenance of erection after penetration

ICI vs PDE5 Inhibitors with ICI

- Yang et al. (2012) demonstrated papaverine aided achieving full erection (80%) significantly more than sildenafil (60%) and tadalafil (56%)
- Clinical and CPDU responses to ICI greater than sildenafil with AV stimulation

Utilizing ICI Therapy

- Discuss benefits, contraindications, AEs
  - Contraindications: hemoglobinopathy, bleeding diathesis, Peyronie’s disease, and idiopathic priapism; ? Poor vision or poor dexterity, unstable CV disease
  - Adverse effects: pain, priapism, penile fibrosis
- Initiate by titrating dose in the office setting
  - 50-75% of max erection as noted by patient
  - Escalate doses after a period of at least 24 hours

Utilizing ICI Therapy

- Dosage at home is generally less than maximal dosage in office due to differences in environment and sexual stimulation
- Patients must be educated on proper administration
  - Must also be educated on response to adverse effects
Medications Used for ICI

- Alprostadil
- Papaverine
- Phentolamine
- Combinations
  - Bimix: PGE1 + phentolamine or chlorpromazine
  - Trimix: PGE1 + phentolamine + papaverine
Alprostadil

- First-line agent for ICI
- Prostaglandin E1 (PGE1): blocks alpha-1 receptors
  - Most common dose 10-20 mcg
- Pain with injection is common, especially at higher doses\(^1\)
  - Pain reduced with 0.7% sodium bicarbonate or procaine\(^2,3\)

Papaverine

- An opium alkaloid that inhibits PDE leading to accumulation of cAMP
- Higher rate of fibrosis, priapism, and hematoma when compared to alprostadil\(^1\)
  - Associated with elevated liver enzymes\(^1\)
- Used in bi- and trimix solutions
  - Smaller doses to potentially limit adverse effects

Other Agents

- Phentolamine
- Moxisylyte
- Vasoactive intestinal peptide (VIP)
- Calcitonin gene-related peptide (CGRP)
- Linisidomine
- Sodium nitroprusside
- Atropine
Efficacy and Safety of Alprostadil

- Linet and Ogrinc (1996) studied 683 men with ED of various causes
  - 11,924/13,762 (87%) of injections after which sexual activity was recorded resulted in satisfactory sexual activity
  - 50% of men reported pain, but only after 11% of injections
    - Only 6% of men withdrew due to pain
  - Fibrosis was observed in 2% of patients, priapism in 1% of patients

Satisfaction with ICI

- Porst et al. report that 78-89% of patients and their partners report a positive impact of ICI on self-esteem and partner relationship
- Alexandre et al. found an overall satisfaction rate of 78% of 596 men that regularly use ICI²
  - 70% report improvement of sex life
  - 45% report improvement of quality of life
- Despite this, high drop-out rates from ICI therapy

Erectile Dysfunction and Radical Prostatectomy

- 60% of men who were potent prior to surgery report erectile dysfunction 2 years after RP
- Etiology is multi-factorial, including neural injury, tissue changes in the corpora, arterial injury, and venous leak
  - Possible role of hypoxemia in histological changes suggests importance of rehabilitation programs after RP

Erectile Dysfunction and Radical Prostatectomy

- Hypoxemia theory post RRP
- → Early post-op “rehab” to prevent fibrosis and decrease collagen deposition
- Prevent tissue apoptosis
- PDE5-I + VED more often used as first line therapy
- ICI as alternative option
- No direct comparative (PDE5i vs ICI) studies

Men who were potent prior RP most often reported ICI was effective after RP in achieving erection.

Montorsi et al. (1997) examined alprostadil for rehab:
- 1 month after patients had RP → injecting 3 times weekly with alprostadil for 12 weeks
- 67% of patients who completed regimen had return of spontaneous erections after the 3 months
- Compared to 20% in patients who were only observed
- No placebo arm

Efficacy of ICI after RP

Claro et al. (2001) studied 168 patients who had normal erectile function prior to RP and erectile dysfunction after RP
- 94.6% of patients reported achieving erection with successful penetration with ICI
- 42 (40%) patients had failed therapy with sildenafil

Timing of ICI After RP

- Gontero et al. (2003) studied 73 men who received ICI therapy after RP
  - Group 1: therapy within 3 months
  - Group 2: therapy within 4-12 months
  - 22% of patients had a PSV <30 in group 1 as compared to 51% in group 2

- EARLY seems better!

FOR WHEN YOUR PENIS IS JUST TOO SMALL