Running an Intracavernosal Injection Program

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Patient Selection:

- ED not responding/poor response to PDE5-I
- Post radical prostatectomy
- Patients not willing or not a candidate for penile implant
Scheduled for 1-2 sessions with adequate time for all instructions (typically 30-60 minutes)

- Instructed not to take PDE5i night before or day of visit
- Reminded to bring corrective reading lenses
- Encouraged to bring spouse or partner

- Provided verbal and written instructions
  - Signature form confirming they read/acknowledge instructions

- Teaching sessions also involve one-on-one training going through each step of the process and having the patient/significant other demonstrate every step of the process giving the first injection
Injection supplies:

- Vial of Medication or Injection Kit
- Syringe (29 gauge, ½” needle, 0.5 to 1 ml)
- Alcohol swabs
- Sharps container
- Pre-filled syringe

Instructed on drawing medication from multi-dose vial or preparing kit

Taught to alternate sides each injection & what to do if problems occur (i.e. prolonged erections)
Anatomical landmarks

- Avoid visible veins
- Do not twist or rotate penis – accidental urethral injection
- Patient grasps glans with less dominant hand (must retract foreskin if uncircumcised) and gently stretch penis

- Area to be injected located and swabbed with alcohol wipe

- Holding needle as dart or pen position toward area to be injected
- Touching needle to injection site, swiftly slide entire length of needle through tunica albuginea into cavernosal tissue

- Medication instilled into cavernosal tissue by depressing plunger

- Needle swiftly removed

- Direct pressure held with alcohol swab to site for 3–5 minutes, longer if on anti-coagulation
Important Guidelines

- Direct pressure to injection site for 3-5 minutes after injecting
- Pull needle back 1-2 mm if resistance is felt in plunger
- Avoid visible veins
- Do not twist or rotate penis - can lead to accidental urethra injection
- Injection at 90 degrees to penile skin
- Syringes/needles one time use only - disposed in safe manner
- No more than one use per 24 hour period and 3 times a week maximum
Response

- 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
- Erection scale used to grade
  - 0 = no erection
  - 6 = erection just firm enough for penetration
  - 8-10 = Satisfactory for sexual intercourse
  - 10 = 100% erect
Monitoring

- Instructed to increase dose by 0.5 units until full erection is achieved
- May take multiple injections 2-3x/week to reach appropriate dose
- Injects 2-3x/week regardless of sexual activity - penile rehab program
- If poor or no response cannot repeat for 24 hrs
- No PDE5 Inhibitor within 24-36 hours of ICI
- Follow-up scheduled 3 months or sooner for additional teaching session if required
1982 Virag demonstrated intracavernosal injection of papaverine produced rigid erection. Followed by Brindley 1983, but issues with fibrosis nodules and side effects as single agent.


Utilized when first-line therapy not effective or side effects not tolerated
Selecting an Injection Agent

- FDA approved medications have not demonstrated better insurance coverage.
- Reasons for using compounded medications
  - Less Cost
  - Greater Efficacy
  - Availability
- **Papaverine**
  - Vasodilator, smooth muscle spasmolytic producing generalized smooth muscle relaxation (PDE Inhibitor) - drug has longest half life

- **Phentolamine**
  - Non-selective $\alpha$-adrenoceptor blocker, completely blocks $\alpha$-adrenergic receptors to produce brief antagonism of circulating epinephrine and norepinephrine

- **PGE1/Alprostadil** *(Caverject®, Edex®)*
  - Prostaglandin (PGE$_1$). Relaxes trabecular smooth muscle by dilation of cavernosal arteries promoting arterial flow and blood entrapment within the lacunar spaces of the penis

- **Compounded multi-agent mixtures** *(Bimix, Trimix, “Super Trimix”, “Quadmix”)*

- **Maximums:**
  - Alprostadil (no limit) typically up to 40-60 mcg
  - Papaverine max 30 mg/ml
  - Phentolamine max 3 mg/ml
**FDA-Approved Injectable PGE₁**

- **Edex®/ Viridal®**:  
  - 10 mcg  
  - 20 mcg  
  - 40 mcg

- **Caverject®**:  
  - Solution (reconstituted)  
    - 20 mcg  
    - 40 mcg
Compounded Mixtures

- **Papaverine**
  - Papaverine 30 mg/ml

- **Bimix**
  - Papaverine 30 mg/ml
  - Phentolamine 1-1.5 mg/ml

- **Trimix**
  - Papaverine 17.64 mg/ml
  - Phentolamine 0.588 mg/ml
  - PGE₁ 5.88mcg/ml (alprostadil)

- **“Super Trimix”**
  - Papaverine 30 mg/ml
  - Phentolamine 2 mg/ml
  - PGE₁ 20 mcg/ml

- **“Quadmix”**
  - Papaverine 30 mg/ml
  - Phentolamine 2 mg/ml
  - PGE₁ 20 mcg/ml
  - Atropine 0.15 mg/ml
### Precautions

- Obese abdomen
- History vaso-vagal response
- Dexterity problems
- Uncontrolled hypertension
- Severe Deformity of the penis/Peyronie’s Disease

### Contraindications

- Concurrent use of MAO Inhibitors (phenolamine)
- Penile prosthesis
- Sexual activity is inadvisable or contraindicated
- Predisposition to priapism due to hematologic disorders (e.g., sickle cell anemia, multiple myeloma, leukemia)
Advantages

▪ High efficacy rate
▪ Reliable
▪ Suitable for travel but agents with PGE$_1$ requires refrigeration

Disadvantages

▪ Invasiveness and anxiety of injecting needle into penis
▪ Cost/insurance coverage
▪ Side effects:
  • Priapism
  • Bruising/bleeding
  • Hematoma
  • PGE$_1$ pain
▪ Papaverine may test (+) for opiates on urine screen$^1$
Priapism

- 0.5–11.3% incidence\(^1\) (0.2% MSKCC)
- Ischemic in nature
- Post-training education on management essential
- Off label pseudoephedrine 30 mg (1-2 tablets- if they can take this medication- anecdotal support from patients) or terbutaline 5 mg (1-2 tablets; this medication has limited research support)\(^2\)


Management of Prolonged Erection

- Instructed to take 2-4 tablets of pseudoephedrine (Sudafed®) 30mg if erection 6 or firmer > two hours
- Erection remains ≥ 6/10 at third hour after pseudoephedrine, patient contacts office
- By fourth hour, at Emergency Department for priapism take-down procedure and intracavernosal injection of phenylephrine. ER contacted by provider.
Aspiration of Priapism

- AUA guidelines for phenylephrine or irrigation:

Aspiration of Priapism

- **Kit:**
  - Phenylephrine 10,000 mcg/ml vial
  - 10ml of Normal Saline
  - Dose: 100-500 mcg/ml solution- typically ½ to 1 ml slowly for detumescence
  - 500 mcg solution: mix 0.5 cc of 1% phenylephrine (10 mg/cc) in 9.5 cc normal saline
  - 200 mcg solution: mix 0.2 cc of 1% phenylephrine in 9.8 cc normal saline
  - 19 gauge butterfly needle
  - 5 ml syringe
  - 10-30ml syringe
  - Basin
  - 4x4 & 2x2 gauges
  - Coban
FAQs

- Can I use a smaller needle?
- Can I use an injection and pill together?
- Why have injections stopped working?
- I have pain with an injection of Alprostadil? Why is that? What can I do to prevent it?
- How can I travel with my medication?
- Why can’t I get Trimix at my local pharmacy?
- How do I dispose of the needles?
- I’m a doctor, why do I need training visits?
- Does my health insurance cover the cost of the medication?
- I have a tremor, can I be trained to inject?
- Can I inject more than 3 times a week?
- Is it safe to resume injections if it has been 6 months since my last injection?
- Can I do injections if I have extensive Peyronie’s disease?
- Can I use injections if I am taking anti-coagulants?
Pain: Needle and Medication

Albaugh & Ferrans (2009) (n=65)

- 40% (n = 26) no pain with the needle insertion
- Those with pain (n=39) from needle insertion
  - Mean injection pain score = 1.33 (SD = 0.63); range of 0.5 to 3.0
- Medication pain occurred in 35% (n = 23)
- For those with pain, the mean pain rating was 2.6 (SD = 1.27) (range 0-10) with reports of pain ranging from 0.5-5
- A comparison of men who had radical prostatectomy (n = 27) with those who had not (n = 38) revealed:
  - A significantly larger proportion of post radical prostatectomy men experienced pain from the medication (51.9% vs 23.7%) 
    $\chi^2(1, n = 65) = 5.5, p = .02$

Needle Insertion Pain and Anxiety

  - Pain and anxiety with use measured at two training sessions and 4-month follow-up
  - No significant difference in men who scored ≤ 2 vs. > 2 on pain scale at 1st training session (59% vs. 41%) compared to 4 month follow-up (53% vs. 47%)
  - Mean injection pain score = 2.2±1.8 (range 0-10) (SD = 0.63); range of 0.5 to 3.0
  - Mean injection anxiety score at 1st injection was 5.7±2.8 (range 0-10) and significantly decreased to 4.1±3 at 4 months (p<00.1)

Injections and Quality of Life
Post-prostatectomy

- Erectile function improved
  - Erection strength Mean at 1 month = 7.75 (SD = 1.80); 3 months = 7.47 (SD = 1.68)
  - Mean erection strength at 1 and 3 months - both over the 7/10 strength threshold indicating erection rigid enough for sexual relations.

- Overall Self Esteem and Relationship (SEAR) scores and the scores for the sub-domains for sexual relationship and sexual confidence improved significantly from baseline to one month and three months\(^1\)\(^-\)\(^2\).

Benefits to Injections

- Penile injections effective associated with improved satisfaction with sexual relationship and improved sexual confidence and self-esteem.\(^1\)

- Erections can last after orgasm

- Patient’s reported advantages of: quick & easy, less messy; more natural erection without rings.\(^2\)

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Barriers to Injections

- Reasons for dropping out of self-injection program ($n=720$)$^1$:  
  - Too expensive: 28.3%  
  - Did not like idea of injecting penis: 27.6%  
  - Partner did not like injections: 19.3%  
  - Partner not available: 17.0%  
  - Erections improved spontaneously: 15.3%  
  - Not effective: 14.2%  
  - Development of penile curvature: 11.2%  
  - Development of other medical problems: 10.6%  
  - Lost interest in sex: 8.1%  
  - Undertook alternative treatment: 7.6%  
  - Lost interest in partner: 7.2%  
  - Developed penile lump: 5.8%  
  - Injections thought to be unnatural: 6.1%  
  - Erections lasted too long: 4.9%  
  - Injections painful: 4.9%  
  - Fear of needles: 4.5%

Conclusions: Injections

Pros: They Work!
- Improve Erections, Improve Sexual Self Confidence, Improve Sexual Relationship
- No Tension Rings!

Cons: Although the injections do not hurt, some men just don’t like doing penile injections

Fear of more serious side effects like priapism and Peyronies

✓ Not safe for injections: pendulous abdomen, tremor, severe visual/cognitive impairment, anxiety disorders