Intracavernosal Injection Therapy in the Management of ED

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Disclosures

- Auxilium: Principal Investigator
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- ISSM (Communications Committee Chair)

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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

1. Lewis et al. J Sex Med, 2010, vol 7, pp.1598-1607.
2. Virag, J Urol, 2002, vol 167, pp. 1196.

"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

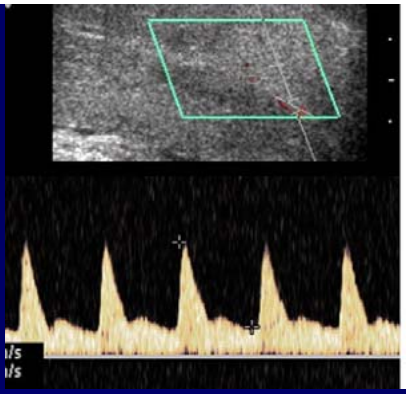
Brindley GS. Cavernosal alpha-blockade: a new technique for investigating and treating erectile impotence. Br J Psychiatry 1983;143:332-337.

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]

1. Quam et al. AJR Am J Roentgenol, 1989, vol. 153, pp. 1141-7.

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

1. Sadeghi-Nejad et al. Ultrasound Clinics. 2007 Volume 2, Issue 1, 57-71
2. Sikka et al. J Sex Med, 2013, vol. 10, pp. 120-9.

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]

1. Porst. J Urol, 1996, vol. 155, pp. 802-15.
2. Golijanin et al. Int J Impot Res, 2007, vol. 19, pp. 37-48.

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 sildenafil[1]
  - Also noted improved sexual penetration and maintenance of erection after penetration

1. Shabsigh R et al. Urology, 2000, vol. 55, pp. 477-80.

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[2]

1. Yang Y et al. Int J Impot Res, 2012, vol. 24, pp. 191-5.
2. Copel L. Radiology, 2005, vol. 237, pp. 986-91.

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

1. Hatzimouratidis K, Hatzichristou DG. Drugs, 2005, vol. 65, pp. 1621-50.

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]

1. Montsori F et al. Int J Impot Res, 2002, vol. 14, pp. S70-S81.
2. Moriel EZ et al. J Urol, 1993, vol. 149, pp. 1299-1300.
3. Schramek P et al. J Urol, 1994, vol. 152, pp. 1108-10.

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

1. Porst H. J Urol, 1996, vol. 155, pp. 802-15.

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[1]
  - 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

1. Linet OI. N Engl J Med, 1996, vol. 334, pp. 873-7.

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 ICI[2]
  - 70% report improvement of sex life
  - 45% report improvement of quality of life
- Despite this, high drop-out rates from ICI therapy

1. Porst H et al. Int J Impot Res, 1998, vol. 10, pp. 225-31.
2.Alexandre B et al. J Sex Med, 2007, vol. 4, pp. 426-31.

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

1. Alemozaffar M et al. JAMA, 2011, vol. 306, pp. 1205-14.
2. Iacono F et al. J Urol, 2005, vol. 173, pp. 1673-76.
3. Moreland RB. Int J Impot Res, 1998, vol. 10, pp. 113-20.

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

1. Alemozaffar M et al. JAMA, 2011, vol. 306, pp. 1205-14.
2. Iacono F et al. J Urol, 2005, vol. 173, pp. 1673-76.
3. Moreland RB. Int J Impot Res, 1998, vol. 10, pp. 113-20.

Role of ICI in Penile Rehabilitation

- 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

1. Alemozaffar M et al. JAMA, 2011, vol. 306, pp. 1205-14.
2. Montorsi F et al. J Urol, 1997, vol. 158, pp. 1408-10.

Efficacy of ICI after RP

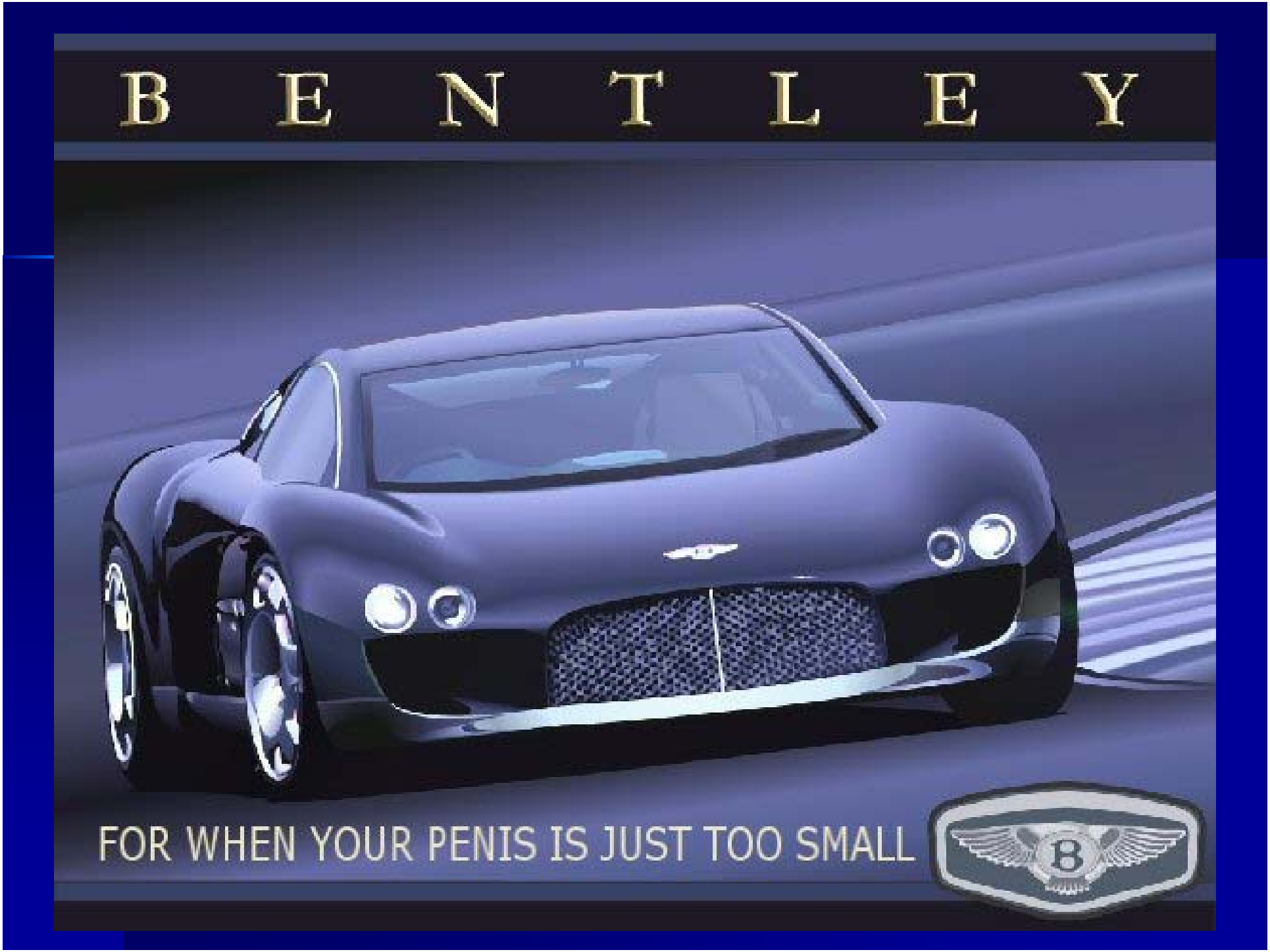
- Claro et al. (2001) studied 168 patients who had normal erectile function prior to RP and erectile dysfunction after RP
  - 94.6% of patients reported achieving erection with successful penetration with ICI
  - 42 (40%) patients had failed therapy with sildenafil

1. Claro Jde A et al. Sao Paulo Med J, 2001, vol. 119, pp. 135-7.

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 I as compared to 51% in group 2
- EARLY seems better!

1. Gontero P et al. J Urol, 2003, vol. 169, pp. 2166-9.
2. Mosbah A et al. J Sex Med, 2011, vol. 8, pp. 2106-11.
3. Mulhall JP et al. BJU Int 2010; 105:37-41.


B E N T L E Y
FOR WHEN YOUR PENIS IS JUST TOO SMALL