Update on the Management of Priapism

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Disclosure

- Consultant for Coloplast but have no conflicts regarding this presentation.
Introduction

- **Priapism - Definition**
  - A full or partial penile erection that continues more than 4 hours beyond sexual stimulation and orgasm or is unrelated to sexual stimulation
History

- First recorded account of Priapism in English medical literature in the Lancet in 1845
- 1914- Frank Hinman, Sr. published landmark article describing the natural history of priapism
- 1960- Frank Hinman, Jr. proposed mechanism of venous stasis, increased blood viscosity, and ischemia were responsible for priapism
- 1983- radiologic differences demonstrated between veno-occlusive and arterial priapism
Ischemic Priapism

- Veno-occlusive or low flow
- Characterized by reduced or absent intracavernous blood flow and rigidity of the copora cavernosa with little or no cavernous arterial inflow
  - Compartment syndrome
- Cavernous blood gases are hypoxic, hypercarbic, and acidotic
- More than 95% of men with priapism
Causes of Ischemic Priapism

- Idiopathic (most common)
- Hematologic dyscrasias
  - SCD, thalassemia, leukemia, myeloma, hemodialysis, G6PD deficiency, Factor V Leiden
- ICI medications
  - Since the mid 1980’s, ICI has become one of the leading causes of priapism
- Recreational drugs
  - Alcohol, cocaine, crack, marijuana
- Hormones
  - GnRH, testosterone
- Neoplastic
- Neurogenic
  - Syphilis, spinal cord injury, CVA, autonomic neuropathy
- Anesthesia
Medications Associated with Ischemic Priapism

- Alpha blockers
- Antianxiety agents (hydroxyzine)
- Anticoagulants (heparin, warfarin)
- Antidepressants and antipsychotics
  - Trazodone, bupropion, fluoxetine, sertraline, lithium, clozapine, risperidone, olanzapine, chlorpromazine, thioridazine, phenothiazines,
- Antihypertensives
  - Hydralazine, propranolol, guanethidine
Sickle Cell Disease and Priapism

- Mechanism presumed to be stagnation of blood within the sinusoids of the corpora during erections and sickled erythrocytes obstructing venous outflow.

- Lifetime probability of a man with SCD developing ischemic priapism ranges from 29% to 42%.
Stuttering Priapism

- Intermittent or recurrent ischemic priapism with intervening periods of detumescence
- Each episode carries a risk of fibrotic damage to the corpora cavernosa if not reduced promptly
- Association with nocturnal erections
Molecular Basis for Ischemic Priapism

- Imbalance between vasoconstrictive and vasorelaxatory mechanisms
- Upregulation of hypoxia induced growth factors (TGF-β)
  - Progression to overt fibrosis
- Data suggests a NO (nitric oxide) imbalance results in aberrant molecular signaling, PDE5 dysregulation, adenosine overproduction, and reduction in Rho-kinase activity
  - Results in enhanced corporal smooth muscle relaxation and inhibition of vasoconstriction
SCD and Hemolysis Associated Endothelial Dysfunction

- Hemolysis releases Hgb which reacts with NO to produce methhemoglobin and nitrate.
- Sickled erythrocytes release arginase I which converts L-arginine into ornithine.
  - Effectively removing substrate for NO synthesis.
- Oxidant radicals further reduce NO.
- Results in a state of NO resistance and insufficiency.
Pathogenesis of Ischemic Priapism


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Time Course of Physiologic Changes

- 12 hours - histologic changes in the cavernous smooth muscle
- 24 hours - loss of sinusoidal endothelium
- 48 hours - sinusoidal thrombosis and smooth muscle necrosis are found
- >48 hours - irreversible corporal fibrosis and severe ED
Functional Erections after Priapism

- Burnett and Mulhall
  - Review of 39 cases of priapism
    - Less than 12 hours- 100%
    - 12-24 hours- 78%
    - 24-36 hours- 44%
    - More than 36 hours- 0%

Conservative Management of Ischemic Priapism

- Patients must be thoroughly counseled regarding risks and benefits of interventions as well as natural history of priapism
  - Discuss likelihood of ED and penile damage regardless of clinical management.
  - Document and consent
Conservative Management of Ischemic Priapism

- Oral medications such as terbutaline, pseudoephedrine, and etileferine reported to be superior to placebo in 28-36% of prolonged erections <4 hours after ICI

- Recommended treatment is decompression of the corpora cavernosa by corporal aspiration
  - Aspiration alone may relieve priapism in 36% of cases
  - Insufficient data regarding saline irrigation
Conservative Management of Ischemic Priapism

- Ateyah et al (2005)- aspiration with cold saline irrigation 66% resolution vs. 24% with aspiration alone
- Aspiration followed by ICI of sympathomimetic drugs is standard of care
  - Phenylephrine- selective alpha 1 agonist diluted 100-500 mcg/ml and given 1ml every 3-5 minutes over
Treatment of Stuttering Priapism

- Home injection of phenylephrine
- GnRH analogues
- Antiandrogens
- Ketoconazole and steroids
  - reduce androgen synthesis
- Baclofen
- Gabapentin
- PDE5 inhibitors
- 5 alpha reductase inhibitors
Ketoconazole Protocol

- Originally 200mg KTZ TID with prednisone for 6 months
- Currently 200mg KTZ TID with prednisone for 2 weeks, then taper to 200mg nightly for 6 months
- Obtain total testosterone and LFTs prior to starting therapy, at weeks 2 and 4 and then monthly.

Outcomes with Ketoconazole

- Hoeh and Levine- 2014
  - 94 % complete resolution of priapism while on KTZ therapy
  - Effects noted immediately and with no reported sexual side effects
  - 29% with no recurrence of discontinuation
  - 78.6% with partial or complete of symptoms after KTZ discontinued

PDE5’s for Stuttering Prapism

- Surges of cGMP go unchecked due to down-regulated PDE5 and NO imbalance
  - stimuli like nocturnal erections result in unchecked smooth muscle relaxation
- Daily sildenafil or tadalafil shown to reduce ischemic episodes
- Results in upregulation and correction of the PDE5 system
- May be effective in sickle cell patient’s given pathogenesis
Burnett et al.- 2014
- 13 patients with SCD at least twice weekly recurrence of priapism
- Randomized to either 50mg daily sildenafil or placebo for 8 weeks followed by 8 week open label
- During open label portion, 62.5% were noted to have priapism frequency reduction by 50%
- No significant difference in adverse effects but a 4 fold decrease in major priapism episodes
PDE5 Inhibitors and Priapism

- Nardozza and Cabrini- 2017
  - 7 patients in Brazil with recurrent priapism
  - Treated with daily 5mg tadalafil
  - Mean follow up 6.6 months
  - Decreased priapism recurrences in all patients
    - 5 patients with no recurrence
    - 2 patients with decreased recurrences
Surgery for ischemic priapism

- Required to relieve penile ischemia and mitigate pathologic effects including penile deformities and erectile dysfunction

- Role for surgery persists due to the limitations of medical interventions
Distal percutaneous shunts

Winter

Ebbehoj

T Shunt

Open distal shunts

- Al Ghorab
- Burnett

Open Proximal Shunts

- Quackles
  - Perineal approach

- Sacher
  - Peno-scrotal approach
Vein Shunts

- **Grayhack**
  - Saphenous vein

- **Barry**
  - Superficial or deep dorsal vein
Shunt modifications

- **Intracorporeal tunneling**
  - After T shunt pass a 20-24Fr straight urethral sound

- **“Snake” procedure**
  - After Al-Ghorab pass 7/8 Hegar dilator

- **Cavernous tunneling with blunt cavernosotomy**
  - Large drainage route made by partial blunt excision of the cavernous tissue with Pean forceps


T shunt with cavernosal tunneling

“Snake” Procedure

Outcomes of tunneling/snake procedures

- Brant et al.
  - 12/13 with restoration of cavernous blood flow, 1/13 required a repeat procedure
  - 11/13 with recovery of erectile function

- Segal et al. – Long term followup
  - 8/10 with resolution without recurrence of priapism
  - 2/10 with recurrent and refractory priapism
  - Only 2/10 achieved partial erections postoperatively


45 patients with prolonged, ischemic priapism
Resolution in all patients with priapism <24 hours duration
Resolution in only 30% in patients with priapism >48 hours
IIEF reduced from a mean of 24 to 7.7, related to duration of priapism

Transient Distal Shunt

- Uses a sterile closed system blood collection set with 21G needles x2
- Removed after flaccid for at least 10 minutes
- 10/15 patients with priapism <18 hours successfully treated without further therapy

Penoscrotal Decompression

- Fuchs et al. J Sex Med March 2018
  - Penoscrotal approach to expose the corpora
  - Unilateral corporotomy with dilation of the corpora with a pediatric yankeur
  - Bilateral dilation performed if necessary
  - 6 patients with median priapism duration of 60 hours with failed irrigation and distal shunt in all
    - 100% detumescence
    - 1 patient with spontaneous return of erections
Importance of Timing

- Efficacy for restoring erectile function controversial
  - But long duration (>36 hours) likely to irreversibly impair erectile tissue viability and function
  - If prolonged then may serve to mitigate local pathologic effects and pain.

- ISSM Standards Committee- shunting has limited benefit for priapism >72 hours
Is there an ideal shunt?

- Lack of data comparing the efficacies of shunt procedures
- May be decided on surgeon preference
- Typically may progress from least to most invasive
  - Distal shunts prior to proximal shunts
- Consider proceeding to tunneling if prolonged (more than 2-3 days) or difficulty expressing old blood

Is there a possible role for anticoagulation?
Vascular Anastomosis

- Endothelium to endothelium is important in vascular anastomoses to prevent thrombosis
- Tissue injury leads to activation of the clotting cascade
  - Exposure of highly thrombogenic factors in the sub-endothelial matrix
- Anticoagulation is utilized to prevent thrombosis
How does this relate to priapism?

- Old blood in the corpora does not clot due to endothelium derived anticoagulating and fibrinolytic factors within the corpora.
- Penile shunt is not endothelium to endothelium.
  - Vascular spaces of the corpora cavernosum and spongiosum are separated by the collagen rich tunica albuginea.
- Newly created shunt cuts through the tunica leading to collagen activated platelets and fibrin.
- Early postoperative shunt closure
  - Postoperative thromboembolic complication.

Proposed mechanism of shunt clotting

Proposed Anticoagulation Protocol

- Preoperatively
  - 5000 units subQ heparin and 325mg aspirin

- Postoperatively
  - 81mg aspirin for 3 weeks

- Given the resulting morbidity of premature shunt closure, should this be treated with the same precautions as other thrombo-embolic complications?

Prosthesis for Acute Priapism

- Ralph et al. (2009) *Eur Urol*
  - 50 patients unresponsive to conventional treatment
    - 13 patients with unsuccessful shunt surgery
  - 43 malleable prostheses and 7 IPP’s
  - After 6 months, 42 patients resumed sexual activity.
  - 3 patients (6%) with infection
  - 6 patients needed revision
  - Overall satisfaction rate of 96%
Cost Effectiveness of Prosthesis

- Tausch et al. (2015) *J Sex Med*
  - 14 patients with average duration of priapism 82 hours underwent malleable prosthesis placement
  - Prior to implant, average cost of care- $83,818
  - Discharged home 24 hours after prosthesis
  - Cost of implant- $4,200 + OR fees
  - 1 infection and 1 urethral erosion

Early vs. Delayed Prosthesis

- Zacharakis et al. 2014
  - 68 men with early prosthesis- median 7 days
  - 27 men with delayed prosthesis- median 5 months
  - MRI before intervention +/- frozen section of cavernosal smooth muscle were utilized to confirm smooth muscle necrosis prior to early implant placement.
  - All had prior attempted aspiration and alpha agonists
  - 28 patients with prior T shunts

Early vs. Delayed Prosthesis

- **Early implant outcomes**
  - 96% patient satisfaction with penile shortening
  - 7% revision for infection (all with prior T shunt)
  - 2% revision for curvature

- **Delayed implant outcomes**
  - 60% patient satisfaction with 40% penile shortening
  - 19% revision for infection
  - 4% revision for erosion

Use of MRI with gadolinium

- Ralph et al. 2010 BJU Int
  - The use of high resolution magnetic resonance imaging in the management of patients presenting with priapism.
  - 23 patients with MRI and corporal biopsy - 10% sensitivity predicting nonviable smooth muscle
  - 10 patients with nonviable smooth muscle without biopsy developed ED
  - 5 patients with viable smooth muscle maintained erectile function at 1 year
Lack of corporal enhancement

Ralph et al. The use of high resolution magnetic resonance imaging in the management of patients presenting with priapism. 2010. BJU Int. 106: 1714-1718.
Patchy perfusion with distal viability

Ralph et al. The use of high resolution magnetic resonance imaging in the management of patients presenting with priapism. 2010. BJU Int. 106: 1714-1718.
Segmental priapism with unilateral viability

Ralph et al. The use of high resolution magnetic resonance imaging in the management of patients presenting with priapism. 2010. BJU Int. 106: 1714-1718.
Proposed Algorithm

Prosthesis for Acute Priapism

- Prosthesis placement in setting of prolonged ischemic priapism is an option
- Relieve pain, quicker resolution and discharge, and treat resulting ED
- Increased risk of complications
  - Infection, erosion
  - Caution if prior distal shunt
- USF protocol- prefer placement of malleable in the acute priapism setting
  - Consider if priapism >36-48 hours
Thank You

Priapus