

10. PRIAPISM

Principles

- To educate patients about the risks of priapism in boys, adolescents and men with SCD.
- To teach patients to recognize priapism and bring it to rapid medical attention.
- To ensure rapid medical treatment by the emergency medical team.
- To appropriately involve consultants, including Urology and Hematology.
- To select appropriate medical and/or surgical intervention, tailored to the individual patient and episode.

Recommendations

Patient Education

- Educate patients about risk of priapism in boys, adolescents, and men with SCD.
- Educate as to possible measures for self-treatment of priapism at home.
- Instruct patients to seek medical attention if the episode lasts for longer than 2 hours.
- Emphasize the nature of this problem as a medical emergency that requires rapid assessment and attention, so that the patient can advocate for himself at the emergency department.

Acute Treatment

- Patients should be treated rapidly and in a sensitive manner.
- First-line therapy includes:
 - Intravenous fluids and narcotic analgesia
 - Supplemental oxygen should be administered if the patient is hypoxic
 - Oral pseudoephedrine may be considered
- If first-line therapy is not rapidly effective, and the total duration of priapism has been or will soon be longer than 4 hours, urologist consultation should be obtained.
 - Urologist to consider corporeal aspiration and irrigation with or without vasoactive agent.
 - Consider cavernosum-spongiosum shunts if the above measures are ineffective.
- Hematologist to consider risks vs. benefits of exchange transfusion.

Prevention

- No preventive measure has been confirmed in randomized studies.
- Chronic hydroxyurea use may be effective in preventing episodes of priapism.
- Other preventive measures that may be considered include daily pseudoephedrine, sildenafil, or chronic RBC exchange transfusion.

Background

Priapism is a prolonged, full or partial erection that “persists beyond or is unrelated to sexual stimulation”.¹ Prolonged priapism lasting more than 4 hours is a medical emergency. Prolonged or recurrent priapism can result in erectile dysfunction.

Priapism occurs when there is an imbalance in the arterial inflow and venous outflow from the penile vascular chambers. SCD-related priapism is classically low-flow (ischemic), with sickle veno-occlusion and endothelial dysfunction causing a pathological decrease in venous outflow, in contrast to increased arterial flow seen in high-flow (non-ischemic) priapism.¹ Minor episodes can be uncomfortable but tolerable and self-limiting, lasting up to several hours. Recurrent self-limiting “minor” episodes, referred to as stuttering or intermittent priapism, may be a precursor to a major episode. Major episodes can last a few hours to several days, and are often extremely painful.² Patients may not report episodes until they are very severe or prolonged.³

Epidemiology

In regions of high prevalence, sickle cell disease is the most common cause of priapism. Priapism can first occur in early childhood, sometimes as early as 5 or 6 years of age.⁴ The lifetime risk of priapism in men with SCD is estimated at 29% to 42%.^{5,6} Based on patient questionnaires, the probability of having at least one episode by 10, 15, or 20 years of age is 12.9%, 50.3%, and 89%, respectively.⁷

Risk Factors and Triggers

Risk factors for priapism include higher sickle hemoglobin (HbS) levels,²⁴ increased hemolytic rate,²⁵ and sleep hypoxemia.²⁶ It is more common in sickle cell anemia (HbSS) than HbSS-alpha thalassemia and hemoglobin SC disease (HbSC).²⁷ Priapism may occur spontaneously, but potential triggers include sexual activity, fever, dehydration, and cold weather.^{3,8}

Diagnosis and Triage

Diagnosis is made by patient report of erection lasting beyond or unrelated to sexual stimulation, typically more than 30 minutes.^{1,9} A history should be taken to determine the time of onset and any potential precipitating events.⁹ Priapism can be confirmed by physical examination and Doppler penile ultrasound. Priapism in patient with SCD is usually bicorporal – affecting both corpora cavernosa bodies but leaving the glans penis and corpus spongiosum soft, which enables normal urination during the episode. Patients with prior episodes or at high risk should be instructed not to wait for the arbitrary 4-hour cut-off time to seek care. Instead, they should be instructed to go to the emergency room urgently while fasting (in case surgical treatment is required). Triage staff should be notified about the critical nature of the condition and the need to be urgently evaluated by specialists familiar with this condition.

Management

Management of priapism in patients with SCD is based largely on small case series and expert opinion.

a) Home Management

Initial self-treatment by patients has some reported benefit, including analgesia, oral hydration and light exercise.⁸ There may also be benefit in voiding, ejaculating, or having a warm shower or bath.⁷

b) First-line Medical Therapy

First-line medical interventions include supportive-care measures such as intravenous hydration, narcotic analgesia, and supplemental oxygen (if the patient is hypoxic). Oral vasoactive agents (terbutaline, phenylephrine, and pseudoephedrine) have been reported to be effective in reversing pharmacologically induced priapism,⁹ and may be considered.

If the episode persists for more than two hours, additional measures must be considered.

c) Aspiration/Irrigation

Institution of supportive measures should not delay urological consultation and subsequent consideration for decompression, which includes corporal aspiration, irrigation, and administration of intracorporeal epinephrine solution.¹⁰

- Study: Prospective, case series of 15 boys and teenagers.
- Indication: Priapism persisting 1 hour after arrival at the emergency department (total duration of episode = 4 to 6 hours).
- Procedure (more detailed instructions available in reference 9):
 1. Conscious sedation and local anesthesia.
 2. Aspiration of blood from corpus cavernosum with 23-gauge needle. A sample should be sent to the lab for blood gas, which confirms a low-flow (ischemic) state.

3. Irrigation of the corpus cavernosum with normal saline, followed by diluted epinephrine (1:1,000,000 dilution of epinephrine to saline). This should be done under hemodynamic monitoring (heart rate, blood pressure).

- Results of the study: Rapid detumescence in 37 of 39 episodes.

d) Surgical Shunts

If the above measures are ineffective, surgical procedures may be required to create a cavernosum-spongiosum distal shunt.^{4,11}

e) Transfusion

Depending on the patient's hemoglobin level, exchange transfusion may be used, although there is conflicting evidence as to its efficacy.^{12,13} Transfusion may be associated with equivalent or worse clinical outcomes compared to more conservative management, including risk of neurological events (referred to as ASPEN syndrome).^{14,15}

Prevention

One study has suggested that patients with high levels of fetal hemoglobin (HbF) are unlikely to suffer from priapism.¹⁶ Hydroxyurea has been demonstrated in case reports to be effective in preventing recurrent priapism.^{17,18}

There is some scientific evidence that chronic phosphodiesterase type 5 (PDE5) inhibitor therapy in patients with recurrent priapism reconditions PDE5 regulation in the penis (Burnett, Bivalacqua *et al.* 2006). Long-term, continuous PDE5 inhibitor (tadalafil or sildenafil) was shown retrospectively to be associated with decreased priapism recurrences over 2 years of clinical follow-up in 3 out of 4 SCD patients with a history of disease-associated “stuttering” priapism.¹⁹ A small, randomized controlled trial of 13 patients showed no difference in priapism frequency between the sildenafil and placebo groups during the eight-week double-blind phase. Mild reductions in priapism were seen during eight weeks of open-label assessment,²⁰ suggesting a possible role for further study of this therapy.

Other prevention methods that have not been extensively studied include: oral or self-administered intracavernous injection of etilefrine²¹; self-administered intracavernosal metaraminol²²; ketoconazole and prednisone²³; daily, oral pseudoephedrine⁹; or chronic exchange transfusion.⁹ Well designed, randomized trials are required to further evaluate these and other potential therapies.

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