Pharmacologically-induced Recreational Priapism: Case Report and Review

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Introduction: Priapism, a time-sensitive urologic emergency, is associated with hematologic disorders, malignancies, trauma, pharmaceuticals, and recreational drugs.

Case Report: A 51-year-old male presented with 36 hours of priapism after recreational use of nonprescribed pharmaceuticals including an oral phosphodiesterase inhibitor and intracorporally injected erectile medications, together with unspecified quantities of cocaine and alcohol. Venous blood gas confirmed ischemic priapism. Detumescence was achieved with intracavernosal phenylephrine injection, aspiration, and irrigation.

Conclusion: This case highlights the risk that recreational use of vasoactive medications by patients who seek to prolong sexual activity may lead to delayed presentation for ischemic priapism. [Clin Pract Cases Emerg Med. 2020;4(4):591–594.]

Keywords: ischemic priapism; phosphodiesterase inhibitor; intracorporal injection.

INTRODUCTION
Numerous factors may lead to priapism, defined as penile erection in the absence of active sexual stimulation that persists for a minimum of four hours due to persistent engorgement of the corpora cavernosa and disruption of normal detumescence mechanisms.¹ Priapism is a time-sensitive urologic emergency that is relatively rare in the general population; priapism disproportionately affects patients with hematologic and neurologic disorders, notably sickle cell disease and spinal cord injury, and is associated with a number of pharmaceuticals and recreational drugs.²,³ Although the mean duration is just over two hours per episode, delayed presentation can be associated with use of medications intended to stimulate potency or manage erectile dysfunction.¹ Including tissue necrosis, fibrosis and scarring, and subsequent erectile dysfunction.¹,²

CASE REPORT
A 51-year-old male presented to the emergency department (ED) with a chief complaint of persistent erection that had been present for approximately 36 hours after he ingested 20 milligrams (mg) of tadalafil followed by penile self-injection with approximately one milliliter (mL) of Trimix, a compound containing alprostadil, papaverine, and phentolamine. He had no history of erectile dysfunction. Neither medication had been prescribed to him, and his intention was to achieve a sustained penile erection to facilitate prolonged sexual activity with a group of people. There was concomitant use of an unspecified quantity of alcohol as well as intranasal cocaine. The patient reported mild discomfort and some difficulty passing urine due to his prolonged erection, but reported he was still able to void. He denied hematuria, dysuria, or penile discharge. There was no past history

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of malignancy or hematologic disorders. His medical issues included stable human immunodeficiency virus (HIV) disease and reported compliance with antiretroviral medication (emtricitabine-tenofovir); there was no history of hypertension.

On examination the patient did not appear to be in distress; his demeanor was consistent with mild intoxication, but he was fully alert and oriented to person, place, time, and situation. His initial vital signs were notable for hypertension, with a blood pressure of 161/104 millimeters of mercury (mm Hg), heart rate of 88 beats per minute, and an afebrile temperature of 36.1 degrees Celsius. His penis was erect and engorged; glans and spongiosum were soft without tenderness to palpation. The examiner was unable to bend the shaft due to rigidity. The testes and vas were nontender.

Initial laboratory evaluation included normal hemogram and renal function; urinalysis showed three white blood cells and six red blood cells per high-powered field. Urologic consultation was requested and ice packs were applied to the penile shaft for several minutes without response. Aspiration of the corpora was performed. Penile venous blood (VBG) was remarkable for pH of 7.00 (reference [ref] range 7.31-7.41), partial pressure of carbon dioxide of 88.4 mm Hg (ref range 40-52 mm Hg), calculated venous oxygen saturation of 8.0 % (ref range 75%), and lactic acid level of 14.4 millimoles per liter (mmol/L) (ref range 0.5-2.2 mmol/L), consistent with ischemic priapism. After local anesthetic, corporal injection of phenylephrine 500 µg/mL, diluted in 10 mL of normal saline, followed by aspiration and irrigation with an additional 10 cubic centimeters (cc) of sterile saline, resulted in gradual detumescence. A compression dressing was then applied to the penile shaft. The patient reported no discomfort after the procedure; blood pressure on discharge was normalized to 124/81 mm Hg. The patient was given instructions to remove the pressure dressing in 24 hours and abstain from sexual intercourse for a minimum of seven days.

On follow-up in urology clinic 11 days after his presentation to the ED, the patient reported ability to achieve normal erections; he was noted to have minimal ecchymosis at the base of the penile shaft. He was advised to refrain from using erectogenic medications in the future.

DISCUSSION

Penile erections are a result of vasodilation in the corpora cavernosa, mediated by inhibition of the cyclic guanosine monophosphate (cGMP) hydrolyzing enzyme phosphodiesterase-5 (PDE5). With ischemic priapism, venous outflow is reduced and venous congestion leads to diminished or loss of arterial inflow.1 Tadalafil is one of several available PDE5 inhibitors. Trimix, a compound intended for intracorporal injection (ICI), consists of alprostadil, phentolamine, and papaverine. The three pharmaceuticals act in different ways to stimulate penile vasodilation. Alprostadil acts directly to stimulate the production of cyclic adenosine monophosphate (cAMP), which like cGMP leads to penile tumescence from smooth muscle relaxation. Phentolamine is an antagonist of alpha adrenergic receptors, resulting in further vascular dilation, while papaverine inhibits several subclasses of PDEs, causing cGMP and cAMP accumulation.2

While the above described medications are intended to facilitate erections for a safe duration in persons with erectile dysfunction, this case describes a patient with normal erectile function who recreationally misused a combination of pharmaceuticals resulting in a prolonged, unsafe erection. A retrospective study of 169 priapism encounters highlighted growing recreational use of ICIs within a metropolitan community, finding nearly 50% of cases to be due to ICIs.3 Numerous cases of priapism with various medication classes, in addition to ICIs and PDE inhibitors, have been documented. Psychotropic medications implicated in recreational misuse include the following: serotonin specific reuptake inhibitors, most notably trazodone; amphetamines; pregabalin; and typical and atypical antipsychotics (due to alpha-blocking characteristics).4,5 Tamsulosin, due to alpha blocking effects, as well as alpha-receptor antagonist antihypertensives have been associated with ischemic priapism.6,7 Priapism associated with cocaine use has long been observed.8 Some herbal supplements marketed for
sexual enhancement have been reported in cases of prolonged priapism. *Tribulus terrestris* has been associated with protracted episodes of priapism (between 48-72 hours), as well as the herbal product yohimbine, ranging between 20-72 hours in case reports.\textsuperscript{12,13} Pharmaceutical agents reported in association with priapism are summarized in the following table.

Regardless of etiology, ischemic or low-flow priapism is a urologic emergency requiring prompt intervention. Diagnosis should be accomplished through history and physical exam, followed by corporal VBG. Venous blood in ischemic priapism is characterized by an acidic pH (below 7.1).\textsuperscript{2} Hematologic studies can be obtained and duplex ultrasonography can be done to assess arterial blood flow but is not required.\textsuperscript{2} Once ischemic priapism is suspected, management should begin promptly to prevent compartment syndrome and future fibrosis, which then may contribute to permanent impotence. Urologic input is appropriate if feasible. Initial conservative measures may include application of ice packs to the genital area and asking the patient to perform vigorous physical exercise of the lower limbs.\textsuperscript{14} Aspiration of blood from the corpora cavernosa is used both for blood gas analysis and to remove blood to relieve cavernosal compartment pressure, which then should be followed by saline irrigation.

If detumescence does not occur, the next step is ICI of an alpha-adrenergic sympathomimetic; this is generally preceded by local anesthetic or nerve block.\textsuperscript{2} The preferred sympathomimetic agent is phenylephrine hydrochloride 10 mg/mL; 0.1-0.5 mL (1-5 mg) is diluted in 10 cc normal saline to give a concentration of 100-500 µg/mL, injected at a rate of 1 mL over three to five minutes until detumescence is achieved. Diluted epinephrine 1:10,000 solution may be used if phenylephrine is unavailable.\textsuperscript{2,15} Sonographic guidance may be used to facilitate cavernosal needle placement but is not a requirement. Oral pseudoephedrine as well as subcutaneous terbutaline are other options, but are less effective and not recommended for priapism of duration greater than four hours. If these measures fail, a surgical procedure to implant shunts may need to be performed.\textsuperscript{2}

By contrast, non-ischemic priapism, which is rarer and usually a result of trauma or congenital arterial malformation, occurs from unregulated arterial inflow to the corpora cavernosa, creating an arteriolar-sinusoidal fistula. Due to constant high inflow of arterial blood, the corpora cavernosa is not at risk for ischemia and the condition is, therefore, non-ischemic priapism. Non-ischemic priapism is generally painless; treatment is routinely conservative, as most cases resolve spontaneously.\textsuperscript{2}

**CONCLUSION**

Numerous pharmaceutical agents have been associated with priapism; in addition to medications used to treat erectile dysfunction, several psychotropic medications have been implicated. Recreational use of vasoactive pharmaceuticals with the intention of prolonging sexual activity can lead to delayed presentation for ischemic priapism. In particular, patients who misuse intracorporally injected medications present four hours later on average than those with priapism from other etiologies, more frequently have comorbid HIV disease, and more commonly co-ingest recreational drugs and alcohol, which can exacerbate priapism and likely contribute to delayed presentation.\textsuperscript{3} A patient presented with an episode of ischemic priapism of approximately 36 hours in duration after use of diverted erectogenic pharmaceuticals, likely exacerbated by concomitant use of cocaine. The patient underwent active intervention in the ED to achieve detumescence, with no apparent permanent sequelae. This case adds to the growing literature on pharmacologically induced priapism. Emergency clinicians should be aware of the potential for misuse of medications prescribed for erectile dysfunction and the need for active management to achieve a favorable outcome.

The authors attest that their institution requires neither Institutional Review Board approval, nor patient consent for publication of this case report. Documentation on file.

**Table.** Pharmaceutical agents associated with priapism.

<table>
<thead>
<tr>
<th>Category</th>
<th>Agent(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erectile dysfunction medications</td>
<td>ICI agents, PDE inhibitors</td>
</tr>
<tr>
<td>Antidepressants/SSRIs</td>
<td>Paroxetine, citalopram, trazodone</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Atypical and typical (haloperidol, chlorpromazine, quetiapine, clozapine, olanzapine, risperidone)</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Methylphenidate, dexamphetamine, lisdexamphetamine</td>
</tr>
<tr>
<td>Anti-epileptic/pain management</td>
<td>Pregabalin</td>
</tr>
<tr>
<td>Alpha-adrenergic blockers</td>
<td>Antihypertensives (terazosin), tamsulosin</td>
</tr>
<tr>
<td>Herbal products</td>
<td><em>Tribulus terrestris</em>, yohimbine</td>
</tr>
<tr>
<td>Recreational drugs</td>
<td>Cocaine, ethanol</td>
</tr>
</tbody>
</table>

ICI, intracorporal injection; PDE, phosphodiesterase; SSRI, selective serotonin reuptake inhibitor.


\textsuperscript{2} Conclusions of this study can be found in the literature on pharmacologically induced priapism. Emergency clinicians should be aware of the potential for misuse of medications prescribed for erectile dysfunction and the need for active management to achieve a favorable outcome.

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**Conflicts of Interest:** By the CPC-EM article submission agreement, all authors are required to disclose all affiliations, funding sources and financial or management relationships that could be perceived as potential sources of bias. The authors disclosed none.

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