

Supplementary Material

Article Title: Psychotropic Medication-Induced Priapism: An Approach to Diagnosis and

Treatment

Author(s): Andrea DeSimone, DO; Ezra Rudinoff, DO; Moon Young Lee, DO; James K.

Rustad, MD; Michael Zaragoza, MD; and Theodore A. Stern, MD

DOI

Number: https://doi.org/10.4088/PCC.25f03942

LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

- 1. Supplementary Appendix A
- 2. Supplementary Appendix B

DISCLAIMER

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Appendix A

Table 1. Comprehensive List of Medications Associated With Drug-Induced Priapism

Elevated risk medications are bolded, with the percentages of the individual cases of priapism in Schifano and colleagues' review of the US Food and Drug Administration Adverse Event Reporting System pharmacovigilance database arranged in relative order of incidence by class^{7,12,18}

Medication class	Medications					
	Atypical: Quetiapine (12.48%), risperidone (10.54%), olanzapine (8.60%), aripiprazole					
A4:14:	(6.49%), clozapine (2.51%), paliperidone, iloperidone, ziprasidone					
Antipsychotics	Typical: Chlorpromazine, fluphenazine, trifluoperazine, haloperidol, thioridazine,					
	zuclopenthixol, pipamperone					
	SARIs: Trazodone (15.98%)					
Antidomessants	SSRIs: Sertraline (4.70%), citalopram, escitalopram, fluoxetine, paroxetine					
Antidepressants	SNRIs: Venlafaxine, duloxetine, atomoxetine					
	NDRIs: Bupropion					
CNS stimulants	Methylphenidate (2.68%), dexmethylphenidate, lisdexamfetamine					
Vagagativa quatila accepta	Sildenafil (3.16%), tadalafil (6.00%), alprostadil (2.60%) (intracavernosal injection),					
Vasoactive erectile agents	papaverine (intracavernosal injection)					
Alpha-adrenergic receptor	Selective: Tamsulosin, terazosin					
antagonists	Nonselective: Doxazosin, prazosin					
Anesthetics	Morphine (epidural), propofol					
Hormonal therapy	Testosterone enanthate, gonadotropin releasing hormone, androstenedione,					
Hormonar therapy	cabergoline/bromocriptine					
Anxiolytics	Hydroxyzine					
Antihypertensives	Hydralazine, guanethidine, propranolol					
Anticoagulants	Unfractionated heparin, low molecular weight heparin, warfarin, acenocoumarin					
Chemotherapy	Oxaliplatin					
Dopamine agonist	Rotigotine					
Herbal supplements	Tribulus terrestris, Rhino 7 Platinum 3000, All Nite Long, horny goat weed					
Anticonvulsant	Topiramate, valproate, pregabalin, gabapentin, lamotrigine					
Monoclonal antibody	Adalimumab					
Antibiotics	Vancomycin					
Melanocortin	Melanotan-II					
Parenteral nutrition	20% fat emulsion					
Recreational substances	Cocaine, cannabis, MDMA, alcohol					

SARIs: serotonin receptor antagonists and reuptake inhibitors

SSRIs: selective serotonin reuptake inhibitors

SNRIs: serotonin and norepinephrine reuptake inhibitors NDRIs: norepinephrine and dopamine reuptake inhibitors

MDMA: 3,4-methylenedioxymethamphetamine

Supplementary Appendix B

Table 2. Agents Used to Treat or Prevent Subsequent Episodes of Priapism

Medication/FDA Indication and Off-Label Uses	Mechanism of Action for Priapism	Typical Dose	Dosing Strategies for Priapism	Common Side Effects	Serious Reactions	Caution/Other Information			
HORMONAL THERAPIE	HORMONAL THERAPIES								
GnRH agonists									
Leuprolide acetate Central precocious puberty, endometriosis, advanced prostate cancer, uterine leiomyoma Off label: premenopausal ovarian preservation during chemotherapy and endocrine therapy, breast cancer in male patients, hormone therapy for transgender males, paraphilias (male)	Central androgen ablation; causes initial increase in FSH and LH; chronic use	Adult: 3.75 mg every 4 weeks (endometriosis) 7.5 mg every 4 weeks (prostate cancer); available in long- acting injectable formulations (45 mg every 6 months) Pediatric: Weight-directed dosing: 7.5 to 15 mg every 4 weeks Fixed dosing: 7.5 mg every 4 weeks	Men: 7.5 mg every 4 weeks; 45 mg every 6 months	ECG changes, hypertension, ischemia, peripheral edema, diaphoresis, pruritis, abdominal pain, constipation, diarrhea, nausea, vomiting, psychiatric side effects, fever, fatigue	Decreased bone density, hypersensitivity reactions, cardiovascular events, pituitary apoplexy, psychiatric side effects, QT prolongation, seizures, tumor flare, gynecomastia (men), decreased libido (men)	Used for refractory cases due to poor tolerability; 50% efficacy with preventing future priapism episodes			
Goserelin acetate Advanced breast cancer, endometrial thinning, endometriosis, advanced prostate cancer, locally advanced prostate cancer Off label: combination therapy for breast cancer, premenopausal ovarian preservation during chemotherapy, breast cancer in male patients, hormone therapy for transgender women	leads to suppression of pituitary gonadotropins with serum testosterone levels comparable to surgical castration	Adult: 3.6 mg SUBQ every 4 weeks	3.6 mg SUBQ every 4 weeks	Women: peripheral edema, vasodilation, acne, diaphoresis, seborrhea, decreased/increased libido, abdominal pain, nausea, infection, depression, asthenia, emotional lability, headache, insomnia Men: hot flashes, abdominal pain, nausea, vasodilation, asthenia, insomnia, decreased libido, fatigue	Decreased bone density, worsening glycemic control, psychiatric side effects, tumor flare, cardiovascular events, gynecomastia	Used for refractory cases due to poor tolerability			
Antiandrogens	Antiandrogens								
Flutamide Metastatic prostate cancer	Inhibits binding of androgen in target tissues	Adult: 250 mg TID with LH agonist	125 to 250 mg TID ³⁷	Hot flashes, diarrhea, galactorrhea, vomiting,	Loss of libido, impotence, gynecomastia,	Liver function monitoring necessary; hepatic toxicity			

Medication/FDA Indication and Off-Label Uses	Mechanism of Action for Priapism	Typical Dose	Dosing Strategies for Priapism	Common Side Effects	Serious Reactions	Caution/Other Information
Off label: paraphila (men)				impotence, cystitis, rectal hemorrhage	hepatotoxicity	can occur
Bicalutamide Metastatic prostate cancer Off label: locally advanced prostate cancer, salivary gland tumors		Adult: 50 mg once daily with LH agonist	50 mg daily ³⁸	Peripheral edema, pain, hot flashes, gynecomastia, constipation, nausea, diarrhea, mastalgia, anemia, infection, dyspnea, decreased libido, fatigue	Hepatotoxicity, anemia, gynecomastia, interstitial lung disease	May increase the risk of cardiovascular disease, decreased bone mineral density, diabetes
Chlormadinone [Not approved in the United States]		Adult: 1 to 100 mg daily depending on indication	100 mg daily ³⁹	Menstrual irregularities, headaches, nausea, sexual dysfunction	Sexual dysfunction, adrenal insufficiency	
Internationally: birth control, hot flashes, prostate cancer, BPH						
5-alpha reductase inhibitor	s					
Finasteride BPH, male pattern hair loss Off label: hirsutism	Inhibits conversion of testosterone to dihydrotestosterone	Adult: 1 to 5 mg once daily Pediatric: not recommended	3 to 5 mg daily ³⁶	Impotence, hypotension, orthostasis, peripheral edema, rhinitis	Sexual dysfunction, prostate cancer, gynecomastia, increases risk of self-harm and depression	Requires no kidney or liver dosing
Dutasteride BPH Off label: male pattern baldness	(DHT), thereby suppressing serum DHT levels	Adult: 0.5 mg once daily Pediatric: not recommended	0.5 mg daily ³³	Decreased libido, impotence, prostate cancer	Prostate cancer, gynecomastia, increases risk of self-harm and depression	
Antifungals						
Ketoconazole (oral) Systemic fungal infections Off label: Cushing syndrome, prostate cancer	Inhibits adrenal enzymes responsible for androgen and cortisol synthesis	Adult: 200 - 600 mg in 1 to 3 divided doses; max 1.2 g/day Pediatric: - 2 years+: 3.3 to 6.6 mg/kg/day	Ketoconazole 200 mg + prednisone 5 mg TID for 2 weeks, then ketoconazole 200 mg nightly for 6 months ⁴⁰	Headache, stomach pain, diarrhea, constipation, heartburn, gas, taste alteration, nervousness, numbness in hands or feet, hair loss, flushing, sensitivity to light, decreased libido	Hepatotoxicity, gynecomastia	Black box warning: hepatotoxicity, QTc prolongation Hepatic dosing needed, not renal
DRUGS THAT ALTER TH	HE CORPORAL MUSCLE T	ONE				

Medication/FDA Indication and Off-Label Uses	Mechanism of Action for Priapism	Typical Dose	Dosing Strategies for Priapism	Common Side Effects	Serious Reactions	Caution/Other Information
Alpha agonists						
Pseudoephedrine Nasal congestion Off label: hyperlactation		Adult: -IR: 60 mg every 4-6 hours -ER: 120mg every 12 hours or 240 mg every 24 hours; max 240 mg daily Pediatric: - <4 years: 1 mg/kg/dose every 6 hours; max 15 mg/dose - 4-6 years: 15 mg every 4-6 hours; max 60 mg daily - 6-<12 years: 30 mg every 4-6 hours; max 120 mg/24 hours - >12 years: same as adult	50 - 100 mg nightly ¹	Palpitations, nausea, dizziness, xerostomia, anxiety, tremor, insomnia, headaches	Persistent palpitations, dyspnea, allergic reaction, chest pain, urinary retention	Requires renal dosing Do not use with or within 2 weeks of discontinuing a monoamine oxidase inhibitor
Etilefrine [not approved in the United States] Internationally: Hypotension in patients with circulatory failure, anesthesia-induced hypotension, postoperative hypotension	Promotes vasoconstriction, thereby assisting corporal drainage	Adult: 5-10 mg TID; max 30 mg/day Pediatric - <2 years: 1 - 2.5 mg TID; max 7.5 mg/day - 2-6 years: 2.5-5mg TID; max 15mg/day ->6 years: 5-10 mg TID; max 30 mg/day	5-10 mg nightly ³⁴	Palpitations, nausea, dizziness, xerostomia, anxiety, tremor, insomnia	Persistent palpitations, dyspnea, allergic reaction, chest pain, urinary retention	Effective in up to 72% of cases of recurrent priapism ³⁵
Phenylephrine Hypotension in patients with circulatory failure, mydriasis and vasoconstriction of conjunctival blood vessels, nasal congestion Off label: priapism, hypotension in the setting of anesthesia		Adult: IV: 0.1 to 1.5 ug/kg/min	200 ucg/mL every 3 to 5 minutes ⁷ Can be prescribed for outpatient intracavernosal use while awaiting the effect of other agents	Headache, hypertension, bradycardia, palpitations, sweating, insomnia, worsening BPH	Hypertension when using systemically; typically side effects are short lived	Contraindicated in patients with history of epilepsy, on anticonvulsants, cardiac dysfunction, PAH Requires hepatic and renal dosing
Antiarrhythmic agent						

Medication/FDA Indication and Off-Label Uses	Mechanism of Action for Priapism	Typical Dose	Dosing Strategies for Priapism	Common Side Effects	Serious Reactions	Caution/Other Information
Digoxin HFrEF, atrial fibrillation, atrial flutter Off label: sustained fetal supraventricular tachyarrhythmia, supraventricular tachycardia (rate control)	Inhibits corporeal smooth muscle Na ⁺ /K ⁺ pump, leading to inhibition of Ca ²⁺ efflux from smooth muscle cells, which promotes contraction and impedes nitric oxideinduced relaxation	Adult: 0.0625 - 0.25 mg once daily Pediatric: - Dosing strategies range by weight from 2.5 mcg/kg BID to 2.5-4 mcg/kg BID ->10 years or >30 kg: 0.125 mg BID or 0.25 mg once daily	0.25 - 0.5 mg daily ³⁵	Bradycardia, dizziness, confusion, weakness, diarrhea, headache	Gynecomastia, decreased libido Toxicity: arrhythmias, hyperkalemia, lethargy, delirium, xanthopsia	Must be monitored; serum target is 0.5 to <0.9 ng/mL, some guidelines go higher; toxicity arises with levels >2 ng/mL Can use every other day dosing strategies in older patients Renally excreted; GFR adjustments necessary Several pertinent interactions
Beta-2 agonist						
Terbutaline Bronchospasm Off label: tocolysis	Relaxes smooth muscle; mechanism of action for priapism poorly understood	Adult: 2.5-5 mg TID; max 15 mg/day Pediatric: - 12-15 years 2.5 mg TID; mac 7.5 mg/24 hours ->15 years: 5 mg TID; can reduce to 2.5 mg if side effects; max 15 mg/24 hours	5 to 10 mg immediately, then 5 mg taken 15 minutes later; maintenance dose 5 to 10 mg daily ³¹	Nervousness, tremor, hypertension, sweating, xerostomia, muscle cramps	Shortness of breath, allergic reactions, palpitations, seizures, hypokalemia, hyperglycemia	Contraindicated in patients with diabetes, hypertension, hyperthyroidism, seizures
GABA agonists						
Gabapentin Postherpetic neuralgia, partial seizures Off label: alcohol use disorder, alcohol withdrawal, chronic cough, essential tremor, fibromyalgia, generalized anxiety disorder, hiccups, neuropathic pain, panic disorder, restless leg syndrome, social anxiety disorder, vasomotor symptoms of menopause	Inhibits Ca ²⁺ efflux from smooth muscle cells in the corpora, preventing smooth muscle relaxation ⁴²	Adult: 100-300 mg 1-3 times daily to start; max 3600 mg/day Pediatric: - IR, 3 to <12 years: 10-15 mg/kg/day in 3 doses; up to 50 mg/kg/day ->12 years: 300 mg TID; typical 900 to 1800 mg/day; max 2400 mg/day in 3 divided doses	400 mg TID; max 2400 mg daily ⁴³	Dizziness, drowsiness, emotional lability, hostility, ataxia, weight gain	Respiratory depression, anaphylaxis, erectile dysfunction, anorgasmia, DRESS, SJS, TEN, suicidal ideation	Requires renal and hepatic dosing Caution when using concurrently with other CNS depressants due to increased risk of respiratory depression

Medication/FDA Indication and Off-Label Uses	Mechanism of Action for Priapism	Typical Dose	Dosing Strategies for Priapism	Common Side Effects	Serious Reactions	Caution/Other Information
Baclofen Spasticity Off label: alcohol use disorder, hiccups, muscle spasm	Reduces excitatory neurotransmission in presynaptic neurons and inducing inhibitory neurotransmission by GABA agonism; reduction in spasticity can reduce erections	Adult: Oral: 5 to 10 mg TID; max 80 mg/day Intrathecal: 50 mcg; max 100 mcg Pediatric: 12 years+: 5 mg TID; max 80 mg/day Intrathecal: 25 to 50 mcg; max 100 mcg	10 mg TID; increase weekly; max 90 mg ⁴⁴	Dizziness, nausea, vomiting, drowsiness, asthenia, weakness, headache, nausea, constipation, frequent urination	Hallucinations, seizures, potentially addictive; can withdraw if abruptly stopped	Can also be used intrathecally with more efficacy Renal dosing advised; avoid with hemodialysis
Antineoplastic agents						
Hydroxyurea CML, head and neck carcinoma, SCD Off label: AML, differentiation syndrome, essential thrombocytopenia, hypereosinophilic syndrome, meningioma, myelofibrosis, polycythemia vera	Inhibits ribonucleotide diphosphate, arresting cells in S phase; reduces hemolysis and free hemoglobulin levels and, therefore, prevents nitric oxide sequestration	Adult: 15 - 100 mg/kg/day ideal body weight; 500 mg to 3 g daily; depending on indication Pediatric: - 6 months to 2 years: 15 to 20 mg/kg/dose - 2 years+: 20 mg/kg/dose once daily	Used as treatment for SCD only	Eczema, headache, constipation, hair loss, weight gain, loss of appetite, changes in skin and nails	Bone marrow suppression, leg ulcers, secondary primary malignancies, infection, macrocytosis, neutropenia, oligospermia	Renally dosed, no need for hepatic dosing Requires dose adjustment in obesity
PDE-5 inhibitors						
Sildenafil ED, PAH Off label: high altitude pulmonary edema, Raynaud phenomenon, sexual dysfunction associated with SSRIs	Chronic use can prevent the downregulation of PDE-5 and chronic accumulation of cGMP, leading to a reduction on priapism episodes	Adult: ED: 50 to 100 mg once daily PAH: 20 mg TID Pediatric: PAH: 10 to 20 mg TID; max 40 mg/dose	25 to 50 mg daily ³⁵	Flushing, diarrhea, dyspepsia, headache, back pain, myalgias, visual disturbance, epistaxis	Hearing loss, hypotension, priapism, visual disturbance	

Medication/FDA Indication and Off-Label Uses	Mechanism of Action for Priapism	Typical Dose	Dosing Strategies for Priapism	Common Side Effects	Serious Reactions	Caution/Other Information
Tadalafil BPH, ED, PAH Off label: high altitude pulmonary edema, sexual dysfunction associated with SSRIs		Adult: ED: 2.5 mg to 10mg daily depending on formulation PAH: 20 to 40 mg once daily Pediatric: Not FDA-approved	5 mg three times weekly ³⁵	Flushing, dyspepsia, nausea, headache, back pain, myalgia, respiratory infections	Hearing loss, hypotension, priapism, visual disturbance	Renal dosing; not recommended for use with severe hepatic impairment

GnRH: gonadotropin releasing hormone

LH: luteinizing hormone

CML: chronic myeloid leukemia

ED: erectile dysfunction

PAH: pulmonary arterial hypertension

BPH: benign prostatic hyperplasia

HRrEF: heart failure with reduced ejection fraction

AML: acute myeloid leukemia

SCD: sickle cell disease

GABA: gamma amino butyric acid

PDE-5: phosphodiesterase 5

SSRI: selective serotonin reuptake inhibitor