

hemostatic disorders or active pathologic bleeding. Caution advised in pts with a recent ACS/PCI or history of severe tachyarrhythmia.

- Plasma lipids: Has been shown to decrease triglycerides by 15% and increase HDL cholesterol by 10%
- Drug interactions:
  - Dose reduction: Required with medications metabolized by cytochrome p450 pathway. CYP3A4 and CYP2C19 inhibitors may increase

cilostazol levels and require dose reduction to 50 mg (e.g., erythromycin, clarithromycin, ketoconazole, diltiazem, statins, cisapride, ergot, omeprazole).

- Dose increase: Caution with CYP3A4 and CYP2C19 inducers such as statins, which may

decrease cilostazol plasma concentration. Smoking (which induces CYP1A2) has been shown to decrease cilostazol plasma concentrations by 18%.

Assessment Points				
System	Effect	Assessment by Hx	PE	Test
CV	Increased HR and palpitations Decreased BP Increased HDL cholesterol Decreased TG Worsens class 3-4 CHF	Avoid if Hx of severe tachyarrhythmia, ACS, or PCI in last 6 mo, class III-IV heart failure	Two-flight walk, Signs of CHF.	ECG ECHO
PVS	Arteriolar vasodilatation	Walking distance	Peripheral pulses	Ankle-brachial pressure index
GI	GI upset	Diarrhea, bloating		
HEPAT	Metabolized by cytochrome P450 with active metabolites	Hepatic failure, nausea, anorexia	Jaundice	ALT, AST, albumin, bilirubin
RENAL	Renal excretion; not removed by dialysis	Severe renal insufficiency		CrCl <25 mL/min
HEME	Plt dysfunction Agranulocytosis	Temp, sore throat Hx of hemostatic disorders	Evidence of thrombocytopenia	CBC No effect on PT, APTT, INR
CNS	Headaches, dizziness, vertigo			

**Key References:** Rogers KC, Oliphant CS, Finks SW: Clinical efficacy and safety of cilostazol: a critical review of the literature, *Drugs* 75(4):377–395, 2015; Gogarten W, Vandermeulen E, Van Aken H, et al.: Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology, *Eur J Anaesthesiol* 27(12):999–1015, 2010.

### Perioperative Implications

#### Preoperative Concerns

- Discontinue 2–5 d before surgery depending on type and anticipated blood loss. Limited data available on risk of preop surgical bleeding and no standard guidelines available.
- Discontinue 2 d (>42 h according to European Society of Regional Anaesthesia guidelines) before neuraxial or regional anesthesia. Avoid indwelling cath while pt is taking cilostazol.
- Preop: CBC, ECG. No effect on INR/APTT.
- Emergency surgery: No reversal agent. Consider plt transfusion.

- Plt function assessment can be done using cytometry, aggregatory, or point-of-care P2Y12 assays. Thrombin generation does not appear to be affected by cilostazol; therefore no evidence that TEG/rotational thromboelastometry are suitable for monitoring.

#### Induction/Maintenance

- Positive inotrope and chronotrope in pts prone to tachyarrhythmias.
- May cause hypotension due to arteriolar vasodilation.

#### Postoperative Period

- Restart regular dose 24 h postop.
- Wait at least 5 h after regional/neuraxial cath removal to restart dose.

#### Anticipated Problems/Concerns

- Inhibitor of plt aggregation with increased risk surrounding regional anesthesia and invasive monitoring
- Caution in pts with heart failure, tachyarrhythmias, hemostatic disorders, renal or hepatic dysfunction, or concomitant administration of CYP3A4 or CYP2C19 inhibitors
- Predominantly studied in Asian populations; more studies required to extrapolate findings to broader population

## Cocaine

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### Uses

- Cocaine (benzoylmethylecgonine) is a commonly abused stimulant drug isolated from leaves of the coca plant (*Erythroxylon coca*).
- Administered IV, to mucosa, “snorted,” or smoked (“crack”); lipophilic and crosses BBB.
- Extremely addictive; 5 million Americans are regular users and 30 million have tried it at least once (2012 National Survey on Drug Use and Health).
- Drug that is most commonly associated with mortality.

### Perioperative Risks

- Hemodynamic instability, increased sympathetic discharge
- Myocardial ischemia: supply/demand imbalance
  - Increased myocardial O<sub>2</sub> demand (increased HR, BP, and LV contractility)
  - Decreased myocardial O<sub>2</sub> supply (increased endothelin and decreased NO, resulting in coronary vasoconstriction)

### Worry About

- CV: Htn, tachycardia, dysrhythmias, MI, cardiomyopathy, premature coronary atherosclerosis, LV hypertrophy, sudden cardiac death, aortic dissection
- Neurologic: Intracerebral bleed, seizures, euphoria, delusions, hallucinations, coma
- Pulmonary: Pneumomediastinum, cocaine-induced asthma, hypersensitivity pneumonitis, chronic cough, pulm edema, abnormal diffusing capacity, perforation of nasal septum
- OB: Placenta previa, abruptio placentae, premature labor, fetal distress or demise

### Overview/Pharmacology

- Cocaine is an ester local anesthetic and sodium channel–blocking drug; it is a class I antiarrhythmic agent.
- Blocks presynaptic reuptake of norepinephrine, dopamine, and serotonin, resulting in activation of the SNS. Note: Does not release catecholamines.

- Accumulation of dopamine in the synaptic cleft may lead to acute euphoria, increased alertness, and out-of-body experiences.
- The USA FDA approves cocaine 4% topical solution as a local anesthetic to be used on mucous membranes. Cocaine is useful for ENT surgery and awake fiberoptic intubation (dosage not to exceed 1–3 mg/kg).

### Etiology

- Cocaine abuse
- Iatrogenic: OD during ENT surgery; ER use (part of tetracaine, epinephrine, cocaine mix)

### Usual Treatment

- Supportive
- Myocardial ischemia induced by cocaine should be treated initially with O<sub>2</sub>, sublingual aspirin, and benzodiazepines. If there is ongoing myocardial ischemia, use of nitroglycerine, verapamil, or phenolamine to reverse cocaine-induced coronary vasoconstriction may be necessary.

- Consider urgent coronary angiography in clinical setting of acute chest pain with evidence of myocardial ischemia.
- Treat hyperthermia promptly as it increases cardiac demand.
- Beta-blockers may worsen coronary vasoconstriction (because unopposed alpha agonism remains) and should be used with great caution if pt presents with signs of ischemia or acute cocaine toxicity.
- In management of short-lived arrhythmias, drug treatment should be avoided if possible, as antiarrhythmic agents and cocaine may cause a synergistic depression of contractile function.
- For sustained hemodynamically tolerated SVT associated with AV nodal reentry, adenosine is safe and free of major side effects. If adenosine is unsuccessful, administration of an  $\alpha$ -antagonist and a beta-blocker in combination is likely to be both safe and effective.
- No reliable information on the safety and efficacy of other antiarrhythmic drugs.
- Supraventricular or ventricular tachyarrhythmias associated with hemodynamic compromise require urgent DC cardioversion.
- Avoid use of reversal agents including flumazenil or naloxone, because these may further precipitate cardiac dysrhythmia and autonomic instability.

### Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, MI, dysrhythmias, myocarditis, cardiomyopathy, aortic dissection, endocarditis, premature coronary atherosclerosis, prolonged QT	Exposure Chest pain Palpitations	BP/HR Murmur	ECG ECHO CK-MB, troponins I and T
RESP	Pneumomediastinum, bronchoconstriction, pneumothorax, diffuse alveolar hemorrhage, pulm edema	Exposure Hemoptysis SOB	Wheezing Rales	CXR
HEME	Thrombocytopenia, enhanced platelet aggregation promoting thrombus formation	Bleeding problems, vasoconstriction		Plts
OB	Preterm labor, premature rupture of membranes, abruptio placentae, spontaneous abortion, meconium-stained amniotic fluid	Exposure Uterine contractions Abdominal pain	Vaginal bleeding	US
GU	Rhabdomyolysis, ARF, ESRD	Exposure	Oliguria, anuria	K <sup>+</sup> , Cr, CK, urine myoglobin
CNS	Subarachnoid hemorrhage, intracerebral bleed, seizures, CVA	Headache, N/V	Neurologic exam	CT scan

**Key References:** Hernandez M, Birnbach DJ, Van Zundert AA: Anesthetic management of the illicit-substance-using patient, *Curr Opin Anaesthesiol* 18(3):315–324, 2005; Dwarakanath S, Cook AM, Fahy BG: Perioperative care of the cocaine-dependent neurosurgical patient, *J Anesthesiol Clin Sci* 2:12, 2013.

### Perioperative Implications

#### Preoperative Concerns

- Outside of trauma, likelihood of pt presenting to the OR with acute intoxication is low because of rapid metabolism.
- Some recommend at least 1 wk cocaine-free interval before elective surgery.
- Pts who have been chronically abusing cocaine are at risk for catecholamine-induced cardiomyopathy. Inquire about exercise tolerance, chest pain, and DOE.
- Hx of smoking, alcohol use, positive syphilis serology, and use of other illicit drugs should alert to possibility of cocaine abuse.
- Difficult IV access due to sclerosis of peripheral veins.
- Consider urine screen (reliable for only 14–60 h after use). Tests typically screen for benzoylgonine.
- Be alert for polysubstance abuse; rare that only one substance is abused. Cocaine is often “cut” with amphetamines. Check blood alcohol, comprehensive drug screen.

#### Monitoring

- Routine.
- Consider arterial line if Hx of acute intoxication or recent exposure. Consider central access for difficult IV access or if significant hemodynamic lability requiring use of vasoactive agents.

#### Airway

- Intranasal cocaine can cause perforation of nasal septum, oropharyngeal ulcers, and chronic sinusitis.

- Notify ENT surgeons if pt is chronically hypertensive, on MAO-I or a TCA. Usage of cocaine will precipitate hemodynamic instability.

#### Preinduction/Induction

- Benzodiazepines are helpful to decrease HR and BP.
- Severe Htn may occur during direct laryngoscopy.
- Usage of succinylcholine in acutely intoxicated pt can be associated with prolonged paralysis as cocaine is also metabolized by plasma cholinesterase. Succinylcholine may also compete for plasma cholinesterase metabolism and prolong acute cocaine effects. Use with caution.
- Use ketamine with caution; potentiates CV toxicity of cocaine.
- Neuraxial anesthesia may be associated with more frequent episodes of hypotension. Correct hypovolemia/coagulopathies first. Hypotension may be ephedrine resistant and thus more responsive to phenylephrine.

#### Maintenance

- Myocardial ischemia can manifest as CV instability, ECG changes.
- With acute exposure, anesthetic requirements may be increased (increased MAC with acute intoxication, decreased MAC with chronic abuser not using periop)
- Increased catecholamine levels due to inadequate anesthesia; cocaine in blood may result in cardiac dysrhythmias.
- Long-term cocaine abuse may downregulate postsynaptic catecholamine receptors such that indirect

vasoconstrictors (ephedrine) are not as effective as direct vasoconstrictors (phenylephrine).

- Despite having alpha-antagonist effects, nonselective beta antagonist effects of labetalol are much more potent, leaving it as a questionable choice for hemodynamic control.
- Temperature rise, sympathomimetic effects associated with cocaine can mimic malignant hyperthermia.

#### Extubation

- No special issues

#### Adjuvants

- Ester local anesthetics and succinylcholine, which undergo metabolism by plasma ChE, may compete with cocaine, resulting in decreased metabolism of both.
- Cocaine decreases seizure threshold and enhances convulsant effect of other local anesthetics.
- Dexmedetomidine may be useful as an adjuvant because it counteracts cocaine's sympathomimetic cardiovascular effects. Use with caution if hemodynamics have not been optimized.

#### Postoperative Period

- Myocardial ischemia
- Pain medication requirements for chronic abusers are same as for nonabusers.
- Consider poor home social environment; may call for vigilant work with case management for pt's posthospital transitions in care that optimize longitudinal recovery.

## Colchicine

### Uses

- Specifically indicated for treatment and relief of pain in acute attacks of gouty arthritis. Often effective in aborting an attack when taken at initial sign of discomfort.
- Not an analgesic and should not be used for other causes of pain.
- Recommended for prophylaxis of gouty attacks with regular use between attacks.

- Well documented use in familial Mediterranean fever.
- Also used in other conditions such as Behcet disease, pericarditis, atherosclerosis, osteoarthritis, and prophylaxis for postop atrial fibrillation.

### Preoperative Risks

- Narrow therapeutic window and possibility of toxicities. In view of its potential side effects—including renal, hepatic, respiratory, and gastrointestinal side

effects—dosage adjustments must also be considered, especially in cases of renal and hepatic impairment.

- In animals, has been shown to alter neuromuscular function, intensify gastrointestinal activity, increase sensitivity to central depressants, heighten response to sympathomimetic compounds, depress the respiratory center, constrict blood vessels, cause hypertension through central vasomotor stimulation, and lower body temperature.

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