Cocaine Abuse (including in Pregnancy)

Cocaine blocks the pre-synaptic reuptake of MAO neurotransmitters in the CNS and the PNS, resulting in profound stimulation of the sympathetic nervous system; acute intoxication and chronic use present marked physiologic derangements in drug users as well as complications for parturients and fetal well-being

ANESTHETIC CONSIDERATIONS:

- Risk of significant hemodynamic instability (HTN/hypotension/arrythmias)
  - avoid indirect acting vasopressors
    - treat HTN and tachycardia with alpha and beta blockade (consider phentolamine/esmolol)
    - avoid isolated beta blockade due to unopposed alpha blockade
- Multisystem manifestations
  - CNS – hyperthermia, seizure (benzodiazepines), stroke, bleeds, psychosis
  - CVS – HTN, arrhythmias, coronary vasospasm, cardiomyopathy, aortic dissection
  - Resp – bronchospasm (crack cocaine), aspiration, pulmonary edema
  - GI / GU – renal failure, GI ischemia, hepatic failure, thrombocytopenia, DIC
- Risk of co-intoxicants
  - Alcohol, marijuana, heroin, methamphetamines, opioids
- Complications related to anesthesia
  - Potential exacerbation of SNS stimulation
  - **Neurotransmitter depletion**
  - Neuraxial anesthesia and thrombocytopenia, DIC
- Infection risk associated with IVDU
- Cocaine effects in Pregnancy
  - Maternal - decreased uteroplacental perfusion, spontaneous abortion, premature labor, premature ROM, placental abruption
  - Fetal – increased congenital abnormalities, cardiomyopathy, MI, intra-cerebral bleeding, CNS irritability

ANESTHETIC GOALS:

- Preoperative optimization:
  - Consider postponing or canceling elective/semi-urgent cases if acute intoxication
- Caution with regional and neuraxial techniques (thrombocytopenia)
- Supportive management of acute cocaine intoxication
  - Control hemodynamics
    - Uppers: Direct acting: phenylephrine, vasopressin, norepinephrine
    - Downers: phentolamine + esmolol, magnesium, nitroglycerin, nitroprusside, hydralazine
  - Benzodiazepine for seizure prevention
  - Invasive BP monitoring
  - Postoperative disposition
- Anticipate perioperative hemodynamic instability
  - Utilize direct acting vasopressors

HISTORY

- Use of cocaine – duration, frequency
- Use of other intoxicants – alcohol, tobacco, marijuana, heroin, crystal-meth
- Consider alternate diagnosis for HTN, particularly in pregnancy
- Sequelae of physiologic effects
  - CNS – seizures, stroke, psychosis
  - CVS – arrhythmias, chest pain, cardiomyopathy
  - Resp – pulmonary edema (primary respiratory or cardiac), bronchospasm
  - GI / GU / heme – renal failure, hepatic failure (mostly related to hepatitis infections), bleeding, bruising, petechiae
- Obstetric history – prenatal care, abstinence from substances
  - Spontaneous abortion, placental abruption, premature labor and ROM
  - Fetal well-being – IUFD, congenital abnormalities, cardiomyopathy
  - HTN, rule out PIH
- Pain management issues – history of methadone use, opioid use

PHYSICAL

- Standard physical exam, especially vitals
- FHR in pregnancy

INVESTIGATIONS

- **Labs**
  - CBC, lytes, BUN, Creatinine (PLT, renal failure)
  - INR, PTT, glucose (DIC, hepatic dysfunction)
  - X-match (placental abruption in pregnancy)
  - EtOH, toxicology screen
  - TSH
- **Imaging**
  - ECG (arrhythmias)
  - CXR – pulmonary edema, infection, aortic dissection
  - Appropriate cardiac investigations (accelerated CAD)
  - ECHO (cardiomyopathy)
  - Pregnancy – fetal heart, NST, fetal ultrasound (abruption, IUFD)

OPTIMIZATION

- Acute intoxication can be treated with **benzodiazepines** (CNS effects)
- Active **cooling** for hyperthermia
- Pregnancy – management of hypertension:
    - **Hydralazine** can reduce BP, but increases maternal tachycardia with NO improvement of uteroplacental perfusion
    - **Labetalol** has been used in acutely intoxicated parturients, with the theoretical risk of worsening HTN due to unopposed alpha-vasoconstriction
        - Labetalol does reduce BP and maintain HR at baseline, but NO improvement of uteroplacental perfusion

ANESTHETIC OPTIONS

- Local, regional, neuraxial, GA (recognize implications of potentially uncooperative patient)
- Caution with neuraxial in patients with potential thrombocytopenia and risk of hemorrhage (placental abruption)
    - Profound hypotension may result with neuraxial – indirect vasopressors may be ineffective (SAB > epidural)
- GA – increased MAC with acute intoxication, decreased MAC with chronic use
    - Profound increases in SNS stimulation may result from laryngoscopy, surgical stimulation
    - Avoid SNS agonists (ketamine, atropine)

ANESTHETIC SETUP

- **Drugs**
    - Uppers – phenylephrine, epinephrine, norepinephrine, indirect acting may be ineffective
    - Downers – NTG, **phentolamine + esmolol in combination OK**, hydralazine, ?labetalol
    - Rate Control – avoid β-blockers, CCBs have been used (verapamil 2.5-5 mg slow IV over 2-3 minutes q5-10min up to 20 mg)
- **Equipment**
    - CAS + 5-lead
    - Low threshold for invasive BP monitoring
    - Large-bore IV
    - Temperature monitoring
    - Medications for hemodynamic control
    - FHR monitoring in pregnancy

MANAGEMENT OF ANESTHESIA

- **Induction / Maintenance / Emergence**
    - Increased anesthetic requirements in acutely intoxicated patient
    - Patient should be deep prior to laryngoscopy or surgical stimulation (risk of profound hypertension & myocardial ischemia)
    - Concerns of regional anesthesia
        - Compliance
        - Thrombocytopenia
    - Avoid drugs which ↑ SNS: ketamine, atropine, ?desflurane
    - Note that catecholamines should be used cautiously:
        - Ephedrine may not work because it is indirect, and catecholamine store may be depleted
        - Phenylephrine should be used in a reduced concentration as it may have an exaggerated effect

DISPOSITION & MONITORING

- Ongoing cardiovascular monitoring – risk of arrhythmias, MI, impaired cardiac output
- Management of CNS symptoms of intoxication or withdrawal
- Multimodal analgesia plan

COMPLICATIONS

- **Myocardial Ischemia**
    - Mechanisms
        - Coronary artery vasospasm
        - ↑ MVO_2
        - Coronary artery thrombosis
        - Coronary artery aneurysm
    - Medications:
        - Mainstay of treatment are **BDZ** and **ASA**
        - Beta-blockers are contra-indicated
            - **Labetalol** has been used safely despite preferential β-blockade although this is controversial
        - For rate control, consider **Calcium Channel Blockers**
            - **Verapamil 2.5 – 10 mg IV**
        - **NTG** is also used
        - **Phentolamine**
    - Should refer to cardiology for possible catheterization
- **Arrhythmias**
- **HTN**

COCAINE AND PREGNANCY

- Fetal and neonatal effects
    - ↑ incidence of spontaneous abortions
    - ↑ premature labor and PROM
    - ↑ incidence of placental abruption
    - ↓ uteroplacental perfusion → fetal distress
    - ↑ intrauterine fetal death

- ↑ risks to neonate: MI, ICH, congenital malformations
- Maternal risks as above:
  - Myocardial ischemia
  - Aortic dissection
  - ICH

PATHOPHYSIOLOGY

- **History**
  - Tropane ester alkaloid from the leaves of the Erythroxylum coca plant of South America
  - Cocaine isolated from coca leaves in 1860
  - Cocaine hydrochloride registered as a local or topical anesthetic as a controlled substance
  - Cocaine is the illegal drug of abuse most often associated with ER visits in the US, including patients requesting detox and suicide attempts
  - Cocaine use highly associated with use of other illegal and legal substances of abuse, as well as psychiatric disorders
- **Mechanism of action** is by inhibition of the presynaptic reuptake of MAO neurotransmitters (dopamine, norepinephrine, serotonin) in the CNS and PNS
  - Cocaine also blocks voltage-gated Na channels and is effective as a local anesthetic and contributes to cardiac arrhythmias
  - Metabolized by hydrolysis via plasma cholinesterases to largely inactive metabolites, excreted in urine
  - Rapidly redistributed to most organs, crosses placenta
  - Chronic use results in depletion of MAO transmitters norepinephrine, dopamine, serotonin
- Alteration of expression of mu and kappa opioid receptors can contribute to altered pain perception and complex pain management problem
- **Cocaine Effects**
  - The euphoric and 'loss of fear' effects of cocaine are tachyphylactic, however, the CVS effects of cocaine are only PARTIALLY tachyphylactic which explains why catastrophic CVS events are seen during cocaine binges as the addict attempts to get their fix
  - Classic S&S include HTN, hyperthermia, tachycardia, mydriasis, seizures, stupor, cardiorespiratory depression, & death
  - Significant adverse effects including coronary vasoconstriction persist up to 6 weeks after last ingestion
  - Death can occur within 2-3 min so ABCs are the priority
  - Complications are NOT dose related & can occur up to 6 weeks after exposure apparently
  - Hyperthermia results from altered autoregulation, increased muscular activity & intense vasoconstriction
- **Clinical Manifestations**
  - CNS:
    - Ischemic CVA d/t vasospasm, thrombosis, or vasculitis
    - Hemorrhagic CVA d/t HTN crisis ruptured aneurysm or AVM
    - Seizures d/t serotonin accumulation, anticholinergic sigma & muscarinic receptor stimulation, or hyperthermia
    - Cocaine associated delirium occurs in up to 10% of abusers in which cocaine levels are modest, but benzylecgonine, the principal metabolite, levels are high
    - Psychiatric d/o are often exacerbated by cocaine use
    - Movement d/o result from dopamine accumulation in basal ganglia and can present diagnostic confusion in postoperative emergency surgery patients as resulting from therapeutic drug effects or e-lyte abnormalities
  - A/W:
    - Epistaxis, nasal septal perforation, & oropharyngeal ulcers
    - Sinusitis, necrosis & cellulitis are all common
    - A/W fires assoc. w/ ether contamination if smoked freebase (crack)
  - Resp:
    - RAD d/t inflammatory bronchospasm
    - Pulmonary infarction (rare) & hemorrhage (25%) d/t direct lung injury from cocaine / impurities & vasoconstriction injury
    - Hypersensitivity pneumonitis, a.k.a. "crack lung", is commonly seen
    - Pulmonary edema d/t increased permeability & LV failure
    - Pulmonary HTN & hypertrophy can lead to cor pulmonale (independent of dose, frequency, or route of administration)
    - Pneumothorax, pneumomediastinum, & pneumoperitoneum occur d/t deep inhalations w/ Valsalva maneuvers to increase absorption and CNS stimulation (worsened by alveolar damage)
  - CVS:
    - Acute MI can occur d/t:
      - O_2 demand / supply mismatch:
        - Increased demand - tachycardia, HTN, increased contractility (increased Ca d/t NOR / EPI effects)
        - Decreased supply - intense vasoconstriction
      - Accelerated atherosclerosis
      - Direct endothelial damage + prothrombotic state
    - Myocarditis
    - NOR / EPI, increased Ca, & Na channel blockade can cause:
      - Increased arrhythmias including VF / VT / sudden death
      - Conduction blockade & re-entrant tachyarrhythmias
    - Dilated cardiomyopathy & LV diastolic dysfunction occur in up to 50% of chronic abusers
  - GI:
    - Decreased gastric emptying
    - Vasoconstrictive ischemia leads to ulcers & perforations
    - Vasospasm induced splenic infarct that leads to hemorrhage after vasospasm resolves
  - Renal:
    - ARF d/t infarcts d/t vasoconstriction & thrombosis in setting of accelerated renal atherosclerosis
    - ARF d/t rhabdomyolysis d/t trauma, IM vasoconstriction, & seizures
  - Vascular & Heme:
    - Small & large vessel vasospasm & thrombosis +/- direct endothelial damage

        - Decrease in Protein C & AT III
        - Increase in plasminogen activator inhibitor activity
        - Increase in PLT activation & aggregation
    - Accelerated atherosclerosis
    - Aortic dissection d/t endothelial damage, HTN, & tachycardia
    - Thrombocytopenia:
        - Catecholamine-induced vasospasm and activation of platelets leads to binding w/in microvasculature
        - Other theories - bone marrow suppression, autoimmune response, hypersplenism
        - Evidence suggests that while this consideration is worth mentioning, it is a rare occurrence in reality

REFERENCES

- Stoelting Anesthesia and Co-Existing Disease 5th Ed. pp 642- 643
- Chestnut Obstetric Anesthesia 4th Ed. pp 929- 933
- Uptodate.com – cocaine abuse, substance abuse in pregnancy