

APPENDIX T: SPECIAL CONSIDERATIONS FOR TREATMENT OF SEVERE HYPERTENSION: AMPHETAMINE/COCAINE DRUG ABUSE AND HYPOTENSION

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Drug abuse is very common in women of childbearing age, with 12-21% of women 18-35 years using illicit drugs,¹ especially cocaine and methamphetamine.² Many drugs not only affect maternal and fetal well-being, as well as alter maternal responses to prescribed medications and treatment. In particular, acute and chronic amphetamine or cocaine use may result in physiologic and pharmacodynamic changes that prove difficult to manage in the parturient.

Cocaine blocks the presynaptic reuptake of sympathomimetic neurotransmitters including dopamine, serotonin and norepinephrine. Thus, the acute use of cocaine results in the relative neurotransmitter concentrations increasing at the catecholamine's site of action, producing adrenergic stimulation both centrally and peripherally. Cocaine may cause intense vasoconstriction producing hypertension, coronary ischemia, and reduced uterine artery blood flow; other effects include tachycardia, arrhythmias, altered sensorium, and hyperthermia. With chronic abuse of cocaine the sympathomimetic neurotransmitters become depleted and hypotension and lethargy may ensue.

Common treatment of cocaine/amphetamine induced hypertension and tachycardia may include the use of hydralazine and labetalol.³ However beta-blockers, including labetalol (beta-adrenergic to alpha-adrenergic blocking 7:1 when administered IV⁴) may produce unopposed alpha-adrenergic stimulation with worsening of coronary and peripheral vasoconstriction.⁵ Indeed, phentolamine may be the drug of choice for cocaine/amphetamine-induced hypertension.

Treatment of hypertension in the patient with chronic cocaine/amphetamine abuse may cause an exaggerated decrease in blood pressure. Hypotension may be difficult to treat due to altered vasopressor response and depleted endogenous catecholamine stores. Unexpected, severe hypotension may also occur after regional anesthesia or general anesthesia.

Please note the following references for this statement:⁶⁻⁸

Also noteworthy, ketamine administration may exacerbate symptoms of acute cocaine use, due to ketamine's sympathetic nervous system stimulation.

Amphetamines indirectly stimulate the sympathetic nervous system, causing the release of catecholamines from presynaptic vesicles. The symptoms are similar to cocaine intoxication and may include hypertension, arrhythmias, tachycardia, dilated pupils, hyperreflexia and even hyperthermia. Use of regional anesthesia may be associated with unpredictable hypotension, resistant to treatment. Cardiac arrest has also been reported following both regional and general anesthesia.

Parturients chronically using either cocaine or amphetamines are in a state of catecholamine depletion and potentially altered adrenergic receptor responses. Trauma patients may also exhibit catecholamine depletion, having maintained their blood pressure through extensive release of stored catecholamines. The initial antihypertensive treatment of elevated blood pressure due to acute intoxication with cocaine/amphetamine or even pain with coincident significant trauma may exacerbate subsequent hypotension.

Treatment of hypotension may be difficult in the catecholamine-depleted patient.

Ephedrine's mechanism of action includes a direct effect as well as a significant secondary release of norepinephrine, which would be decreased in the catecholamine-depleted state, considerably blunting ephedrine's effectiveness. The vasopressors of choice should be direct acting agents, administered intravenously. Preferred agents include phenylephrine, epinephrine and norepinephrine. While norepinephrine has the strongest direct acting vasoconstriction, it should be administered via central access. Please note that greater than typical bolus doses may be required. Infusions may also be very useful, depending on circumstances. Typical doses of direct acting vasopressors are listed below:

Phenylephrine 100 mcg IV bolus

Epinephrine 50-100 mcg IV bolus (stronger)

Norepinephrine 4-8 mcg IV bolus or infusion 2-20 mcg/min⁴ (risk of skin ischemia if given through small peripheral IV, prefer central line or secondarily large bore IV fast flowing)

Note that the same phenomenon of hypotension 'resistant' to vasopressor treatment has been reported following double calcium channel blocker usage – i.e., magnesium sulfate plus nifedipine. The physiologic difficulty with dual calcium channel blockers is post-depolarization low intracellular calcium. Normally the rise in intracellular calcium triggers a much greater release of calcium from the sarcoplasmic reticulum, causing contraction of the muscle cell. In the setting of post-dual calcium channel blocker hypotension, vasopressors may not be effective, because of calcium depletion. Fortunately, treatment with calcium (1 gram CaCl₂ IV) may reverse the primary problem – low intracellular calcium.

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