Cocaine-Related Psychiatric Disorders

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Introduction

Background

Cocaine is a naturally occurring alkaloid found within the leaves of a shrub, *Erythroxylon coca*. The earliest reported use of cocaine dates back to times when the ancient inhabitants of Peru used the leaves for religious ceremonies. Cocaine was first isolated from the coca leaf in 1859. Its first use as a local anesthetic was reported in 1884. In the late 19th century, Sigmund Freud proposed cocaine for the treatment of depression, cachexia, and asthma. It later became prescribed for almost any illness and could be found in numerous tonics. In 1885, John Styth Pemberton registered a cocaine-containing drink in the United States. This drink was later named Coca-Cola. In 1914, the Harrison Narcotics Act banned all nonprescription use of cocaine. Finally, in 1970, the Controlled Substances Act prohibited the possession of cocaine in the United States, except for limited medical uses.

Cocaine may be abused through a number of different routes. The most widespread routes of administration include inhaling (snorting), subcutaneous injection (skin popping), intravenous injection (shooting-up), and smoking (freebasing or smoking crack). Because of poor absorption and significant first-pass metabolism, cocaine is rarely ingested.

Cocaine abuse is associated with numerous detrimental health effects. All organ systems can be adversely affected by its use. Cocaine-related psychiatric disorders have been well-documented in the literature. Ten cocaine-induced psychiatric disorders are described in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (*DSM-IV-TR*)[1]. These cocaine-induced disorders include the following:

- Cocaine intoxication
- Cocaine withdrawal
- Cocaine intoxication delirium
- Cocaine-induced psychotic disorder with delusions
- Cocaine-induced psychotic disorder with hallucinations
- Cocaine-induced mood disorder
- Cocaine-induced anxiety disorder
- Cocaine-induced sexual dysfunction
- Cocaine-induced sleep disorder
- Cocaine-related disorder not otherwise specified

Pathophysiology

The time to peak effects of cocaine depends on the dose and route of administration. When cocaine is injected intravenously or crack is smoked, the onset of action is within seconds and peak effects occur within 5 minutes. When snorted, the onset of action of cocaine is within the first 5 minutes and its effects typically peak within 30 minutes. Cocaine can be absorbed across any mucosal surface, including the respiratory, gastrointestinal, and genitourinary tracts.

Two major routes account for cocaine's metabolism: (1) enzymatic metabolism by both liver esterases and plasma cholinesterase to ecgonine methyl ester and (2) nonenzymatic degradation to benzoylecgonine. The half-life of cocaine is 30-90 minutes. The metabolites ecgonine methyl ester and benzoylecgonine are excreted in the urine. Drug screens detect the presence of benzoylecgonine, which may be present in the urine for 2-3

days, depending on the dose and chronicity of usage. Rare cases of benzoylecgonine detection in the urine for 22 days following cocaine use have been reported.

Cocaine has a number of pharmacologic effects on the human body. Neuronal fast sodium channel blockade produces a local anesthetic effect that continues to be used in medicine today. During myocardial fast sodium channel blockade, cocaine blocks fast cardiac sodium channels, which results in type I antidysrhythmic activity. This may lead to prolongation of the QRS complex and contribute to the induction of the dysrhythmias associated with cocaine use.

Blockade of catecholamine reuptake (ie, norepinephrine, dopamine, and serotonin reuptake blockade) occurs in both the central and peripheral nervous systems. Blockade of reuptake of norepinephrine leads to the sympathomimetic syndrome associated with cocaine use. This syndrome consists of tachycardia, hypertension, tachypnea, mydriasis, diaphoresis, and agitation. Inhibition of dopamine reuptake in the CNS synapses, such as in the nucleus accumbens, contributes to the euphoria associated with cocaine. Norepinephrine release augments norepinephrine reuptake blockade effects.

Frequency

United States

The following statistics are from the 2005 National Survey on Drug Use & Health (NSDUH) for the age group 12 years and older.[2]

- Approximately 33.7 million Americans have tried cocaine at least once in their lifetimes, representing 13.8% of the 12 years and older population.
- Approximately 5.5 million (2.3%) used cocaine in the past year and 2.4 million (1%) used cocaine in the past month.
- The incidence of cocaine use generally rose throughout the 1970s to a peak in 1980 (1.7 million new users) and subsequently declined until 1991 (0.7 million new users). Cocaine initiation steadily increased during the 1990s, reaching 1.2 million in 2001.
- Within the past 12 months of the time the survey was taken, 872,000 persons used cocaine for the first time. That is a statistically significant reduction from 2002 when there were more than 1 million past-year cocaine initiates.

International

Cocaine continues to be a major drug of abuse internationally. In Mexico, for example, patients in drug abuse treatment programs in 16 cities report cocaine as the primary drug of choice.

Mortality/Morbidity

The Drug Abuse Warning Network (DAWN) reports drug-related deaths. For 2003, 122 jurisdictions in 35 metropolitan areas and 6 states submitted mortality data to DAWN.

- In drug misuse deaths, cocaine was among the top 5 drugs in 28 of the 32 metropolitan areas and in all of the 6 states.
- On average, cocaine alone or in combination with other drugs was reported in 39% of drug misuse deaths.
- The etiologies of some of the deaths associated with cocaine abuse include cardiac dysrhythmias, myocardial infarctions, intractable seizures, strokes, and aortic dissection.

Race

- In the 2005 Youth Risk Behavior Survey, Hispanic and white students were significantly more likely than African American students to report lifetime cocaine use (12.2% and 7.7%, respectively, vs 2.3%).
- The 1999 Drug Abuse Warning Network data reported cocaine as an agent in 59%, 36%, and 35% of drug-related emergency department visits among African Americans, Hispanics, and whites, respectively.

Sex

In the 2005 National Youth Risk Behavior Survey, 8.4% of males and 6.8% of females had used cocaine at least once in 2005. According to DAWN, males are disproportionately represented among deaths related to drug misuse or abuse. After adjusting for population size, the rate of drug misuse deaths per 1,000,000 population for males was 2.4 that for females.

Age

Among students surveyed as part of the 2006 Monitoring the Future study, 3.4% of eighth graders, 4.8% of tenth graders, and 8.5% of twelfth graders reported lifetime use of cocaine. Approximately 8.8% of college students and 14.3% of young adults (aged 19-28) surveyed in 2005 reported lifetime use of cocaine.

Clinical

History

The *DSM-IV-TR* describes 10 cocaine-induced psychiatric disorders. A thorough history pertaining to the type of symptoms experienced by the patient and the timing of these symptoms in association with cocaine abuse is necessary to make each diagnosis. Other cocaine-induced medical problems may be present and/or coexistent with any of these 10 cocaine-induced psychiatric conditions. For example, a patient may present with specific clinical criteria that lead to the diagnosis of a cocaine-induced psychotic disorder with hallucinations. That same patient also may report chest pain, a symptom that could be associated with cocaine-induced acute coronary syndrome, pneumothorax, or pulmonary edema. The following are described in the *DSM-IV-TR*:

- Cocaine intoxication
    - To be diagnosed with cocaine intoxication, a patient must have used cocaine recently and must have developed clinically significant behavioral or psychological changes.
    - These changes may consist of euphoria, hypervigilance, talkativeness, grandiosity, anxiety, impaired judgment, anger, tension, changes in sociability, or changes in occupational functioning. Impaired judgment, anger, and tension can be extreme and increase the risk for violent and even homicidal behavior. In addition, the patient must demonstrate 2 or more of the following 9 signs or symptoms during or shortly after the cocaine use:
        - Tachycardia or bradycardia
        - Mydriasis
        - Blood pressure change
        - Perspiration
        - Nausea or vomiting
        - Weight loss
        - Psychomotor agitation or retardation
        - Weakness, respiratory depression, chest pain, or dysrhythmia
        - Disorientation, seizures, dyskinesias, dystonias, or coma
    - Mental status examination may show a patient who is agitated and restless with a labile affect, irritable or anxious mood, poor judgment, and impaired attention. Assess for homicidal ideation and be aware of increased risk of violence.
- Cocaine withdrawal
    - The diagnostic criteria for cocaine withdrawal include cessation or reduction in previously heavy or prolonged cocaine use.
    - The patient also must have a dysphoric mood associated with 2 of the following 5 physiological changes:
        - Fatigue
        - Vivid unpleasant dreams
        - Insomnia or hypersomnia
        - Increased appetite
        - Psychomotor agitation or retardation
    - These signs or symptoms result in significant distress in the patient clinically and may impair the patient's social or occupational areas of functioning. The patient may experience significant depressed mood with suicidal ideation.
    - Mental status examination may show a sleepy, slowed-down patient who complains of depressed mood and has a restricted affect. They may express suicidal ideation.

- Cocaine intoxication delirium
    - The diagnosis of cocaine intoxication delirium is made instead of the diagnosis of cocaine intoxication only when the cognitive symptoms are in excess of those typically encountered in cocaine intoxication. These symptoms are of such severity as to warrant independent clinical attention.
    - The diagnostic criteria of cocaine intoxication delirium include both a disturbance in consciousness resulting in a reduction of the patient's ability to focus, sustain, or shift attention and a change in cognition. These changes must develop over a short period and fluctuate in severity throughout the day.
    - Patients with delirium demonstrate impairment in their ability to receive, process, store, and recall information. They are easily distracted by irrelevant stimuli. Reasoning and problem solving is difficult. Orientation to time and place may be impaired, but orientation to person typically is intact except in the most severe cases. Cocaine-induced delirium is usually transient and reversible.
    - Evidence must show that the above changes occur during or are related to cocaine intoxication.
    - Mental status examination would show a patient who is very distractible and confused with a variable affect and mood. Visual illusions (visual misperception of stimuli) may also be present. Judgment is extremely poor, as is orientation. Although suicidal and homicidal ideation may not be present, the patient may be at risk for harm due to their poor judgment and orientation.
- Cocaine-induced psychotic disorders with delusions
    - The diagnosis of cocaine-induced psychotic disorder with delusions is made instead of a diagnosis of cocaine intoxication or withdrawal only when the psychotic symptoms are in excess of those typically encountered in intoxication or withdrawal. Delusions may be of any type but typically are paranoid and/or grandiose in nature.
    - Patients presenting with psychosis demonstrate a gross distortion of their mental capacity, communication, interactions with others, ability to recognize reality, and affective response. These distortions interfere with their ability to cope with the ordinary demands of everyday life.
    - A person demonstrating delusions clings to a false belief or judgment despite incontrovertible evidence to the contrary. For example, a female abusing cocaine may demonstrate delusions of grandeur and believe that she possesses great wealth, intellect, and power, despite the fact that she is homeless and without education. Suicidal or homicidal ideation can occur in response to delusional beliefs.
    - The diagnostic criteria for this disorder include prominent delusions developing during or within a month of cocaine intoxication or withdrawal.
    - Mental status examination often shows a guarded, tense patient who may appear fearful or anxious. They may or may not reveal their paranoid delusions and may be suspicious of questions asked. Judgment is impaired by their beliefs and may add to homicidal or suicidal ideation.
- Cocaine-induced psychotic disorders with hallucinations
    - The diagnosis of cocaine-induced psychotic disorder with hallucinations is made instead of cocaine intoxication or withdrawal only when the psychotic symptoms are in excess of those typically encountered in intoxication or withdrawal.
    - A person demonstrating hallucinations has a strong subjective perception in any sensory modality of an object or event when no such object or event is present. Auditory and tactile are the 2 types of hallucinations encountered most frequently. For example, a person may be witnessed in conversation with himself or herself and may state that he or she is talking with someone else in the room when, in fact, no one else is present. Hallucinations can contribute to suicidal or homicidal ideation; therefore, risk of harm to self or others must be assessed.
    - The diagnostic criteria for this disorder include prominent hallucinations developing during or within a month of cocaine intoxication or withdrawal.
    - Mental status examination shows a patient who is distracted by internal stimuli, may show thought blocking (verbal outflow is stopped mid thought by internal stimuli), and has a reactive affect and labile mood influenced by internal voices. Attention is variable, and homicidal and suicidal ideation may be fueled by the internal voices.
- Cocaine-induced mood disorder

    - In cocaine-induced mood disorder, a prominent and persistent disturbance in mood that arises only in association with the abuse of cocaine must occur. The symptoms must develop during or within 1 month of cocaine use, and the use of cocaine closely corresponds to these symptoms.
    - The mood changes may be depressive, manic, or mixed (neither mania nor depression predominates). The symptoms must not be better accounted for by another mood disorder that is not induced by cocaine, must not occur only during delirium, and must cause significant impairment in areas of functioning, such as social or occupational.
    - A patient demonstrating a depressed mood may show a loss of interest in daily activities, apathy, weight changes, fatigue, feelings of worthlessness, excessive guilt, indecisiveness, diminished ability to concentrate, and/or recent thoughts of death.
    - A patient presenting with acute mania may demonstrate inflated self-esteem, decreased need for sleep, talkativeness, flight of ideas, distractibility, increased goal-directed activity, and/or irritability.
    - Mental status of the depressed mood shows a patient with restricted or flat affect, depressed mood, and slowed movements and responses. They may have reduced concentration and suicidal ideation. Orientation is intact. If manic, their affect is reactive, mood is elevated and/or irritable, speech is pressured, and thoughts are tangential. Judgment is often impaired, but orientation is intact.
- Cocaine-induced anxiety disorder
    - To be diagnosed with cocaine-induced anxiety disorder, a patient must have prominent anxiety, panic attacks, obsessions, or compulsions. The symptoms must develop during or within 1 month of cocaine use, and the use of cocaine closely corresponds to these symptoms.
    - The symptoms must not be better accounted for by another anxiety disorder that is not induced by cocaine, must not occur only during delirium, and must cause significant impairment in areas of functioning, such as social or occupational.
    - A patient presenting with a cocaine-induced anxiety disorder demonstrates a diffuse, highly unpleasant, often vague feeling of apprehension accompanied by one or more bodily sensations, such as tightness in the chest or pounding heart.
    - Mental status examination shows a patient with a reactive affect, anxious mood, possible restlessness, and difficulty concentrating. Judgment and orientation are usually intact. Due to distress, suicidal ideation may be present.
- Cocaine-induced sexual dysfunction
    - To be diagnosed with cocaine-induced sexual dysfunction, a patient must have prominent sexual dysfunction that results in distress or interpersonal difficulty.
    - The symptoms of sexual dysfunction include impaired sexual desire, impaired arousal, impaired orgasm, or sexual pain.
    - The symptoms must develop during or within 1 month of cocaine use, and the use of cocaine closely corresponds to these symptoms. The symptoms must not be better accounted for by another sexual dysfunction that is not induced by cocaine.
- Cocaine-induced sleep disorder
    - To be diagnosed with cocaine-induced sleep disorder, a patient must have a prominent disturbance in sleep.
    - The 4 types of sleep disorder include insomnia, hypersomnia, parasomnia, and a mixed sleep disorder in which more than one sleep disturbance occurs and none predominates.
    - The symptoms must develop during or within 1 month of cocaine use, and the use of cocaine closely corresponds to these symptoms. The symptoms must not be better accounted for by another sleep disorder that is not induced by cocaine, must not occur exclusively during delirium, and must cause significant impairment in areas of functioning, such as social or occupational.
- Cocaine-related disorder not otherwise specified: This category is for disorders associated with the abuse of cocaine that are not otherwise classifiable as 1 of the 9 disorders noted above.

Physical

Cocaine affects multiple organ systems. A thorough physical examination must be performed on patients suspected of cocaine abuse.

- Vital signs
    - Acute cocaine intoxication is most commonly associated with tachycardia and hypertension due to an induced sympathomimetic syndrome.
    - Any patient presenting with a history of cocaine abuse and altered mental status must have an adequate temperature taken, preferably a core temperature, such as rectal. Hyperthermia associated with acute cocaine toxicity must be closely monitored.
    - Tachypnea may be simply a result of cocaine's stimulant effects. However, other etiologies of tachypnea include pulmonary edema, pneumothorax, pulmonary embolism, acute coronary syndrome, panic attacks, and withdrawal syndromes.
- Skin and extremities
    - Acute cocaine toxicity is typically associated with diaphoresis.
    - The skin may be cool as a result of the vasoconstrictive effects of cocaine, despite an elevated core temperature.
    - Examine the skin for evidence of intravenous (track marks) or subcutaneous (skin popping) drug abuse.
- Head, ears, eyes, nose, and throat
    - Close inspection of the head for signs such as edema, ecchymosis, or bony deformity is necessary to help exclude the possibility of head trauma.
    - Examine the eyes for pupil size (mydriasis with acute cocaine abuse), presence of nystagmus, and extraocular muscle function.
    - Individuals who chronically abuse cocaine who insufflate cocaine may have nasal septa perforations as a result of necrosis from repetitive cocaine-induced vasoconstriction and subsequent ischemia.
- Cardiovascular: Heart sounds may reveal murmurs (endocarditis and/or valvular damage), rubs (pericarditis), or dysrhythmias.
- Pulmonary
    - Rales due to pulmonary edema (cardiac and noncardiac etiologies associated with cocaine), pneumonia (infectious or aspiration), or atelectasis (pulmonary embolism) may be present.
    - Decreased breath sounds may be noted as a result of a pneumothorax.
    - Acute bronchospasm (wheezing) may be noted secondary to smoking crack cocaine or cocaine insufflation abuse.
- Gastrointestinal: Vomiting, diarrhea, and hyperactive bowel sounds may be noted with acute cocaine abuse.
- Neurologic
    - People who abuse cocaine may present with seizures, agitation, tremor, and hyperreflexia.
    - Focal muscular weakness or sensory changes may occur secondary to cerebral vascular accident.
- Psychiatric
    - The American Psychiatric Association recognizes a number of cocaine-induced psychiatric conditions.
    - Patients may present with delirium, psychosis, delusions, hallucinations, depression, mania, and anxiety (see History).

Causes

Numerous potential causes and risks factors have been cited as associated with cocaine abuse.

- The US National Institute on Drug Abuse estimates that approximately 10% of people who begin to use cocaine progress to heavy, chronic abuse.
- A family history of substance abuse directly correlates both with the development of cocaine abuse and with earlier age of onset of cocaine abuse.
- Approximately 50% of those who abuse illicit drugs also have a co-occurring mental disorder.
- For example, individuals who abuse cocaine have higher rates of antisocial personality disorder, depression, anxiety, and attention-deficit/hyperactivity disorder.
- Low levels of family bonding and high levels of peer antisocial activity were consistently associated with higher prevalence of illicit drug initiation among youths aged 12-21.

Differential Diagnoses

Amphetamine-Related Psychiatric Disorders
Anxiety Disorders
Attention Deficit Hyperactivity Disorder
Bipolar Affective Disorder
Delirium
Delusional Disorder
Depression
Hallucinogens
Panic Disorder
Phencyclidine (PCP)-Related Psychiatric Disorders
Schizoaffective Disorder
Schizophrenia
Schizophreniform Disorder
Sleep Disorders

Other Problems to Be Considered

Thyrotoxicosis
Major depressive disorder (agitated) with psychotic features

Workup

Laboratory Studies

- When caring for patients with suspected cocaine-induced psychiatric disorders, a number of laboratory studies may be considered. For example, a patient with marked agitation with or without psychotic features may have complications from cocaine intoxication, such as rhabdomyolysis, myocardial infarction, or renal failure. The need for specific laboratory and ancillary tests noted below will vary depending on the clinical scenario.
- Electrolytes
    - Typically, hypokalemia occurs in acute cocaine intoxication from intracellular shifts of potassium ions. This corrects as the intoxication resolves. In severe cocaine toxicity, hyperkalemia may develop and lead to cardiac dysrhythmias. The exact etiology of this is unclear, but rhabdomyolysis may be a contributing factor.
    - Metabolic acidosis (a decreased serum bicarbonate level) also may be observed in acute cocaine intoxication. This also corrects as the toxicity resolves. A progressively worsening metabolic acidosis associated with progressive altered mental status is a poor prognostic sign. Closely monitor these patients.
- Glucose: In any patient presenting with altered mental status, obtain a rapid glucose determination to rule out hypoglycemia.
- Renal function tests: Renal failure due to rhabdomyolysis and renal artery thrombosis has been reported with cocaine abuse.
- Creatine kinase: This test may help diagnose rhabdomyolysis.
- Urinalysis: If an agitated patient shows a urine-dip test result that is positive for blood but microscopic analysis reveals no red blood cells, consider urine myoglobin and rhabdomyolysis as the cause.
- Pregnancy test: All women of childbearing age should receive a pregnancy test.
- Liver function tests: Hepatic damage may occur in the acutely intoxicated patient. In addition, patients who use cocaine are at risk for infectious hepatitis, which also may result in acute mental status changes.
- Complete blood cell count: Anemia, leukocytosis, and leukopenia all may lead the clinician to consider other disease entities.
- Toxicology
    - Urine drug screens: Benzoylecgonine, a metabolite of cocaine, may be present in the urine for 60 hours after a single use of cocaine. In heavy cocaine use, it has been found in the urine as much as 22 days after cessation of cocaine use. Positive screen results are typically verified with gas chromatography with mass spectrometry.
    - Plasma cocaine levels: Because cocaine has a short half-life of 30-45 minutes and the metabolites are present in the urine for a much longer period, plasma cocaine levels typically are not as helpful as the tests that analyze for cocaine metabolites in the urine.
- Cardiac enzymes: Because of the significant prevalence of myocardial infarction associated with cocaine use, patients presenting with chest pain and cocaine abuse should be considered candidates for cardiac enzyme monitoring.

Imaging Studies

- Chest radiographs: Chest radiographs should be obtained in patients exhibiting pulmonary signs or symptoms after cocaine use. Pneumomediastinum, pneumothorax, pneumonia, pulmonary embolism, atelectasis, and other air-space diseases have been reported with cocaine use.
- Head CT scan: Patients exhibiting acute mental status changes or focal neurological signs and symptoms may require a head CT scan. Cocaine use has been associated with intracranial bleeding and embolic and thrombotic strokes.

Other Tests

- Arterial blood gas determination: This test may be useful in patients with either marked tachypnea or a decreased serum bicarbonate level to further delineate the etiology.
- ECG: An ECG should be obtained if an individual who abuses cocaine reports chest pain, shortness of breath, syncope, or palpitations. Cocaine-induced myocardial ischemia, infarction, and dysrhythmias have been reported.
    - Cocaine is a known fast sodium channel blocker of cardiac myocytes. This can lead to a delay in the upstroke of phase 1 of depolarization and subsequent widening of the QRS duration.
    - Cocaine can cause either myocardial ischemia or infarction. This can subsequently lead to ST depression or elevation depending on the ischemia/infarct region. However, many young patients who abuse cocaine have a baseline J-point elevation that may be difficult to differentiate from an infarct pattern. In addition, normal ECG findings do not rule out the possibility of myocardial injury in a patient who abuses cocaine who has chest pain.
    - Acute cocaine toxicity also may result in hyperkalemia. This can lead to a diffuse peaking of T waves, widening of the QRS, loss of P waves, or, in the most severe cases, a sinusoidal wave pattern.

Treatment

Medical Care

People who abuse cocaine present with many different medical symptoms. At times, clinicians may have difficulty determining which signs and symptoms are significant and which are not. For example, cocaine-induced chest pain is usually benign. However, these patients may have an acute coronary syndrome, pneumothorax, pulmonary embolism, pulmonary edema, or aortic dissection. Before these patients are discharged home or admitted to a psychiatric ward, the clinicians involved must evaluate the patient for other nonpsychiatric medical problems.

- Cocaine intoxication
    - Acute cocaine intoxication is usually self limited and can be managed with supportive care.
    - Benzodiazepines are the first-line therapy in treating patients who are intoxicated from cocaine and are extremely agitated. Typically, benzodiazepines can be titrated until the patient is calm and the pulse and blood pressure have stabilized.
    - Use neuroleptics with caution in acute intoxication. Acute hyperthermia syndromes associated with acute cocaine intoxication have been reported, and the use of neuroleptics with the risk of neuroleptic malignant syndrome may confuse this situation.
    - Specific laboratory tests can be ordered as necessary.
- Cocaine-induced chest pain
    - Chest pain associated with cocaine use may be from musculoskeletal, cardiovascular, or pulmonary etiologies.
    - Obtain a chest radiograph to exclude localized infiltrates, pneumothorax, pneumomediastinum, and pulmonary edema. An ECG and serial cardiac enzyme evaluation assist in excluding acute myocardial infarction and acute coronary syndromes.
    - If an acute coronary syndrome is suggested, then oxygen, aspirin, benzodiazepines, and nitroglycerin can be administered. Nonselective beta-blockers are best avoided in all patients who are intoxicated with cocaine.
- Hypertension

    - Cocaine-induced hypertension is treated first with benzodiazepines. Benzodiazepines decrease the cocaine-induced sympathomimetic drive from the CNS.
    - If this fails, phentolamine may be considered. Phentolamine is an alpha-antagonist and counteracts cocaine's vasoconstrictive effects.
    - Nitroprusside and nitroglycerin also may be considered.
- Seizures
    - Cocaine-induced seizures may be either generalized or partial and result from cocaine toxicity itself or from a cocaine-induced process, such as a cerebral vascular accident.
    - The first-line therapy is benzodiazepines, followed by barbiturates.
    - Consider a head CT scan for seizures associated with the use of cocaine.
    - No evidence exists that anticonvulsants prevent cocaine-induced seizures, and they are not recommended for this purpose.
- Rhabdomyolysis
    - Rhabdomyolysis may manifest in patients who are agitated and intoxicated with cocaine. This disorder must be recognized early to prevent secondary renal failure.
    - Obtain a creatine kinase measurement and test the urine for myoglobin. If the urinalysis reveals blood on the dipstick but no red blood cells upon microscopic examination, then myoglobinuria may be present.
    - Treatment of rhabdomyolysis focuses on ensuring adequate urine output and, possibly, alkalization of the urine.
- Dyspnea
    - Cocaine-induced dyspnea has multiple causes.
    - Obtain a chest radiograph to exclude pulmonary edema, focal infiltrate, pneumothorax, and pneumomediastinum
- Sleep disturbance: In a study by Morgan et al, modafinil was evaluated for its ability to normalize sleep patterns in chronic cocaine users. Progressive cocaine abstinence is associated with disruptive sleep outcomes. In patients who received modafinil each morning, nocturnal sleep was promoted and daytime sleepiness decreased compared with those taking placebo.[3]
- Psychiatric symptoms (see Further Inpatient Care)

Recent work has suggested that a cocaine vaccine may induce the formation of sufficient antibodies to reduce cocaine use.

Martell et al conducted a phase IIb randomized, double-blind, placebo-controlled trial to evaluate the immunogenicity, safety, and efficacy of a cocaine vaccine in cocaine-dependent and opioid-dependent individuals. Of the 115 patients recruited, 94 (82%) completed the trial. Participants were administered 5 vaccinations with placebo or succinylnorcocaine over 12 weeks. Within the vaccine group, those with serum IgG anticocaine antibody levels $\geq$43 mcg/mL had significantly more cocaine-free urine samples than those with serum levels <43 mcg/mL and those who received placebo. Reduction of cocaine use by 50% was significantly greater if a high IgG level was achieved (53% of participants) compared with a low IgG level (23% of participants) (P =0.048).[4]

Consultations

A number of consultations may be necessary when caring for a patient who abuses cocaine. Consultations to consider include medical toxicologists, regional poison control center personnel, cardiologists, neurologists, psychiatrists, substance abuse clinicians, and social services personnel, depending on the presenting signs and symptoms.

Medication

Cocaine induces 10 psychiatric disorders described in *DSM-IV-TR*. Treatment of each disorder varies. Benzodiazepines are the drugs of choice for acute cocaine intoxication with extreme agitation. Pharmacologic therapy depends on presenting signs and symptoms (eg, treat chest pain with oxygen, benzodiazepines, aspirin, and nitroglycerin). All possible pharmacotherapies for various cocaine-induced medical conditions are beyond the scope of this article. For a complete review of treating cocaine-induced nonpsychiatric effects, refer to Toxicity, Cocaine.

Avoid use of beta-blockers because of the unopposed alpha-agonist activity. The mood shifts, abnormal sleep and even delusions associated with acute cocaine intoxication or withdrawal often are transient and do not

require medications. Persistent mood disorders with mania may be treated with lithium, whereas antidepressants are advocated for mood disorders with depressive features. Antipsychotics are advocated to treat persistent psychotic disorders.

Benzodiazepines

Bind specific benzodiazepine receptor on GABA-receptor complex, thereby increasing GABA affinity for its receptor. Increase the frequency of chlorine channel opening in response to GABA binding. GABA receptors are chlorine channels that mediate postsynaptic inhibition, resulting in postsynaptic neuron hyperpolarization. The final result is a sedative-hypnotic effect that counteracts the stimulant effect of cocaine.

Diazepam (Valium)

Depresses all levels of CNS (eg, limbic and reticular formation) possibly by increasing activity of GABA. Individualize dose and increase cautiously to avoid adverse effects.

Dosing

Adult

2-10 mg PO/IV q3-4h, repeat q2-4h prn; not to exceed 30 mg/8 h; may give IM in similar doses, but absorption is erratic

Pediatric

0.05-0.3 mg/kg/dose over 2-3 min IV/IM, repeat in 2-4 h prn
0.12-0.8 mg/kg/d PO divided q6-8h; not to exceed 10 mg/dose

Interactions

Coadministration of phenothiazines, barbiturates, alcohols, or MAOIs may increase CNS toxicity

Contraindications

Documented hypersensitivity; pregnancy; severe CNS or respiratory depression

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Caution with other CNS depressants, low albumin levels, or hepatic disease (may increase toxicity); prolonged use may cause dependance; do not discontinue abruptly following prolonged use

Lorazepam (Ativan)

Sedative hypnotic with short onset of effects and relatively long half-life. Increases action of GABA (ie, major inhibitory neurotransmitter in brain). May depress all levels of CNS, including limbic and reticular formation.

Dosing

Adult

1-10 mg/d PO/IV/IM divided bid/tid

Pediatric

0.05 mg/kg/dose PO q4-8h; not to exceed 2 mg/dose

Interactions

Toxicity of benzodiazepines in CNS increases when used concurrently with alcohol, phenothiazines, barbiturates, and MAOIs

Contraindications

Documented hypersensitivity; preexisting CNS depression; hypotension

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Caution in renal or hepatic impairment (adjust dose), myasthenia gravis, organic brain disease, dehydration, and Parkinson disease
Hepatic disease is less of a concern with lorazepam than many other benzodiazepines, such as diazepam (lorazepam is only glucuronated in the liver)
Prolonged use may cause dependance; do not discontinue abruptly following prolonged use

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Midazolam (Versed)

Short-acting benzodiazepine used for acute or short-term sedation. Also exhibits amnestic effects.

Dosing

Adult

Loading dose: 0.05-0.2 mg IV over 2 min
Maintenance dose: Infuse 1-2 mcg/kg/min IV titrated to desired effect
Dosing range: 0.4-6 mcg/kg/min IV
Alternatively: 0.07-0.08 mg/kg IM

Pediatric

Sedation, anxiolysis, or amnesia
<2 years: 1-2 mg intranasally, limited by volume delivered
>2 years: 0.1-0.15 mg/kg IV over 2-3 min; as much as 0.5 mg/kg may be needed for severe anxiety

Interactions

Sedative effects may be antagonized by theophylline; coadministration with other CNS depressants increases sedation and respiratory depression; erythromycin may enhance sedative effects as a result of decreased clearance

Contraindications

Documented hypersensitivity; preexisting hypotension; sensitivity to propylene glycol (the diluent)

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Caution in congestive heart failure, pulmonary disease, renal impairment, and hepatic failure; prolonged use may cause dependance; do not discontinue abruptly following prolonged use

Antipsychotic agents

High-potency antipsychotic agents in the butyrophenone class (eg, haloperidol, droperidol) are used for rapid sedation. Easily titrated and cause less sedation and orthostasis; however, they cause extrapyramidal symptoms more often than lower-potency agents. Used short term to rapidly control psychosis.

Newer antipsychotics (eg, risperidone, olanzapine, quetiapine) are used for long-term management. Improvements over earlier antipsychotics include fewer anticholinergic effects and less dystonia, parkinsonism, and tardive dyskinesia. Affect dopamine and serotonin receptors.

Haloperidol (Haldol)

DOC for acute psychosis. Parenteral dosage form may be admixed in same syringe with 2 mg lorazepam for better anxiolytic effects.

Dosing

Adult

0.5-5 mg PO bid/tid; may titrate prn to 30 mg/d; some patients require 100 mg/d
2-5 mg IM (as lactate) q4-8h prn

Pediatric

<3 years: Not established
3-12 years: 0.25-0.5 mg/d PO bid/tid initially, increase by 0.25-0.5 mg q5-7d; not to exceed 0.15 mg/kg/d
Maintenance dose: 0.05-0.15 mg/kg/d PO divided bid/tid; not to exceed 0.15 mg/kg/d
>12 years: Administer as in adults

Interactions

May increase TCA serum concentrations and hypotensive action of antihypertensive agents; phenobarbital or carbamazepine may decrease effects; coadministration with anticholinergics may increase intraocular pressure; encephalopathylike syndrome associated with coadministration of lithium

Contraindications

Documented hypersensitivity; bone marrow suppression; severe cardiac disease; severe hypotension; liver disease; subcortical brain damage

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Severe neurotoxicity manifesting as rigidity or inability to walk or talk may occur in patients with thyrotoxicosis also receiving antipsychotics; monitor BP with parenteral administration; caution in CNS depression or cardiac disease; with history of seizures, benefits must outweigh risks; may cause neuroleptic malignant syndrome, restlessness, anxiety, extrapyramidal symptoms, dystonia, tardive dyskinesia, or Parkinsonlike syndrome

Droperidol (Inapsine)

DOC for severely disturbed and/or violent patient. Faster acting and more sedating than haloperidol but more likely to cause hypotension. May exert antipsychotic activity through dopaminergic system. Evidence suggests it alters dopamine action in CNS.

Dosing

Adult

1.25-2.5 mg IV/IM as single dose

Pediatric

<2 years: Not established
2-12 years: 1-1.5 mg/9-11 kg/dose (20-25 lb) IV/IM as single dose
>12 years: Administer as in adults

Interactions

May increase toxicity of CNS depressants

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Monitor BP if hypovolemic or administered parenterally; may decrease pulmonary arterial pressure; high incidence of tardive dyskinesia (ie, 40%); elderly patients more vulnerable to extrapyramidal symptoms; may cause life-threatening arrhythmias

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Risperidone (Risperdal)

Binds to dopamine D2-receptor with 20-times lower affinity than for 5-HT2-receptor. Improves negative symptoms of psychoses and reduces prevalence of adverse extrapyramidal effects.

Dosing

Adult

1 mg PO bid initially, slowly increase to optimum range of 4-8 mg/d; not to exceed 10 mg/d

Pediatric

Not established

Interactions

Carbamazepine may decrease serum levels; may inhibit effects of levodopa; clozapine may increase levels

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

May cause extrapyramidal symptoms (especially > 6 mg/d), hypotension/orthostasis, tachycardia, arrhythmias, amenorrhea, galactorrhea, sexual dysfunction, GI toxicity, and cholestatic jaundice

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Olanzapine (Zyprexa)

May inhibit serotonin, muscarinic, and dopamine effects.

Dosing

Adult

5-10 mg PO qd, increase to 10 mg qd within 5-7 d, adjust by 5 mg/d at 1-wk interval; not to exceed 20 mg/d

Pediatric

Not established

Interactions

CYP1A2 inhibitors (eg, fluvoxamine) may increase effects; antihypertensives may increase risk of hypotension and orthostatic hypotension; CYP inducers (eg, levodopa, pergolide, bromocriptine, charcoal, carbamazepine, omeprazole, rifampin, cigarette smoking) may decrease effects

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in narrow-angle glaucoma, cardiovascular disease, obesity, diabetes, lipidemias, prostatic hypertrophy, seizure disorders, hypovolemia, dehydration

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Quetiapine (Seroquel)

May act by antagonizing dopamine and serotonin effects.

Dosing

Adult

Initial: 25 mg bid/tid PO, increase by day 4 to 300-400 mg/d divided bid/tid; not to exceed 750 mg/d
Maintenance: 150-750 mg/d PO

Pediatric

Not established

Interactions

May antagonize levodopa and dopamine agonists; CYP3A4 inducers (eg, phenytoin, thioridazine) may reduce levels; CYP3A4 inhibitors (eg, itraconazole, erythromycin) may increase levels; may decrease warfarin clearance, monitor aPTT

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

May induce orthostatic hypotension associated with dizziness, tachycardia, and syncope; neuroleptic malignant syndrome has been reported; caution with seizures, cerebrovascular disease, and hepatic dysfunction (adjust dose); common adverse effects include somnolence, agitation, headache, and dizziness

Antidepressants

While numerous antidepressants are currently available, selective serotonin reuptake inhibitors (SSRIs) provide many advantages over past antidepressants. MAOIs should be avoided in mood disorders with depressive features. MAOIs are lethal if patient relapses from abstinence and combines them with cocaine.

Citalopram (Celexa)

Enhances serotonin activity by selective reuptake inhibition at the neuronal membrane.

Dosing

Adult

20-60 mg PO qd; 10 mg/d initially, titrate by 10 mg/wk

Pediatric

Not established

Interactions

Serotonin syndrome (ie, myoclonus, rigidity, confusion, nausea, hyperthermia, autonomic instability, coma, eventual death) may occur with simultaneous use of other serotonergic agents (eg, anorectic agents, tramadol, buspirone, trazodone, clomipramine, nefazodone, tryptophan), discontinue other serotonergic agents at least 2 wk prior to administering SSRIs; may be potentiated by azole antifungals, omeprazole, and macrolides
Despite this precaution, trazodone, nefazodone, and, to a lesser extent, buspirone, are commonly prescribed with SSRIs with very few scattered case reports of serotonergic syndrome
Has been speculated that the low prevalence of serotonergic syndrome with these medications in combination with SSRIs is due to postsynaptic serotonin receptor–blocking activity

Contraindications

Documented hypersensitivity; administration within 2 wk of MAOIs

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in cirrhosis (adjust dose), suicidal tendencies, SIADH, DM, and breastfeeding; common adverse effects include fatigue, GI toxicity, and sexual dysfunction; symptoms of weakness, lethargy, headache, anorexia, weight gain, confusion, or constipation may indicate hyponatremia

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Fluoxetine (Prozac)

Selectively inhibits presynaptic serotonin reuptake with minimal or no effect on reuptake of norepinephrine or dopamine.

Dosing

Adult

20 mg/d PO qam, increase after several wk by 20 mg/d; not to exceed 80 mg/d

Pediatric

<18 years: Not established; initial doses of 20 mg/d in children 6-14 y have been used

Interactions

Inhibits CYP3A4 and CYP2D6, therefore increases toxicity of isoenzyme substrates (eg, diazepam, trazodone, TCAs) by decreasing clearance; increases toxicity of MAOIs; may displace highly protein–bound drugs (eg, warfarin); serotonin syndrome (ie, myoclonus, rigidity, confusion, nausea, hyperthermia, autonomic instability, coma, eventual death) may occur with simultaneous use of other serotonergic agents (eg, anorectic agents, tramadol, buspirone, trazodone, clomipramine, nefazodone, tryptophan), discontinue other serotonergic agents at least 2 wk prior to administering SSRIs
Despite this precaution, trazodone, nefazodone, and, to a lesser extent, buspirone, are commonly prescribed with SSRIs with very few scattered case reports of serotonergic syndrome
Has been speculated that the low prevalence of serotonergic syndrome with these medications in combination with SSRIs is due to their postsynaptic serotonin receptor–blocking activity

Contraindications

Documented hypersensitivity; administration within 2 wk of MAOIs

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in hepatic impairment (adjust dose) and history of seizures; common adverse effects include headache, somnolence, nervousness, dizziness, nausea, diarrhea, xerostomia, general weakness, and sexual dysfunction; symptoms of weakness, lethargy, headache, anorexia, weight gain, confusion, or constipation may indicate hyponatremia

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Fluvoxamine (Luvox)

Inhibits neuronal serotonin reuptake. Does not significantly bind to alpha-adrenergic, histamine, or cholinergic receptors, thus has fewer adverse effects than TCAs.

Dosing

Adult

50 mg PO hs initially, titrate by 50 mg/d q4-7d, divide total daily dose into 2 doses once maximum therapeutic benefit achieved; if doses are unequal, administer larger dose hs; not to exceed 300 mg/d

Pediatric

<8 years: Not established
8-18 years: 25 mg PO hs initially, titrate by 25 mg/d q4-7d; divide doses >50 mg/d into 2 doses; if doses are unequal, administer larger dose hs; not to exceed 200 mg/d

Interactions

Coadministration with MAOIs increases risk of hypertensive crisis; inhibits CYP1A2, 2C9, 2C19, 2D6, and 3A4 and may potentiate effects of isoenzyme substrates (monitor plasma levels and adjust dose accordingly, consider alternative SSRI); alcohol, cimetidine, sertraline, phenothiazines, and warfarin increase toxicity; serotonin syndrome (ie, myoclonus, rigidity, confusion, nausea, hyperthermia, autonomic instability, coma, eventual death) may occur with simultaneous use of other serotonergic agents (eg, anorectic agents, tramadol, buspirone, trazodone, clomipramine, nefazodone, tryptophan), discontinue other serotonergic agents at least 2 wk prior to administering SSRIs
Despite this precaution, trazodone, nefazodone, and, to a lesser extent, buspirone, are commonly prescribed with SSRIs with very few scattered case reports of serotonergic syndrome
Has been speculated that the low prevalence of serotonergic syndrome with these medications in combination with SSRIs is due to postsynaptic
serotonin receptor–blocking activity

Contraindications

Documented hypersensitivity; administration within 2 wk of MAOIs

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in liver dysfunction (adjust dose), cardiovascular disease, history of seizures, or suicidal tendencies; common adverse effects include headache, somnolence, nervousness, dizziness, nausea, diarrhea,

xerostomia, general weakness, and sexual dysfunction; symptoms of weakness, lethargy, headache, anorexia, weight gain, confusion, or constipation may indicate hyponatremia

Paroxetine (Paxil)

Alternative DOC. Potent selective inhibitor of neuronal serotonin reuptake. Weak effect on norepinephrine and dopamine neuronal reuptake.

Dosing

Adult

10 mg/d PO initially, increase by 10 mg/d prn qwk; usual dose range is 10-60 mg/d; not to exceed 60 mg/d

Pediatric

<18 years: Not established
>18 years: Administer as in adults

Interactions

Phenobarbital and phenytoin decrease effects; alcohol, cimetidine, sertraline, phenothiazines, and warfarin increase toxicity; weak inhibitor of CYP 2D6, 1A2, and 3A4; serotonin syndrome (ie, myoclonus, rigidity, confusion, nausea, hyperthermia, autonomic instability, coma, eventual death) may occur with simultaneous use of other serotonergic agents (eg, anorectic agents, tramadol, buspirone, trazodone, clomipramine, nefazodone, tryptophan), discontinue other serotonergic agents at least 2 wk prior to administering SSRIs
Despite this precaution, trazodone, nefazodone, and, to a lesser extent, buspirone, are commonly prescribed with SSRIs with very few scattered case reports of serotonergic syndrome
Has been speculated that the low prevalence of serotonergic syndrome with these medications in combination with SSRIs is due to their postsynaptic serotonin receptor–blocking activity

Contraindications

Documented hypersensitivity; administration within 2 wk of MAOIs

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in history of seizures, mania, renal or hepatic disease (adjust dose), and cardiac disease; common adverse effects include headache, somnolence, nervousness, dizziness, nausea, diarrhea, xerostomia, general weakness, and sexual dysfunction; symptoms of weakness, lethargy, headache, anorexia, weight gain, confusion, or constipation may indicate hyponatremia

Sertraline (Zoloft)

Selectively inhibits presynaptic serotonin reuptake.

Dosing

Adult

50 mg/d PO qam, increase by 50 mg/d q2-3d to 100 mg/d, if tolerated; not to exceed 200 mg/d

Pediatric

<6 years: Not established
6-12 years: 25 mg PO qd
13-18 years: 50 mg PO qd

Doses in clinical trials ranged from 25-200 mg/d; adjust dose gradually, taking into consideration lower body weight

Interactions

Coadministration with MAOIs increases risk of hypertensive crisis; inhibits CYP2C9, 2D6, 2C19, and 3A4; may displace highly protein–bound drugs (ie, warfarin); serotonin syndrome (ie, myoclonus, rigidity, confusion, nausea, hyperthermia, autonomic instability, coma, eventual death) may occur with simultaneous use of other serotonergic agents (eg, anorectic agents, tramadol, buspirone, trazodone, clomipramine, nefazodone, tryptophan), discontinue other serotonergic agents at least 2 wk prior to SSRIs
Despite this precaution, trazodone, nefazodone, and, to a lesser extent buspirone, are commonly prescribed with SSRIs with very few scattered case reports of serotonergic syndrome
Has been speculated that the low prevalence of serotonergic syndrome with these medications in combination with SSRIs is due to their postsynaptic serotonin receptor–blocking activity

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in seizure disorders, recent MI, unstable heart disease, hepatic dysfunction (adjust dose), or renal impairment; common adverse effects include headache, somnolence, nervousness, dizziness, nausea, diarrhea, xerostomia, general weakness, and sexual dysfunction; symptoms of weakness, lethargy, headache, anorexia, weight gain, confusion, or constipation may indicate hyponatremia

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Venlafaxine (Effexor)

Inhibits neuronal serotonin and norepinephrine reuptake. Also causes beta-receptor down-regulation.

Dosing

Adult

IR: 75 mg/d PO divided bid/tid with food; may titrate by 75 mg/d q4d to 225-375 mg/d
ER: 75 mg PO qd with food; may titrate by 75 mg/d q4d to 225 mg/d

Pediatric

Not established

Interactions

Cimetidine, MAOIs, sertraline, fluoxetine, class IC antiarrhythmics, TCAs, and phenothiazine may increase effects; CYP2D6 substrate; serotonin syndrome (ie, myoclonus, rigidity, confusion, nausea, hyperthermia, autonomic instability, coma, eventual death) may occur with simultaneous use of other serotonergic agents (eg, anorectic agents, tramadol, buspirone, trazodone, clomipramine, nefazodone, tryptophan), discontinue other serotonergic agents at least 2 wk prior to SSRIs

Contraindications

Documented hypersensitivity; administration within 2 wk of MAOIs

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Coadministration or use within 2 wk of MAOIs may cause hypertensive crisis; caution in cardiovascular disorders, renal or hepatic dysfunction (adjust dose), seizure disorder, suicidal tendency, or mania; common adverse effects include headache, somnolence, nervousness, dizziness, nausea, diarrhea, xerostomia, general weakness, and sexual dysfunction; symptoms of weakness, lethargy, headache, anorexia, weight gain, confusion, or constipation may indicate hyponatremia

Follow-up

Further Inpatient Care

- Patients with marked cognitive impairment, acute psychosis, severe depression, delirium, mania, and medical complications should be considered for admission to an inpatient facility. Achieving and maintaining stable abstinence depends on the specific treatment of addiction and on the detection of comorbid psychiatric and general medical disorders. These disorders may include conditions such as anxiety, depression, and bipolar disorder.
- All patients should also be assessed for risk of harm to self or to others. This also may mandate further inpatient care. Careful assessment for suicidal ideation, plans, and level of intent to act on such ideation is crucial. If a plan and intent to act is present, psychiatric hospitalization is almost always warranted, even if requiring involuntary commitment. Also, assessing homicidal ideation, intent, and plan is critical. Not only may the patient require voluntary or involuntary psychiatric hospitalization, but one also may have a duty to warn an intended victim.
- For patients with the more severe additive problems that have not been amenable to outpatient therapy, relatively long stays in residential programs are associated with better outcomes.

Further Outpatient Care

- Outpatient treatment is effective for many patients with cocaine addiction. The goals of treatment for cocaine addiction are 3-fold: (1) achievement of abstinence, (2) prevention of relapse, and (3) rehabilitation. Treatment is available to assist individuals who are addicted to cocaine to achieve these goals.
    - Unlike the use of methadone therapy for the treatment of opiate addiction, no safe and effective cocaine replacement therapy is available as an alternative to abstinence. Currently, no FDA-approved pharmacological therapy is available for any stage of cocaine addiction treatment.
    - Numerous medications have been studied for the treatment of cocaine addiction, and many show promise. Topiramate, an anticonvulsant, shows some promise for cocaine-dependent patients. Baclofen and tiagabine, as well as modafinil have also shown promise in reducing cocaine use. Disulfiram may increase the aversive effects of cocaine and reduce its use.
    - Cognitive and behavioral therapies have been designed to prevent relapse in patients addicted to cocaine. These therapies help minimize exposure to drug cues and help modify patients' responses to cues they encounter. For example, a relapse prevention strategy may include minimizing the free cash the cocaine addict has available to buy drugs. Another example is behavioral therapy such as contingency management, in which vouchers are provided and are redeemable for goods or services contingent on performance of desired behaviors.
    - Tragically, access to existing outpatient treatments is often limited. In addition, if the addicted patient has insurance, many times the coverage for such therapy is limited, placing further stress on the patient.
- Programs specifically structured for substance abuse should be arranged for patients who abuse cocaine. Twelve-step programs for cocaine addiction may be useful. These self-help groups are based on the principles of Alcoholics Anonymous and include a commitment to abstinence. Psychiatric follow-up at a minimum of within 2 weeks of the initial evaluation aids compliance.
- A more intensive outpatient regimen of daily individual and group therapy and weekly family therapy typically is necessary for many patients. Close monitoring of patients for relapse should be part of treatment. When patients who are addicted relapse, many physicians are too ready to give up. An all-

or-nothing attitude by physicians is unrealistic with addiction. Initial treatment may fail, and relapses may occur before a stable remission is achieved.

- Patients with significant mental illness, such as major depressive disorder, bipolar disorder, posttraumatic stress disorder, and anxiety disorders, frequently require treatment specific to their illness (eg, medication, psychotherapy) in addition to a 12-step program. Programs that offer dual-diagnosis groups and 12-step programs are ideal if available. Inadequate treatment of either the mental illness or cocaine addiction increases the risk of relapse of both.
- Multiple drug addictions can also occur, such as addiction to cocaine and alcohol. Treatment, to be successful and safe, requires careful assessment of intake of all possible drugs of addiction and a treatment plan designed to both detoxify from each drug and treat each addiction.

Inpatient & Outpatient Medications

- Cocaine-induced mood disorder: Pharmacotherapy with antidepressant medications, such as SSRIs, may be necessary.
- Cocaine-induced psychotic disorder: Pharmacotherapy with antipsychotic medications may be necessary.
- Cocaine-induced anxiety disorder: Pharmacotherapy with anxiolytics, such as benzodiazepines, may be necessary. Several of the SSRIs and venlafaxine have been approved for generalized anxiety disorder, and, if anxiety or panic attacks persist, these medications may be helpful.

Transfer

- If adequate psychiatric inpatient services are not available, consider transfer to a facility with such services.
- If the patient is critically ill due to cocaine intoxication, transfer to a facility with critical care services.

Deterrence/Prevention

- The key to deterrence and prevention is education.
- Thoroughly review the complications of cocaine abuse with these patients at a level at which they can understand.
- The earlier the intervention, the more likely the patient will succeed without long-term adverse health effects.

Complications

- Rhabdomyolysis
- Acute coronary syndrome
- Cerebral vascular accidents
- Acute renal failure
- Seizures
- Hyperthermia
- Pneumothorax
- Pneumomediastinum
- Pulmonary infarct
- Pulmonary edema

Prognosis

- Among subjects who present for cocaine dependence treatment, concurrent alcoholism predicts higher relapse risk and poorer outpatient therapy attendance.
- Studies suggest that patients who have used cocaine as a primary drug of abuse for extended periods constitute a group with particularly high underlying psychopathology.

Patient Education

- Education may be a challenge in patients who are addicted to cocaine if they have a limited educational background, have a low intelligence quotient, or are resistant to educational activities.
- Complications associated with cocaine abuse may be difficult for people who are addicted to understand. An understanding of medical pathophysiology may be difficult for some patients to comprehend. They may be either resistant to the concept or lack insight into the cause-and-effect relationship of their disease process and cocaine abuse.
- Intensive education is an important part of the success of any drug treatment program.
- For excellent patient education resources, visit eMedicine's Substance Abuse Center. Also, see eMedicine's patient education articles Cocaine Abuse and Substance Abuse.
- For further family and patient education, see the following Web sites:
    - Substance Abuse Treatment, Facility Locator
    - MyAddiction.com
    - Free Vibe.com
    - Drugs of Abuse Information
    - Principles of Drug Addiction Treatment

Miscellaneous

Medicolegal Pitfalls

- Failure to thoroughly evaluate cocaine-induced chest pain in a monitored setting: In 1995, Hollander et al reported a prevalence of myocardial infarction in 5.7% of patients reporting of cocaine-induced chest pain.
- Failure to obtain a chest radiograph in cocaine-induced dyspnea: Cocaine can induce significant pulmonary pathology, including pulmonary edema, pneumothorax, pneumomediastinum, and focal parenchyma infarcts.
- Failure to adequately sedate a patient with benzodiazepines who abuses cocaine and is agitated: Benzodiazepines act to suppress the sympathomimetic drive induced by cocaine. Large doses of benzodiazepines may be required to adequately calm these patients. If adequate sedation is not obtained, complications such as rhabdomyolysis may occur. In the patient who is acutely intoxicated with cocaine, antipsychotics should be used with caution. Hyperthermic syndromes are a dreaded complication of acute cocaine intoxication and can lead to the rapid demise of such a patient. Antipsychotics are associated with hyperthermic syndromes (eg, neuroleptic malignant syndrome) and may complicate the clinical picture in a patient acutely intoxicated with cocaine.
- Failure to obtain an adequate temperature in a patient who is febrile and intoxicated with cocaine: Fever associated with cocaine abuse can be a harbinger of serious complications such as seizures, rhabdomyolysis, and renal failure. Adequate core temperatures must be obtained in patients who are intoxicated with cocaine.
- Failure to recognize the risk associated with the use of a nonselective beta-blocker in patients who are intoxicated with cocaine: Unopposed alpha-agonist activity may result in and lead to a hypertensive crisis, coronary vasospasm, or both.

Special Concerns

- Pregnancy: A significant association is evident between cocaine abuse and complications such as spontaneous abortion, placental abruption, low birth weight, intrauterine fetal demise, meconium staining, and low Apgar scores.
- Pediatrics
    - Cocaine-induced withdrawal syndromes may be observed in neonates born to women addicted to cocaine.
    - Toddlers are at increased risk of toxicity, especially seizures, if they are exposed to cocaine.
    - Cocaine crosses into breast milk and may lead to toxicity in children who are exposed.
    - Child abuse and neglect are more prevalent in families in which cocaine abuse is present.

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