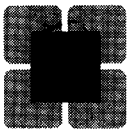

The pulmonary effects of free-base cocaine: a review

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The number of people smoking free-base cocaine, or "crack," has increased dramatically in recent years. Concomitantly, the literature describing complications of such use has grown as well. Adverse pulmonary effects are being increasingly noted, such as respiratory symptoms, pulmonary hemorrhage, pulmonary edema, asthma, and pulmonary barotrauma. These and other pulmonary effects are reviewed.

INDEX TERMS: CRACK COCAINE; RESPIRATORY TRACT DISORDERS
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THE USE OF SMOKEABLE cocaine has reached epidemic proportions in recent years. Cocaine powder, cocaine hydrochloride, cannot be effectively smoked because it decomposes when heated.[1] Rather, the "free-base" form of cocaine is prepared by adding an alkaline solution such as buffered ammonia or baking soda (sodium bicarbonate) and extracting the free base into a solvent which can then be evaporated, leaving cocaine crystals. These volatile crystals are then most often smoked through a water pipe; they may also be mixed into a cigarette and smoked. Some users prepare their own free base from cocaine powder, whereas some buy the ready-made form on the street known as "rock" or, more commonly, "crack." The smoking of free base results in rapid absorption and a rapid increase in plasma concentration resulting in a rapid "high."[1] However, the high typically is short-lived, lasting only 2 to 5 minutes, after which an intense "crash" sets in. It is this quality of rapid, intense high followed by rapid, intense crash which leads to repeated use and is a

highly addictive characteristic of free-base cocaine Typically, the user may go on binges of repeated use which may last days.[2]

COCAINE PHARMACOLOGY

Pharmacologically, cocaine has two principal effects. First, it is a local anesthetic and was widely touted as such in the 1880s before its addictive properties became known.[3] This local anesthetic effect is due to its ability to prevent the initiation and conduction of nerve impulses.[4] Second, cocaine blocks the presynaptic reuptake of catecholamine neurotransmitters, producing an excess of these transmitters at the postsynaptic receptor, which results in effective activation of the sympathetic nervous system.[4] This second property is known to cause local small-vessel vasoconstriction when cocaine is applied to mucous membranes.[5] It is also this property that likely accounts for many of the signs and symptoms of cocaine use, which may include anxiety, tremulousness, psychomotor hyperactivity, and tachycardia.[6] Cocaine may lead to complications involving many organ systems, including cardiovascular, gastrointestinal, and neuromuscular.[7] Only the pulmonary effects of cocaine are discussed in this review.

RESPIRATORY SYMPTOMS

Respiratory symptoms reported by smokers of free base include cough, sputum production, and mild shortness of breath on exertion. In addition, a proportion of free-base smokers report sputum with black or brown specks and sputum which is occasionally blood-tinged.[8]

PULMONARY HEMORRHAGE

Pulmonary hemorrhage has been reported following cocaine use. Murray et al[9] reported a case of alveolar hemorrhage in a previously healthy 36-year-old woman who had been smoking free base heavily for 2 weeks prior to admission. Her white blood count included a high percentage of eosinophils (26%). Other etiologies including vasculitis and collagen vascular disorders were effectively ruled out, and cocaine was advanced as the likely cause. The authors postulated that cocaine-induced vasoconstriction of the pulmonary circulation could result in anoxic cell damage to endothelial and epithelial cells leading to hemorrhage, or, alternatively, a direct toxic effect of cocaine or one of its adulterants could be the cause; the eosinophilia may suggest an allergic or hypersensitivity reaction. In a follow-up study by Murray,[10] 20 individuals who died from cocaine intoxication with various forms of use were studied at autopsy. In 35% of those studied, hemosiderin-laden macrophages were noted in lung tissue, and it was suggested that occult pulmonary hemorrhage may occur more commonly than is recognized. In addition, 20% had evidence of medial hypertrophy of either small or medium muscular arteries in the absence of foreign-particle embolization, suggesting an effect of cocaine on the pulmonary circulation. Whether this will cause pulmonary hypertension in the long term remains to be elucidated.

Forrester et al[11] reported four cases of an acute pulmonary syndrome temporally related to smoking free base. All patients presented with acute dyspnea and alveolar infiltrates; in addition, three had experienced hemoptysis. Biopsies performed in two of the patients revealed numerous hemosiderin-laden macrophages, as well as a prominent inflammatory-cell infiltrate. Corticosteroid treatment resulted in marked improvement in both of these patients; the other two patients experienced spontaneous improvement.

PULMONARY EDEMA

Pulmonary edema with no other identifiable etiology has been reported following cocaine use. Allred et al[12] reported a case of fatal acute pulmonary edema developing soon after intravenous use of free-base cocaine. Cucco et al[13] reported a case of noncardiogenic pulmonary edema developing 6 to 8 hours after smoking free base; bronchoalveolar lavage fluid revealed a protein concentration higher than that usually seen in normal patients or asymptomatic cigarette smokers. The authors suggested that cocaine may cause either changes in endothelial permeability or a capillary leak. More recently, five cases of pulmonary edema following the smoking of crack, with no evidence of a cardiogenic cause, have been reported[14]; all cases resolved within 24 to 72 hours, three with the help of diuretics. Of note, one patient had experienced multiple episodes of acute pulmonary edema temporally related to smoking free base in each instance.

COCAINE-INDUCED ASTHMA, HYPERSENSITIVITY LUNG DISEASE

Rebhun[15] reported three cases of an association between free-base smoking and asthma. Two of the patients had no previous history of asthma; they each developed typical asthma symptomatology with chronic use of free base. The third had a childhood history of asthma and experienced cough and shortness of breath temporally related to the use of free base; these symptoms improved with the use of theophylline and albuterol. Whether cocaine is a nonspecific irritant to the airways in susceptible individuals or whether another mechanism is responsible is unclear. The first two patients reported sputum with black specks in it while freebasing, and analysis of the first patient's sputum revealed macrophages with black pigment which proved to be hemosiderin. Recently, Rubin et al[16] reported six cases of severe asthma exacerbations requiring hospitalization provoked by cocaine use in known asthmatics. We have also seen several cases of asthmatic exacerbations requiring hospitalization secondary to smoking free base (unpublished observations). Kissner et al[17] reported a 47-year-old woman with a history of atopy who repeatedly developed transient pulmonary infiltrates, bronchospasm, eosinophilia, and pruritus after intensive use of free base on three separate occasions.[17] The eosinophilia and pruritus may make this a type of hypersensitivity lung reaction to the cocaine or one of its adulterants.

OTHER EFFECTS

Pulmonary barotrauma, including pneumomediastinum and pneumothorax, has been reported following both snorting and smoking of free-base cocaine.[18,19] The frequent, prolonged Valsalva maneuvers often performed by both snorters and smokers of cocaine in an effort to enhance the drug's effects are the most likely cause of the barotrauma; similar cases have been reported among marijuana smokers who perform the Valsalva maneuver frequently.[20]

Pulmonary infarction has been reported[21] after the use of free base and without evidence of an embolic source. The possibility of local vascular spasm and in situ thrombosis was advanced.

Nasal and nasopharyngeal complications of nasal cocaine use have been well described[22,23] and include nasal septal perforations, epistaxis, chronic rhinitis, diminished olfaction, and intranasal and pharyngeal necrosis. In free-base cocaine use, a case of inhalational upper and lower airway injury and tracheal stenosis possibly due to the intratracheal ignition of the ether vehicle used in freebasing cocaine has been reported.[24]

In 1987, Patel et al[25] reported a case of bronchiolitis obliterans organizing pneumonia confirmed by open-lung biopsy in apparent association with the use of free base; the pneumonia resolved with corticosteroids.[25] The authors speculated that the injury was related to toxins generated by the combustion of the cocaine or to unknown contaminants in the mixture.

Due to the mixing of cocaine with talc, a patient developed pulmonary talc granulomatosis after snorting cocaine; he emphatically denied any intravenous use.[26] A young user of free base developed pulmonary infiltrates after heavy use; bronchoalveolar lavage revealed large amounts of carbonaceous material thought to result from inhalation of nonvolatile by-products of cocaine burning.[27] A case of hypodermic needle aspiration in a free-base smoker has been reported[28]; the needle was used in the preparation of the free base and may have been inhaled into an airway partially anesthetized by the cocaine.

FREE-BASE COCAINE AND PULMONARY FUNCTION

There is a varied body of literature on the effects of free-base smoking on pulmonary function as measured by standard pulmonary function tests.

In 1981, Weiss et al[29] described reduction of the diffusing capacity of the lungs for carbon monoxide (DLCO) in two free-base smokers admitted to the hospital for treatment of their drug abuse. The authors hypothesized that the reduction in DLCO seen in both patients was attributable to use of free base and that free base may damage the pulmonary gas-exchange surface as a result of vasoconstriction of the pulmonary vasculature; however, one of the patients used intravenous drugs heavily and had experienced septic pulmonary emboli in the past, which may have contributed to his abnormality.

Itkonen et al[30] studied 19 free-base smokers admitted to the hospital for treatment of drug abuse and found reductions in DLCO to 70% of the predicted value or less in 10 of these patients (53%).[30] Other lung-function parameters were es-

sentially normal. To exclude acute effects, subjects did not use cocaine for at least several days before testing; most were cigarette smokers and prior marijuana smokers; all but one denied prior intravenous drug abuse. No correlation was seen between duration of use and abnormal DLCO. More recently, the Weiss group[31] reported a study of 10 free-base smokers, all of whom were also cigarette smokers; in addition, 4 of the 10 were marijuana smokers. Two different control groups were used: cigarette smokers, and those who neither smoked cigarettes nor used drugs. They found that the mean DLCO of the 10 cocaine users was 73.7% of the predicted value; the mean DLCO of the cigarette smokers was 84.4%, and that of the nonsmokers who did not use drugs was 96%. Statistical significance was seen only between the cocaine users and the nonsmokers but not between the cocaine users and the cigarette smokers.

In contrast, two uncontrolled studies reported in 1988,[32,33] as well as an uncontrolled study recently completed in our laboratory,[34] failed to find reductions of the DLCO in free-base smokers.

In order to control for the possible confounding influences of marijuana and cigarette smoking on lung function,[35] Tashkin et al[36] compared two groups of marijuana and cigarette smokers: one that also smoked cocaine, and one that did not. The incidence of spirometric abnormalities of both large and small airways was significantly higher in those who smoked cocaine compared with those who did not; however, there was no increased incidence of abnormal DLCO in the cocaine smokers. In a follow-up study, Tashkin studied subjects who were *primarily* cocaine smokers compared with a control group of nonusers of cocaine[37]; the groups were stratified according to concomitant cigarette and marijuana use. Abnormal DLCO was significantly more prevalent among cocaine users, but only in those who did not smoke marijuana or cigarettes; in those who smoked cigarettes or marijuana or both, cocaine had no additive effect on the DLCO. Spirometric abnormalities were not observed in this study.

SUMMARY

The effect of cocaine smoking on pulmonary function remains unclear; further studies with adequate controls are needed to help resolve the issue. Nevertheless, it is well documented that smoking cocaine may lead to various respiratory complications. Physicians caring for users of "crack" need to be aware of the potential disease presentations in these patients. Conversely, a thorough review of drug use is necessary in any young patient presenting with a pulmonary abnormality.

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