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Chest 2005;128;1951-1957
DOI: 10.1378/chest.128.4.1951

ISSN: 0012-3692.

The Effects of Cocaine and Heroin Use on Intubation Rates and Hospital Utilization in Patients With Acute Asthma Exacerbations*

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Background: **The use of both heroin and cocaine has been associated with asthma exacerbations. However, the magnitude of this effect has not been adequately described. The purpose of this study was to examine the association between cocaine or heroin use and asthma severity.**
Methods: **We conducted a retrospective chart review of adult patients who had been admitted to an inner-city hospital and who subsequently had received a hospital discharge diagnosis of acute asthma exacerbation. Patients were classified as *cocaine users* if they had admitted to using cocaine within 24 h of symptom onset, or if a positive drug screen result was obtained. A similar classification was employed for heroin. The severity of asthma exacerbations among cocaine and heroin users was compared to severity among *nonusers* (*ie*, individuals without evidence of having used either drug within the 24 h preceding symptom onset).**
Results: **One hundred sixty-six unique patient encounters were identified, and 152 patient records were analyzed. Of these, 27.6% (42 of 152 patients) used cocaine with or without heroin and were classified as cocaine users, while 30.9% (47 of 152 patients) used heroin with or without cocaine and were classified as heroin users. Cocaine users had longer mean lengths of hospital stay than nonusers (3.4 days vs 2.5 days; $p < 0.049$). Intubation and ICU admission were more common among cocaine users than nonusers (21.4% vs 2.3%, respectively [$p = 0.0006$]; 31.0% vs 11.5%, respectively [$p = 0.0068$]). Heroin users were also intubated more frequently than nonusers (17.0% vs 2.3%, respectively; $p = 0.0036$). Neither the length of hospital stay nor the percentage of ICU admissions was significantly different between heroin users and nonusers.**
Conclusion: **Heroin and cocaine use are common among adult asthmatic patients admitted to an inner-city hospital. Both cocaine and heroin are significantly associated with the need for intubation. Based on these findings, it may be prudent to screen adults with asthma presenting to an urban emergency department for cocaine and heroin use.**

(CHEST 2005; 128:1951–1957)

Key words: asthma; cocaine; drug abuse; heroin; intubation; status asthmaticus

Abbreviations: AMA = against medical advice; CI = confidence interval; OR = odds ratio

Asthma is a chronic, inflammatory disease, primarily involving the lower airways. It has been estimated that 14 to 15 million Americans currently have asthma,[1] and the prevalence is increasing. While individuals of all ages and races are affected, children and African Americans have some of the highest hospitalization rates for acute asthma exacerbations.[2,3] In addition, some Hispanic individuals and individuals of lower socioeconomic status have a higher prevalence and severity of asthma.[4] Leikauf and colleagues[5] cite environmental factors as one of the causes for the increasing prevalence of asthma. Some specific reasons cited for the increasing prevalence of asthma in lower socioeconomic regions

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Manuscript received August 10, 2004; revision accepted February 28, 2005.

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include poor access to health care, crowded living conditions, and the use of illicit drugs.[6]

Substance abuse, a common problem in many inner-city environments, has substantial social, economic, and medical ramifications. Cocaine was first temporally associated with the development of an acute asthma exacerbation in 1932.[7] Since that time, numerous other reports[8–25] have associated both cocaine and heroin use with asthma exacerbations. Other pulmonary complications of cocaine use have been described elsewhere.[8,9,23]

While cocaine and heroin use have been associated with asthma exacerbations, the magnitude of this effect has not clearly been established. Therefore, we conducted this study in order to quantify the magnitude of this association. Specifically, we assessed whether patients who had been admitted to the hospital for an asthma exacerbation who used these drugs experienced more severe exacerbations than patients not using these drugs.

Materials and Methods

This study was conducted at an inner-city, university-affiliated teaching hospital in Chicago. We conducted a retrospective medical record review of all adult patients (age ≥ 16 years) who had been admitted to the hospital during the calendar year of 2003 and who ultimately received a hospital discharge diagnosis of acute asthma exacerbation. If a person had multiple hospital admissions for asthma exacerbations during the calendar year, only the first hospitalization was included in the analysis.

Study Subjects

Patients were classified as *cocaine users* if they either had admitted to using cocaine within the 24 h preceding the onset of dyspnea or if they had a urine drug screen finding that was positive for cocaine metabolites. A similar classification was used for heroin. The comparison group (*nonusers*) consisted of individuals with no evidence of having used either drug within the 24 h preceding the onset of dyspnea. Patients with a positive urine drug screen finding, who reported using cocaine or heroin within the week but > 24 h before the onset of dyspnea, were also classified as nonusers. Patients were excluded from analysis if there was no documentation of drug use or a urine drug screen had not been performed.

Data Collection

Data abstracted from medical records included patient age, sex, date of visit, smoking history, history of prior intubations, initial vital signs in the emergency department, and disposition from the emergency department (*ie*, admission to a hospital floor vs ICU admission). In addition, information was collected pertaining to the use of cocaine or heroin (by patient admission), the results of a urine drug screen (if performed), intubation during the hospitalization, and length of time receiving ventilation for those patients who had been intubated. Last, information on length of stay, including the number of days spent in the ICU and the total number of days spent in the hospital were obtained.

The data were collected on a preprinted data abstraction form and then were entered into a standard spreadsheet (Excel 2000, version 9.0.2720; Microsoft; Redmond, WA) by one author (M.L.). Following data entry, the data were independently checked for accuracy by another investigator (M.E.I.).

The urine drug screen for both cocaine and heroin is performed via a homogenous immunoassay method. The urine drug screen for cocaine detects the primary inactive metabolite of cocaine, benzoylecgonine, rather than the cocaine itself. A cutoff of 300 ng/mL is considered to be a positive result for a cocaine metabolite assay by our hospital laboratory. The detection of benzoylecgonine in concentrations of > 300 ng/mL generally implies use within 1 to 2 days.[10] For opiates, the urine drug screen detects morphine and 6-acetylmorphine in the urine; a positive result indicates exposure to morphine, diacetylmorphine (heroin), codeine, hydromorphone, levorphanol, meperidine, or oxycodone/morphine. A cutoff of 2,000 ng/mL is considered to be a positive result by our hospital laboratory. Using the cutoff value of 2,000 ng/mL, a positive result generally indicates use within the previous 12 h.[26]

The need for mechanical ventilation or ICU admission, along with the total length of stay were used as markers for asthma severity. Patients who left the hospital against medical advice (AMA) were included in all data analyses except for length of stay.

Data Analysis

Independent associations were assessed via χ^2 test and Fisher Exact Test (as appropriate) for categoric variables, and *t* tests were used for assessing continuous variables. Logistic regression analysis was utilized to identify variables that were independently associated with endotracheal intubation and ICU admission. Logistic regression models were also used to obtain odds ratios (ORs) and 95% confidence intervals (CIs) for the association between risk factors (cocaine or heroin) and outcome variables (endotracheal intubation and ICU admission), after adjustment for identified confounders. All statistical analyses were performed using a statistical software package (SAS, version 8.2; SAS Institute; Cary, NC). The study received approval from the institutional review board.

Results

Between January 1, 2003, and December 31, 2003, a total of 166 unique patient encounters were identified. Of the 166 patients, 3 were excluded because neither had a urine drug screen been performed nor was there any documentation of drug use in the chart. Of the remaining 163 charts, 152 (93.3%) were located and included in the study analysis.

Eighteen patients (11.8%) had exclusively used cocaine, and 23 patients (15.1%) had exclusively used heroin. An additional 24 patients (15.8%) had used both cocaine and heroin. Thus, a total of 42 patients (27.6%) used cocaine, and 47 patients (30.9%) used heroin. The overall prevalence of either illicit drug in our study population was 42.8% (65 of 152 patients).

More than half of all subjects were women (62.5%), and the mean age of subjects was 43.2 years. African-Americans accounted for 88.1% of the

sample, with the remainder being Hispanic (11.3%) or white (0.7%). Fifty-four percent of the patients were current tobacco smokers, and 33.6% of the patients had been intubated at least once in the past. The characteristics of cocaine users compared to nonusers are presented in Table 1, and the characteristics of heroin users compared to nonusers are presented in Table 2.

Cocaine users were more likely to be tobacco smokers than were nonusers (69.2% vs 41.9%, respectively; p = 0.0046) [Table 1]. Similarly, heroin users were more likely to be tobacco smokers than were non-drug users (75.0% vs 41.9%, respectively; p = 0.0003) [Table 2].

Patients who used either cocaine or heroin were significantly more likely to be intubated during the hospitalization than were those who used neither drug. Among cocaine users, 21.4% were intubated compared to only 2.3% of non-drug users (p = 0.0006) [Table 1]. In the heroin group, similar results were obtained (17% vs 2.3%, respectively; p = 0.0036) [Table 2]. Even after adjusting for tobacco smoking, patients who used cocaine were still more likely to be intubated than those who had not used either cocaine or heroin (adjusted OR, 15.3; 95% CI, 2.7 to 86.7). A similar phenomenon was observed in the heroin group (adjusted OR, 16.5; 95% CI, 2.8 to 97.2).

Patients who used cocaine were more likely to be admitted to the ICU than those who had not used drugs (31.0% vs 11.5%, respectively; p = 0.0068) [Table 1]. Even after adjusting for tobacco smoking, patients who used cocaine were more likely to be admitted to the ICU (adjusted OR, 4.7; 95% CI, 1.6 to 13.8). When comparing the patients who used heroin to those who had not used drugs, there was no statistical difference with regard to ICU admission (Table 2).

Among cocaine users, 14% (9 of 42 patients) left the hospital AMA compared to 25% of heroin users (12 of 47 patients). Only 3% of patients (3 of 87 patients) who had used neither drug left the hospital AMA. Patients leaving the hospital AMA were not included in the analysis of length of stay.

Patients who used cocaine had significantly longer total mean (± SD) lengths of stay in the hospital than did the non-drug users (3.4 ± 2.3 days vs 2.5 ± 1.8 days, respectively; p = 0.049) [Table 1]. Among patients who had been admitted to the ICU, cocaine users received an average of 4.2 ± 2.2 days of critical care compared to 1.8 ± 1.5 days among non-drug users (p = 0.0268) [Table 1]. There was no statistical difference noted when comparing the total length of hospital stay for heroin users compared to non-drug users. However, heroin users admitted to the ICU did spend significantly more days in the ICU than did non-drug users (3.9 days vs 1.8 days, respectively; p = 0.0420) [Table 2].

Discussion

Our results found a 42.8% prevalence of cocaine or heroin use among adult patients who had been admitted for acute asthma exacerbations to an inner-city Chicago hospital. We also found that both cocaine and heroin use were associated with higher intubation rates. Cocaine use, but not heroin use, was also associated with longer lengths of stay and a higher likelihood of being admitted to the ICU. To

Table 1—*Characteristics of Cocaine Users and Non-Drug Users

Characteristics	Cocaine Users (n = 42)	Non-Drug Users (n = 87)	p Value
Mean age, yr	41.0	46.0	0.0132
Gender			
Female	52.4 (22/42)	74.7 (65/87)	0.0112
Male	47.6 (20/42)	25.3 (22/87)	
Race			
African American	42/42 (100)	79.3 (69/87)	0.0005
Hispanic	0/42 (0)	19.5 (17/87)	
White	0/42 (0)	1.2 (1/87)	
Current tobacco smokers	69.2 (27/39)	41.9 (36/86)	0.0046
Admitted to ICU	30.9 (13/42)	11.5 (10/87)	0.0068
Intubated in ED	21.4 (9/42)	2.3 (2/87)	0.0006
Mean time received mechanical ventilation,† d	3.2	2.5	0.6362
Mean time in ICU,‡ d	4.2	1.8	0.0268
Mean total length of hospital stay,§ d	3.4	2.6	0.0490

*Values given as % (No. of patients/total No. of patients), unless otherwise indicated. ED = emergency department.
†Limited to those patients who were intubated.
‡Limited to those patients who were admitted to the ICU and did not leave AMA.
§Limited to persons who did not leave the hospital AMA.

Table 2—*Characteristics of Heroin Users and Non-Drug Users

Characteristics	Heroin Users (n = 47)	Non-Drug Users (n = 87)	p Value
Mean age, yr	38.2	46.0	0.0002
Gender			
Female	55.3 (26/47)	74.7 (65/87)	0.0005
Male	44.7 (21/47)	25.3 (22/87)	
Race			
African American	100 (47/47)	79.3 (69/87)	0.006
Hispanic	0 (0/47)	19.5 (17/87)	
White	0 (0/47)	1.2 (1/87)	
Current tobacco smokers	75.0 (33/44)	41.9 (36/86)	0.0003
Admitted to ICU	21.3 (10/47)	11.5 (10/87)	0.1294
Intubated in ED	17.0 (8/47)	2.3 (2/87)	0.0036
Mean time received mechanical ventilation,† d	2.8	2.5	0.8651
Mean time spent in ICU,‡ d	3.9	1.8	0.0420
Mean total length of stay In hospital,§ d	2.9	2.5	0.2965

*Values given as % (No. of patients/total No. of patients), unless otherwise indicated.
†Limited to those patients who were intubated.
‡Limited to persons who were admitted to the ICU and who did not leave AMA.
§Limited to persons who did not leave the hospital AMA.

our knowledge, this study is the first to place numerical values on the extent to which both cocaine and heroin affect acute asthma exacerbations.

We used the length of stay as well as the need for ICU admission or intubation as markers for asthma severity. We chose these parameters because they are readily quantifiable, and subject to little interobserver variability.

In our hospital, patients < 16 years of age are admitted to the pediatric service, while patients ≥ 16 years of age are admitted to the medicine service. However, neither asthma nor illicit drug use is uncommon among teenagers. Nonetheless, in order to further minimize the confounding variables, we opted to include only those patients who were ≥ 16 years of age, in order to ensure that the same group of physicians had been responsible for the care of all patients in the study.

Pathophysiologically, there are several reasons why both cocaine and heroin might induce an acute asthma exacerbation. Direct thermal injury can occur following the inhalation of either cocaine or heroin. The bronchoconstrictive effects of morphine, which is a metabolite of heroin, have been known since the early 1900s.[27] It is now known that bronchoconstriction after heroin use is likely because of the ability of heroin to directly cause the degranulation of the mast cells, with the subsequent release of preformed inflammatory mediators such as histamines.[28] Furthermore, under normal circumstances, asthmatic patients will increase their respiratory rate in an effort to compensate for the relative hypoxemia caused by bronchoconstriction. Since opioids cause respiratory depression, it is possible that the heroin-induced respiratory depression at least partly thwarts the ability of the body to adequately compensate, thus exacerbating the severity of an asthma attack.

Heroin users were clearly intubated more frequently than patients who had used neither cocaine nor heroin. However, unlike cocaine users, heroin users did not have any longer lengths of hospital stay or more days spent receiving mechanical ventilation when compared to non-drug users. Thus, it is certainly possible that heroin induced some degree of respiratory depression, and this respiratory depression contributed to a worsening initial presentation. Nonetheless, all patients were thought to be experiencing an asthma exacerbation, and not simply respiratory depression, by at least two board-certified attending physicians (*ie*, an emergency medicine physician, who saw the patient in the emergency department, and an internist or pulmonary/critical care specialist, who treated the patient once they had been admitted to the hospital). Regardless of the etiology, the use of heroin was associated with a more severe acute asthma exacerbation than was observed in non-drug users. This initial presentation has significant implications for the early management and disposition of heroin-using patients experiencing an acute asthma exacerbation.

Cocaine and its adulterants can cause inflammation of the respiratory epithelium.[6,9] It is most likely that inhaled cocaine serves as a topical irritant on the airways.[9] In addition, some cases of cocaine-induced asthma exacerbations may occur through an IgE-mediated sensitivity.[15]

There have been several case reports[8,20] of life-threatening or fatal status asthmaticus following heroin insufflation in the same geographic region as ours. Krantz and colleagues[20] examined the preva-

lence of drug use in asthmatic patients who had been admitted to the ICU and compared the pattern of drug use in these patients to patients in the ICU who had been admitted for diabetic ketoacidosis. The authors observed that asthmatic patients in the ICU were more likely to have used heroin than were the diabetic ketoacidosis patients in the ICU. They did not observe any difference between the two groups regarding cocaine use. The reasons for the discrepancies observed in our study compared with the study by Krantz and colleagues[20] are not entirely clear. It is possible, however, that the small number of patients who used only cocaine in their study merely did not permit Krantz and colleagues[20] to appreciate the effect of cocaine.

In our study, there were no fatalities. Levenson and colleagues[13] examined asthma deaths in Cook County, IL, where our hospital is located. They reported that 31.5% of asthma deaths were confounded by substance abuse or alcohol ingestion. Cocaine was the most frequently identified drug found on toxicologic analysis in their study. Weitzman and colleagues[29] examined asthma deaths in the state of Maryland. They reported that 17.5% of asthma patients who died had a history of drug abuse, and that 12.7% of them had toxicology screens that were positive for drugs that are normally abused. While our study revealed a much higher rate of drug use, the study by Weitzman and colleagues[29] included young children. Therefore, it is likely that among adults, the percentage of patients with toxicologic screens that were positive for drugs of abuse would be higher. The study by Weitzman et al[29] also demonstrated that the majority of fatal asthma attacks are likely to begin at home. Thus, it is possible that many patients who die from an acute asthma exacerbation would do so either prior to arriving in the emergency department or while in the emergency department. Therefore, they would not have been admitted to the hospital. If this scenario is correct, we might have missed patients with the most severe cases of asthma, as we included only those patients who had been admitted to the hospital.

Given the high prevalence rate of both cocaine and heroin use in our population, it is unlikely that patient underreporting of their drug usage contributed significantly to our findings. However, even if underreporting were to occur, one would expect our observed differences to be even larger. Thus, if any drug-using patients were incorrectly categorized into a nonuser group rather than a user group, we would expect the true differences between the two groups to be even greater.

Our study was limited by its retrospective nature. As a result, we were limited to the data that were recorded in the medical chart, and our conclusions are limited by the quality and completeness of those data. Gilbert and colleagues[30] have noted that retrospective reviews can further be limited by the specific variables that are chosen for examination. For example, parameters such as medication histories, ECG results, or "appropriateness of care" are subject to much interrater variability during retrospective reviews.[30] However, in our study, most of the data abstracted included continuous variables (*ie*, days in the hospital) and dichotomous variables (*ie*, intubated or not). This fact likely reduced any bias on behalf of the abstracter and, thus, reduced some of the limitations of a retrospective study.

The routes of drug consumption were too inconsistently documented to permit any meaningful analysis. In our experience, however, most of our patients smoke these drugs, rather than inject or insufflate them. It is likely that drug-induced asthma will primarily be observed in patients who smoke the drug, as this route is associated with the most direct damage and inflammation of the bronchial epithelium.[15] Support for this theory has come from a study by Tashkin and colleagues,[31] who examined airway dynamics in patients who consumed cocaine via various routes. They observed that smoking cocaine, but not injecting cocaine, produced acute bronchoconstriction. However, it should be noted that the insufflation of cocaine has also been linked to near-fatal status asthmaticus.[18]

Another limitation of the study is that the limited sample size made it difficult to distinguish between individuals who had used one drug vs both drugs in the analysis. In other words, when assessing the association between cocaine use and the severity of asthma exacerbations, cocaine users, whether they had used only cocaine or both cocaine and heroin, were compared to non-drug users. Similarly, when assessing the relationship with heroin use, heroin users, whether they had used only heroin or both heroin and cocaine, were compared to non-drug users. It would have been ideal to have examined individuals who had used only cocaine ($n = 18$), individuals who had used only heroin ($n = 23$), and individuals who had used both ($n = 24$) separately, but the small numbers of patients would have made the adjusted logistic regression models unstable. It could, however, be argued that this detail is irrelevant. For example, if a clinician knows that a patient has used cocaine, then the clinician knows that the patient is at risk for a more severe exacerbation, regardless of whether or not other drugs were consumed simultaneously.

We only examined cocaine and heroin. While we did correct for tobacco smoking, we neither investigated nor corrected the data for other potentially confounding variables such as exposure to marijuana smoke or second-hand tobacco smoke, as well as for

the concurrent use of alcohol. Other potential confounding variables such as a history of allergies, current medications being used, and access to medical care were also not measured. The consideration of marijuana might have been important, as marijuana smoking has several pulmonary effects. While marijuana is associated with increased airway injury and hyperresponsiveness,[32,33] it is also associated with bronchodilation.[34] The combination of cocaine and ethanol produces the metabolite cocaethylene, which is believed to be more toxic to the brain and heart than either parent compound alone.[35] It is not known whether cocaethylene produces specific pulmonary complications beyond that produced by cocaine alone.

The high prevalence of both tobacco use and drug use in our population may reduce the generalizability of our study to regions where drug use is less prevalent. While there is clearly an association between cocaine use and asthma, and possibly between heroin use and asthma, the limited sample size makes it difficult for us to conclude anything about the strength of the association. Also, our study design does not permit us to evaluate a dose-response relationship. A prospective study is needed to evaluate whether the route of administration affects the degree of bronchoconstriction. In addition, a prospective study would allow us to further correct for some additional confounding variables.

It is interesting to note that there is a higher prevalence of male patients in the drug-abusing groups. This finding likely reflects the overall patterns of drug abuse, as men use drugs more frequently than women.[36] In addition, patients who used these illicit drugs left the hospital AMA much more frequently than did patients who did not use drugs. The exact reasons are not entirely clear, but could be further investigated in a prospective study. In addition, this observation would imply that clinicians should commence patient education early in the course of a hospital stay.

Conclusion

We have reported a surprisingly high prevalence of cocaine and heroin use among adults who were admitted to an inner-city hospital for asthma exacerbation. The use of cocaine is a risk factor for triggering severe acute asthma exacerbations. Heroin also appears to be a risk factor for intubation. It is probable that the high prevalence of drug use in inner-city populations contributes to the high rates of asthma exacerbations in patients in inner-city settings. Patients who have been admitted to the hospital with acute asthma exacerbations in areas where illicit drug use is prevalent should be screened for the use of cocaine or heroin.

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