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Selected Topics: Toxicology

RETROSPECTIVE REVIEW OF NEED FOR DELAYED NALOXONE OR OXYGEN IN EMERGENCY DEPARTMENT PATIENTS RECEIVING NALOXONE FOR HEROIN REVERSAL

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☐ **Abstract—Background: Emergency departments (EDs) are experiencing an increasing number of heroin overdose visits. Currently, there is no generally agreed upon ED observation period for heroin overdose patients who receive naloxone. Objectives: We aimed to determine the safety of a 2-h observation period for heroin overdose patients who receive naloxone. Methods: We performed a chart review of all patients who presented with any opioid-related complaint between 2009 and 2014 to our urban academic trauma center. Subset analysis of patients with isolated heroin overdose who received naloxone was performed, with the intent of excluding patients intoxicated with long-acting/enteral opioids. The primary outcome was the number of patients who required delayed intervention—specifically, additional naloxone or supplemental oxygen. Results: Between 2009 and 2014, we recorded 806 visits to our ED for heroin use after receiving naloxone. Twenty-nine patients (3.6%) received a repeat dose of naloxone, and 17 patients (2%) received oxygen ≥2 h after initial naloxone administration. Our 2-h intervention rate was 4.6% (N = 37). This decreased to 1.9% (N = 15) after 3 h and 0.9% (N = 7) after 4 h. Patients with polysubstance use were more likely to receive repeat naloxone ($p < 0.01$), but not oxygen ($p = 0.10$). Preexisting cardiopulmonary conditions did not correlate with a need for supplemental oxygen ($p = 0.24$) or repeat naloxone ($p = 0.30$). Conclusions: A 2-h ED observation period for heroin overdose patients reversed with naloxone resulted in a delayed intervention rate of 5%. Clinicians may consider a 3-h observation period, with extra scrutiny in polysubstance abuse.**

☐ **Keywords—emergency department; heroin; naloxone; observation period; overdose**

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INTRODUCTION

As heroin use increases, emergency departments (EDs) will continue to observe an increasing number of visits related to heroin overdose (1–3). The number of heroin users in the United States rose from 373,000 to 669,000 from 2007 to 2012 according to the National Survey on Drug Use and Health (4). Between 2005 and 2014, the national rate of opioid-related ED visits increased 99.4% from 89.1 to 177.7 per 100,000 population (2). This trend continues to effect metrics, such as ED volume, bed occupancy, and length of stay. While shorter periods of ED observation for heroin overdose patients that received naloxone could help offset this burden, safety is unknown.

After naloxone reversal, heroin overdose patients require a period of observation to monitor for

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complications, such as pulmonary edema, aspiration pneumonia, and rebound intoxication before discharge. There is currently no medically agreed upon standard observation period (5).

Goldfrank's Toxicologic Emergencies takes a conservative approach, recommending an observation period of 6 to 24 h, while the most recent systematic review suggests that 1 h may be safe (5,6). The conclusions drawn in this systematic review were based on studies conducted >10 y ago, which is problematic given the recent increase in substance use and change in heroin composition (7–10). Samples patients believe to be heroin are increasingly adulterated with many substances, the most dangerous of which are fentanyl and other synthetic opioids. The increased rate of combined overdoses and variability in opioid purity and potency differentiates today's heroin overdose patients from those studied in the past (11–14). It is not currently known whether previously recommended shorter observation periods are safe given these differences. Standard management of heroin overdose patients at our facility includes a 4-h observation period, based on our local poison control center recommendations, provider experience, and current literature.

The purpose of this study was to determine the intervention rate after a 2-h ED length of stay in naloxone-reversed heroin overdose patients. We hypothesized that decreasing our current observation period to 2 h would not cause significant risk to our patients given the known duration of action of naloxone (20–90 min) (15). We sought to determine the associations between coingestions (termed "polysubstance use") and preexisting cardiopulmonary or neuromuscular disease on rate of delayed intervention. Our intent is to inform the current discussion on ED observation periods for patients with heroin overdose after naloxone administration.

METHODS

Study Design and Setting

A retrospective chart review was performed on patients presenting to the University Hospital ED during a 6-year period from January 1, 2009 through December 31, 2014 after obtaining approval from our institutional review board. University Hospital is an urban level 1 trauma center with approximately 60,000 annual ED visits. A database was built with ED patients during this time period, comparing rates of heroin overdose–related visits to those of prescription opioids after the implementation of comprehensive opioid state regulations (termed Kentucky House Bill 1) (16). The following terms were searched in chief complaint and clinical impression fields to identify prescription opioid and heroin-related visits: overdose, OD, heroin, opiate, opioid, drug, substance abuse, Lortab, Vicodin, Opana, Percocet, needle, hydrocodone, and oxycodone.

Trained reviewers (the principal investigator and additional abstractors) filtered these visits manually. The principal investigator trained all the reviewers on inclusion/exclusion criteria. Reviewers were trained to include ED visits if the patient visit was determined to be caused directly by prescription opioid or heroin abuse. Toxicology results were viewed and recorded but were not used in isolation to determine the presence or absence of drug-related presentation. Visits were excluded if prescription opioids or heroin were not the substance abused or if they were only discovered incidentally on toxicology. We test for 3 different types of opioids ("opiates," "methadone," and "oxycodone") on urine samples, and have no opioids on the standard serum toxicology. Four thousand sixteen visits were included in the database, 692 of which were duplicates of the same patient and were excluded, leaving 3324 unique patients. Patients were categorized into 2 groups based on the drug reported: prescription opioids or heroin. Patients who abused both, or those who abused opioids but the type of opioid could not be determined, were excluded from statistical analysis.

For the current study, subset analysis was performed on patients from the above database who presented with heroin overdose and received naloxone either prehospital or in the ED. Because of the statewide prescription opioid regulations and because of a sharp increase in regional heroin use, this study focused on heroin overdoses only. A team of 4 abstractors reviewed these charts after standardized coding instruction by the principal investigator and first author to add several data points related to naloxone administration. The first author audited every record in the database for discrepancy and worked with the principal investigator to make a final determination. Because of this redundancy, no formal interobserver verification testing was performed.

Patients were excluded from the study if the history, physical, and laboratory findings did not support heroin use as the cause for ED presentation. Patients were also excluded if charts were missing key prehospital or ED data, including route, dosage, and time of initial naloxone dose. Figure 1 shows the flow diagram of subject derivation.

Methods and Measurements

Data from the electronic medical record were entered into REDCap, an online encrypted software system, to create the original database. Information was obtained from prehospital emergency medical services (EMS) run sheets that are scanned into the patient's chart, as well as ED technician, nursing, and physician documentation. Data

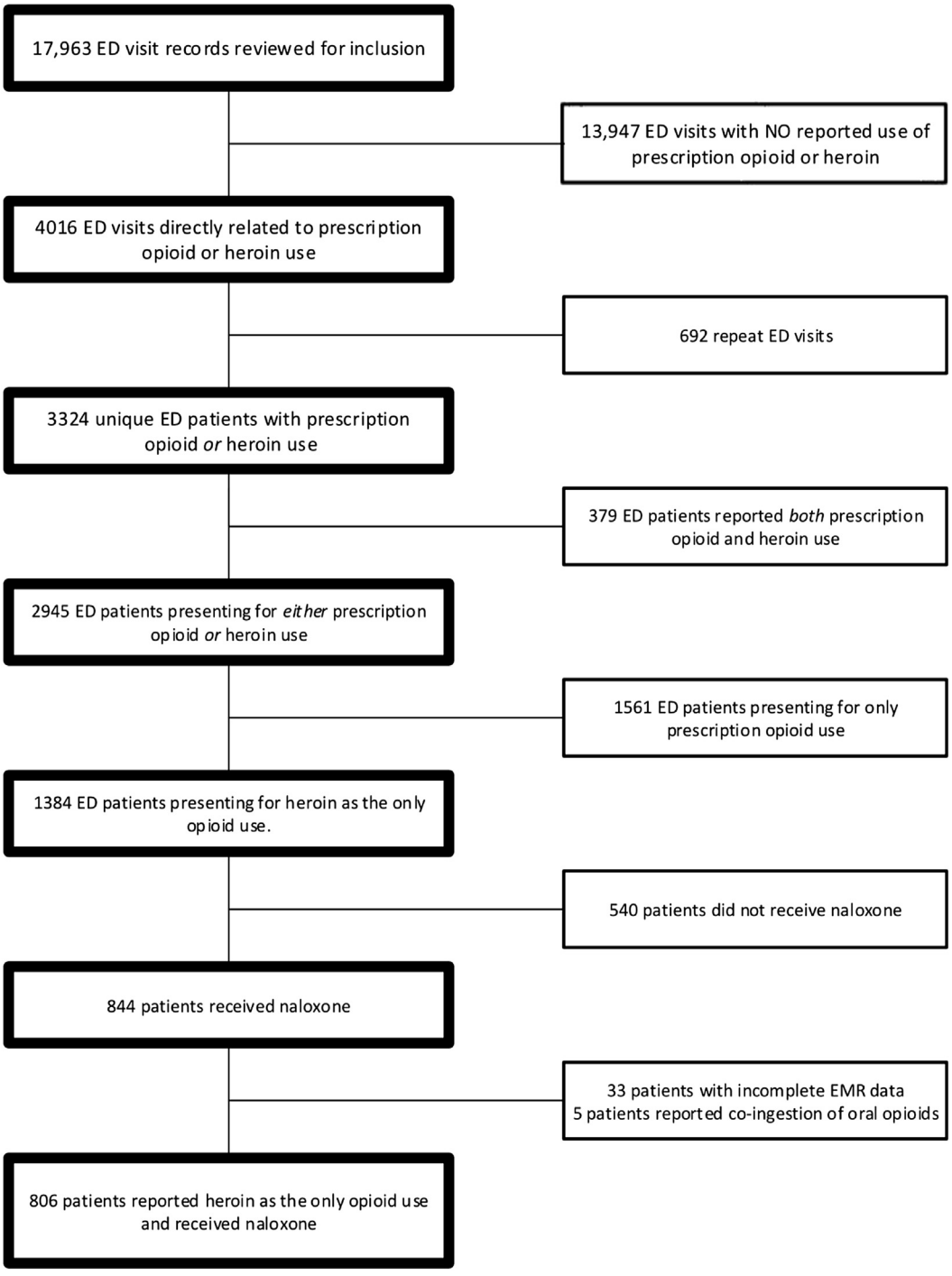

Figure 1. Flow diagram illustrating the derivation of patients for the naloxone cohort. ED, emergency department; EMR, electronic medical record.

points from the previous study included: time of ED arrival; gender; race; street address; ZIP code; departure time; mode of arrival; date of birth; insurance status; total ED visits during study period; whether home medications included opioids; coingestants (based on self-report or positive toxicology screen); naloxone use; intubation; and other complications of use (16). Study abstractors reviewed all electronic medical record charts of the heroin and naloxone subset to obtain the following additional data points: need for higher level of care; time, route, and dosage of initial naloxone administration and any subsequent doses; need for supplemental oxygen and

method of delivery; presence of preexisting cardiopulmonary disease (chronic obstructive pulmonary disease, asthma, congestive heart failure, coronary artery disease or neuromuscular disorders); toxicology results (both serum and urine); and return visits within 24 h.

Coingestants were divided into 4 categories: alcohol; depressants (including benzodiazepines, barbiturates, and antipsychotic medications); stimulants (amphetamines and cocaine); other (including tetrahydrocannabinol, phencyclidine, and lysergic acid diethylamide). Additional substances not identified as either a depressant or stimulant that were self-reported or detected on serum or urine toxicology were included in the "other" category. If naloxone was given by EMS in the prehospital setting, time of ED arrival was used as time of initial naloxone dose (time 0 min). EMS run sheets were often not available or incomplete; therefore, prehospital naloxone was considered time 0 because this represented the start of the ED observation period.

Data Analysis

In this study, we defined delayed intervention as a patient receiving either a repeat dose(s) of naloxone or supplemental oxygen. Descriptive statistics were used to characterize the patient's demographic information. The chi-square test of independence was used to determine the relationship of supplemental oxygen administered to comorbid conditions and polysubstance use. Chi-square analysis was used to determine relationships between hospital readmission and repeated naloxone, and between comorbid conditions and polysubstance use. An odds ratio generated from chi-square test of independence was reported for each outcome. We used SAS software (SAS Institute Inc, Cary, NC) for data analysis.

RESULTS

Demographic Characteristics

We found 1384 patient visits in our ED with a heroin-related complaint, and 844 received naloxone. Thirty-three visits had missing prehospital data, and 5 patients admitted to oral prescription opioid use. Statistical analysis was conducted on the remaining 806 visits (Figure 1). The 806 heroin overdose ED visits involved 713 individual patients; 76 patients had >1 visit, with the most being 5 visits. Most patients were male (n = 495, 69%) and white (n = 646, 91%).

Of the 806 different patient visits, the most common mode of transport was ambulance (n = 742, 92%). Six hundred forty-five (80%) visits ended in discharge home; 5 (0.62%) died in the ED as a direct result of heroin overdose. Thirteen subjects (2%) left the ED against medical advice. Ninety-five percent of patient visits (n = 769) remained in the ED for >2 h, while 5% (n = 37) were discharged at or before 2 h. Demographics, disposition, comorbidities, and intubation data are shown in Table 1. Most patients in this cohort abused heroin intravenously.

Patterns of Naloxone Administration

Most patient visits (n = 682, 85%) required only 1 dose of naloxone. There were 106 patient visits (13%) where 2 doses of naloxone were given and 18 (2.5%) with ≥3 doses of naloxone. Most visits received the first dose of naloxone in the prehospital setting (n = 626, 78%), while 180 (22%) received the first dose in the ED. Naloxone was administered in subjects for the indications of opioid overdose and respiratory depression from opioids. Additional doses of naloxone were administered at the discretion of the treating provider to manage recurrent

Table 1. Demographic Characteristics of Emergency Department Heroin Overdose Patients, 2009–2014

Patient Characteristics	n (%)
Gender	
Male	495 (69)
Female	218 (31)
Race	
White	646 (91)
Black/African American	62 (9)
Other	5 (0.62)
Mode of transport	
Ambulance	742 (92)
Private vehicle	61 (8)
Helicopter	2 (0.36)
Disposition	
Home	645 (80)
Admission floor/progressive care unit	68 (8)
Emergency psychiatric services	42 (5)
Admission intensive care unit	23 (3)
Against medical advice	13 (2)
Substance abuse treatment center	10 (1)
Death	5 (0.62)
Duration of ED stay	
>2 h	769 (95)
≤2 h	37 (5)
Polysubstance use	
Alcohol	142 (18)
Depressants	134 (17)
Stimulants	125 (15)
Other	52 (6)
Intubation	
Before arrival (prehospital)	40 (5)
By emergency physician	12 (2)
Preexisting cardiopulmonary or neuromuscular disease	
Asthma	23 (3)
COPD	11 (1.36)
CAD	5 (0.62)
Neuromuscular disease	4 (0.5)
CHF	4 (0.5)

CAD = coronary artery disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; ED = emergency department.

Table 2. Naloxone Administered to Patients

Description of Naloxone Administration	n (%) or Median ± IQR (Range)
Patients receiving an additional dose of naloxone, n (%)	
Patients receiving a single dose	682 (85)
Patients receiving 2 doses of naloxone	106 (13)
Patients receiving 3 doses of naloxone	14 (2)
Patients receiving 4 doses of naloxone	4 (0.5)
Naloxone doses, median ± IQR (range)	
First dose (n = 806)	2.0 ± 1.0 (0.50–10.0)
Second dose (n = 124)	1.0 ± 1.0 (0.50–4.0)
Third dose (n = 18)	1.0 ± 1.0 (0.50–2.0)
Fourth dose (n = 4)	1.0 ± 0.75 (0.50–2.0)

IQR = interquartile range.

symptoms of overdose including respiratory depression, hypoxia, and profound alteration in level of consciousness.

The median (± interquartile range) initial dose of naloxone was 2.0 mg ± 1.0 (0.4–10 mg). The initial naloxone dose included the sum of all naloxone administered within 15 min of ED arrival (Table 2). The average cumulative naloxone dose across all subjects was 3.08 mg, with a range of 1–15 mg. Nineteen patients were placed on a continuous infusion of naloxone, at rates of 1 to 6 mg per hour (average 2.37 mg/hr).

Intervention Rates 2 H after Initial Naloxone Dose

The primary outcome was the observed rate of intervention, specifically repeat naloxone or supplemental oxygen, 2 h after the initial naloxone dose (Table 3). Patients were not included if they received either oxygen or repeat naloxone >2 h after initial naloxone dose. If a patient received both interventions after 2 h, their time to intervention was defined by which intervention (oxygen or naloxone) occurred first. Figure 2 displays the time of each delayed intervention.

Repeat naloxone after 2 h. Twenty-nine patient visits involved a repeat dose of naloxone >2 h after the initial dose. Most of these patients received their initial dose prehospital (n = 22, 76%). Fourteen of these patients presented with polysubstance use, and 4 patients used >2 substances (alcohol, n = 2; stimulants, n = 7; depressants, n = 9). Three patients had documented preexisting conditions. The number of patients with polysubstance use and preexisting conditions was too small for chi-square analysis in this subgroup. After receiving a repeat dose of naloxone, 20 patients were discharged, 7 patients were admitted, and 2 patients were medically cleared for psychiatric evaluation.

Table 3. Number of Patients Who Received Repeat Naloxone or Supplemental Oxygen by Hours after Initial Naloxone Dose

Intervention, n	>2 h	>3 h	>4 h
Repeat naloxone	29	11	6
Supplemental oxygen	17	8	3
Both	9	4	2
Patient total, n (%)	37 (4.6)	15 (1.9)	7 (0.9)

Supplemental oxygen after 2 h. Seventeen patient visits involved initiation of supplemental oxygen >2 h after their initial naloxone dose. Most of these patients received their initial naloxone dose prehospital (n = 13, 76%). Eight patients presented with polysubstance use, and 3 of these presented with >2 substances (alcohol, n = 3; stimulants, n = 4; depressants, n = 4). Two patients had preexisting conditions; 1 patient had asthma and another patient had chronic obstructive pulmonary disease. After receiving supplemental oxygen, 14 patients were discharged and 3 were admitted. Nine patients received both supplemental oxygen and repeat naloxone >2 h after their initial naloxone dose and were therefore included in both groups.

Polysubstance Use and Preexisting Cardiopulmonary or Neuromuscular Disease, Irrespective of Initial Naloxone Dose

Polysubstance use was seen in >50% of patients (n = 453, 56%) (Table 1). Polysubstance use was determined based on a combination of self-report and positive toxicology results (urine or serum). There was a significant correlation between patients with polysubstance use and repeat naloxone ($p < 0.01$) as well as admission rate ($p < 0.01$), when compared with isolated heroin use. Polysubstance use was not significantly correlated with increased rate of supplemental oxygen administration ($p = 0.10$) compared with patients with isolated heroin use. There was significant correlation between the depressant subgroup and repeat naloxone administration ($p < 0.01$) as well as admission rate ($p < 0.01$). Patients in the stimulant subgroup were more likely to be admitted to the hospital compared with patients with heroin use only ($p < 0.01$) (Table 4).

In total, 47 patients had a preexisting cardiopulmonary or neuromuscular disease (Table 1). Preexisting conditions did not correlate with need for supplemental oxygen ($p = 0.24$), hospital admission ($p = 0.12$), or repeat naloxone ($p = 0.30$) (Table 4).

Additional Adverse Events

Before ED arrival, 42 patients (5.1%) were intubated; in the ED, 12 patients (1.5%) were intubated for airway

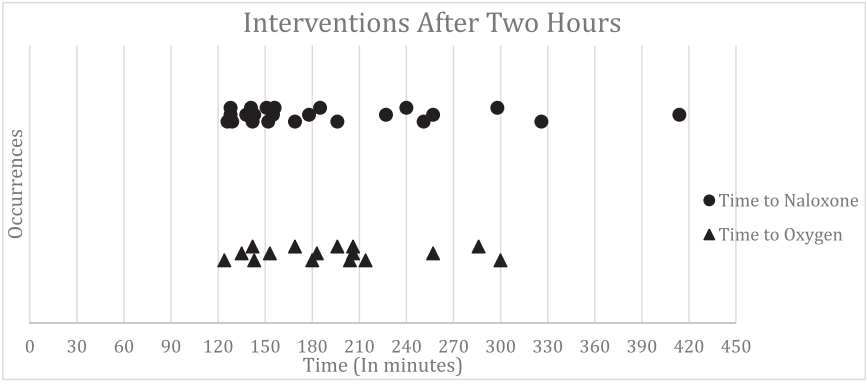

Figure 2. Time to repeat naloxone or supplemental oxygen for patients with heroin overdose after initial naloxone dose, from 2009 to 2014.

protection or respiratory depression with hypoxia. Other adverse medical events included aspiration pneumonia (n = 17, 2%), pulmonary edema (n = 7, 0.9%), non–ST-elevation myocardial infarction (n = 3, 0.4%), and cardiac arrest (n = 5, 0.6%). Of the 5 deaths, 3 were intubated by EMS, and 1 was intubated in the ED. Of patients diagnosed with aspiration pneumonia, 12 (70%) coingested other depressants, specifically alcohol or benzodiazepines. Fourteen (2%) patients returned to the ED within 24 h. None of these patients appeared to have returned to the ED because of adverse events from the initial overdose. Of these 14 patient visits, 9 presented because of repeat heroin overdose, 1 presented with alcohol intoxication, 1 presented with heroin and alcohol withdrawal, and 3 had non–opioid-related complaints.

DISCUSSION

The results of our study show a delayed intervention rate (oxygen or repeat naloxone after a 2-h ED observation period) of almost 5%. A hypothetical observation period of 1 h, as recommended in previous studies, may have led to a higher rate of delayed intervention (5,7). Further analysis showed our intervention rate decreased to 1.9% at 3 hours and 0.9% at 4 hours. Our data show the need for intervention decreases as the ED observation period increases.

Several factors differentiate current heroin overdose patients from those studied previously. First, the rate of combined overdoses with other drugs has increased nationally (11). In addition to a rise in polysubstance abuse, there has been an increased presence of more potent opioids as adulterants (fentanyl and other potent synthetic opioids) (12,17–19). The presence of these more potent adulterants further complicates the evaluation and management of the current heroin overdose patient. In addition, we observed both a higher mean initial naloxone dose and broader range of naloxone dosages than previous studies (8–10). This variability in initial naloxone dosing was observed among prehospital

Table 4. Need for Supplemental Oxygen, Admission, and Repeat Naloxone in Patients with Polysubstance Use and Preexisting Conditions during the Entire Emergency Department Visit

	Supplemental Oxygen	*p* Value, OR (CI)	Admission	*p* Value, OR (CI)	Repeat Naloxone	*p* Value, OR (CI)
Preexisting conditions, n (%)	Yes, 14 (33) No, 187 (25)	0.24, 1.49 (0.77–2.87)	Yes, 8 (19) No, 83 (11)	0.12, 1.86 (0.83–4.14)	Yes, 9 (21) No, 115 (15)	0.30, 1.49 (0.70–3.19)
Polysubstance use, n (%)	Yes, 83 (28) No, 118 (23)	0.10, 1.31 (0.95–1.82)	Yes, 55 (19) No, 36 (7)	<0.01,* 3.03 (1.94–4.74)	Yes, 59 (20) No, 65 (13)	<0.01,* 1.73 (1.17–2.54)
Depressants, n (%)	Yes, 34 (25) No, 167 (25)	0.90, 1.03 (0.67–1.58)	Yes, 24 (18) No, 67 (10)	<0.01,* 1.98 (1.19–3.29)	Yes, 31 (23) No, 93 (14)	<0.01,* 1.87 (1.19–2.96)
Alcohol, n (%)	Yes, 41 (29) No, 160 (24)	0.23, 1.28 (0.85–1.92)	Yes, 13 (9) No, 78 (12)	0.36, 0.75 (0.41–1.39)	Yes, 20 (14) No, 104 (16)	0.64, 0.88 (0.53–1.48)
Stimulants, n (%)	Yes, 27 (22) No, 174 (26)	0.35, 0.80 (0.51–1.27)	Yes, 31 (25) No, 60 (9)	<0.01,* 3.39 (2.09–5.50)	Yes, 25 (20) No, 99 (15)	0.12, 1.47 (0.90–2.39)
Other, n (%)	Yes, 15 (29) No, 186 (25)	0.50, 1.24 (0.66–2.31)	Yes, 6 (12) No, 85 (11)	0.97, 1.02 (0.42–2.46)	Yes, 3 (6) No, 121 (16)	0.05, 0.32 (0.10–1.04)

CI = confidence interval; OR = odds ratio.
* Statistically significant ($p < 0.05$).

providers (EMS) as well as emergency physicians. In some cases, initial dosages of 10 mg were given. We attribute our rate of delayed intervention and the broad range of naloxone doses to increased polysubstance abuse and increased presence of more potent opioid adulterants in our study population.

It is possible that higher dosages of naloxone contributed to the rate of interventions that were observed after 2 h. Although naloxone's rapid onset of action is ideal for reversal of opioid overdose, its duration of action (approximately 20–90 min) can be insufficient given the longer duration of heroin (3–5 h) (1,15,20–23). Fentanyl is 50 to 100 times more potent than heroin and requires significantly higher dosages of naloxone to reverse its effects, though fentanyl does have a shorter duration of action (18,19). Higher doses of naloxone effectively increase its duration of action, and in turn warrant longer periods of observation, given that rebound toxicity from the opioid will be delayed (24). The majority (60%) of patients who required interventions after 2 h received naloxone dosages ≥2 mg, and almost all (90%) received naloxone dosages ≥1 mg. By comparison, Christenson et al. reported an average naloxone dose of 0.5 mg, which may have contributed to their conclusion that a 1-h ED observation period is safe (7). It is also unclear to what degree opioid adulterants such as fentanyl played in their study.

Polysubstance abuse in our patients was associated with higher odds of requiring hospital admission and receiving additional dosages of naloxone; however, it was not associated with increased odds of requiring supplemental oxygen when compared with patients who used heroin alone. Additional substances likely cause persistent intoxication and altered mental status that is not reversed by naloxone alone. We also observed that most patients with aspiration pneumonia coingested either benzodiazepines or alcohol. The presence of coingestants is relevant to emergency providers when considering length of observation period, level of monitoring, and resource use.

Contrary to our hypothesis, the presence of preexisting cardiopulmonary or neuromuscular disease did not increase the rate of delayed intervention. The lack of statistical significance may be related to the low prevalence of comorbid conditions in this study population; therefore, our study was likely underpowered to detect an association. Heroin users are typically younger, with the majority between 20 and 30 years of age, predicting a lower rate of cardiopulmonary disease (8,10,25,26). To date, we have found no literature describing the effects of heroin use on underlying cardiopulmonary disease.

Other significant complications included aspiration pneumonia, pulmonary edema, non–ST-elevation myocardial infarction, and cardiac arrest. These adverse outcomes were observed to a far lesser extent as compared with our primary interventions. The rate of pulmonary edema in our study is consistent with previous studies (27,28). In our study, most presentations of pulmonary edema (6 of 7 patients) were detected within 2 h of ED arrival. Only 1 patient manifested symptoms of pulmonary edema after 3 h. This suggests that in our patient population, this rare but fatal complication would be detected in almost all cases if an observation period of 3 h were maintained.

Aspiration pneumonia as a complication of heroin overdose has not been well described in the literature. Our cohort had twice as many cases of aspiration as pulmonary edema. In our patients who developed aspiration pneumonia, 70% (12 of 17) coingested either alcohol or benzodiazepines compared with 43% (3 of 7) of those that developed pulmonary edema. Trends in increasing polysubstance abuse may explain why this complication was not addressed in previous literature. Of the 17 patients who developed aspiration pneumonia, 16 were evident within 2 h of ED arrival. Only 1 patient manifested signs of aspiration pneumonia 3 h after arrival. Like pulmonary edema, an observation period of 3 h would have identified all but 1 case of aspiration pneumonia.

This study contributes to the published literature by informing the discussion on an acceptable observation period for patients who receive naloxone for heroin overdose. Current literature proposes observation periods ranging from 1 to 24 h (5,6). While we found intervention rates of almost 5% after a 2-h period of observation, ED operations and throughput may suffer if observation periods are extended beyond 6 h (29).

Clemency et al. recently published a validation study using the St. Paul's Early Discharge Rule after a 1-h observation period (30). Their rule achieved a sensitivity of 84.1%, specificity of 62.1%, and a negative predictive value of 95.6%. Of note, only 1 patient with a normal screen at 1-h length of stay received an additional dose of naloxone. In our cohort of subjects, a 1-h observation period would have missed significantly more complications (repeat naloxone dosing or oxygen administration) (30).

Despite initially hypothesizing the safety of a 2-h period of observation, the authors recommend a 3-h period of observation to balance clinical safety and ED throughput. Further prospective studies similar to that performed by Christenson et al. and Clemency et al. should be conducted to validate the ideal observation period in the current population of patients who overdose on heroin (7,30). Additional studies may also seek to determine the time to recurrent opioid toxicity in patients receiving high initial doses of naloxone.

Limitations

One of the major limitations of this study is recall bias because of our reliance on patients' disclosure of heroin and polysubstance use to EMS or ED personnel. The overall prevalence of preexisting conditions is reliant on self-reporting and subject to recall bias. The use of objective data, specifically toxicology screens and provider diagnosis codes, helped to mitigate this bias. Although data were collected from the entire medical record, all variables of interest (such as the reason for supplemental oxygen) were not present for every patient. Importantly, we used repeat naloxone administration as a surrogate for recurrent opioid toxicity. It is difficult to ascertain retrospectively if repeat doses were given because of bradypnea, hypoxia, altered mental status, or other reasons, but rather the authors relied on provider clinical judgement to determine need for repeat dosing. Future prospective studies with documented reasoning for naloxone dosing and oxygen administration could overcome this limitation.

Not all patients had toxicology screens, and these were performed based on individual provider discretion. It is known that serum and urine toxicology screens are incomplete, and therefore our results likely underestimate the true rate of polysubstance abuse. We did not review all patients who presented to the ED with positive opioid toxicology screens; therefore, some patients who did not present with historical details of opioid use or diagnosis of heroin overdose could have been missed. Although confirmatory toxicology testing can be performed, literature has supported the reliability and validity of self-report (31). In addition, a positive toxicology screen does not necessarily indicate intoxication with a particular substance at the time the test was performed.

This study captured ED complications and deaths that occurred either within our ED or during inpatient admission. Out of hospital complications and deaths were not reported. The authors did not access other local community ED or medical examiner data. Only return visits to our facility within 24 h were included in statistical analysis. In addition, 37 (5%) patients were discharged at $\leq$2 h; it is possible these patients developed complications that would not have been reported if they did not seek treatment at our facility. While the overall practice pattern of emergency providers during this time period was an observation period of 4 h, individual practice patterns varied and the ultimate disposition of the patient was subject to provider discretion.

CONCLUSIONS

A 2-h ED observation period for heroin overdose patents after naloxone administration resulted in a delayed intervention rate of almost 5% in our patient population. Intervention rates decreased to 1.9% after 3 hours and 0.9 % after 4 hours of observation after initial naloxone dose. Serious complications, such as aspiration and pulmonary edema, manifested before 3 h in almost all cases. Given these rates, clinicians may consider a 3-h observation period, with extra scrutiny in polysubstance abuse.

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ARTICLE SUMMARY

1. Why is this topic important?

Patients who receive naloxone for heroin overdose continue to present in large numbers to emergency departments (EDs). There is no agreed upon ED observation period for these patients.

2. What does this study attempt to show?

We aimed to determine the expected safety of a 2-h observation period by studying the rate of interventions (oxygen or repeat naloxone) after an ED length of stay of 2 h.

3. What are the key findings?

Almost 5% of subjects in our study received naloxone or oxygen after 2 h observation in the ED. Patients with polysubstance abuse were more likely to require additional naloxone doses and were more likely to be admitted.

4. How is patient care impacted?

This analysis informs the discussion on safe observation time for patients who receive naloxone for heroin overdose. The ideal observation period could be 3 h.