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Use of Naloxone by Emergency Medical Services During Opioid Drug Overdose Resuscitation Efforts

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Abstract

Naloxone administration is an important component of resuscitation attempts by emergency medical services (EMS) for opioid drug overdoses. However, EMS providers must first recognize the possibility of opioid overdose in clinical encounters. As part of a public health response to an outbreak of opioid overdoses in Rhode Island, we examined missed opportunities for naloxone administration and factors potentially influencing EMS providers' decision to administer naloxone. We reviewed medical examiner files on all individuals who died of an opioid-related drug overdose in Rhode Island from January 1, 2012 through March 31, 2014, underwent attempted resuscitation by EMS providers, and had records available to assess for naloxone administration. We evaluated whether these individuals received naloxone as part of their resuscitation efforts and compared patient and scene characteristics of those who received naloxone to those who did not receive naloxone via chi-square, t-test, and logistic regression analyses. One hundred and twenty-four individuals who underwent attempted EMS resuscitation died due to opioid overdose. Naloxone was administered during EMS resuscitation attempts in 82 (66.1%) of cases. Females were nearly three-fold as likely not to receive naloxone as males (OR 2.9; 95% CI 1.2–7.0; *p*-value 0.02). Additionally, patients without signs of potential drug abuse also had a greater than three-fold odds of not receiving nalox-one (OR 3.3; 95% CI 1.2–9.2; *p*-value 0.02). Older individuals, particularly those over age 50, were more likely not to receive naloxone than victims younger than age 30 (OR 4.8; 95% CI 1.3–17.4; *p*-value 0.02). Women, older individuals, and those patients without clear signs of illicit drug abuse, were less likely to receive naloxone in EMS resuscitation attempts. Heightened clinical suspicion for opioid overdose is important given the recent increase in overdoses among patients due to prescription opioids.

Keywords

naloxone; opioid; heroin; emergency medical services; resuscitation

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Introduction

From 1980 to 2013 deaths due to drug poisoning in the United States increased more than 600%, from about 6,100 to 43,982.[1,2] Prescription drugs currently account for the largest share of drug overdose deaths, with opioid analgesics involved in 74.2% of prescription drug deaths.[3] Opioid analgesics, including prescribed medications such as oxycodone, methadone, and fentanyl, are intended primarily for pain relief under the direction of a physician. However, such medications are often diverted from controlled medical use through misuse, illicit trade, and sales.[4] Indeed, deaths due to opioid analgesics now surpass total deaths involving heroin or cocaine.[4]

The rapid rise in opioid overdose deaths is also associated with a rise in related emergency medical service (EMS) encounters.[5] Naloxone is an opioid antagonist whose administration during resuscitation efforts serves as an important component in EMS response to opioid overdoses.[6,7] However, appropriate administration of naloxone depends first on recognition of the possibility of opioid overdose in an EMS encounter.

To date, research on the use of naloxone in opioid overdoses has largely focused on heroin abuse. Furthermore, there remains a paucity of published information on EMS clinical decision making in potential opioid overdose cases.[8] In one previous study of opioid overdose in Rhode Island from 1997 to 2002, EMS run data indicated that such overdoses were primarily among males younger than age 50, suggesting illicit opioid use according to the authors.[9] In this study, records of physical exam findings were not sufficiently available to fully assess EMS clinical decision making around naloxone administration.

Given that most opioid overdoses have traditionally been related to heroin, for which injection paraphernalia and injection stigmata are clues to the type of drug involved, EMS providers may have difficulty identifying prescription opioid overdose cases. Patient and scene characteristics can be critical as they may be the only factors which lead providers to contemplate naloxone use, particularly if the resuscitation or treatment protocol being followed does not explicitly mention consideration of opioid intoxication. Consequently, without clear signs of drug abuse, EMS providers may not consider administering naloxone and the potential for effective opioid overdose reversal in prescription drug overdose cases could be decreased.

Beginning in November 2013, the state of Rhode Island experienced a rapid rise in drug overdose deaths.[7] In response, we conducted a comprehensive review of all Rhode Island drug overdose deaths that occurred between January 1, 2012 and March 31, 2014, to identify potential public health responses. This analysis was conducted in April 2014 and reports on one component of the investigation. Specifically, the purpose of this study was to identify factors related to nalox-one administration in EMS resuscitation efforts among medical examiner-reviewed opioid overdose deaths in Rhode Island. A better understanding of factors potentially affecting clinical decision making on nalox-one use could potentially help to increase the success of some resuscitation attempts.

Methods

Study Design and Participants

This cross-sectional study examined patient and scene characteristics of individuals who died from a drug overdose involving any opioid (including illicit substances such as heroin and/or opioid analgesics) in Rhode Island from January 1, 2012 through March 31, 2014. All study subjects were certified by the Rhode Island Office of the State Medical Examiners (OSME) to have a cause of death attributable to a drug overdose involving an opioid (multiple causes of death can be specified by a medical examiner), underwent attempted resuscitation by EMS providers, and had EMS or Emergency Department records available to assess for naloxone administration in the field. Individuals that were 15 years old or younger and those whose cases were reviewed *in absentia* (without autopsy or inspection of the body) were excluded from the study.

Rhode Island maintains a single, centralized OSME office through which all drug overdose deaths are assessed. Where available, OSME records include a scene narrative prepared by a state death investigator, police reports, EMS run sheets, Emergency Department and medical records, autopsy reports, and toxicology results. Rhode Island medical examiners can test for multiple opioids, including fentanyl, methadone, and oxycodone, as well as other opioids and opioid metabolites. Demographic information on each individual was supplemented with death certificates from Rhode Island's Office of Vital Records. Information on patient and scene characteristics was abstracted by study investigators.

In this cross sectional study, individuals who received naloxone as part of EMS resuscitation efforts were compared to those who did not receive nalox-one as part of EMS resuscitation efforts. EMS providers included both fire department and ambulance responders; it was not possible to disaggregate the identity of the provider-type.

Statistical Analyses

Among individuals deceased due to opioid overdose, we calculated the proportion who received nalox-one during their attempted resuscitation by EMS providers. Additionally, we coded patient and scene characteristics potentially observable by EMS and explored to what degree such factors predict naloxone administration. Factors examined include age, gender, race/ethnicity, body mass index (BMI), location of the overdose, signs of drug abuse, and medical examiner determination that the overdose was a suicide attempt. Signs of drug abuse were defined as any mention of drug paraphernalia from scene reports (includes needles, syringes, crude illicit substances, objects with drug residue, crack pipes, tourniquets, drug preparation tools, and others); a needle found directly in the vein of the patient by EMS, police, or other investigators; or visualization of fresh track marks noted by any official involved. For this item, only signs of illicit drug abuse were considered and thus would not include details on prescription medication bottles. Chi-square, Fisher exact, and t-tests were used to assess statistically significant differences.

Finally, unadjusted and adjusted multivariable logistic regression models were used to explore how observable patient and scene characteristics predict naloxone administration.

Adjusted models included all terms found to be significant predictors ($p < 0.05$) of naloxone administration at the unadjusted level. All analyses were conducted in SAS (version 9.3).

RESULTS

One hundred twenty-four individuals met our inclusion criteria. Of these individuals, all of whom were determined by the medical examiner to have a cause of death attributable to opioids, 82 (66.1%) received naloxone as part of EMS resuscitation attempts. Over the entire study period, January 1, 2012 through March 31, 2014, the percentage of all overdose patients who received naloxone during EMS resuscitation attempts varied by quarter, ranging from 57% to 92% (Figure 1). The highest rates of naloxone administration were observed from January 1, 2014 through March 31, 2014.

Individuals whose final toxicology results indicated the presence of heroin had received naloxone (75%) to a greater degree than individuals dying of non-heroin opiates (57.8%) (Table 1). To explore factors that may have influenced EMS providers' decisions to give naloxone in resuscitation attempts, we examined various patient and scene characteristics (Table 1). While 86.7% of patients younger than age 30 received naloxone, only 65.4% of those age 30 to 50, and 52.4% of those older than age 50 received naloxone (p-value <0.01). Females were also significantly less likely to receive naloxone than males (46.9% vs. 74.2%, *p*-value 0.01). Lastly, in situations where visible signs of potential drug abuse such as drug paraphernalia or track marks were not present, fewer patients received naloxone (55.6% vs 86.1%, *p*-value 0.04). Of the three deaths ultimately determined by the medical examiner to be suicides, none received naloxone. Naloxone administration did not differ significantly by race/ethnicity, BMI, or location of the overdose (home vs. other residence/hotel vs. outdoors/car/other/unknown).

After adjusting for all patient and scene characteristics significant at the unadjusted level, multivariable logistic regression analyses found that age, gender, and the presence of signs of potential drug abuse were associated with naloxone administration (Table 2). When compared to individuals younger than age 30, those patients age 30 to 50 were approximately three times as likely not to have received naloxone (OR 3.2; 95% CI 0.9–11.3; *p*-value 0.07) and those over age 50 were nearly five times as likely not to have received nalox-one (OR 4.8; 95% CI 1.3–17.4; *p*-value 0.02). Females were approximately three-fold as likely not to receive naloxone as males (OR 2.9; 95% CI 1.2–7.0; *p*-value 0.02). Finally, patients without signs of potential illicit drug abuse, such as drug paraphernalia or track marks, also had a three-fold increased odds of not receiving naloxone (OR 3.3; 95% CI 1.2–9.2; *p*-value 0.02).

Discussion

In this study we identified differences in the use of naloxone during EMS resuscitation attempts in Rhode Island by certain patient and scene characteristics. Among those patients found by the medical examiner to have died of an opioid overdose, a significant proportion did not receive naloxone per documented records. Consequently, our findings suggest there may exist missed opportunities for successful resuscitation. Findings demonstrate

differences in naloxone administration, favoring its administration in cases where scene characteristics suggest illicit drug use.

The proportion of resuscitation attempts in which naloxone was administered was highest in the most recent quarter. Indeed, during January through March, 2014, 92% of patients who died of an opioid overdose appropriately received naloxone in the attempted resuscitation. This may have occurred because of a higher index of suspicion among EMS personnel during a concurrent statewide overdose epidemic that was attributed largely to fentanyl produced in a clandestine laboratory and sold illegally.[10,11] However, in February 2014, Rhode Island also issued a revision to permit emergency medical technicians to administer an initial dose of intranasal naloxone by standing order.[12] It is possible that this provision also contributed to the increased naloxone usage noted during the final period of our study.

Patient-level factors that affect whether EMS providers decide to administer naloxone have not been fully elucidated. Prior literature on naloxone use by EMS has focused largely on naloxone dosing,[8,13] efficacy of administration route,[14–16] and protocol and policy formation.[6,17] Thus, we analyzed several patient and scene characteristics available to EMS providers to explore characteristics associated with naloxone administration. We found that older individuals, females, and those without signs of illicit drug use were at higher likelihood of not receiving naloxone during resuscitation attempts. These treatment patterns are consistent with the historically higher rates of heroin overdose among younger males who injected heroin.[18]

With the rise in prescription opioid abuse affecting older, female, and more chronically ill patients who use opioid analgesics orally, EMS responders must also consider opioid overdose among this patient population. Indeed, from 1999 to 2010, deaths from opioid pain medications among women increased five-fold, a rate of increase greater than that among men.[19] Raised suspicion for potential opioid overdose among broader demographic categories is important in EMS clinical decision-making. In general, naloxone is a medication with an excellent safety profile and infrequent reports of side effects. Some case reports have posited a possible rare association with pulmonary edema, seizures, or arrhythmias; however, such patients are often critically ill and these conditions may be a consequence of the underlying disease or injury process, such as extreme opioid toxicity or hypoxia.[20] Patients undergoing opioid intoxication reversal can also become combative. Nonetheless, in patients undergoing EMS resuscitation where there is suspicion for opioid intoxication, empiric naloxone administration may help save patient’s lives.

Some important limitations of this study should be noted. First, analysis of naloxone use patterns was dependent on documentation of naloxone use in clinical records, which often occurred through hand written notes. In some instances, naloxone may have been used but not recorded by providers. Other research on EMS systems has detected a need for improvement and standardization of data collection[21] and Rhode Island has since adopted an improved method to capture naloxone use. Additionally, record of what scene and patient characteristics (e.g., evidence of illicit drug use) were present is also dependent on official documentation; misclassification could occur in the event of incomplete recording of such characteristics. Second, as in many states, naloxone administration by emergency medical

technicians traditionally required authorization by medical control. Third, our analysis was restricted to those individuals who met all inclusion criteria and who had records available at the time of the study. Some degree of selection bias, though unquantifiable, may be present. Fourth, it is impossible to determine retrospectively the degree to which naloxone was clinically indicated. Although we have included all patients in whom resuscitation was attempted, all patients in our sample ultimately died. Providers may have felt that naloxone would not benefit the patient if it appeared that an early window for intervention had passed. Nonetheless, naloxone may lead to rhythm improvement in cardiac arrest and has been recommended with suspicion of opioid overdose.[22] Lastly, although we focused our analysis on patient and scene characteristics, it remains unclear to what degree providers use these clues to guide treatment decision making.

Conclusion

This research suggests that some individuals who die of opioids may not be initially recognized by EMS providers as suffering from opioid intoxication. Because of the growing diversity of individuals who are victims of opioid overdose, there exists a need for a high level of clinical awareness of the possibility of opioid overdose among first responders. Education of first responders on the changing demographics of opiate overdose patients may help in increasing recognition of those patients who may benefit from nalox-one administration. Treatment of opioid overdose with naloxone is highly effective,[23] and interventions provided by EMS on scene could lead to improved patient outcomes. Multifactorial strategies are needed to effectively prevent and respond to opioid overdose deaths, including early administration of nalox-one by bystanders,[24] improved physician prescribing practices,[25] and targeted state policies and laws.[26] For EMS, improving response to opioid overdose may result in additional successful resuscitations.

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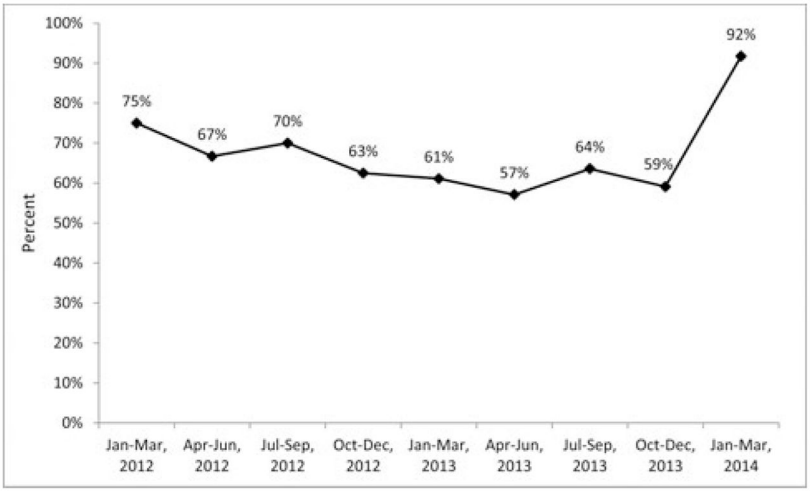

Figure 1.

Proportion of opioid-related deaths in which naloxone was administered by emergency medical services, Rhode Island, January 2012–March 2014 (*N* = 124).

Table 1

Administration of naloxone during emergency medical services resuscitation attempts by patient and scene characteristics of individuals deceased due to opioid overdose (*N* = 124)

		Naloxone administered		Naloxone not administered		
		n	**%**	***n***	**%**	***p*-value**
Heroin present on toxicology at death	Yes (*N* = 60)	45	75.0	15	25.0	0.04
	No (*N* = 64)	37	57.8	27	42.2	
Age (in years)	Younger than 30 (*N* = 30)	26	86.7	4	13.3	< 0.01
	30 to 50 (*N* = 52)	34	65.4	18	34.6	
	Older than 50 (*N* = 42)	22	52.4	20	47.6	
Gender	Male (*N* = 89)	66	74.2	23	25.8	<0.01
	Female (*N* = 35)	16	45.7	19	54.3	
Race/ethnicity[a]	Non-Hispanic White (*N* = 99)	66	66.7	33	33.3	0.85
	Non-Hispanic Black[b] (*N* = 8)	6	75.0	2	25.0	
	Hispanic (*N* = 11)	6	54.6	5	45.5	
Body Mass Index (mean)			31.0		32.5	0.33
Location of overdose	Home (*N* = 81)	52	64.2	29	35.8	0.21
	Other residence/hotel (*N* = 28)	22	78.6	6	21.4	
	Outdoors/Car/Other/Unknown (*N* = 15)	8	53.3	7	46.7	
Visible signs of potential drug abuse present (e.g., paraphernalia, track marks)	Yes (*N* = 43)	37	86.1	6	14.0	< 0.01
	No (*N* = 81)	45	55.6	36	44.4	
Suicide attempt	Yes (*N* = 3)	0	0.0	3	100.0	0.04
	No (*N* = 121)	82	67.8	39	32.2	

Percentages represent row percentages.

P-values from chi-square, Fisher exact, or t-test, where appropriate.

[a] Race/ethnicity information missing for 6 individuals.

[b] Includes one individual for whom mixed race (Black and White) was reported.

Table 2

Association of patient and scene characteristics with no administration of naloxone during emergency medical services resuscitation attempts among individuals deceased due to an opioid overdose (*N* = 124)

		Unadjusted			Adjusted[a]		
		OR	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Age (in years)	Younger than 30 (*N* = 30)	1 (ref)	–	–	1 (ref)	–	–
	30 to 50 (*N* = 52)	3.4	1.0–11.4	0.04	3.2	0.9–11.3	0.07
	Older than 50 (*N* = 42)	5.9	1.8–19.9	<0.01	4.8	1.3–17.4	0.02
Gender	Male (*N* = 89)	1 (ref)	–	–	1 (ref)	–	–
	Female (*N* = 35)	3.4	1.5–7.7	<0.01	2.9	1.2–7.0	0.02
Race/ethnicity[b]	Non-Hispanic White (*N* = 99)	1 (ref)	–	–			
	Non-Hispanic Black[c] (*N* = 8)	0.7	0.1–3.5	0.63			
	Hispanic (*N* = 11)	1.7	0.5–5.9	0.43			
Body Mass Index (per point increase)		1.02	0.98–1.07	0.33			
Location of overdose	Home (*N* = 81)	1 (ref)	–	–			
	Other residence/hotel (*N* = 28)	0.5	0.2–1.3	0.17			
	Outdoors/Car/Other/Unknown (*N* = 15)	1.6	0.5–4.8	0.43			
Visible Signs of potential drug abuse (e.g., paraphernalia, track marks)	Yes (*N* = 43)	1 (ref)	–	–			
	No (*N* = 81)	4.9	1.9–13.0	<0.01	3.3	1.2–9.2	0.02
Suicide attempt	Yes (*N* = 3)	NA[d]					
	No (*N* = 121)						

Percentages represent row percentages.

[a] Adjusted model includes all variables with $p < 0.05$ at the unadjusted level.

[b] Race/ethnicity information missing for 6 individuals.

[c] Includes one individual for whom mixed race (Black and White) was reported.

[d] NA = Not applicable. Unable to be estimated due to cell size of 0.

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