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Use of Intranasal Naloxone by Basic Life Support Providers

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Abstract

Study Objectives: Intranasal delivery of naloxone to reverse the effects of opioid overdose by Advanced Life Support (ALS) providers has been studied in several prehospital settings. In 2006, in response to the increase in opioid-related overdoses, a special waiver from the state allowed administration of intranasal naloxone by Basic Life Support (BLS) providers in our city. This study aimed to determine: 1) if patients who received a 2-mg dose of nasal naloxone administered by BLS required repeat dosing while in the emergency department (ED), and 2) the disposition of these patients. **Methods:** This was a retrospective review of patients transported by an inner-city municipal ambulance service to one of three academic medical centers. We included patients aged 18 and older that were transported by ambulance between 1/1/2006 and 12/12/2012 and who received intranasal naloxone by BLS providers as per a state approved protocol. Site investigators matched EMS run data to patients from each hospital's EMR and performed a chart review to confirm that the patient was correctly identified and to record the outcomes of interest. Descriptive statistics were then generated. **Results:** A total of 793 patients received nasal naloxone by BLS and were transported to three hospitals. ALS intervened and transported 116 (14.6%) patients, and 11 (1.4%) were intubated in the field. There were 724 (91.3%) patients successfully matched to an ED chart. Hospital A received 336 (46.4%) patients, Hospital B received 210 (29.0%) patients, and Hospital C received 178 (24.6%) patients. Mean age was 36.2 (SD 10.5) years and 522 (72.1%) were male; 702 (97.1%) were reported to have abused heroin while 21 (2.9%) used other opioids. Nasal naloxone had an effect per the prehospital record in 689 (95.2%) patients. An additional naloxone dose was given in the ED to 64 (8.8%) patients. ED dispositions were: 507 (70.0%) discharged, 105 (14.5%) admitted, and 112 (15.5%) other (e.g., left against medical advice, left without being seen, or transferred). **Conclusions:** Only a small percentage of patients receiving prehospital administration of nasal naloxone by BLS providers required additional doses of naloxone in the ED and the majority of patients were discharged. **Key words:** naloxone; opioid overdose; basic life support

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Introduction

Opioid overdose and death has reached epidemic proportions in the United States and is continuing to increase even in the most recent national data.[1,2] Opioids were responsible for 28,647 deaths in 2014 alone.[3] The problem is exacerbated by stronger heroin formulations as well as adulteration by potent synthetic opioids like fentanyl and its analogues.[4–7] Furthermore, there is evidence that prescription opioid use has waned while heroin abuse has increased.[8] The antidote for opioids is naloxone, a competitive inhibitor of the opioid mu receptor that attenuates the effects of overdose, most importantly respiratory depression that portends death.[9]

Although typically administered via the intramuscular (IM) or intravenous (IV) route, the rich blood supply of the nasal mucosa allows for efficient drug absorption and the avoidance of first-pass hepatic metabolism that would be seen with oral administration.[10,11] Studies have highlighted the possibility of intranasal (IN) delivery of naloxone to reverse the effects of opioid overdose in the prehospital setting.[12–17] These prior studies have largely focused on naloxone delivery administered by paramedics with specialized training serving as Advanced Life Support (ALS) providers. In 2006, in response to the increase in opioid-related overdoses, Boston EMS (the city's ambulance provider) obtained a Commonwealth of Massachusetts Office of Emergency Medical Services Special Project Waiver for the administration of intranasal naloxone by Basic Life Support (BLS) providers.[18]

Allowing BLS providers to provide treatment vs. ALS providers for opioid overdose would be advantageous to EMS systems. If the practice proves to be safe, it can lead to dispatching BLS providers to presumed opioid overdoses, which in turn has potential for significant operational cost savings to the EMS program.[19] As there are far more BLS providers than ALS providers in most systems,[20] nasal naloxone by BLS could shorten the time from overdose to antidote administration.[21]

In this study, we aimed to determine the clinical course of patients receiving intranasal naloxone by BLS providers. We collected data from electronic EMS records of the documented cases of intranasal naloxone administration by BLS providers and then matched these patients with their hospital electronic medical record (EMR). The primary objective was to determine if the 2-mg dose of nasal naloxone administered by BLS was sufficient or if the patient required a repeat dosing while in the emergency department (ED). The secondary objective was to determine the ED dispositions for these patients.

METHODS

This was a retrospective chart review of patients who received intranasal naloxone by Boston EMS BLS providers between January 1, 2006 and December 12, 2012 and were transferred to one of three hospitals in the city of Boston. These hospitals received about 75% of the BLS transports for suspected opioid-related overdose during the study period. Boston EMS is the primary ambulance service for the City of Boston and is responsible for dispatching all of its 9-1-1 calls. It employs a two-tiered, third service model, serving an area with a daytime population of approximately 1,000,000. Annually, there are about 110,000 calls for service and 85,000 transports.

Under this program, medics were trained with a 1-hour lecture and 30 minute practical session on the use and administration of nasal naloxone, including the need for bag-valve-mask ventilation prior to administration. Naloxone was provided as a kit containing a prefilled syringe containing 2 mg of naloxone with a mucosal atomizing device. The indications for use was altered mental status with respiratory rate <8 breaths/minute and a known or suspected opioid abuse based on history, presentation and/or supporting information at the scene.

The Boston EMS database maintains a record of each instance in which nasal naloxone was administered. The EMS electronic patient care record data included medications administered and also documentation of whether or not the naloxone given had an effect on the patient. Effect, for the purpose of BLS naloxone administration, was defined as improvement in respiratory rate over 8 breaths per minute and/or improvement in mental status using the AVPU scale. Improvement was defined as increased level from either unresponsive or responsive to pain only.

After appropriate data use agreements and institutional board approvals were obtained from all three sites, an investigator at each hospital received the following information: study ID number, date and time of presentation, gender, age, and suspected overdose etiology. Based on this information, the electronic medical record of each hospital was queried to match the prehospital data with the correct hospital EMR of each patient for further analysis. Further information (e.g., recorded name) was provided only if the patient data was still not located with the initial information. This step was utilized to protect patient confidentiality as much as possible. Basic demographic information was recorded for all patients.

The primary outcome of interest was the number and percent of patients who received an additional dose of naloxone post-BLS administration. Site investigators reviewed all matched EMRs, including all physician orders, notes, and nursing notes, to determine if a second administration of naloxone was documented. The secondary outcome was the disposition of each patient (i.e., discharged, admitted to an inpatient or intensive care unit, transferred, left against medical advice, or left without being seen). We report the frequencies and percentages of patients discharged or admitted to an inpatient or intensive care unit. Data were analyzed using SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

During the study period, 793 patients received nasal naloxone by BLS and were transferred to one of the three hospitals. Nasal naloxone was documented to "have an effect" for 747 (94.2%) patients. BLS transported 677 (85.4%) times, and there was ALS intervention for 116 (14.6%) patients. Eleven patients (1.4%) were intubated prehospital. Of the total cohort, 724 (91.3%) were successfully matched to the receiving hospital's EMR. Hospital A received 336 (46.4%) patients, Hospital B received 210 (29.0%) patients, and Hospital C received 178 (24.6%) patients. Mean age was 36.2 (SD 10.5) years and 522 (72.1%) were male. An additional naloxone dose was given in the ED to 64 (8.8%) patients. ED dispositions were: 507 (70.0%) discharged, 105 (14.5%) admitted, and 112 (15.5%) other (73 left without being seen, 27 left against medical advice, 7 transferred to other facilities, 4 unknown, and 1 expired). Detailed results are displayed in Table 1.

DISCUSSION

Our research indicates that the 2-mg dose of nasal naloxone administered by BLS had an effect in over 95% of patients, and that <10% of patients required a repeat dose in the ED. Furthermore, about 15% of patients who received IN naloxone by BLS required subsequent admission to the hospital. Based on these findings, our EMS system has continued to allow BLS providers to provide the antidote in this fashion. Expansion of naloxone availability is paramount toward responding to the opioid epidemic.[22,23] Communities that enacted programs for overdose education and nasal naloxone distribution among the lay public had lower rates of opioid-related overdose death than communities that did not[24] and both community and ED based naloxone distribution programs have proliferated.[25,26] Law enforcement has also demonstrated ability to safely reverse opioid overdose.[27]

TABLE 1. Descriptive analysis: naloxone administered by Basic Life Support (BLS) providers

	Hospital A ($n = 336$)	Hospital B ($n = 210$)	Hospital C ($n = 178$)	Total ($n = 724$)
Mean (SD); median (min, max)				
Age	36.6 (10.6); 36 (18, 61)	36.3 (10.9); 34 (18, 69)	35.3 (9.8); 33.5 (18, 64)	36.2 (10.5); 35 (18, 69)
Not Documented/Unknown	2	0	0	2
n (column %)				
Gender				
Male	250 (74.4)	150 (71.4)	122 (68.5)	522 (72.1)
Female	86 (25.6)	60 (28.6)	56 (31.5)	202 (27.9)
Overdose etiology				
Heroin overdose	328 (97.6)	201 (95.7)	174 (97.8)	703 (97.1)
Other opioid abuse	8 (2.4)	9 (4.3)	4 (2.3)	21 (2.9)
Naloxone had an effect				
Yes	318 (94.6)	204 (97.1)	167 (93.8)	689 (95.2)
No	11 (3.3)	5 (2.4)	7 (3.9)	23 (3.2)
Not Documented/Unknown	7 (2.1)	1 (0.5)	4 (2.3)	12 (1.7)
Additional dose of naloxone in ED				
Yes	16 (4.8)	21 (10.0)	27 (15.2)	64 (8.8)
No	320 (95.2)	188 (89.5)	151 (84.8)	659 (91.0)
Not Documented/Unknown	0	1 (0.5)	0	1 (0.1)
ED Disposition				
Admitted	52 (15.5)	31 (14.8)	22 (12.4)	105 (14.5)
Discharged	220 (65.5)	162 (77.1)	125 (70.2)	507 (70.0)
AMA	11 (3.3)	0	16 (9.0)	27 (3.7)
Transfer	5 (1.5)	0	2 (1.1)	7 (1.0)
AWOL/LWBS/LWT	44 (13.1)	17 (8.1)	12 (6.7)	73 (10.1)
Deceased	1 (0.3)	0	0	1 (0.1)
Not Documented/Unknown	3 (0.9)	0	1 (0.6)	4 (0.5)

Note: n = 724. AMA = left against medical advice; ED = emergency department; AWOL = absent without leave/eloped; LWBS/LWT = left without being seen/left without treatment.

Barton and colleagues have demonstrated the safety of nasal naloxone by pre-hospital providers.[12,13] They discovered that >80% of patients responded to nasal naloxone, which had the further benefit of reducing the risk of blood-borne exposure and disease that can occur with needle-based administration of the antidote.

Davis and colleagues conducted a national systematic legal review of naloxone policies for EMS in the prehospital setting.[28] The group found that the *National EMS Scope of Practice Model* created by the National Highway Traffic Safety Administration (NHTSA) in 2007 listed administration of a narcotic antagonist as a requisite skill for ALS and intermediate life support (ILS) staff but not for BLS providers.[29] Furthermore, in rural areas BLS providers may be the only level of service available.[20] Respiratory support in the form of bag-valve-mask ventilation with supplemental oxygen is available to BLS providers until ALS arrival. However, bag-valve-mask ventilation may lead to the dangerous complication of aspiration.[30] The only definitive treatment is reversal of the underlying cause of hypoventilation. As of November 1, 2013 in the 53 jurisdictions studied, only 12 (23%) permitted BLS providers to administer naloxone.[28] Additionally, there was wide variation in the dosing protocols and routes of administrations between jurisdictions.

The question that remains is why layperson administration of naloxone has become commonplace[26] while BLS administration has not. Talking auto-injectors (Evzio, kaléo Pharma, Richmond, VA) and nasal devices that require no assembly (Narcan, Adapt Pharma, Radnor, PA) have been approved and clearly target non-medical providers. The vast majority of drug users (88.5%) said that they would be willing to administer a medication to another drug user in the event of an overdose.[31]

For prehospital providers, the question may be one of patient safety. As recently as 2008, there was not enough evidence to support the IN route for prehospital administration.[17] However, several subsequent studies have demonstrated that it is safe, that rates of response are within 10 minutes are similar to the IM or IV route, and that there was no difference in mean response time.[11–15] Supplemental naloxone may need to be given more frequently after the IN route (compared to IM),[16] but there is likely minimal harm incurred by giving a second dose of naloxone, and since the IN route works in the vast majority of cases, it can decrease time to antidote.

Kerr and colleagues also did a similar study of 172 patients in the prehospital setting.[32] There were no differences in rates of response in 10 minutes (IN 72% vs. IM 78%) and mean response time (IN 8.0 minutes vs. IM 7.9 minutes), although need for supplementary naloxone was higher in the IN group (IN 18.1% vs. IM 4.5%). In their study, only one patient had a major adverse event, a seizure in a patient who received IM naloxone. That said, EMS personnel should be aware of minor adverse events that are common with both IM and IN delivery, such as agitation and/or violence (IN 6.0% vs. IM 7.9%), nausea and/or vomiting (IN 8.4% vs. IM 7.9%), and headache (IN 4.8% vs. IM 3.3%), as reported by Kerr et al.[28] Another paper found that only 1.3% suffered severe adverse effects within ten minutes after naloxone administration (one asystole; three generalized convulsions; one pulmonary edema; and one violent behavior).[33]

In addition to the adverse effects, IN naloxone is not a panacea solution. Although IN naloxone has reversed a patient who mistakenly overdosed on fentanyl that was sold to him as heroin,[34] another case report of failure of IN naloxone to reverse a fentanyl overdose is illustrative.[35] Intoxication with longer-acting, higher potency opioids, such as fentanyl and other synthetic opioids, may not be as easily reversed as heroin, and the increased prevalence of these medications will likely portend more naloxone treatment failures and more deaths.[3] Furthermore, EMS providers need to first recognize the possibility of opioid overdoses to administer the antidote. One study demonstrated that about 35% of patients who died of an opioid-related overdose after EMS resuscitation did not have naloxone administered, most commonly for women, individuals over age 50, and those without clear signs of potential drug abuse.[36]

In our cohort, there was a documented effect of nasal naloxone in 95% of patients, as reported by EMTs on their electronic patient care report documentation. This number is higher than that documented in prior studies, but may be due to our definition of "effect." This response rate could also be a function of the emphasis in the protocol to start with effective bag-valve-mask ventilation prior to administration of naloxone. A more accurate measure is the need for additional naloxone administered in the ED. The fact that <10% required this intervention indicates success in the vast majority of cases.

In addition to being the largest cohort of pre-hospital IN naloxone administration described, a particularly novel part of our study is the evaluation of the final ED dispositions of patients after transport. We found that about 15% of these patients were admitted. Determining the cause of admission was not an aim of the study, so it is unknown if the admission was for opioid overdose or for concomitant diagnoses where opioid overdose was not the reason for the patient's altered mental status. Although not an aim of our study initially, we did however review the Massachusetts Registry of Vital Records for all 105 subjects that were admitted. Fourteen death records were identified, but only two of those occurred within close proximity of the initial EMS transport for overdose. Perhaps most importantly is that only one patient did not survive beyond the emergency department treatment, indicating that this is likely a safe practice.

Our study has a number of limitations. We are reporting on opioid overdose transports of one EMS system and our findings may not be generalizable, particularly as transport times in our city are relatively short. Secondly, this was a retrospective analysis and results were therefore based solely on what was documented in the record. For example, we relied on the medics' documentation of suspected opioid use, including their determination if the intoxicant was heroin or another opioid, but we were unable to confirm their suspicions, particularly as confirmatory urine toxicology screening is not commonly obtained for these patients. Data abstraction is also a limitation, as there were two reviewers of EMS data who reviewed different records, and only one abstractor at each of the three hospitals; therefore, no determination of inter-rater reliability was made. We did not compare patient outcomes with either historical data or concurrent data in which ALS providers administered naloxone, so do not know if outcomes such as need for repeat naloxone administration in the ED or admission rates vary with this protocol. Finally, we do not know what happened to the patients who left against medical advice or were not matched into the three hospitals' EMR after transport, and the analysis only included patients transported to hospital and did not consider those who refused transport. Prior evidence does show that death after reversal with naloxone and refusal of transport is unlikely to occur,[37,38] but we did not study such patients in this study.

CONCLUSIONS

Only a small percentage of patients receiving prehospital administration of nasal naloxone by BLS providers required additional doses of naloxone in the ED and the majority of patients were discharged. ALS intervention occurred for about 15% of patients and prehospital intubation was rare. Based on these results, we propose that BLS administration of IN naloxone is a safe practice and offer our experience as a potential model for other EMS systems.

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