

BRIEF REPORTS

Assessment for Deaths in Out-of-hospital Heroin Overdose Patients Treated with Naloxone Who Refuse Transport

Gary M. Vilke, MD, Christian Sloane, MD, Alan M. Smith, MPH,
Theodore C. Chan, MD

Abstract

Naloxone frequently is used to treat suspected heroin and opioid overdoses in the out-of-hospital setting. The authors' emergency medical services system has operated a policy of allowing these patients, when successfully treated, to sign out against medical advice (AMA) in the field. **Objectives:** To evaluate the safety of this AMA policy. **Methods:** This is a retrospective review of out-of-hospital and medical examiner (ME) databases over a five-year period. The authors reviewed all ME cases in which opioid overdoses were listed as contributing to the cause of death. These cases were cross-compared with all patients who received naloxone by field paramedics and then refused transport. The charts were reviewed by dates, times, age, sex, location,

and ethnicity when available. **Results:** There were 998 out-of-hospital patients who received naloxone and refused further treatment and 601 ME cases of opioid overdose deaths. When compared by age, time, date, sex, location, and ethnicity, there were no cases in which a patient was treated by paramedics with naloxone within 12 hours of being found dead of an opioid overdose. **Conclusions:** Giving naloxone to patients with heroin overdoses in the field and then allowing them to sign out AMA resulted in no identifiable deaths within this study population. **Key words:** out-of-hospital; naloxone (Narcan); release; against medical advice; paramedic. *ACADEMIC EMERGENCY MEDICINE* 2003; 10:893-896.

In many emergency medical services (EMS) systems, a patient given naloxone (Narcan) for heroin overdose must be transported to an emergency department for physician evaluation. This overdose reversal often leads to a combative, withdrawing patient who does not want to be transported, who then potentially could bring risks to the out-of-hospital and hospital staff. Paramedics in San Diego County have standing orders to treat a suspected heroin overdose patient with naloxone. Protocols give medics the authority to treat with 2 mg of naloxone intravenously/intramuscularly or 4 mg via endotracheal tube and to repeat the dose if no response is observed.¹ If the patient has a favorable response to the medication and wants to leave and if the answers to all six questions in the county protocols for releasing a patient against medical advice (AMA) are in the affirmative (Table

1), the patient can be released AMA at the scene by paramedics without base hospital contact.² Although question 2 seems to be violated by use of heroin, the use of naloxone reverses the opioid effect and enables the medics to answer this question in the affirmative, provided that no other coingestants are impairing the patient. An additional dose of naloxone can be ordered by the paramedics' base hospital before the patient's release.

A preliminary study was performed to assess whether this practice results in subsequent death from recurrent heroin overdose after naloxone wears off.³ The results showed no deaths during the one year of data collection. To the best of our knowledge, there are no other published articles looking at this out-of-hospital topic. Our current study is a five-year review to evaluate whether the practice of releasing heroin-overdose patients AMA after treatment with naloxone by paramedics is safe. We hypothesize that releasing patients AMA after reversing heroin overdose with naloxone would not result in subsequent death.

From the Department of Emergency Medicine, University of California, San Diego Medical Center (GMV, CS, TCC), and the San Diego County Division of Emergency Medical Services (GMV, AMS), San Diego, CA.

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Address for correspondence and reprints: Gary M. Vilke, MD, Department of Emergency Medicine, UC San Diego Medical Center, 200 West Arbor Drive, Mailcode #8676, San Diego, CA 92103. Fax: 619-543-3115; e-mail: gmvilke@ucsd.edu.

METHODS

Study Design. This study was a retrospective review of records using the San Diego County Quality Assurance Network (QANet) computer database for out-of-hospital providers and the San Diego County Medical Examiner's (ME) Office database. The study was approved by the University of California, San

TABLE 1. Six Questions of County Protocol for Releasing Patients Against Medical Advice (AMA)

1. Is the patient oriented?
2. Is the patient not impaired by drugs or alcohol?
3. Is the patient competent to refuse care?
4. Have risks and consequences been discussed?
5. Has the patient been advised that medics will return if called back?
6. Has AMA form been signed?

Diego Investigational Review Board and the San Diego County Out-of-hospital Audit Committee.

Study Setting and Population. The study location is a county with a population of approximately 2.8 million people residing in urban, suburban, and rural areas. Approximately 150,000 calls are received annually by nine 9-1-1 dispatch agencies. Eighteen advanced life support (ALS) ground transport agencies and one airmedical rotor-wing agency operate in the county, employing about 900 paramedics to provide EMS to these areas. There are about 37 basic life support units that respond primarily, with ALS backup available. The study location has 21 basic emergency departments with one Level 1 trauma center and five Level 2 trauma centers. Medical oversight is provided by written protocols with available direct medical oversight via a mobile intensive care nurse (MICN) or a base hospital physician when necessary.

Study Protocol. The QANet is a customized database, which has a comprehensive collection of prospectively entered, out-of-hospital data, entered by out-of-hospital providers and MICNs from calls run throughout the county, including all ALS level calls. The ME database contains records on all ME-reviewed cases, which include all victims who were found dead in public or private residences or died in emergency departments of reasons other than natural causes or progression of known disease (i.e., cardiovascular disease or end-stage carcinoma). All suspicious deaths and suspected overdose deaths are examined by the ME. All of these patients undergo routine toxicologic screening.

Measures. Using the QANet, a list of all paramedic 9-1-1 responses over a 5-year period from January 1, 1996, through December 31, 2000, was generated based on whether the patient received naloxone, had an improvement in mental status, and signed out AMA. Naloxone is reserved for patients with suspected opioid overdose with an obtunded level of consciousness. A second list covering the same period was generated by the ME's office of all deaths who had the metabolite of morphine as contributing to the cause of death. The ME is unable to identify

specifically whether heroin is in the bloodstream because their assay tests only for morphine, heroin's metabolite. The initial screen is performed using a radioimmunoassay screening kit by Immunalysis (San Dimas, CA). This kit screens for morphine and codeine. If this test is positive, a confirmatory gas chromatography mass spectrograph analysis is performed at the ME's laboratory to confirm morphine as the metabolite. All heroin-overdose deaths would be contained in this group. Both lists included date, time, sex, ethnicity, location, and name when available.

The lists were reviewed and cross-referenced by name when available, date, and time to assess whether any patients had been evaluated and treated with naloxone by paramedics within 12 hours preceding the documented times of death by the ME's office. When date and time overlapped, other identifying information, including race, sex, estimated age, and location, was reviewed to identify whether the patient and the victim were the same person. Care was given to look closely for potential misspellings in name. If the name was phonetically close, and the individuals were similar in other physical characteristics, this would be considered a match. The ME database also would keep reports on AKAs ("also known as"), and these were checked. Locations were compared by zip codes, with any neighboring zip codes considered as possible local movements by a patient after treatment and before relapse. Additional identifying information was compared closely to confirm whether a patient and victim were the same. Any questionable cases were evaluated by a second independent reviewer.

Data Analysis. Routes of naloxone and numbers of doses were documented. Descriptive statistics were calculated and reported as means and ranges using software for SPSS version 9.0.

RESULTS

A total of 556,427 paramedic 9-1-1 responses with base hospital contact occurred over the five-year study period, with 35,957 (6.5%) of these patients signing out AMA. During the study period, 8,366 patients received naloxone. A total of 998 patients received naloxone *and* were released AMA by paramedics. The mean age of patients was 37.7 years (range 16 to 83 years), and 834 (83.8%) were male. Of the patients who received naloxone, 260 (26.1%) received a single dose, 714 (71.5%) received two doses, and 24 (2.4%) received three doses. Of the single doses of naloxone, 179/260 (68.8%) were intravenous and 80/260 (30.8%) were intramuscular. Route was not specified for one patient. Tables 2 and 3 show the different routes when two or three doses of naloxone were given. The ME database over this period included 601 deaths with morphine listed as the cause of death or contributing to the cause of

TABLE 2. Number of Patients Who Received Two Doses of Naloxone (n = 714)

IV→IM	552	(77.3%)
IM→IV	40	(5.6%)
IM→IM	47	(6.6%)
IV→IV	74	(10.4%)
IM→I(?)	1	(0.1%)

IV = intravenous; IM = intramuscular.

death. The mean age was 40.1 years (range 18 to 86 years) with 509 (83.6%) male. There were no cases in which a time of death was unavailable.

The QANet and ME groups were cross-referenced as described earlier, with results showing that none of the 998 (97.5% confidence interval = 0% to 0.37%) patients who were treated by paramedics with naloxone and released AMA matched to any of the ME victims within 12 hours of treatment. There were 62 cases that had some similarities regarding time, date, gender, and age and required closer evaluation using the full ME report and EMS narrative run information. All of these were determined by two independent reviewers to not be the same patient.

DISCUSSION

Naloxone is a derivative of oxymorphone and acts as an opioid antagonist by competitive binding of opioid receptors at the cellular level. The medication commonly is used to reverse the effects of opiates and is the most frequently prescribed specific antidote for human poisonings.⁴

There are case reports of rare adverse reactions after naloxone, including seizures, hypertension, dysrhythmias, and precipitation of an anticholinergic syndrome. Naloxone also can induce non-life-threatening opioid withdrawal. Despite these reports, naloxone is a safe medication with which to treat opioid overdoses, with most reports of its adverse effects occurring early after the drug's administration.⁵⁻⁸ Given its excellent safety profile, naloxone has been used extensively in the out-of-hospital, emergency department, and inpatient settings to reverse the effects of opioid intoxication.

In this study, most patients received an intravenous dose followed by a second dose of intramuscular

TABLE 3. Number of Patients Who Received Three Doses of Naloxone (n = 24)

IV→IV→IM	16	(66.7%)
IM→IM→IM	1	(4.2%)
IV→IM→IM	3	(12.5%)
IV→IV→IV	2	(8.3%)
IM→IV→IM	1	(4.2%)
IM→IV→IV	1	(4.2%)

IV = intravenous; IM = intramuscular.

naloxone. This practice gives the patient a longer duration of action before the naloxone wears off.

Previous work has evaluated the safety of out-of-hospital naloxone administration for opioid overdose patients. Sporer et al.⁹ retrospectively reviewed 726 cases of presumed opioid overdose treated with naloxone in the out-of-hospital setting. He reported low rates of adverse reactions, and nearly all patients who had an initial pulse and blood pressure responded and improved with out-of-hospital naloxone administration. Yealy et al.⁷ reported on 813 out-of-hospital patients with depressed level of consciousness who received out-of-hospital naloxone during a one-year period and found few adverse reactions. Other studies have suggested that out-of-hospital naloxone use is effective in reducing opioid-related morbidity and mortality.¹⁰ In comparing patient demographics, our study exhibited similar age and gender distributions compared with other studies.^{9,11}

Although the immediate effectiveness and safety of out-of-hospital naloxone has been well shown, the need for transport and further medical evaluation in opioid-overdose patients who improve after naloxone administration in the field has been less clear. Because of its short half-life (20 to 30 minutes), there is concern that patients who improve after this intervention need to be observed medically should the effectiveness of naloxone subside before that of the initial, potentially longer acting opioid intoxication.⁶ Work done evaluating the potency and duration of action of naloxone compared with nalmefene showed that these agents were equipotent in terms of dose and plasma concentration; however, nalmefene was shown to have slower clearing and a prolonged effect compared with naloxone.¹² Similar results were shown clinically by Kaplan et al.¹³; naloxone and nalmefene were found to be safe and efficacious in a population of emergency department patients. Besides the intravenous and intramuscular routes used in our study, other work has shown effectiveness in subcutaneous and intranasal routes of naloxone.^{11,14}

Previous work has evaluated fatal outcomes in patients receiving naloxone by paramedics and being released AMA. Vilke et al.³ had found no deaths in 317 patients over a one-year period. In this study, we reviewed all cases of out-of-hospital naloxone in which patients refused transport after receiving the medication and cross-referenced these cases with ME reports of opioid-related deaths during a five-year period. We found no cases of out-of-hospital naloxone use that potentially could be associated temporally or otherwise with an opioid-related death in our county. Sporer et al.⁹ also reviewed ME reports in their study, but all patients in their study with measurable pulses and blood pressures were transported to a medical facility.

Christenson et al.¹⁵ attempted to develop a clinical predictive rule for patients presenting with presumed opioid overdose. They found it safe for early

discharge from the ED in their patient population but noted that the rule requires prospective validation. Similar results were found by Smith et al.,¹⁶ who determined that on retrospective review there was no evidence to support that hospital admission and 24 hours of observation were of any benefit to heroin-overdose patients who were awake, were alert, and lacked evidence of pulmonary complications.

Our study offers support that many heroin overdoses do not likely require ambulance transport and emergency department evaluations when treated with naloxone. This finding has implications for EMS systems that already are stretched to capacity.

LIMITATIONS

This study looked specifically at mortality from the practice of releasing patients AMA after treating heroin overdose with naloxone but did not assess morbidity; an EMS system considering implementing a similar protocol must be aware of this limitation. Other limitations to this study include retrospectively reviewing the data from a computerized database. Because the paramedics and MICNs are instructed to transport patients with opioid intoxications or overdoses other than heroin to the emergency department for evaluation, we believe that most, if not all, of the overdoses in patients who were released AMA were due to heroin alone. Additionally, the ME database would capture more than heroin overdoses in the 601 autopsy reports; however, all deaths attributed to heroin would be included in that total.

We did not determine whether patients treated by the paramedics with naloxone and released AMA sought follow-up health care via reaccessing 9-1-1 or by being driven by car to a clinic or emergency department for additional treatment. If any of these patients had died, however, they would have been in our ME database based on criteria for ME review. Another possibility that would not have been captured in the ME database is that a patient could have been treated by paramedics, then fled across the border to Mexico and died. The 12-hour time frame to compare EMS treatment and ME determination of the time of death could have caused cases to be missed. If the ME was inaccurate in determining the time of death, a patient seen by EMS and treated may have died but not be found in our query because of timing issues by the ME. We chose 12 hours as a cutoff because there were no previous studies done for reference, and with the short half-life of naloxone coupled with a buffer time period for ME error in determining the time of death, 12 hours seemed reasonable.

CONCLUSIONS

In our review of out-of-hospital and ME databases over five years, no deaths were found in 998 suspected heroin-overdose patients who refused transport to a hospital after receiving naloxone by paramedics.

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