The Safety of Prehospital Naloxone Administration by Paramedics

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We performed a retrospective review to investigate the safety of prehospital naloxone administration by paramedics as part of a protocol for all patients presenting with an acutely depressed level of consciousness (LOC). The prevalence of naloxone-induced vomiting, seizures, hypotension, hypertension, and cardiac arrest was sought from the prehospital records of 813 patients treated during a 12-month period. The mean age of the treated patients was 42.4 ± 9.7 years. The initial dose of naloxone was 0.4 to 0.8 mg, and the mean total dose was 0.9 ± 0.6 mg. No patients lost a pulse within ten minutes of receiving naloxone. Two patients (0.2%) experienced a significant drop in systolic blood pressure, and one patient (0.1%) demonstrated a significant rise in systolic blood pressure within five minutes of naloxone administration. Vomiting occurred in two patients (0.2%), and one patient (0.1%) suffered a tonic-clonic seizure within five minutes of naloxone administration. Of the 813 patients treated, 60 patients (7.4%; mean age, 32.3 ± 6.7 years) were judged to have an improved LOC after naloxone, with 27 (3.3%) regaining a normal LOC. We conclude that in the above doses, naloxone is safe as part of prehospital protocols for paramedics treating patients with an acutely depressed LOC. However, the vast majority of patients treated empirically with naloxone in the field demonstrated no benefit. [Yealy DM, Paris PM, Kaplan RM, Heller MB, Marini SE: The safety of prehospital naloxone administration by paramedics. Ann Emerg Med August 1990;19:902-905.]

INTRODUCTION

Patients with an acutely depressed level of consciousness (LOC) often are initially treated by paramedics in the field. Among the many etiologies responsible for a depressed LOC, hypoglycemia and opiate narcosis are easily reversed when the appropriate therapies are given. The initial treatment of opiate overdose is based on the maintenance of adequate oxygenation and ventilation. Following steps to achieve these goals, specific antidote therapy is indicated in narcotic-overdose patients. Naloxone is the preferred agent for reversal of opiate-induced altered sensorium and respiratory depression.[1-3] Although widely used, naloxone has been associated with such complications as vomiting, seizures, hypertension, hypotension, ventricular arrhythmias, and cardiac arrest.[4-9] The magnitude of the risk of these complications in the prehospital setting is undefined. Because of the potential for complications, some suggest smaller initial doses[7] and routine intubation before naloxone administration.[4]

We performed a retrospective review to define the safety of naloxone administration by paramedics as part of a protocol for the treatment of patients with an acutely depressed LOC. Specifically, the prevalence of vomiting, seizures, significant hypertension, hypotension, and precipitation of cardiac arrest was sought from the records of patients treated with naloxone.

METHODS

The Pittsburgh Bureau of Emergency Medical Services (EMS) is staffed by 170 full-time paramedics and supervisory personnel, with 16 mobile advanced life support units (ALS) available for dispatch. Patients are transported to one of 16 hospital emergency departments in the metropolitan

area. Each year, there are approximately 40,000 responses attended by the EMS personnel, with approximately 15% requiring ALS interventions. Second- and third-year emergency medicine residents serve as primary medical command for all ALS calls by a two-way radio, with continual monitoring of all calls by a faculty backup physician. In addition, residents respond to many ALS calls in a separate vehicle to assist with diagnosis and treatment. Consult with the medical command physician is required before administration of any medications.

The protocol for the management of patients with an acutely altered LOC requires the paramedic to obtain a directed history, perform a brief physical examination, place ECG leads, administer supplemental oxygen, and insert a peripheral IV line while obtaining blood for glucose estimation. If hypoglycemia is diagnosed (Chemstrip® bG reagent strip reading of 80 mg/dL or less), 50 to 100 mL of a 50% dextrose solution is administered. Patients with a depressed LOC and no response to IV glucose or those with a depressed LOC and a glucose estimation of more than 80 mg/dL received 0.4 to 0.8 mg naloxone by the IV catheter. In some cases, naloxone was given before glucose estimation, particularly if the history and surrounding circumstances suggested opiate overdose. The IV route was preferred, but IM, sublingual, SQ, and intratracheal (if intubated) routes were considered acceptable when approved by the command physician when IV access was unobtainable.

The initial dose of naloxone was based on published recommendations for the field treatment of opiate overdose at the time of treatment.[10] Only after recontact with the command physician were additional doses administered as needed based on initial response.

Patients were maintained in the lateral decubitus position with nearby suction after the administration of naloxone until normal LOC had returned; they were immobilized if cervical-spine injury was suspected. If clinically indicated, bag-valve-mask or endotracheal intubation was performed by the paramedics or field physicians. Detailed trip sheets were maintained, with an emphasis on the presenting history, physical examination, and vital signs, as were chronological recordings of all interventions and clinical responses.

The prehospital charts of all patients treated with naloxone during the 12-month period from January through December 1986 were reviewed. Any patients without a palpable pulse at the time of naloxone administration or who were treated as part of a combination of the altered response and multiple trauma protocols were excluded. In addition, although the altered LOC protocol is applicable for patients with any change in sensorium, naloxone was administered only to patients with a subjective depressed sensorium or respiratory drive as judged by the paramedics.

The charts were reviewed for age and sex; vital signs, subjective LOC (as judged by paramedics and recorded in the narrative), and cardiac rhythm before and after each intervention; initial and total doses of naloxone and route; and development of vomiting or seizures within five minutes of the administration of naloxone and before admission to an ED.

Before data analysis, we arbitrarily defined "significant hypotension" after naloxone administration as occurring when the measured systolic blood pressure decreased to less than 30 mm Hg and obtained an absolute value of less than 120 mm Hg, and "significant hypertension" after naloxone administration as occurring when the systolic blood pressure increased to more than 30 mm Hg and obtained an absolute value of more than 160 mm Hg.

The data were analyzed using descriptive methods, with continuous variables reported as the mean ± standard deviation. Ninety-five percent upper limits of confidence (ULC) were calculated for the risk of each complication.[11]

RESULTS

A total of 813 patients met the criteria for review, with no patients excluded because of missing charts. There were 480 male (59%) and 333 female (41%) patients (mean age, 42.4 ± 9.7 years). The total naloxone doses ranged from 0.4 to 2.4 mg (mean, 0.9 ± 0.6 mg). Administration routes were IV (800), intratracheal (seven), sublingual (four), IM (one), and SQ (one). Of all patients treated with naloxone, 60 (7.4%) developed some subjective improvement in their LOC within five minutes of administration as recorded by the attending paramedics. The mean age of the patients with any subjective improvement in LOC after naloxone was 32.3 ± 6.7 years. Also, 27 patients (3.3%) were judged to have regained a normal LOC before arrival at the receiving ED. In 22 of these 27 patients (82%), the prehospital chart stated that witnesses observed or paramedics or peace officers found evidence of recent opiate use at the scene.

No patient developed ventricular tachycardia, fibrillation, or asystole after naloxone administration (0%, ULC = 0.4%). One patient (0.1%, ULC = 0.5%) developed a generalized tonic-clonic seizure after receiving 0.8 mg IV naloxone; no improvement was noted, and further history revealed an underlying seizure disorder. Two patients (0.2%, ULC = 0.6%) vomited after receiving 0.8 mg IV naloxone; one of these patients demonstrated a rapid improvement in the observed LOC before emesis. The other patient, initially described as "slightly drowsy," had received ipecac before naloxone administration. The ED records of both patients reported no evidence of aspiration, and they were discharged by the treating physician without further follow-up.

One patient (0.1%, ULC = 0.5%) developed significant hypertension after naloxone administration. This patient was observed to have no improvement in the subject LOC by the paramedics, with a total dose of 1.2 mg administered. Another seven patients (8.6%) had increases of more than 30 mm Hg, yet their post-treatment systolic blood pressures either remained at or returned to 100 to 160 mm Hg. Two patients (0.2%, ULC = 0.6%) developed significant hypotension after naloxone administration; each received 0.8 mg, but only a partial improvement in LOC was observed in one patient.

DISCUSSION

These data confirm the safety of empiric naloxone therapy by paramedics when treating patients with an acutely depressed LOC; there was little risk of precipitating vomiting, seizures, cardiac arrest, or significant

hypertension and hypotension. This was true for patients with a clinical improvement after naloxone and for those with no subjective improvement who were given naloxone as part of a protocol.

Case reports documenting cardiac arrest after naloxone reversal of opiate anesthesia in young, healthy adults have surfaced,[5] yet no data exist on the overall prevalence of this complication in either the postoperative or emergency settings. In the aforementioned case reports, ventricular fibrillation developed rapidly after 0.2 to 0.4 mg IV naloxone, presumably from a catecholamine surge precipitated by the agent. However, these patients may differ from those treated for acutely depressed LOC. Postoperative patients have often received a variety of agents capable of altering circulatory physiology and are still subject to the stress of surgery. Also, vomiting and seizures have been reported as a direct side effect of IV naloxone.[4]

A literature search found no data on the prevalence of vomiting or seizures after naloxone administration. Nonetheless, it has been suggested that routine endotracheal intubation be performed before naloxone administration to lessen the risk of aspiration of vomitus.[4] Others have suggested smaller initial doses of naloxone (0.04 mg) in patients with a suspected opiate overdose to decrease the risk of complications.[7] However, present data do not support these recommendations.

There are limitations to our study. One potential design bias lies within the data collection technique. The paramedics' recording of the pre- and post-treatment LOC was subjective; no predetermined ordinal scale (eg, modified Glasgow Coma Score) was used. Only systolic blood pressures were consistently available for evaluation on each patient, thus interfering with analyses of diastolic and mean arterial blood pressure changes. The accuracy of blood pressures obtained in the field may be questioned, but previous researchers have suggested that any errors may be clinically insignificant.[12] Furthermore, it is unlikely that an important bias was encountered because the arbitrary criteria for significant hypertension or hypotension were selected after the care was delivered but before chart review.

Our data collection was primarily from prehospital charts, with limited ED chart review. This was omitted because of the logistic difficulties in obtaining a standardized set of data on each patient when 16 receiving facilities were involved. This does not allow analyses of response and complication rates based on final diagnoses. Also, no toxicologic screening data were available for analysis on the vast majority of patients. For similar reasons, we are not able to completely exclude the possibility of late development of symptoms consistent with pulmonary aspiration in the two patients who vomited after treatment. However, even if both developed aspiration syndromes, the overall prevalence of this complication would be equal to that seen with vomiting (0.2%).

The retrospective nature of the present study does raise the issue of data accuracy. We chose to concentrate on complications that were easily observed and routinely recorded by the prehospital care personnel. The quality assurance system used by the EMS bureau stresses detailed, uniform data collection, with strict guidelines for documentation after all interventions during ALS calls. The presence of continuous on-line medical command physicians, with many ALS calls attended by the resident physicians, also assists with detection of complications after therapy. Given the above system and study design, we feel that no cases of cardiac arrest, seizures, or vomiting were unrecorded.

Pulmonary edema, another rare complication associated with naloxone therapy,[13,14] was not studied because the field documentation of this disease is difficult. Opiate overdose alone can lead to pulmonary edema,[3] further clouding any conclusions about a direct cause-and-effect relationship between naloxone administration and this side effect.

We did not assess the cost-effectiveness of routine prehospital naloxone administration to all patients with an acutely depressed LOC; in our series, more than 92% of patients treated had no observable benefits. In addition, the vast majority of patients who experienced a complete return to a normal LOC after naloxone administration had a history strongly suspicious for recent narcotic use. Our design does not allow accurate identification of all patients likely to respond to naloxone therapy, although those with evidence of recent opiate use are very likely to demonstrate the most improvement. However, it is clear that some patients exhibited a complete response to naloxone when opiate narcosis was not suspected. The partial responses of some patients may be the result of inadequate doses, multiple drug ingestions, or the alleged nonspecific arousal properties of naloxone in certain non-narcotic-induced conditions of depressed LOC.[15]

Prospective research to identify the characteristics of patients most likely to respond to naloxone is needed to better tailor the use of this agent in the field. Furthermore, analysis of the costs and benefits of selective versus routine use of naloxone in patients with an acutely depressed LOC in a variety of prehospital systems is needed before definitive recommendations concerning protocols can be made.

Our conclusions may not be valid with the use of larger doses of naloxone, which are often used to counteract the more potent synthetic opiate cogeners. Previous research with higher doses of naloxone in overdose patients and healthy subjects has failed to document any significant side effects.[16,17] The conclusions may also not apply with the use of newer opiate antagonists, such as nalmefene.

CONCLUSION

The use of naloxone in initial doses of 0.4 of 0.8 mg for the prehospital treatment of patients with acutely depressed LOC is safe, with little risk of precipitating vomiting, seizures, significant hypertension, hypotension, or cardiac arrest. Smaller doses and routine preadministration intubation appear unwarranted from our data. When given to all patients with a depressed LOC, the majority will not demonstrate any benefit, yet the overall cost-to-benefit ratio remains undefined.

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ERRATUM

In the article "The Ability of Physicians to Predict Electrolyte Deficiency From the ECG," by Wrenn, Slovis, and Slovis [May 1990;19:580-583], parts A and B of the figure were inadvertently switched.