

Prescribing Naloxone to Actively Injecting Heroin Users: A Program to Reduce Heroin Overdose Deaths

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ABSTRACT. Heroin overdose deaths have increased alarmingly in Chicago over the past decade. Naloxone, an opioid antagonist with no abuse potential, has been used to reverse opiate overdose in emergency medical settings for decades. We describe here a program to educate opiate users in the prevention of opiate overdose and its reversal with intramuscular naloxone. Participant education and naloxone prescription are accomplished within a large comprehensive harm reduction program network. Since institution of the program in January 2001, more than 3,500 10 ml (0.4 mg/ml) vials of naloxone have been prescribed and 319 reports of peer reversals received. The Medical Examiner of Cook County reported a steady increase in heroin overdose deaths since 1991, with a four-fold increase between 1996 and 2000. This trend reversed in 2001, with a 20% decrease in 2001 and 10% decreases in 2002 and 2003. [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <<http://www.HaworthPress.com>> © 2006 by The Haworth Press, Inc. All rights reserved.]

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INTRODUCTION

Fatalities related to accidental overdose of illicit opiates have risen alarmingly in the past decade, in Europe and Australasia as well as in the United States.¹⁻⁶ This trend has been very steep in Chicago. Between 1988 and 1998, hospital emergency room (ER) mentions of heroin/morphine increased 400%, ranking Chicago third in the US for ER mentions of heroin.⁷ In 1996, the Medical Examiner for Cook County documented 198 deaths related to heroin overdose. By 2000 this number had increased to 466, a 425% increase over five years, and her-

oin was a factor in more Chicago area deaths than any other illicit drug.

In a San Francisco study, 89% of drug users reported having witnessed an overdose,⁸ and injection drug users at a Chicago needle exchange program report witnessing an average of 3 opiate overdose events, one of them fatal (Bigg, unpublished data). In the San Francisco study, 91% of respondents had tried various measures to revive their peers, the most common involving painful stimuli (physical striking; ice on genitals; injection of concentrated saline), but only half reported summoning emergency help for fear of reprisal from author-

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ities responding to the emergency call. This fear is by no means unfounded: another San Francisco study found at least three instances where the persons who sought emergency help for their peer were arrested.¹

Naloxone is a pure opiate antagonist that has been used routinely for decades in the emergency treatment of opioid overdose. Naloxone has no physiological effect other than opiate blockade, and no adverse reactions save precipitation of opiate abstinence syndrome in opiate-dependent individuals. Intravenous naloxone was long a component of the "coma cocktail" empirically given to comatose patients in ERs.⁹ Although routine administration of the 'coma cocktail' is becoming obsolete, the safety and efficacy of naloxone has never come into question. Naloxone has no abuse potential whatsoever, no potential for overdose,¹⁰ and the generic formulation is extremely inexpensive.

Prescription of antidotes for peer administration in emergency situations has become routine medical practice in certain situations. Diabetic patients are prescribed glucagon and instructed to educate their family and friends regarding its use in reversing insulin shock.¹¹ Persons hypersensitive to insect stings are prescribed equipment for emergency administration of epinephrine in case of anaphylaxis.¹² Both of these examples involve medications that have far greater potential for adverse reactions than does naloxone.

The idea has been advanced that naloxone, a pure opioid antagonist that definitively reverses opiate overdose, be prescribed to injection drug users, instructing these individuals in how to utilize this treatment 'in the field.'^{8,13,14} There has been heated debate on the topic, but little information and virtually no controlled studies have been published.¹⁵

This report describes a program that has been prescribing injectable naloxone to heroin addicts since 2001.

METHODS

The Chicago Recovery Alliance (CRA) has done outreach in prevention of HIV infection and other drug-related harms to active injection drug users (IDUs) since 1991. CRA operates 16 van-based sites, 6 storefront-based sites, and 10

areas of cell phone and pager access each week, seven days a week. Every week CRA's outreach workers directly contact over 340 IDUs, who then reach an additional 780 people. CRA's history as a widespread and trusted harm reduction program make it a perfect vehicle for intervention in the epidemic of opiate overdose deaths, and volunteer physicians began prescribing and dispensing naloxone from the CRA outreach van in 1998. In 2000, the authors began formulating a program to widen the availability of naloxone to IDUs for use by their families and peers in reversing accidental opiate overdose.

A curriculum was developed that includes basic opioid neurophysiology, pharmacodynamics and pharmacokinetics of commonly used opiates, pharmacology and pharmacokinetics of naloxone and other opiate antagonists, risk factors and prevention techniques for opiate overdose, signs and symptoms for the early recognition of opiate overdose, prevention of choking and aspiration in the unconscious patient, techniques of rescue breathing, routes of administration and dosing guidelines for naloxone, and protocols for follow-up care. All CRA outreach specialists are trained via this curriculum to engage and inform participants regarding naloxone and its availability through CRA.

A medical history is collected on all participants to be prescribed naloxone. The lay operative provides standardized education about overdose and naloxone, and documents their instructions to the participant. The participant is dispensed a 10ml multi-dose vial of naloxone, 0.4 mg/ml, a supply of sterile syringes with long (1-1½") intramuscular needles, a pocket-sized instruction card of instructions for overdose recognition and treatment, and documentation that the participant's possession of the medication is legal and medically sanctioned. The order to dispense naloxone is signed by the physician, who retains the medical history in the patient's record.

Files of the curriculum and the forms can be downloaded free of cost at www.anypositivechange.org

RESULTS

Formal compilation of the data regarding IDUs who have been prescribed naloxone and

those who have used it in overdose reversal is in progress. However, we can offer the informal reports that we have found to be sufficient justification for us to not only continue but aggressively expand this program.

To date we have received 319 reports of peer overdose reversals. These reports are usually spontaneous, often presenting as a rapid aside while the participant is busy exchanging needles (e.g., “Oh, and can I have more of that overdose medicine? I used all mine up”). In these spontaneous situations we elicit from the participant a full report of the event, and add their report to our tally.

One unsuccessful revival has been reported. In this case, the victim was known to have drunk at least nine shots of alcohol, taken 8 mg of alprazolam, and smoked several rocks of cocaine in addition to heroin. The total dose of naloxone given, 1.6 mg in two doses over a 3-5 minute period, failed to revive the victim, who expired.

In five instances it was reported that the victim did not respond until a second injection of naloxone was given, however in four of these cases the second dose was given within less than two minutes of the first and may not have been clinically necessary. There have been no reports of victims requiring a second dose of naloxone because of return of the overdose after naloxone has been metabolized, although in one case the victim (who was a very large man that had been revived by a very small woman) suggested that he take a second dose prophylactically, because rescue breathing had been physically very difficult for the rescuer. In contrast to the severe opiate abstinence syndrome (OAS) observed with the 2 mg of intravenous naloxone commonly administered in medical situations, we have received only one report of naloxone precipitating OAS severe enough to induce vomiting. One case of seizures was reported, but there was also a history of alprazolam use (6-8 mg/day) in that situation. One rescuer reported using five sequential doses (0.4 mg each), each having a partial reviving effect, before full reversal was achieved.

Approximately one-third of the reversals occurred in persons who were reinstating heroin use after a period of abstinence. In many cases this period was as brief as three days, com-

monly a hospital detoxification program or a weekend incarceration.

We also present as results the reports from the Office of the Medical Examiner of Cook County (Figure 1). A consistent trend of increasing heroin overdose deaths, from 198 to 466 in 2000, was reversed in 2001, the year that we instituted this program, with 374 deaths in 2001, 344 in 2002, and 324 in 2003.

DISCUSSION

We describe here our experience with a program that has, to date, prescribed more than 3,500 multi-dose vials of naloxone and received 319 reports of peer reversals.

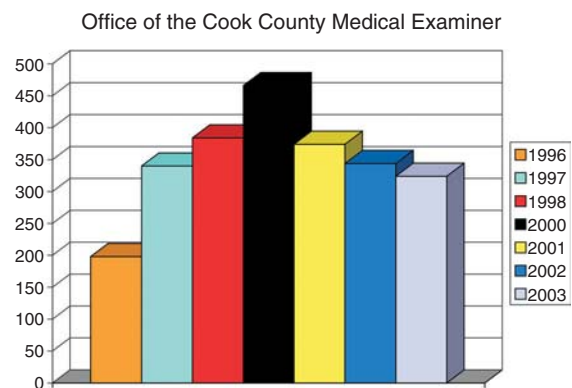
There has been much discussion but little information about the practice of prescribing injectable naloxone to IDUs for use in reversing opiate overdose.¹⁵ A survey in San Francisco revealed that 87% of IDUs were in favor of a program that would train them to administer naloxone to their peers.⁸

*I was just freakin' out, thinking: 'I wish I knew how to do CPR' . . . and I didn't know none of that and I was like, 'Oh, why don't I know this?'**

In New York, 33.4% of providers responding to a random postal survey reported that they would consider prescribing naloxone to patients at risk for opiate overdose.¹⁶

In most clinical situations outside pediatrics, medication is prescribed for the patient to ad-

FIGURE 1. Opiate Overdose Deaths in Cook County



minister to himself. It is not customary for a patient to be prescribed medication to administer to another, or to have another administer to him. There are, however, precedents for prescription of medications intended for peer administration. In most instances the medication is an antidote for inadvertent overdose or poisoning, the two most common situations being glucagon for reversal of inadvertent insulin overdose, and epinephrine for treatment of anaphylaxis following insect sting.^{11,12}

In neither of these situations is it generally required that the laypersons who will actually administer the medication be involved in the prescription process; customarily the patient is educated and provided with written instructional materials, and he then educates his peers. In both cases the patient may also wear a medical bracelet with brief instructions for emergency situations, with the implication that a totally untrained lay bystander may safely administer the antidote.

We suggest an exactly analogous situation in the case of naloxone for inadvertent opiate poisoning, with one important difference: both glucagon and epinephrine are medications with significant risk of adverse events. Naloxone, however, has virtually no known adverse effects beyond the precipitation of opiate abstinence syndrome in opiate-dependent individuals.

*If you ever get in a meeting with some professional-type people, tell 'em that, you know, people like us—no, we're not professionals, but if we have it at hand we can save somebody's life with this stuff [naloxone] . . . it's a lifesaver, there's no question.**

One concern often voiced is that availability of naloxone will encourage IDUs to use more heroin and deter them from seeking treatment. This concern is contradicted by results of a pilot study in San Francisco, which found that during the six months following training in naloxone administration, participants had a statistically significant *decrease* in injection frequency, and a non-significant *increase* in participants entering treatment (Seal KH, personal communication).

*It doesn't influence me to do more; it actually influences me to do less . . . knowing that if they go out I could help them.**

In every report that we have received, the rescuer and the victim were specifically asked if availability of naloxone made them feel comfortable using heroin more often or in higher doses, and in every case this was specifically and emphatically denied. In all cases, the overdose reversal experience was extremely frightening and aversive, particularly for the rescuer. No rescuers reported any difficulty in convincing the victim to abstain from opiates to prevent worsening the overdose. In situations where the rescuer was a significant other or close friend, the experience was often powerfully bonding.

*I've saved three people's lives . . . each time that I've helped someone out it's touched me somehow. I start crying because I think, that could've been me, you know, if I was still on the heroin.**

Interestingly, many participants involved in an overdose reversal, both as victim and as rescuer, report that the education about and availability of naloxone has opened new avenues of thought regarding safety and personal health. Some participants, after being dispensed naloxone, have returned to be tested for HIV and HCV, telling us that they are now feeling a greater sense of hope that they may live to see a long-term future. As one participant eloquently put it, "People who overdosed used to be past tense—I *knew* a guy who overdosed. Now we can talk about them in the present: I *know* a guy who overdosed and he's ok now." Our finding of improved personal health care is only anecdotal at this point, but one fact is irrefutable: *Dead addicts never recover.*

*Life is precious. I hope to god I'm never on it again, but if I do relapse I hope someone has it [naloxone] on them to save my life. Life is definitely precious.**

Legal and Ethical Concerns

A physician may prescribe medication only within the confines of a physician/patient relationship. Establishment of a legal physician/pa-

tient relationship is accomplished in our program by meeting three requirements: (1) formation of a clinical chart for each participant; (2) documentation within the chart that the participant has been informed of the risks, benefits, alternatives, and proper use of the treatment; and (3) evidence of the physician's good faith.¹⁷

Medical liability is another concern voiced by some physicians. Anxiety can be minimized by the extremely low risk/benefit ratio for naloxone, as well as by recognizing the low potential for litigation in this patient population. A physician who is providing service on a volunteer basis will also be protected by the Good Samaritan Act. In New Mexico, Jennison and colleagues took advantage of a positive political climate to introduce and see enacted into law a bill exempting physicians from any liability in connection with the prescription of naloxone, as well as protecting the laypersons who actually administer the medication.¹⁸

*We got no haloes on our heads but ... a lot of these people are good people still. They have a lot of good qualities. And if I see 'em fall out, if I got it [naloxone] I'm gonna hit 'em with it. I think it's a wonder-drug.**

The medication is dispensed as a 10 ml multidose vial (0.4 mg/ml naloxone) inside a cardboard box to protect the medication from exposure to light. In the first two years we provided each participant with a prescription to document that their possession of this medication was medically sanctioned. There was only one incident of prescription alteration, with more than 2,500 prescriptions written over 28 months. However, because there was no DEA number printed on the prescription, the pharmacist sought physician verification for prescription of a controlled substance, and the falsification was quickly identified. Recently, we have found it simpler to use a pharmacy-type label sticker on the medication box to verify that the medication is legally prescribed.

We instruct all participants to seek or summon emergency assistance, particularly if the victim fails to respond to initial doses of naloxone, if the victim responds acutely to naloxone but is known to have taken a very

long-acting opiate such as methadone, or if the victim is known to have taken other drugs besides the opiate. All drug users are familiar with reports of legal repercussions when professional help is summoned for an opiate-overdosed peer.

*I'm thinkin', 'Oh my god, I'm going to jail. Oh, my god, my friend's gonna die.' I don't want him to die, but yet I'm looking at ... I got, like, 20 bags of dope in the car. I don't want to go to jail.**

Unfortunately, these reports are not exaggerated, and it is not unknown for a peer to face charges as severe as manslaughter as a consequence of trying to assist a dying friend. One huge advantage of naloxone is that it defers the emergency: an overdose victim can be restored to consciousness and spontaneous breathing long enough to be transported to the hospital, thereby avoiding invitation of law enforcement personnel into the using environment. Also, several studies have examined cases where overdose victims refused follow-up treatment after administration of naloxone, either by paramedics in the field or in the ED.¹⁹⁻²² There was no evidence of increased mortality with this practice, suggesting that simple reversal with naloxone may be all the acute treatment that most opiate overdose victims require.

*I carry naloxone with me ... I went and got it and they're, like, showering him with water and I just, um, injected a cc into his arm and he came out of it pretty quick.**

Participant Instruction

Several salient points are addressed in the instruction of participants prior to prescription of naloxone. First, we discuss overdose prevention and risk factors. Injection techniques that allow titration of the injected dose rather than uncontrollable bolus administration are described. Risk factors that are stressed include polydrug use, lack of tolerance (the occasional user) and recent abstinence. We have seen that a period of abstinence as brief as 72 hours (e.g., a 3-day hospital detoxification or a weekend incarceration) can be associated with overdose; other investigators have also identified brief

periods of abstinence as a risk factor for overdose.^{15,16,23} Repeated administration of opioid antagonists may also precipitate changes in opioid tolerance and increase risk for subsequent overdose;^{24,25} this phenomenon must be explored vis a vis the prescription of naltrexone in detox programs.

*Two days fresh out of jail... this guy dies.
So many days clean . . . that person dies.
So you watch 'em . . .**

Another significant risk factor is use of multiple drugs. Alcohol and benzodiazepines have synergistic effect on CNS depression, but cocaine and other stimulants also increase risk for opiate overdose. We have found it important to instruct participants specifically about this interaction, as it is in contradiction to street folklore that cocaine use protects against heroin overdose. We stress to participants that reversal of opiate overdose in mixed overdose situations can only improve the clinical picture, so naloxone should be administered in any case where opiates are suspected as a component of the overdose.

*It saved his life. It saved mine. I know it was the naloxone . . . yeah, I'm proud of what I did. You're damn right I am.**

Early recognition of opiate overdose is discussed. Most opiate users realize that an overdose has occurred when cyanosis develops. We urge participants to make the diagnosis early, based on unresponsiveness to verbal and painful stimuli, rather than to wait for cyanosis. We stress the safety and specificity of naloxone and recommend that it be used whenever opiate overdose is suspected.

*They do it their way and then there's my way [naloxone]. Too many people die in the tub with the shower on 'em. That don't work.**

Most IDUs have at least indirect experience with the severe opiate abstinence syndrome (OAS) that can be precipitated by naloxone administration. The Physician's Desk Reference¹⁰ recommends a dose of 0.4-2 mg of naloxone, administered either intravenously or

intramuscularly. It is more common for the higher dose and the intravenous route to be utilized by medical personnel. This dose can (and often does) illicit very severe OAS. Our experience (with 319 reversal reports to date) is that a dose of 0.4-0.8 mg intramuscularly is sufficient in virtually all cases, and that the opiate reversal symptoms are mild and abate within 40-60 minutes as the naloxone is metabolized. However, it should be noted that heroin in the Chicago area tends to be approximately 25% pure, and in areas where the available heroin is of greater purity, a higher dose of naloxone may be necessary.

The pharmacokinetics of naloxone, particularly the brevity of its half life in comparison to the opiate agonists it is intended to reverse, is another point that is stressed in participant education. We instruct participants that the mild OAS symptoms resulting from naloxone administration will wear off within 40-60 minutes, but so will the antidote effect of naloxone. We stress that (1) the victim must be deterred from using more opiate, and (2) the victim must be observed for at least two hours after the overdose reversal, and naloxone re-administered if symptoms of overdose recur. No rescuers have reported any difficulty in convincing the victim to abstain from opiates, and we have had no reports of instances where a second dose of naloxone was necessary to treat return of overdose. This is in accordance with studies previously cited documenting the efficacy of a single dose of naloxone in the field by medical personnel.¹⁹⁻²²

*I think it's important that people should . . . that this [naloxone] be made available to most people. I mean, 'cause it's a life-saver.**

Formulation of Medication

We researched several formulations and preparations of naloxone. A single-dose preloaded syringe appeared at first glance to be desirable, but was discarded because of cost, fragility of the apparatus, and fear that the apparatus would be dismantled for use in heroin injection (thereby making the naloxone unavailable). We also investigated a single-dose glass

ampoule, but that was rejected as being too fragile and unwieldy to use.

We settled, via consensus of our participant consumer advocate groups, on a multi-dose vial of generic medication (10 ml of 0.4 mg/ml). This formulation is the most inexpensive (\$2.54/vial, or approximately \$0.25/dose), but has other distinct advantages as well. The vial is small and can be easily carried in a pocket. It does not bend or break like a pre-loaded syringe or single-dose glass ampoule can. Most importantly, a significant number of the reports we have received of overdose reversals involve more than one person overdosing in a single situation. This makes intuitive sense, as groups of people tend to purchase heroin at the same time from the same source before using together. In this situation, a single-use formulation would put the rescuer in an impossible dilemma: either give all his friends a partial dose, and give all but one of his friends an injection with a used needle; or choose which friend to save.

*So, like, FOUR of 'em go down and we're just freaking out . . . but I just kept loading up needles with the stuff [naloxone] and my husband just went down the line and gave 'em all a shot, boom, boom, boom . . . they all came around.**

We stress the importance of introducing only sterile needles into the sterile vial, and provide several intramuscular needles. We also urge our participants to return any used vials to us, to be replaced with a new, sterile, unused vial.

CONCLUSIONS

We present here our experiences with a program to help educate opiate users in the use of naloxone to reverse overdose. Participants are educated, and naloxone prescribed, throughout CRA's extensive harm reduction outreach network. To date, approximately 3,500 10-dose vials of naloxone have been prescribed. No clinical, legal or liability repercussions have ensued. To date we have received reports of 319 peer reversals, with only one report of an unsuccessful reversal in a complicated multi-drug overdose situation. Only two reports of adverse events have been received: one case of severe

OAS and one case of seizures (in a participant with high-dose alprazolam use). There has been a reversal in the upward trend of opiate overdose deaths reported by the Cook County Medical Examiner's office since initiation of this overdose prevention program.

*I did SOMETHING, you know, that made a difference. The whole world can't see it but I know it made a difference. And that's important . . . to me.**

NOTE

*All quotes were collected by Suzanne Carlberg-Racich, MSPH, in her study of participants' responses and attitudes to CRA's overdose prevention program.

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