

Review of the current Milwaukee County EMS Narcotic/Opiate Overdose Protocol in light of new toxicological threats in Milwaukee County

BACKGROUND

Based on the rise in overdose deaths, and several weekends with particularly large death tolls in Milwaukee County, we conducted a review of the literature on prehospital overdose treatments to determine if there should be any recommended changes to the emergency medical service (EMS) overdose treatment protocols in Milwaukee County. We also obtained and reviewed EMS protocols from Cincinnati and Columbus, Ohio in light of their recent surge in opioid overdoses and the identification of increased presence of fentanyl derivatives such as carfentanil.

Naloxone dosing: There are no definitive studies that have determined the optimal dose of naloxone to administer to a patient with suspected overdose. Recommendations for initial dose can vary 10-fold based on reference and medical specialty. In general, emergency medicine and anesthesia references suggest higher doses (0.4mg) while medical toxicology and general medicine references suggest much lower doses (0.04mg).⁶

Intranasal versus IM/IV: In the prehospital setting, 2mg IN naloxone was as effective as 0.4mg IV naloxone at reversing opioid induced bradypnea.¹² Per the manufacturer's guidelines of a popular nasal atomizer device, the maximum volume per dose is 2mL. Most naloxone comes in a concentration of 1mg/mL. Intranasal naloxone has an approximate bioavailability of 4% while IM naloxone has a bioavailability of 36%.⁷

Adverse events after naloxone reversal of opioid overdose: There is concern that following naloxone administration and reversal of opioid intoxication that patients may have one of many adverse events. The most concerning adverse events are pulmonary complications such as pulmonary edema and severe opioid withdrawal causing vomiting leading to aspiration pneumonitis. Other concerns are potential unmasking of other drug intoxications such as methamphetamine, cocaine, or other stimulants, leading to behavioral disturbances. The actual rate of these adverse events witnessed by EMS was addressed in a one year prospective study in Oslo Norway. The total number of events in those who received naloxone was 45% and vomiting was only seen in 9% of patients. Overall, only 0.3% of cases led to hospitalization.⁴ Another retrospective study done in Pittsburgh, found a much lower rate of adverse events following naloxone administration. Only 0.2% of patients vomited and none developed aspiration pneumonitis.³ Furthermore, take home naloxone kits have been shown to be safe and reduce mortality.^{8,11} Based on a survey by the Harm Reduction Coalition, 140 organizations known to provide naloxone kits to laypersons reported the distribution of 152,283 naloxone kits and 26,463 overdose reversals.¹⁵ The rate of adverse events seen following naloxone administration is low and even administration by lay persons with no medical training has been shown to be safe. To date, there has been no direct comparison of the safety and/or outcomes of assisted ventilation/intubation versus naloxone for opioid overdoses in the prehospital setting.

Increasing appearance of fentanyl contaminated drugs of abuse: Fentanyl is 100 times more potent than morphine and 600 times more lipid soluble; increasing its penetration into the brain. Multiple outbreaks of fentanyl contamination leading to sudden increases in overdoses has occurred throughout North America.^{1,5,10,13} Fentanyl overdoses often require higher doses of naloxone to reverse respiratory depression.⁴ There has also been an influx of synthetic opioids and illicitly manufactured fentanyl into the illegal drug market. It is either found as a heroin contaminant or being sold in pill form.^{2,9} Typically, once these compounds show up in the market, there is a significant time delay to the development of an assay to identify these chemicals in post-mortem samples. By the time the chemical is identified with reliability, either from post mortem samples or seized drug samples, the synthetic drug manufacturers have already flooded the market with a new compound. The primary effects of these synthetic opioid compounds are on the mu-opioid receptor leading to respiratory depression that is reversed by naloxone. Thus, although there are new opioids potentially contaminating illicit pills and heroin, the only change in management from an EMS standpoint would be to consider higher doses of naloxone. There is unlikely to be a role for real-time substance identification in EMS response to overdose since there are no new or different treatments that can be used to improve outcomes. As these new and more potent substances are sold on the illicit drug market, EMS providers will need to be aware that more naloxone may be needed to reverse the respiratory depression associated with overdose.

Key roles of EMS in preventing opioid overdose deaths:

- Administering naloxone
- Supporting oxygenation and ventilation
- Transport to a medical facility

Recommended changes to the current MCEMS opioid overdose protocol:

1. *Increase the initial dose of intranasal naloxone to 2mg.* This is based on less bioavailability than IM/IV forms and the recommended maximum volume to be administered.
2. *Remove the maximum dose limit of 2mg requiring medical consult.* This recommendation is based on the low incidence of adverse events with naloxone administration and the increasing appearance of fentanyl contaminated drugs of abuse throughout North America and within Milwaukee County (unpublished medical examiner data).

However, it is understood that these recommendations are based on toxicological principals. Implementation into EMS practice should be made based also on EMS principals of protocol development and the minimization of error. For example, medical directors will need to balance the risk of having differing drug dosages by administration route and choose between higher intranasal doses versus multiple administrations of a dose that can be administered by any available route. In reviewing the proposed changes to the Milwaukee County EMS protocols we believe that they meet these recommendations and should be implemented as soon as possible.

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