

Pre-Hospital Administration of Naloxone with No Indication in Opioids Overdose

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Abstract

Background: Overdose of opioids is one of the most common medical problems that requires medical staff to have enough information for minimizing its mortality. Naloxone is used as an antidote to reverse the signs and symptoms of opioid toxicity such as respiratory depression. Indications for naloxone administration in opioid poisoning are well known. While naloxone administration without indication has some complications and may put financial burden on the patient's shoulder, it can be also considered a medical error. The aim of this study was to evaluate the frequency of pre-hospital administration of naloxone without an accurate indication for the poisoned patients.

Methods: In this retrospective cross-sectional study, all poisoned patients hospitalized in northwest toxicology center of Iran who had received naloxone before hospitalization were included. Data collection was performed by reviewing patients' files. Since indications for naloxone in overdose of opioids are well known, any other administrations out of the specified indications is considered as prescriptions without indication.

Results: Our results show that 178 of the study subjects were men and 22 were women. Naloxone was administered in 57% of the patients that of them 31.57% had specified indication. Among these patients, 19.44% had respiratory rate less than 12 breaths per minute, 66.66% had decreased level of consciousness, and 13.88% had both conditions. All patients with oxygen saturation less than 90% had respiratory rate below 12.

Conclusion: Results of this study showed a high administration rate of naloxone without an appropriate indication. We suggest that it is necessary to reduce such medication errors by continues training of healthcare providers.

Keywords: Antidotes, Drug overdose, Naloxone, Opioids

Introduction

Generally, any synthetic, semi synthetic and natural substance with morphine-like effects that is able to bind and act via the opioid receptors are called opioids¹⁻³. Opioids toxicity manifests as loss of consciousness, decreased Respiratory Rate (RR) and apnea, ileus and pinpoint pupils when opioid receptors are affected in the central nerves system^{1,2}.

Unfortunately, there is no available national data either for the frequency of poisonings among drug abusers or its causes. One study revealed that the incidence of drug abuse had been increased within the past 30 years. Studies on cases referred to legal medicine organizations, medical toxicology and poisoning wards of hospitals in different provinces of Iran report opioids as a relatively common cause of acute poisoning⁴⁻⁶.

High doses of opioid agonists can cause respiratory depression, miosis and finally coma and death. If serious symptoms of opioids overdose are timely diagnosed, possible respiratory arrest and death can be prevented by the administration of opioids receptor antagonists such as naloxone⁷.

Since 1996, many programs have been developed in order to use the opioid antagonist naloxone hydrochloride to reverse the effects of heroin and other opioids, particularly the respiratory depression⁸⁻¹¹.

Naloxone is used to reverse the signs and symptoms of opioid toxicity such as respiratory depression causing no serious contraindications. For the addicted patients, the starting dose of naloxone is 0.04-0.05 mg to avoid withdrawal syndrome and other complications of naloxone. Response to naloxone is measured through improvement in the respiratory response. Depending on the symptoms and their severity, naloxone is used as either infusion or frequent bolus injections due to its short half-life (30-90 minutes)^{7,12,13}.

Cropey *et al* in 2013 stated that opioids poisoning was one of the most common problems in the societies and suggested that it would be necessary for medical staff to have enough information about naloxone to prevent opioid mortality¹⁴. Acute opioid poisoning has a low mortality rate if it is treated appropriately¹⁵. Studies have

shown that two-third of deaths due to opioids poisoning can be preventable through access to naloxone at home. Naloxone administration and securing the airway are the most vital actions in an opioid-overdosed patient^{7,8,10,16}.

Intravenous administration of naloxone rapidly improves respiratory function. Since the half-life of naloxone is shorter than most of opioids, maintenance administration is necessary to avoid recurrence of respiratory depression. However, in addicted individuals naloxone can exacerbate withdrawal symptoms⁷.

Indications for naloxone administration in poisonings are well known. Naloxone administration without indication has some complications (sometimes life-threatening) and may cause financial burden and it can be also considered a medical error. The aim of this study was to evaluate the frequency of naloxone administration without indication in poisoned patients.

Patients and Methods

This study was a retrospective cross-sectional study on all patients admitted in the northwestern toxicology center of Iran from October 2016 to March 2017 who had received naloxone before hospitalization. Data collection was performed by reviewing the patients' files.

A separate file and a questionnaire were filled out for each poisoned patient who had received naloxone before hospitalization in the toxicology ward, regardless of sex and age. All patients' information such as age, sex, education level, and symptoms of poisoning were recorded.

Presence of opioid-overdose symptoms and naloxone administration were considered as inclusion criteria in this study. Poisoned patients who did not receive naloxone were excluded.

Indications for naloxone administration in poisoned patients with opioid overdose were as follows: respiratory depression RR less than 12 breath per minute or oxygen saturation less than 90% [in the absence of pulmonary edema, Acute Respiratory Distress Syndrome (ARDS) or aspiration pneumonia] and decreased level of consciousness Glasgow Coma Scale (GCS) below 8^{1,7,11-13,17,18}. Any other naloxone administrations

were considered as prescriptions without appropriate indication. Data are depicted as percentage, mean and standard deviation. SPSS version 18 and Chi-square test were used.

Results

In this study, 178 men (89%) and 22 women (11%) were included while the average age of the patients was 40.95 ± 15 years (min = 18, max = 90 years old). Of them, 32% were illiterate, 18% had primary education, 25% had secondary education and 4% had even higher education. Patients' vital signs and level of consciousness (according to GCS) are shown in table 1. Types of poisonings are also analyzed in figure 1.

Table 1. Vital signs, percent of oxygen saturation, and level of consciousness of the patients before hospitalization

Variable	Mean \pm SD	Min	Max
SBP	112.92 \pm 18.52	50	170
DBP	71.54 \pm 12.40	40	105
HR	87.32 \pm 15.23	41	125
BT	36.83 \pm 0.66	35.5	39
RR	19.14 \pm 7.44	6	50
O ₂ Sat (%)	92.67 \pm 4.53	80	98
GCS	10.76 \pm 4.21	3	15

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; BT: Body Temperature; RR: Respiratory Rate; O₂Sat: Arterial Blood Oxygen Saturation; GCS: Glasgow Coma Scale

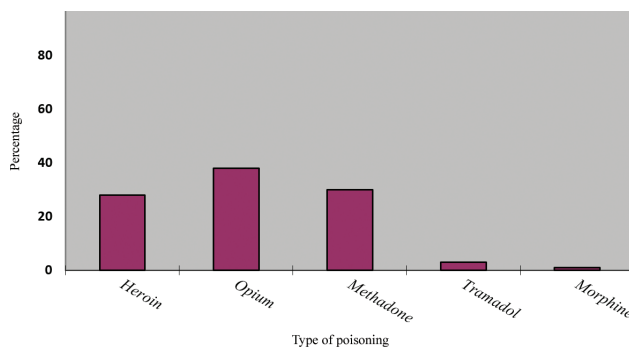


Figure 1. Type of poisonings among the patients: 28% heroin, 38% opium, 30% methadone, 3% Tramadol, and 1% morphine.

We observed that naloxone was given in 57% (114 patients) of the patients that of them 31.57% (36 patients) had indication (RR<12 or decreased level of consciousness defined as coma). Among these patients, 19.44% (7 patients) had RR less

than 12 breaths per minute, 66.66% (24 patients) had decreased level of consciousness, and 13.88% (5 patients) had both conditions. All patients with O₂Sat below 90% had a RR of <12.

The discharge status of the patients was also studied which was as 66% after complete remission, 10% died and 24% left the hospital on their own will.

Discussion

Opioid addiction is a major cause of inefficiencies in young healthy people. This can be the main reason for family breakdown and other behavior problems. Unfortunately, in the past ten years, opioids and particularly methadone abuse have become more than ten times frequent than before^{1,4,8,19,20}. The addicted people have short life span due to various problems including accidents, malnutrition and toxicity. Acute toxicity with opioids is a medical emergency in which prompt diagnosis and treatment can be lifesaving²¹.

Opium receptors are highly concentrated in the brain (the thalamus and amygdala) and are immediately and frequently stimulated by natural morphine-like agents. Unlike natural substances, synthetic opioids usually have long-term effects and decrease the receptors sensitivity after continuous stimulation; so, tolerance and then addiction occurs with prolonged consumption^{3,16,22}.

The first attempt in the management of a case of opioid poisoning is respiratory support. RR less than 12 breaths per minute even in the absence of pinpoint pupils and history of addiction is an indication for immediate supportive therapy¹³. Intravenous injection of naloxone at a dose of 0.04 mg should be administered concurrently¹³. If IV access is not available at the time, the same amount of antidote can be prescribed though nasal rout or tracheal tube. Naloxone acts within two minutes and lasts for 30 to 90 minutes. Depending on the severity of poisoning, further doses may be required up to a maximum of 10-12 mg. Other causes of coma should also be ruled out if the symptoms persist after the maximum dose has been tried^{7,11,13,18}. On the other hand, it is possible to neutralize toxic agents with activated charcoal within less than one hour of the time of using opioids^{7,12,13,18}.

Naloxone given to an addicted person can result

in serious complications such as, arrhythmia, ischemic heart disease, pulmonary edema, acute agitation, delirium and other withdrawal symptoms, and even death^{1,9,11,13,23,24}. Unfortunately, naloxone is prescribed in some hospitals without any medical indications. In fact patients with RR less than 12 and GCS score less than 8 benefit from naloxone administration^{7,12,13,17}.

In this study, 33% of the poisoned patients (36 patients) met the indications for naloxone administration with 7 of them having RR less than 12/minute, 24 GCS<8, and 5 having both conditions. It has been observed that naloxone improved respiratory status and consciousness in such patients.

Berling's study showed that 47% (65 persons) of 137 patients with overdose of oxycodone, who were given naloxone, had appropriate indications²⁵. In a study from China, where the most common drug was heroin, naloxone was indicated only in 63.4% of patients¹⁶.

In our study, naloxone was given in 57% of patients (114 persons) that of them, only 31% had indication for the antidote. The frequency of naloxone administration without indication was higher in this study compared to the previous researches.

One of the important issues that have been discussed in this study is medication error, which is defined as a failure in the treatment process that can be harmful to the patient²⁶. Failure in the treatment shows that the process, which was carried out in order to treat the patient, is not in accordance with the required standards²⁷. An important medication error that may be caused by a physician is to prescribe a wrong medication or administration without indication²⁸.

Medication errors can be also occurred due to adverse effects of drugs in the body. In order to prevent such errors, mutual cooperation is required between the patient, the pharmacist, and the physician, along with other therapeutic factors^{27,28}.

Drug administration errors account for nearly 70% of medical errors, which is accompanied with serious complications. Four out of 1000 people may experience adverse effects of incorrect drug administration. Errors in prescribing appropriate therapeutic dosage of a specific medication account for more than 50% of all medical errors²⁷⁻²⁹. A meta-analysis study suggested that the majority of medication errors in hospitals are by young physicians. These errors can be occurred in 2 to 514 out of 1000 administrations or in other word in 2.4 to 82% of patients³⁰.

In the current study, we have found that there was no indication for naloxone administration in 69% of the patients who received this antidote, and this can be accounted as a medication error. It can be concluded that naloxone was administered by medical staff in 69% of poisoned patients without indication before being hospitalized in toxicology ward of Sina hospital, Tabriz. Sometimes such errors may cause side effects (even life threatening) in addition to financial burdens.

Administration of naloxone with no appropriate indication was calculated as a high as 69% compared with that (2.4 to 82%) observed in other developed countries²⁰⁻²². This indicates a lack of systematic continuous training programs to update medical staffs' information on the treatment of poisoned patients in our country, however there is a potential capacity of presence of medical toxicology experts in most medical universities who can train them.

Conclusion

The results of this study showed a high rate of naloxone administration without appropriate indication and it is necessary to reduce medication errors by continues training of physicians and other medical staffs in healthcare centers and toxicology wards.

Conflict of Interests

None declared.

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