

USE OF NALOXONE FOR REVERSAL OF PICTURES OF OPIOID POISONING

Nathan Augusto de Almeida Santana

Pontifícia Universidade Católica de Goiás
Goiania Goiás

<https://lattes.cnpq.br/0535870805208977>

Alexandre Augusto de Andrade Santana

Pontifícia Universidade Católica de Goiás
Goiania Goiás

<http://lattes.cnpq.br/7288954710999190>

Ana Karla Aguiar de Oliveira Lopes

Pontifícia Universidade Católica de Goiás
Goiania Goiás

<http://lattes.cnpq.br/3929724927856003>

Bernardo Malheiros Tessari

Pontifícia Universidade Católica de Goiás
Goiania Goiás

<http://lattes.cnpq.br/0660469321898622>

Bruna Costa Alves

Pontifícia Universidade Católica de Goiás
Goiania Goiás

<https://lattes.cnpq.br/2566044836908029>

Gustavo Rodrigues Povoá

Pontifícia Universidade Católica de Goiás
Goiania Goiás

<http://lattes.cnpq.br/0380663272451487>

Isabela de Paula Sa

Pontifícia Universidade Católica de Goiás
Goiania Goiás

<http://lattes.cnpq.br/5204595340295968>

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



Lara Pedriel Barreto

Pontifícia Universidade Católica de Goiás
Goiania Goiás
<https://lattes.cnpq.br/6694036166400007>

Natalia Ribeiro Silverio

Pontifícia Universidade Católica de Goiás
Goiania Goiás
<http://lattes.cnpq.br/68733333735498690>

Sergio Gabriell de Oliveira Moura

Pontifícia Universidade Católica de Goiás
Goiania Goiás
<http://lattes.cnpq.br/8428526850411608>

Yuri Borges Bitu de Freitas

Pontifícia Universidade Católica de Goiás
Goiania Goiás
<http://lattes.cnpq.br/1656337426176041>

Luciano Alves Matias da Silveira

Universidade Federal do Triângulo Mineiro
Uberaba – Minas Gerais
<http://lattes.cnpq.br/5516531092140004>

Abstract: Introduction: The consumption of illegal substances is notably a global public health problem. From this, opioid intoxication is, for example, the main cause of drug-related deaths in Austria. In this sense, the administration of Naloxone appears as a tool to combat toxic situations triggered by the use of substances of an opioid nature, given its antagonistic effect on the receptors of this class. **Goals:** to analyze the effects of using Naloxone as an intervention tool in cases of opioid intoxication. **Methods: This is an integrative literature review, in the PubMed database, based on the descriptors: “naloxone” and “opioid intoxication” in the last five years. Seven scientific articles were selected, all written in English and carried out in humans, and articles that did not fit the goals of the present study were excluded. Results:** Naloxone was a significant intervening agent in the absolute majority of cases of opioid intoxication. Select exceptions were observed in which patients required endotracheal intubation and mechanical ventilation due to respiratory failure relatively refractory to large doses of Naloxone. However, the use of opioid antagonist medication has been proven to be the safest and most efficient method of reversing intoxication, with great results even as a treatment for cases of alcohol dependence. **Conclusion:** the use of naloxone to reverse opioid intoxication conditions proved to be safe and efficient, but with some adverse effects when using high doses of this opioid receptor antagonist. It is concluded that the administration of naloxone, in adequate doses, is a useful tool in overdose or acute opioid intoxication.

Keywords: Intoxication; naloxone; opioids.

INTRODUCTION

Illicit substance abuse is a worldwide public health problem, with a high probability of fatal outcome. Currently, opioid intoxication

is the leading cause of deaths associated with illegal drugs in Austria (NICOLAKIS J et al, 2020). Recently in the United States (USA) the increase in opioid deaths in the US has been attributed to the number of opioid prescriptions. In the UK primary care environment, there was also an escalation in opioid prescribing between 2000 and 2010. Although heroin is still the opioid most often involved in fatal overdoses in Europe, the proportion of deaths involving methadone, buprenorphine, fentanyl and tramadol is increasing in several countries. In Norway, the number of fatal opioid overdoses has remained stable at 250-300 per year for the past 15 years, but the proportion caused by prescription opioids has increased from 30 to 50% (GRIMSRUD MM et al, 2019).

Faced with this problem in public health, several factors contribute to its scope and danger, one of these factors stands out for its lethality, which is the practice of co-use of stimulant opioids configured as a complex behavior, which is strongly influenced by the history of use of drugs of an individual and their physical/psychological dependence on opioids. In many cases, concomitant use has been reported as a way of regaining control during heavy periods of crystal methamphetamine use, reducing the negative side effects of opioid withdrawal and satisfying the perceived psychological need to be intoxicated, thus fostering the continuation of this drug addiction. practice of recreationally using opioids in a dangerous way (PALMER A et al, 2020).

As a counterpoint to the above-mentioned aggravation, drug and behavioral therapies were designed to combat opioid abuse and the aggravations resulting from episodes of severe intoxication. Among these resolute proposals, the recommendation to use opioid receptor antagonists has been widely discussed and implemented in different ways, aiming at

improving these health indicators linked to the use of opium-derived substances. Among these medications, naltrexone for sustained-release suspension for injection (XR-NTX) is an FDA-approved opioid antagonist that can be given to people who have had their opioids reduced to help prevent relapse. The duration of action of one month is attractive for patients and professionals looking for an alternative to daily agonist treatment that requires physical dependence on opioids. In cases of emergency treatment linked to opioid overdose, Naloxone is used with the same antagonistic action (FRIEDMANN, PD et al, 2018).

Therefore, the present study seeks, through a comprehensive retrospective bibliographic approach, to evaluate the use of opioid antagonist medications for cases of reversal of opioid intoxication, as well as to evaluate the ways of execution, accessibility and effectiveness of this intervention against intoxication by derivatives of opium.

METHODOLOGY

This is an integrative review of the literature designed according to the criteria of the PICO strategy, an acronym that represents: population, intervention, comparison and outcome, for the elaboration of the guiding question of the research: "What are the benefits of using naloxone for reversal of conditions?" of opioid intoxication?"

In this sense, according to the parameters mentioned above, the population or problem of this research refers to patients who used Naloxone to reverse the condition of opioid intoxication; the intervention has a prognostic character; the comparison is of non-intervention, due to the design of the work; and the expected outcome is the identification of corollary benefits to the use of Naloxone for the aforementioned circumstance.

From this, a search was carried out in the

PubMed (Medline) database, from the Virtual Health Library, with the descriptors *MeSH / DeCS Naloxone* and *Opioid. Intoxication* and the Boolean term AND, that is, the search strategy was: “ *naloxone AND opioid intoxication*”. It is worth remembering that the last search was carried out in September 2022.

Furthermore, for the development of the present study, all complete articles indexed in the last five years, carried out in humans and written in the English language that were related to the evaluation of naloxone in cases of opioid intoxication, without previous period limit, were included, that incomplete articles or that did not fit the objective of the study were excluded and the filters used were, namely, “ *full text* ” “ *5 years* ”, “ *humans* ”, “ *English* ” and “ *clinical trial* ” on PubMed.

From the screening methodology, a total of 239 studies were found in the electronic database search. After applying the filters, 207 were removed from the list, with 32 remaining. After reviewing titles and abstracts, 25 articles were excluded, so that 7 remained for full text analysis and evaluation. Of these, 6 were included in the qualitative analysis synthesis.

Among the reasons for excluding the identified articles are: they do not present the filters indicated in the methodology and do not fit the theme proposed in the goals.

RESULTS

Acute poisoning by the recreational use of prescribed controlled medications is increasing, with benzodiazepines, followed by opioids, the main drugs used for this purpose. In most cases of intoxication (80% of them) an association was found between the use of medication in conjunction with illicit drugs (2 out of 3) and/or alcohol (1 out of 3). The main opioids used in cases of intoxication were methadone and buprenorphine, being brought by ambulance to health centers, where the most severe cases needed to be reversed with

the use of naloxone and some patients required hospitalization in a psychiatric ward for better control. of the picture, since they were with a considerably reduced level of consciousness or even in a coma. (GRIMSRUD et al., 2019).

In view of the cases of intoxication, extended-release naltrexone (XR-NTX) injected intramuscularly monthly has been shown to reduce relapse in people with opioid use disorder. In this regard, the article questions whether variable patient characteristics, including age, sex, depression, suicidal thoughts, risk of drug abuse, substance use, medical, psychiatric and employment status, socialization, legal and family/social issues, abuse history and quality of life measures may moderate the effect of medication for opioid use disorder. As a result, it was reported that XR-NTX appeared to work equally well in subgroups with diverse demographic, addiction, mental health, and environmental characteristics, with the possible exception of working better among those without recent alcohol intoxication. Thus, alcohol use for intoxication in the 30 days prior to randomization was a significant moderator: during the treatment phase, those who reported having recently been intoxicated before randomization to XR-NTX relapsed to opioids at a rate (56%) similar to usual care (58%), while those without alcohol intoxication in the last 30 days had a lower rate of opioid relapse (41% vs. 65%, respectively, $P<0.04$) (FRIEDMANN, PD et al, 2018)).

Another study also showed that the use of Naltrexone, an opioid antagonist of the same class as naloxone, can be used in the treatment of addiction in young addicts. The results were positive in reducing daily consumption and blood alcohol concentration. In addition to having also analyzed its relationships with desire, mood and alcohol use in young adults and how the personal variables of each individual, social and family factors and

consumption desire are a possible variable for the prophylactic use of naltrexone. (BOLD et al., 2016).

However, there are reports of methamphetamine-opioid co-use / co-injection with the motivation that small amounts of crystal methamphetamine used with heroin can prolong the intoxicating effect of heroin and therefore the duration of opioid withdrawal (PALMER et al., 2020).

Thus, it is of great importance for physicians and first responders to be able to recognize the need to administer multiple doses or high doses of naloxone in cases of opioid overdose that do not respond to the administration of a single standard dose of naloxone. It is worth noting that the total dose of naloxone needed will depend on many factors, including the opioid dose, the potency of the opioid at binding receptors, the lipophilicity of the opioid when crossing to the central nervous system, the elimination half-life of the opioid, individual patient factors and the route of administration of naloxone. Furthermore, it was shown that most patients were cocaine users, but not opioid users, which demonstrates that illicit opioids are often mixed with adulterants, as for example in this report in which fentanyl was sold as cocaine (TOMASSONI et al., 2017).

After the rescue of these patients, there is still a need for a process of detoxification and overcoming addiction. However, access to Naloxone Overdose and Distribution Education (OEND) programs is restricted to individuals who access harm reduction services or who have been trained. In this sense, the approach of this article goes through the understanding of how the expansion of such programs to general medical environments can impact society to increase the success of patient adherence. Thus, the provision of OEND in a variety of healthcare settings, such as psychiatric

inpatient units, residential rehabilitation centers, emergency departments, outpatient clinics and pharmacies are not fully explored and in practice, many patients who need this program end up going unnoticed and being discharged before receiving the educational process (JAKUBOWSKI, et al).

CONCLUSION

The use of opium-derived substances dates back thousands of years, but remains a pervasive public health problem. Currently, opioids are controlled medications, but due to their recreational use, they have high lethality associated, mainly, with abuse and intoxication. Thus, therapies to combat opioid abuse and injuries resulting from intoxication were explored, including 2 opioid antagonists, naloxone and naltrexone.

Naloxone proved to be a safe and efficient therapy in reversing the condition of opioid intoxication in emergency cases, with an important caveat in its dose. The total dose used varies by several factors and depends on the healthcare professional's experience in associating a higher dose in non-responsive cases with the standard dose according to the individual clinical picture.

Naltrexone is also an alternative to opioid addiction treatment for its proven prophylactic use in different demographic, mental health, environmental and addiction subgroups, with the exception of recent alcohol intoxication. Due to its monthly application route, it is highly effective in reducing relapses.

REFERENCES

- BOLD, K. W. et al. **Daily relations among affect, urge, targeted naltrexone, and alcohol use in young adults.** *Experimental and Clinical Psychopharmacology*, v. 24, n. 5, p. 367–375, 1 out. 2016.
- FRIEDMANN, P. D. et al. **Do patient characteristics moderate the effect of extended-release naltrexone (XR-NTX) for opioid use disorder?.** *Journal of substance abuse treatment* vol. 85 (2018): 61-65. doi:10.1016/j.jsat.2017.01.018
- GRIMSRUD, M. M. et al. **Acute poisoning related to the recreational use of prescription drugs: An observational study from Oslo, Norway.** *BMC Emergency Medicine*, v. 19, n. 1, 15 out. 2019.
- JAKUBOWSKI, A. et al. **“Development and evaluation of a pilot overdose education and naloxone distribution program for hospitalized general medical patients.”** *Substance abuse* vol. 40,1 (2019): 61-65. doi:10.1080/08897077.2018.1518836
- PALMER, A. et al. **Motivations for crystal methamphetamine-opioid co-injection/co-use amongst community-recruited people who inject drugs: A qualitative study.** *Harm Reduction Journal*, v. 17, n. 1, 27 fev. 2020.
- TOMASSONI, A. J. et al. **Multiple Fentanyl Overdoses — New Haven, Connecticut, June 23, 2016.** *MMWR Morb Mortal Wkly Rep.*, vol 66, n. 4, p. 107-111, 3 fev. 2017. doi: 10.15585/mm6604a4.