Scholars Journal of Medical Case Reports

OPEN ACCESS

Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

Accidental Opioid Intoxication in Children Treated With Low Doses of Naloxone: A Case of Fentanyl Patch Exposure and a Case of Morphine Tablet Ingestion

El Kihel H[1*], Arfaoui M[1], Chaker A[1], Bentalha A[1], Elkoraichi A[1], Echcherif El Kettani S[1]

[1]Intensive care department, Children's Hospital of Rabat, Morocco

DOI: 10.36347/sjmcr.2021.v09i10.016 | **Received:** 07.09.2021 | **Accepted:** 11.10.2021 | **Published:** 14.10.2021

***Corresponding author:** El Kihel H

Abstract **Case Report**

Accidental opioid intoxication in children is a rare affection in morocco, its recognition and management must be immediate to avoid its life threatening complications. In a period of two years (September 2019 - September 2021), two cases of severe opioid intoxication in children have been admitted in the intensive care department of the children's hospital of Rabat. The first case is a 9 years old child admitted for tonic-clonic seizures with acute respiratory distress due to Fentanyl intoxication after being exposed to a skin patch dosed 75 µg/hour, he required mechanical ventilation and was treated with a bolus of 0,8 mg of Naloxone completed with continuous infusion for 48 hours with favorable evolution and hospital release in 5 days. The second case is a 2 years 5 months old child admitted for decreased consciousness with bradypnea due to morphine intoxication after oral ingestion of 5 extended-release morphine tablets dosed 30 mg each, treated with a single bolus of 0,8 mg of Naloxone with rapid improvement.

Keywords: Accidental opioid intoxication, child, tonic-clonic, morphine. awareness

INTRODUCTION

With the increase of prescription, the use of heroine and the lack of awareness; opioid poisoning, accidental or due to substance abuse, increasingly affects children worldwide and has become a danger that threatens their future and their lives. The easy access to pain medications or drugs used by parents or relatives is often the cause of accidental intoxications [1]. It is a life threatening medical emergency that requires early detection and immediate intervention. Respiratory depression and hypoxia are the lead causes of death [2].

Naloxone is the standard treatment; it must be used with precaution and under surveillance. Low doses may allow an efficient treatment and avoidance of the side effects [3].

We would like to report two cases of accidental opioid intoxication in children to highlight the importance of a better parental education and awareness about the dangers of these drugs and to discuss the possibility of use of the lowest doses of Naloxone for opioid antagonism.

CASE REPORT

We report two cases of opioid intoxication admitted in the intensive care department of the Rabat children's hospital in the periode of September 2019-September 2021:

Case 1

AG, a 9 years old child with no reported medical or surgical history who suffered a day before his admission from acute low back pain following a slip and fall accident. His father, in his attempt to relieve his son's pain, applied a Fentanyl patch dosed 75 µg/h on him (borrowed from a cousin). Eight hours later, the child was brought to the children's hospital's emergency department with generalized tonic-clonic seizures; he was placed in a lateral safety position and received a bolus of 2 mg of midazolam. After the management of the seizures, his Glasgow coma scale was evaluated at 3, he had a miosis non reactive to light, bradypnea with stertorous respiration and bilateral rhonchi sounds, his oxygen saturation level was around 88%. His heart rate was 109 bpm and blood pressure was 110/60 mmHg, he had a nonketotic hyperglycemia with capillary blood glucose at 4,5 g/l and his

temperature was 37°C. The child was intubated after a crush induction and transported to the intensive care department. A cranial CT scan and an arterial blood gas analysis were performed, they showed no abnormality. The poison control center was contacted and standard toxicological screening was performed. Naloxone was administered as a bolus of 0,08 mg and then by a continuous infusion pump with a rate of 0,008 mg/h, it was continued for 48 hours until his awakening and extubation. The child was released after 5 days of hospitalization and was referred to the ophthalmology department with a sixth cranial nerve palsy that he kept as a sequela of his intoxication.

Case 2

M.L, a 2 years 5 months old child who was born at term with a normal birth weight and had no medical or surgical history. He accidentally ingested 5 extended-release morphine tablets dosed 30 mg each, the drug belonged to his father who was treated for lung cancer. One hour later, the child was brought to the children's hospital's emergency department for loss of consciousness with a Glasgow coma scale evaluated at 13, he had a miosis non reactive to light, a respiratory rate of 12 breaths/min with breathing pauses and oxygen saturation level around 96%. His heart rate was 136 bpm and his blood pressure was 100/60 mmHg, his capillary blood glucose and temperature were normal. The poison control center was contacted and standard toxicological screening was performed. The child received a single bolus of Naloxone of 0.08 mg, the Glasgow coma scale rapidly raised to 15 and the respiratory rate went back to normal (18 to 22 breaths/min), he had no urinary retention or bowel disorder. The child was released after 48 hours of hospitalization without having any sequelae.

DISCUSSION

The term "Opioid" refers to all compounds both natural, semisynthetic and synthetic that have morphine-like actions. Opioids originate naturally from the poppy plant "Papaver somniferum", there virtues and medicinal uses are known since 2000 years ago. Opium is the dried extract of the plant and Morphine is the principal alkaloid of opium [4].

Based on their affinity and efficacy at the three principal opioid receptors (Mu (μ), Delta (□) and Kappa (□)), opoids are classified into four categories: agonists, partial agonists, agonists-antagonists and antagonists. Morphine is a strong Mu agonist [5], its use as an anesthetic drug is known to be associated with many side effects such as incomplete amnesia, nausea, histamine-release, bradycardia, hyper- or hypotension, and prolonged postoperative respiratory depression, that's why in 1960 Fentanyl was synthesized to give a healthier potent alternative with mild side effects [6, 7].

There is no sufficient data concerning the opioid exposure and poisoning among children in Morocco.

The epidemiology of opioid poisoning in children varies around the world depending on the lifestyle, the education and the amount of prescription.

The incidence of opioid intoxication in children in the Maghreb region seems to be low. A retrospective study conducted in central and southern Tunisia reported only three cases of opioid intoxication among children in a period of 5 years [8].

In the United States, opioid exposure is considered to be epidemic with a high incidence among teenagers and an increase among children aged 1 to 4 years old. The rate of opioid overdose deaths in the US was doubling since 2000 and unintentional poisoning seems to be the leading cause of injury-related mortality [9].

An Iranian study published in 2016 recruited opioid-intoxicated children in a referral center for childhood toxicology and found that the cause of poising was accidental in 58% of the cases. Parents educational levels were low in most cases and 68,3% of the fathers were addicted to opium [10].

In the intensive care department of the children's hospital of Rabat, the two cases reported were the only cases admitted since September 2019. In one case, the father was not aware of the drug's danger; in the other, the drug ingested accidentally by the child was prescribed to the father and was not kept out of the child's reach.

The two children presented the main symptoms of the opioid toxidrome reported in most studies, they both arrived at the hospital with decreased consciousness, bradypnea and miosis [10-12]. The first child had a severe intoxication with an episode of tonic-clonic convulsive seizures, respiratory distress and nonketotic hyperglycemia. N. Ghaemi *et al*., in a study including 126 opioid-intoxicated children reported convulsive seizures in 8,7% of the cases and hyperglycemia was found in 11,1% of the cases. [10]. Zamani N *et al*., in a study including 310 opioid-intoxicated children reported convulsive seizures in 10.3% of the cases [11].

In the two cases we report, there was no use for toxicological testing to initiate the treatment, the toxic was identified and the symptoms were in favor. The toxicological screening was performed to confirm the diagnostic and, mainly, to eliminate the presence of other toxicants.

Naloxone, a Mu receptor antagonist, is the standard treatment for opioid intoxication; it can be administered intravenously, intramuscularly, intranasally, subcutaneously or via inhalation following nebulization or endotracheal tube in intubated patients [13]. It is considered to be a safe drug with rare side effects, but some reports of cardiovascular and pulmonary events raised awareness about the necessity of the titration of the drug with close monitoring and surveillance.

In fact, Naloxone administration can cause an increase in heart rate, cardiac output and arterial blood pressure [14], such side effects are also seen among children [15]. Rare cases of pulmonary edema following Naloxone administration to reverse the effects of opioid anesthesia or in patients with opioid-induced respiratory depression are reported [15-18]. Cardiovascular complications such as severe hypertension, atrial and ventricular tachycardia, fibrillation and sudden deaths are also reported [19, 20]. Those events could be explained by a rise in epinephrine and norepinephrine plasma concentrations observed after the administration of Naloxone causing a cardiovascular stimulation mediated by the sympathoadrenal system [21]. To prevent these complications, the American heart association recommend the usage of the lowest effective dose of Naloxone with an initial dose of 0,04 to 0,4 mg IV or IM [22]. It was demonstrated that low doses of Naloxone can effectively reverse opioid-induced ventilatory depression [23].

It is recommended to give 0.1 mg/kg of Naloxone to infants and children from birth to 5 years of age or 20 kg of body weight, and 2 mg to children older than 5 years of age or weighing more than 20 kg. Lower initial doses and titration with assisted ventilation are also recommended [24, 25].

We gave low doses of Naloxone because of the non availability of the drug in our pharmacies and because we were aware that low doses with proper care and surveillance could have beneficial effects on the respiratory distress and reversing the symptoms. Our two patients were closely monitored in the intensive care unit to detect the signs of withdrawal and to prevent and treat any possible complication. In the case of Morphine intoxication, the symptoms were reversed rapidly and the child regained his initial state hours after the treatment. However, in the case of Fentanyl intoxication, it took more than 48 hours to see the results of the treatment and be able to wean the child from the mechanical ventilation and five days to release him from the intensive care unit, this may be related to the amount of the toxicant and the duration of exposure clearly elevated in this case but also to the potency of the opioid.

The antagonism of opioid toxicity depends on the amount of the opioid, its potency, its interactions with the opioid receptor, the route of administration of Naloxone and the patient's ability to clear the drug [13]. Morphine antagonism by Naloxone is rapid and efficient compared to Fentanyl [26].

Fentanyl is known to be 50 to 100 times more potent than morphine [27]. High doses of the drug can cause accumulation in the fatty tissues thus prolonging its effect and delaying the respiratory distress. Its administration via continuous transdermal patches does not protect against its toxicity [28]. Recurrence of the respiratory distress 8 hours after Naloxone injection in patients with Fentanyl-related overdoses has been reported by Sutter et al. suggesting a possible resistance to the treatment at standard doses and a need for continuous infusion and a prolonged observation period [29].

Cases of children's death by accidental ingestion of Morphine [30], or by accidental exposure to Fentanyl patch (applied by the child or ingested or due to improper use by a relative to relieve the child's pain like the case we report or simply used as a band-aid on a child's skin abrasion) are reported in the literature [31-33]. This should raise awareness about the importance of the correct labeling of the drug and the education of the patient about its dangers, its proper use, storage and disposal. The responsibility falls upon the shoulders of physicians and pharmacists to correctly educate and verify the understanding of the information to prevent the happening of such events, and the patient to keep the drug away from the reach of children and respect the guidelines given to him. More precautions could be taken and takehome Naloxone has been considered as a possible life saver in situations of overdose or child exposure [34, 35].

CONCLUSION

Rapid detection and treatment, and above all, better awareness of the dangers of opioids are the keys to avoid the fatal fate of opioid intoxication in children. Low doses of Naloxone may be efficient to treat the intoxication and avoid its side effects, however caution must be exercised when dealing with potent opioids such as Fentanyl and prolonged infusion could be needed. A multicentric study in Morocco is necessary to identify the incidence and severity of opioid intoxications in children, to compare the different doses of the treatment and to establish a consensual management protocol.

REFERENCES

1. Palmiere, C., Staub, C., La Harpe, R., & Mangin, P. (2010). Parental substance abuse and accidental death in children. *Journal of forensic sciences*, *55*(3), 819-821.

2. Dolinak, D. (2017). Opioid toxicity. *Academic forensic pathology*, *7*(1), 19-35.
3. Fareed, A., Stout, S., Casarella, J., Vayalapalli, S., Cox, J., & Drexler, K. (2011). Illicit opioid intoxication: diagnosis and treatment. *Substance abuse: research and treatment*, *5*, SART-S7090.
4. Williams, R. H., & Erickson, T. (2000). Emergency diagnosis of opioid intoxication. *Laboratory Medicine*, *31*(6), 334-342.
5. Trescot, A. M., Datta, S., Lee, M., & Hansen, H. (2008). Opioid pharmacology. *Pain physician*, *11*(2 Suppl), S133-53.
6. Stanley, T. H. (1992). The history and development of the fentanyl series. *Journal of pain and symptom management*, *7*(3), S3-S7.
7. Kukanich, B., & Clark, T. P. (2012). The history and pharmacology of fentanyl: relevance to a novel, long-acting transdermal fentanyl solution newly approved for use in dogs. *Journal of veterinary pharmacology and therapeutics*, *35*, 3-19.
8. Dakhli, M., Garrab, K., Chemli, S., Besbes, M., & Braham, Y. (2016). Intoxication aux opiacés chez les enfants dans le Centre et Sud Tunisien. *Toxicologie Analytique et Clinique*, *28*(3), 257.
9. Allen, J. D., Casavant, M. J., Spiller, H. A., Chounthirath, T., Hodges, N. L., & Smith, G. A. (2017). Prescription opioid exposures among children and adolescents in the United States: 2000–2015. *Pediatrics*, *139*(4).
10. Ghaemi, N., Alikhani, S., Bagheri, S., & Sezavar, M. (2016). A Cross sectional study of opioid poisoning in children at a tertiary center. *Asia Pacific Journal of Medical Toxicology*, *5*(4), 115-118.
11. Zamani, N., Sanaei-Zadeh, H., & Mostafazadeh, B. (2010). Hallmarks of opium poisoning in infants and toddlers. *Tropical doctor*, *40*(4), 220-222.
12. Farnaghi, F., Pournasir, Z., & Tehranchi, S. (2015). Opioid Poisoning in Children: A Report of 90 Cases. *Journal of Pediatric Nephrology*, *3*(2), 62-66.
13. Rzasa Lynn, R., & Galinkin, J. L. (2018). Naloxone dosage for opioid reversal: current evidence and clinical implications. *Therapeutic advances in drug safety*, *9*(1), 63-88.
14. Huse, K., Hartung, E., & Nadjmabadi, M. H. (1974). The effects of naloxone (Narcan) on circulation and respiration after neurolept anaesthesia for neurosurgical operations (author's transl). *Der Anaesthesist*, *23*(11), 493-499.
15. Hasan, R. A., Benko, A. S., Nolan, B. M., Campe, J., Duff, J., & Zureikat, G. Y. (2003). Cardiorespiratory effects of naloxone in children. *Annals of Pharmacotherapy*, *37*(11), 1587-1592.
16. Schwartz, J. A., & Koenigsberg, M. D. (1987). Naloxone-induced pulmonary edema. *Annals of emergency medicine*, *16*(11), 1294-1296.
17. Nath, S., Tripathi, M., Pandey, C., & Rao, B. (2009). Naloxone-induced pulmonary edema: a potential cause of postoperative morbidity in laparoscopic donor nephrectomy. *Indian journal of medical sciences*, *63*(2), 72.
18. Flacke, J. W., JW, F., & WE, F. (1977). Acute pulmonary edema following naloxone reversal of high-dose morphine anesthesia.
19. Tanaka, G. Y. (1974). Hypertensive reaction to naloxone. *JAMA*, *228*(1), 25-26.
20. Michaelis, L. L., Hickey, P. R., Clark, T. A., & Dixon, W. M. (1974). Ventricular irritability associated with the use of naloxone hydrochloride: two case reports and laboratory assessment of the effect of the drug on cardiac excitability. *The Annals of thoracic surgery*, *18*(6), 608-614.
21. Kienbaum, P., Thurauf, N., Michel, M. C., Scherbaum, N., Gastpar, M., & Peters, J. (1998). Profound increase in epinephrine concentration in plasma and cardiovascular stimulation after [micro sign]-opioid receptor blockade in opioid-addicted patients during barbiturate-induced anesthesia for acute detoxification. *The Journal of the American Society of Anesthesiologists*, *88*(5), 1154-1161.
22. Lavonas, E. J., Drennan, I. R., Gabrielli, A., Heffner, A. C., Hoyte, C. O., Orkin, A. M., ... & Donnino, M. W. (2015). Part 10: special circumstances of resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*, *132*(18_suppl_2), S501-S518.
23. Kim, H. K., & Nelson, L. S. (2016). Reversal of opioid-induced ventilatory depression using low-dose naloxone (0.04 mg): a case series. *Journal of Medical Toxicology*, *12*(1), 107-110.
24. Committee on Drugs. (1990). Naloxone dosage and route of administration for infants and children: addendum to emergency drug doses for infants and children. *Pediatrics*, *86*(3), 484-485.
25. Williams, K., Lang, E. S., Panchal, A. R., Gasper, J. J., Taillac, P., Gouda, J., ... & Hedges, M. (2019). Evidence-based guidelines for EMS administration of naloxone. *Prehospital emergency care*, *23*(6), 749-763.
26. Hill, R., Santhakumar, R., Dewey, W., Kelly, E., & Henderson, G. (2020). Fentanyl depression of respiration: comparison with heroin and morphine. *British journal of pharmacology*, *177*(2), 254-265.
27. Suzuki, J., & El-Haddad, S. (2017). A review: Fentanyl and non-pharmaceutical fentanyls. *Drug and Alcohol Dependence*, 171, 107–116. doi:10.1016/j.drugalcdep.2016.11.
28. Miser, A. W., Narang, P. K., Dothage, J. A., Young, R. C., Sindelar, W., & Miser, J. S. (1989). Transdermal fentanyl for pain control in patients with cancer. *Pain*, *37*(1), 15-21.
29. Sutter, M. E., Gerona, R. R., Davis, M. T., Roche, B. M., Colby, D. K., Chenoweth, J. A., ... &

Albertson, T. E. (2017). Fatal fentanyl: one pill can kill. *Academic emergency medicine*, *24*(1), 106-113.

30. Sachdeva, D. K., & Stadnyk, J. M. (2005). Are one or two dangerous? Opioid exposure in toddlers. *The Journal of emergency medicine*, *29*(1), 77-84.
31. Bakovic, M., Nestic, M., & Mayer, D. (2015). Death by band-aid: fatal misuse of transdermal fentanyl patch. *International journal of legal medicine*, *129*(6), 1247-1252.
32. Teske, J., Weller, J. P., Larsch, K., Tröger, H. D., & Karst, M. (2007). Fatal outcome in a child after ingestion of a transdermal fentanyl patch. *International journal of legal medicine*, *121*(2), 147-151.
33. Hilado, M. A., Getz, A., Rosenthal, R., & Im, D. D. (2020). Fatal transdermal fentanyl patch overdose in a child. *Cureus*, *12*(1).
34. Grissinger, M. (2016). Fentanyl patch fatalities: we all have a role in prevention!. *Pharmacy and Therapeutics*, *41*(7), 405.
35. Bishop-Freeman, S. C., Young, K. A., Aurelius, M. B., & Hudson, J. S. (2021). Pediatric opioid fatalities: What can we learn for prevention?. *Journal of Forensic Sciences*.