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Comparative study of visits to Hospital Emergency Department for opioid overdose in two periods

Estudio comparativo de las visitas a urgencias por intoxicaciones por opiáceos en dos periodos

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Abstract

Objective: The last few years have seen an increase in the use of opioid analgesics and in the incidence of opioid overdoses. The objective of this study was to evaluate the number of overdose-related visits to a university hospital emergency department at two different periods of time to analyze potential differences in terms of patient characteristics, prescription profile, and treatment.

Method: This is a retrospective observational study of opioid overdose-related visits in two periods of time: 2009-2014 and 2018-2020.

Results: The study included 47 cases of opioid overdoses: 20 during the first period (3.3 cases/year) and 27 during the second (9 cases/year). A comparison between the two period showed a decrease in the patients' age (81.1 vs 74.0; $p = 0.044$) and an increase in the number of acute trauma-derived pain treatments at the expense of chronic pain treatments ($p = 0.002$). No differences were observed in the opioids involved. As regards symptoms, there was a decrease in the incidence of confusional syndromes ($p = 0.026$) and an increase in deaths.

Conclusions: Emergency room visits for opioid overdoses have increased in recent years, as has the mortality associated to them. A change has also been observed in the profile of affected patients, with a higher number of cases where pain is derived from acute trauma.

Resumen

Objetivo: El uso de fármacos opiáceos ha aumentado en las últimas décadas, así como las intoxicaciones relacionadas con su uso. El objetivo de este estudio es evaluar el número de visitas a urgencias en un hospital universitario por intoxicaciones por opiáceos entre dos periodos y analizar las posibles diferencias de las características de los pacientes, perfil de prescripción y el tratamiento de dicha intoxicación.

Método: Estudio observacional, retrospectivo de las visitas debidas a intoxicaciones por fármacos opiáceos en dos periodos: 2009-2014 y 2018-2020.

Resultados: Se incluyeron 47 casos de intoxicaciones, 20 en el primer periodo (3,3 casos/año) y 27 en el segundo (9 casos/año). Se observó una disminución en la edad de los pacientes (81,1 versus 74,0; $p = 0,044$) y un incremento de tratamientos debidos a dolor traumático agudo a expensas de menos tratamientos de dolor crónico ($p = 0,002$). No hubo diferencias en el opiáceo implicado. Con respecto a la clínica, se observó una disminución en los síndromes confusionales ($p = 0,026$) y un incremento de fallecimientos.

Conclusiones: Las visitas a urgencias por intoxicaciones a fármacos opiáceos han aumentado en los últimos años, así como la mortalidad asociada. El perfil de los pacientes implicados ha variado, incrementándose el tratamiento de dolor traumático agudo.

KEYWORDS

Analgesics opioids; Drug overdose; Fentanyl; Morphine; Tramadol; Emergency room; Pain; Epidemiology.

PALABRAS CLAVE

Analgésicos opiáceos; Intoxicaciones; Fentanilo; Morfina; Tramadol; Servicio urgencias; Dolor; Epidemiología.



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Introduction

Given their effectiveness in the treatment of pain, opioids have become a widely used analgesic that was prescribed to over 11 million patients in the US in 2016¹. Yet, one in five deaths in Americans aged 24 to 34 years has been attributed to opioid overdoses², which has become a true epidemic. Although use of opioids in Spain has also become more widespread in the last decade³, the data available on inappropriate use and its consequences remains scarce⁴.

The last few years have seen an increase in the number of emergency room visits prompted by opioid intoxication events. The purpose of this study was therefore to carry out a comparative analysis of intoxication-related emergency room visits by patients on active opioid treatment in two different periods of time. Another goal was to analyze possible outcome differences related to patients' characteristics, prescription profiles, and the treatment indicated for the intoxication. The study was carried out in a third-level university hospital.

Methods

This was a retrospective observational study of all the opioid overdose-related visits to the emergency room of a third-level hospital. All adult patients diagnosed with an intoxication following active ambulatory treatment with opioids between 2018 and 2020 (t1) were included in the study. The data obtained was compared with that of a historical series extending from 2009 to 2014 (t2). Improper and/or recreational opioid users were excluded from the study.

The hospital's toxicology unit has a database with information on all medication-induced intoxications that must be treated at the emergency room. Cases were identified by means of a review of diagnoses given at discharge from the hospital's emergency room containing the terms *intoxica-*

tion, overdose, ingestion, and opioid. The idea was to identify those cases where the reason for presentation at the emergency room was an intoxication caused by a prescribed opioid analgesic. Data was extracted from the patients' electronic medical records (EMRs). The information collected included demographic data (age, sex), medical history, prescribing department, opioid involved, indication for the prescription, symptoms of the intoxication, complications, administered treatment and where the patient was transferred on discharge. The contribution of intoxication to the patients' death was classified based on clinical criteria and the EXITOX mortality register into unquestionable, very likely or likely⁵.

The statistical study was performed with the SPSS v25.0 for Windows software package. Values were expressed as means (standard deviation) or percentages. Student's t test was used for comparisons of means, while the chi-squared test with Fisher's Exact Test correction was used for comparisons of proportions, if required. Statistical significance was assumed if $p < 0.05$.

The study was approved by the hospital's Research Ethics Committee.

Results

Forty-seven emergency room visits prompted by opioid overdoses were included in the study. Twenty of them occurred during t1 (3.3 cases/year) and 27 during t2 (9 cases/year). The percentage of opioid overdoses with respect to all toxic substance/medicine-induced intoxications treated during t1 was 0.48% (of a total of 4,141) and rose to 1.38% (of a total of 1,961) in t2 ($p < 0.001$).

Table 1 shows the patients' characteristics. The population in the two periods was rather heterogeneous as regards age and indication for treatment. Mean age was significantly lower in t2 [81.1 (6.2) vs 74.0 (16.3) years; $p = 0.044$]. The majority of patients in the two periods were women, most of whom had been transferred to the emergency room from their homes. No significant differences were found with respect to disease history. The

Table 1. Characteristics of patient suffering from opioid-induced intoxication

	2009-2014 n = 20	2018-2020 n = 27	p
Age (years) (SD)	81.1 (6.2)	74.0 (16.3)	0.044
Female sex, n (%)	13.0 (65.0)	21.0 (77.8)	0.510
Transferring from, n (%)			0.830
Home	15 (75)	19 (70.4)	
Hospital	3 (15)	2 (7.4)	
Primary care/Emergency unit	0	2 (7.4)	
Others/unknown	2 (10)	4 (14.8)	
Disease history, n (%)			
Hypertension	18 (90)	18 (66.7)	0.090
Chronic renal failure	4 (20)	10 (37.0)	0.330
Diabetes mellitus	6 (30)	5 (18.5)	0.490
Cognitive impairment	1 (5)	2 (7.4)	0.610
Reason for treatment (%)			0.002
Acute trauma-related pain	4 (20)	18 (66.7)	
Non-oncologic chronic pain	13 (65)	4 (14.8)	
Oncologic chronic pain	3 (15)	4 (14.8)	
Others/unknown	0	1 (3.7)	
Drugs, n (%)			0.470
Fentanyl patches	10 (50)	16 (59.3)	
Tramadol	3 (15)	3 (11.1)	
Morphine	0	3 (11.1)	
Combination treatment	4 (20)	3 (11.1)	
Others	3 (15)	2 (7.4)	
Prescribing physician, n (%)			0.070
Family doctor	14 (70)	8 (29.6)	
Trauma surgeon	1 (5)	6 (22.2)	
Oncologist	2 (10)	4 (14.8)	
Pain management specialist	2 (10)	3 (11.1)	
Palliative care doctor	0	2 (7.4)	
Others	1 (5)	4 (14.8)	

SD: standard deviation.

reason for prescribing opioids was predominantly related to the presence of non-oncological chronic pain in t1 and trauma-related pain in t2 ($p = 0.002$), with fentanyl patches being the most commonly used medication in both periods (50.0% and 59.3%). Although family doctors were the most common prescribers, prescriptions by these healthcare providers shrank considerably in t2 (70.0% vs 29.6%) as compared with those made by trauma surgeons (5.0% vs 22.2%); this difference was however not statistically significant.

The characteristics of the intoxication episodes are shown in table 2. No differences were found regarding the patients' symptoms, except with respect to the incidence of confusional syndrome, which was lower in t2 (35.0% vs 7.4%; $p = 0.026$). As far as complications are concerned, there were 9 cases of bronchoaspiration (33.3%), all of them in t2 ($p = 0.006$). A trend was observed toward a more assiduous use of naloxone in t2 (25.0% vs 51.9%; $p = 0.064$). One death occurred in t1 and three in t2.

Fentanyl patches were the medication involved in two of the patients who died; oxycodone was involved in one case and codeine in another. Indications for treatment were non-oncologic chronic pain in three patients and oncologic pain in the other. Treatment with opioid analgesics was considered to contribute to death in all cases, and to be likely to be the decisive contributing factor in two cases (a patient receiving palliative treatment with oxycodone for pain control, and a patient where the fentanyl dose was upped to control non-oncologic pain).

Discussion

The results of this study show that opioid analgesic-induced intoxications have become more common in the last few years. The number of intoxications recorded in t2, which only included the last three years, was higher than in t1, which underscores the need to develop intoxication prevention strategies. Moreover, a few changes were observed in the characteristics of the affected patients between the two periods, such that in t2 patients were younger and most had acute trauma-related conditions. This also led to a change in the prescriber's profile, with trauma surgeons being the main prescribers during t2. Although the complexity of the intoxications and their resulting complications did not in general experience too many changes between the two periods, it must be noted that the number of deaths increased threefold. However, the deaths occurred in patients treated for chronic pain, without there being any connection between those deaths and the higher number of opioid-induced intoxications among patients with

trauma-related conditions, who were the ones where the greatest increase in prescriptions was observed.

The age of patients visiting the emergency room in connection with opioid overdoses decreased in t2 from 81 to 74 years. Despite this increase in mean patient age, this finding confirms the data previously reported by our group indicating that opioid-induced intoxications occur mostly in patients over 65 years of age⁶, although the most commonly affected age group is that of patients between 76 and 85 years⁷. The predominance of patients older than 65 years was confirmed by a subsequent multicenter study⁸. The mean age reduction observed in this study could be due to the increased prescription of opioids for treating non-oncologic acute (particularly trauma-related) pain, which tends to occur in younger patients. This increase in the number of patients with acute pain treated with opioid analgesics is in line with the findings of a Chilean study, which reported that up to 7% of patients discharged from the emergency room were prescribed treatment with these drugs, particularly for non-oncologic acute pain⁹.

The absence of bronchoaspiration during t1 must be taken cautiously. Due to the retrospective nature of this study, it cannot be ruled out that some of the complications classified as respiratory infections during t1 were not in fact bronchoaspirations. The diagnoses considered were those reflected in the patients' discharge reports. Decreased levels of consciousness tend to predispose subjects to bronchoaspiration, which means that the difference between a diagnosis of bronchoaspiration and one of respiratory infection is, at best, debatable.

Although the overall complexity of the episodes leading to emergency room visits did not change too much between t1 and t2, there was a trend toward an increase in the number of deaths which, though small in absolute terms, should lead to an increased awareness of the importance of keeping these patients under close surveillance. Even if all the deaths analyzed in this study occurred in patients with chronic pain, strict strategies should be developed to monitor and prevent inappropriate use of opioid analgesics at the beginning of treatment and to optimize their administration as a function of the patients' clinical situation, any physiopathological changes in their metabolism, and the drug's clearance rate. Optimization of the changes of active ingredients is also essential. The above mentioned Chilean study found that prescriptions were in many cases lacking in information, which could induce patients to make mistakes while taking the medication⁸. For these reasons, the health authorities of the United States have issued as series of precise recommendations related to the indications and dosing

Table 2. Characteristics of the intoxication episode

	2009-2014 n = 20	2018-2020 n = 27	p
Symptoms, n (%)			
Decreased consciousness	9 (45)	16 (59.3)	0.380
Respiratory failure	4 (20)	7 (25.9)	0.740
Confusional syndrome	7 (35)	2 (7.4)	0.026
Nausea and/or vomiting	2 (10)	1 (3.7)	0.570
Constipation	2 (10)	0	0.180
General discomfort	2 (10)	3 (11.1)	1.000
Complications, n (%)			
Respiratory infection	6 (30)	7 (25.9)	1.000
Bronchoaspiration	0	9 (33.3)	0.006
Cranioencephalic trauma	4 (20)	2 (7.4)	0.380
Urinary infection	3 (15)	0	0.070
Other trauma	1 (5)	0	0.430
Treatment, n (%)			
Naloxone	5 (25)	14 (51.9)	0.064
Conventional oxygen therapy	5 (25)	13 (48.1)	0.110
Noninvasive ventilation	3 (15)	1 (3.7)	0.710
Transferred to: n (%)			0.450
Discharge	11 (55.5)	15 (55.6)	
Admission	7 (35)	7 (25.9)	
Intensive care unit	1 (5)	0	
Other	0	2 (7.4)	
Deaths n (%)	1 (5)	3 (11.1)	0.050

of, and time of treatment with, opioid analgesics in order to limit potential adverse events and deaths related with their use¹⁰⁻¹². Such recommendations should also be introduced in Spain¹³.

The limitations of this study include its retrospective nature as well as its small sample size. Nonetheless, the increase in the number of cases observed between the two periods, albeit not as alarming as that observed in other countries, does point to the importance of closely monitoring this problem.

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Bibliography

1. Blendon RJ, Benson JM. The public and the opioid-abuse epidemic. *N Eng J Med*. 2018;378(5):407-11. DOI: 10.1056/NEJMp1714529
2. Gomes T, Tadrous M, Mamdani M, Paterson JM, Juurlink DN. The burden of opioid-related mortality in the United States. *JAMA Netw Open*. 2018;1(2):e180217. DOI: 10.1001/jamanetworkopen.2018.0217
3. Agencia Española de Medicamentos y Productos Sanitarios. Utilización de medicamentos opioides en España durante el periodo 2010-2019 [Internet] [accessed 02/22/2021]. Available at: <https://www.aemps.gob.es/medicamentos-de-uso-humano/observatorio-de-uso-de-medicamentos/utilizacion-de-medicamentos-opioides-en-espana-durante-el-periodo-2010-2018/>
4. Coloma-Carmona A, Carballo JL, Rodríguez-Marín J, Pérez-Carbonell A. Uso y dependencia de fármacos opioides en población española con dolor crónico: prevalencia y diferencias de género. *Rev Clin Esp*. 2017;217(6):315-9. DOI: 10.1016/j.rce.2017.03.007
5. Puiguirguer J, Nogué S, Echarte JL, Ferrer A, Dueñas A, García L, *et al*. Mortalidad hospitalaria por intoxicación aguda en España (EXITOX 2012). *Emergencias*. 2013;25:467-71.
6. Supervia Caparrós A, Pallàs Villaronga O, Clemente Rodríguez C, Aranda Cárdenas MD, Pi-Figueras Vallas M, Cirera Lorenzo I. Características diferenciales de las intoxicaciones en los pacientes ancianos atendidos en un servicio de urgencias. *Emergencias*. 2017;29(5):335-8.
7. Béjar Calzada CM, Pi-Figueras Valls M, Clemente Rodríguez C, Pallàs Villaronga O, Arnau Barrés I, Calpe Perarnau X, *et al*. Características de las intoxicaciones agudas en pacientes ancianos según la edad. *Rev Toxicol*. 2020;37(2):44-7.
8. Supervia A, Salgado E, Córdoba F, García Gibert L, Martínez Sánchez L, Moreno A, *et al*. Características de las intoxicaciones agudas atendidas en Cataluña. Diferencias según grupos de edad: Estudio Intox-28. *Emergencias*. 2021;33(2):115-20.
9. Martínez M, Herrada L, Muñoz A, Chávez C, Jirón M. Prescripción de opioides al alta de un servicio de urgencia. *Rev Med Chil*. 2017;145(12):1565-8.
10. Babu KM, Brent J, Juurlink DN. Prevention of opioid overdose. *N Eng J Med*. 2019;380(23):2246-55. DOI: 10.1056/NEJMr1807054
11. American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Opioids, Hatten BW, Cantrill SV, Dubin JS, Ketcham EM, Runde DP, Wall SP, *et al*. Clinical policy: critical issues related to opioid in adult patients presenting to the Emergency Department. *Ann Emerg Med*. 2020;76(3):e13-39. DOI: 10.1016/j.annemergmed.2020.06.049
12. Langabeer JR, Stotts AL, Bobrow BJ, Wang HE, Chambers KA, Yatsco AJ, *et al*. Prevalence and charges of opioid-related visits to U.S. emergency departments. *Drug Alcohol Depend*. 2021;1;221:108568. DOI: 10.1016/j.drugalcdep.2021.108568
13. Roncero C, Grau-López L. Buenos usos y riesgos de los fármacos opiáceos. *Rev Clin Esp*. 2017;217(6):327-8. DOI: 10.1016/j.rce.2017.06.001

Conflict of interest

No conflict of interests.

Contribution to the scientific literature

This study describes the characteristics of the opioid-derived intoxications observed in the last decade.

Analyzing the profile of intoxications resulting in visits to the emergency room could help design strategies to follow-up and prevent inappropriate use of opioid analgesics.