ORIGINAL ARTICLES

Patients with drug-abuse poisoning with and without HIV infection: differential characteristics

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Objective. Persons with HIV infection who use illicit drugs have higher morbidity and mortality rates than nonusers with or without HIV infection. The objetive were to detect differences between acute poisoning from illicit drugs in patients with and without HIV infection who are attended in hospital emergency departments, and to identify independent factors associated with a worse prognosis, defined by hospital admission or death.

Methods. Observational study in 2 hospitals between January 2017 and 31 December 2021. Included were patients with acute illicit drug poisoning with and without HIV infection.

Results. Information for 1132 patients was included. The mean (SD) ages of patients with and without HIV infection, respectively, were 38.9 (9.6) years and 32.6 (10.4) years. In patients with HIV, the main drugs used were opioids (279 [85.3%]), cocaine (226 [69.1%]), and amphetamines (153 [46.8%]. None in this group were on methadone substitution therapy for opioid addiction. In patients without HIV infection the main drugs were cocaine (372 [47.2%]) and cannabis (238 [33.8%]). Alcohol was used along with illicit drugs in 387 cases. Multivariate analysis showed that the only variables independently associated with a poor prognosis were HIV infection (odds ratio [OR], 2.19 [1.29-3.11], $P < .003$), age (OR, 1.20 [1.01-1.05], $P < .003$), and acute poisoning from benzodiazepines (OR, 3.48 [2.14-5.66], $P < .001$). The area under the receiver operating characteristic curve of the model was 0.717.

Conclusion. Certain characteristics distinguish the illicit drug use of patients with HIV infection. HIV infection, age, and the use of benzodiazepines are independently associated with a poor prognosis in acute poisonings.

Keywords: Illicit drugs. Drug overdose. Human immunodeficiency virus (HIV). Acute poisoning.

Intoxicaciones por drogas de abuso: características diferenciales en población VIH

Objetivo. La población VIH, consumidora de drogas de abuso (DA), tiene mayor morbimortalidad en relación con los no consumidores y no VIH. Se investiga si existen diferencias en las intoxicaciones agudas (IA) por DA, en pacientes VIH y no VIH atendidos en los servicios de urgencias hospitalarios (SUH), y se identifican factores independientes de mal pronóstico, definido por ingreso o fallecimiento.

Método. Estudio bicéntrico y observacional de 1 de enero de 2017 al 31 de diciembre de 2021. Se incluyeron pacientes VIH y no VIH atendido en dos SUH por intoxicación por DA. Se recogieron variables demográficas y la sustancia consumida. La variable de resultado principal fue mal pronóstico, definido como ingreso o muerte a los 30 días.

Resultados. Se recogieron 1.132 pacientes. La edad media de los pacientes VIH fue 39 ± 10 años, y 33 ± 10 años para los no VIH. En la población VIH predominaron los opiáceos 279 (85,3%) (ninguno de ellos estaba en tratamiento sustitutivo con metadona), la cocaína 226 (30,9%) y las anfetaminas 153 (69,1%), mientras que en la no VIH predominaron la cocaína 372 (47,2%) y el cannabis 238 (33,8%). El etanol se asoció con otras DA en 387 pacientes. El análisis multivariado mostró que las únicas variables independientes de mal pronóstico fueron el VIH [OR 2,19 (1,29-3,11), p < 0,003], la edad [OR 1,20 (1,01-1,05), p < 0,003], y la IA por benzodiacepinas (BDZ) [OR 3,48 (2,14-5,66), p < 0,001], con un área bajo la curva de la característica operativa del receptor de este modelo de 0,717.

Conclusiones. Existen diferencias en las características de las IA en pacientes VIH. La infección VIH, la edad y el consumo de BZD son factores independientes de mal pronóstico en las IA.

Palabras clave: Drogas de abuso. Sobredosis. VIH. Intoxicación aguda.

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Introduction

The use of drugs of abuse has increased worldwide.[1] According to the last report of the National Plan on Drugs 2020, in Spain, the most abused drug was alcohol, followed by cannabis.[2]

Acute intoxications (AI) account for 0.5-1% of all hospital emergency department (ED) visits.[3] The most frequent drug of abuse involved in ED visits is cocaine.[2] The analysis of patients who consult for problems related to drug abuse use provides reliable information on the main complications derived from such use.[4]

In patients with HIV infection, the use of drugs of abuse causes a higher risk of morbidity and mortality than in patients who do not use them.[5] Many drugs of abuse are used by men who have sex with men (MSM),

known as chemsex.[6] The objective of these sessions is to seek disinhibition to encourage sexual practices,[7] with the risk of AI and sexually transmitted diseases due to the non-use of protective methods.[8]

Drugs as widely consumed as amphetamine and cocaine produce acute or chronic medical and psychiatric disorders (arterial hypertension, acute myocardial infarction (AMI), cerebral vascular accident, paranoia, depression, and violent behavior). When taken up by extracellular vesicles at the neuronal level, they facilitate the passage of the blood-brain barrier, stimulate dopaminergic receptors in an agonistic manner, and cause an increase in circulating dopamine.[9] Although the influence of a drug of abuse in HIV patients has been evaluated previously, few Spanish studies specifically evaluate their influence on the need for admission and death after suffering an AI.[10]

The study aimed to identify the type of drug abuse that produces AI in HIV patients who attended two EDs, as well as the factors of hospital admission and poor prognosis and their differences concerning poisonings in the non-HIV population.

Methods

The observational, retrospective, bi-center study was conducted from January 1, 2017, to December 31, 2021, at Hospital Clínic and Hospital del Mar in Barcelona. The study was conducted following the principles of the Declaration of Helsinki for research in humans. It was approved by the Research Ethics Committee of the Hospital Clínic of Barcelona, with reference HCB-2021-004. According to the World Health Organization, a drug is defined as any substance that, when introduced into the body by any route, alters the functioning of the individual's central nervous system and is also susceptible to creating tolerance and psychological or physical dependence, or both. Intoxication was defined as the acute, adverse reaction associated with the consumption of a drug of abuse that leads to the patient's care in ED.[11] The study investigators made the final diagnosis of substance intoxication after a review of each case based on clinical and analytical data and toxicity tests in the cases in which they were requested. Poly-drug use was defined as the simultaneous consumption of two or more drugs of abuse. The following variables were collected: gender, age, comorbidities, type of substance consumed (cocaine, benzodiazepines -BDZ-, cannabis, ketamine, amphetamine, opiates, gamma-hydroxybutyric acid-GHB-, alcohol), psychiatric history, the reason for drug use (recreational or autolytic), hospital admission, intensive care unit (ICU) admission, and 30-day mortality. In HIV patients, we also collected data on antiretroviral treatment (ART), CD4 lymphocyte count, plasma HIV-1 RNA viral load, and chemsex practice. Psychiatric disorders were included if they met DSM-V criteria.[12]

Drug testing was performed by immunoassay (DRI; Abbott Diagnostics, Texas, USA), and confirmation and interference detection by gas chromatography combined with mass spectrometry (GC-MS) (Agilent 5975/68901, Santa Clara, CA, USA).[13] Diagnosis of GHB use was made by anamnesis, clinical, and by a specific method for its detection.[14]

The primary objective of the study was to identify the drugs consumed in both populations that produced acute intoxication. The secondary objective was to identify the independent factors of poor prognosis, defined by the variables admission to a conventional hospitalization unit, admission to the ICU, and mortality. The data were expressed as mean and standard deviation (quantitative variables) or as absolute and relative frequency (qualitative variables). The Student t-test or Mann-Whitney U test was used to compare quantitative variables, and the chi-square test or Fisher's test was used to compare qualitative variables if necessary. A multivariate study was carried out to identify which epidemiological and clinical variables and which drugs were related to poor outcomes. A value of $P < 05$ was considered statistically significant. The statistical package SPSS version 20.0 (Chicago, USA) was used for data processing and analysis.

Results

1132 patients were collected, and 841 (74.4%) were male. Three hundred and twenty-seven (37.7%) were HIV seropositive and 705 (62.3%) were seronegative. The mean age of HIV patients was 39 ± 10 years and 33 ± 10 years for non-HIV patients (Table 1). Ninety percent of HIV patients were on ART and had virological suppression (viral load, < 30 copies/ml) and high CD4 levels (> 300 cells/µl). One-third of these patients were receiving treatment with cobicistat boosters.

In the overall sample, the drugs of abuse that produced the most AI were cocaine in 598 patients (52.8%) and opiates in 387 (34.1%). In the HIV population, heroin predominated 279 (85.32%), cocaine 226 (69.1%), and amphetamines 153 (46.8%), whereas in non-HIV, cocaine predominated in 372 (47.2%) and cannabis in 238 (33.8%). Ethanol was associated with other drugs of abuse in 387 patients (Table 2). Chemsex occurred in 70% of HIV patients, while no cases were detected among non-HIV patients. None of the patients who used heroin were on methadone substitution treatment.

Poly-consumption was higher in the HIV group, with 52.3% of patients, compared to 43.1% in non-HIV patients ($P < .04$). Psychiatric pathology was more prevalent in the HIV group, with 167 (51.1%) patients, compared to 165 (23.4%) in the non-HIV group ($P < .001$) (Table 1). Depression, anxiety, and schizoaffective disorders were the most diagnosed. In the overall sample, intentional recreational use of drugs of abuse was higher than self-injury, although the HIV group presented a relatively high percentage, with 23.2% of cases ($P < .001$) (Figure 1).

Table 1. Baseline characteristics of the sample

	AIDS patients N = 327 n (%)	AIDS-free patients N = 705 n (%)	*P*
Age [mean (SD)]	39 (10)	33 (10)	< **.001**
Sex			< **.001**
Male	300 (91.7)	541 (76.7)	
Female	27 (8.3)	164 (23.3)	
Aim			< **.001**
Suicide	76 (23.2)	18 (2.6)	
Leisure	251 (76.8)	687 (97.4)	
Psychiatric Background	167 (51.1)	165 (23.4)	< **.001**
Drug poly-consumption	171 (52.3)	304 (43.1)	**.007**

*Polydrug use refers to more than one drug.
Values in bold denote statistical significance ($P < .05$).

Poly-consumption was higher in the HIV group, with 52.3% of patients, compared to 43.1% in non-HIV patients ($P < .04$). Psychiatric pathology was more prevalent in the HIV group, with 167 (51.1%) patients, than 165 (23.4%) in the non-HIV group ($P < .001$) (Table 1). Depression, anxiety, and schizoaffective disorders were the most commonly diagnosed. In the overall sample, recreational intentional use of drugs of abuse was higher than self-injury, although the HIV group presented a relatively high percentage, with 23.2% of cases ($P < .001$) (Figure 1).

HIV patients required more hospital admissions to conventional wards than non-HIV patients, 42 (12.8%) versus 30 (4.3%) ($P < .001$). They also required more ICU admissions: 6.1% vs. 3.3% ($P < .027$). Fifteen non-HIV patients (2.1%) died, compared to 3 HIV patients (0.9%). However, there was no significant difference ($P = .128$) (Figure 2).

Univariate analysis showed that the variables HIV, age, having a psychosomatic disorder, and BDZ intake were associated with poor prognosis, although multivariate analysis showed that the only independent variables with poor prognosis were HIV [OR: 2.19 (1.29-3.11); $P < .003$], age [OR: 1.20 (1.01-1.05); $P < .003$], and BDZ intake [OR: 3.48 (2.14-5.66); $P < .001$]. The area under the curve of the receiver operating characteristic of the module was 0.717.

Table 2. Differences in the type of toxicant consumed

	AIDS patients N = 327 n (%)	AIDS-free patients N = 705 n (%)	*P*
Ethanol	75 (22.9)	312 (44.3)	< **.001**
Cocaine	226 (69.1)	372 (47.2)	< **.001**
Opiates	279 (85.3)	74 (10.5)	< **.001**
Cannabis	51 (15.6)	238 (33.8)	< **.001**
MDMA	3 (3.5)	51 (7.2)	**NS**
Amphetamines	153 (46.8)	125 (17.7)	< **.001**
GHB	105 (32.1)	49 (7)	< **.001**
Methadone	12 (14)	33 (4.7)	**.002**
Ketamine	18 (5.5)	26 (3.7)	NS
LSD	1 (1.2)	9 (1.3)	NS
PCP	0	5 (0.7)	NS
Glue	1 (7.1)	13 (1.8)	NS
Other	7 (8.1)	77 (10.9)	NS
Benzodiazepines	56 (17.1)	124 (17.6)	NS

MDMA: 3,4-methoxymethamphetamine; LSD: lysergic acid diethylamide. PCP: phencyclidine. Others: drugs not identified or not included in the main groups.
NS: not significant.
Bold values denote statistical significance ($P < .05$).

Discussion

The study showed that the profile of the patient presenting to an ED due to an AI due to drugs of abuse was that of a male patient, a recreational user of opiates, cocaine, and amphetamine. It was observed that HIV patients were older than non-HIV patients, probably due to the characteristics of the group studied, with a high percentage of patients who were habitual and chronic users and had developed an addiction to drugs of abuse with the consequences that this implies for their health.[15,16]

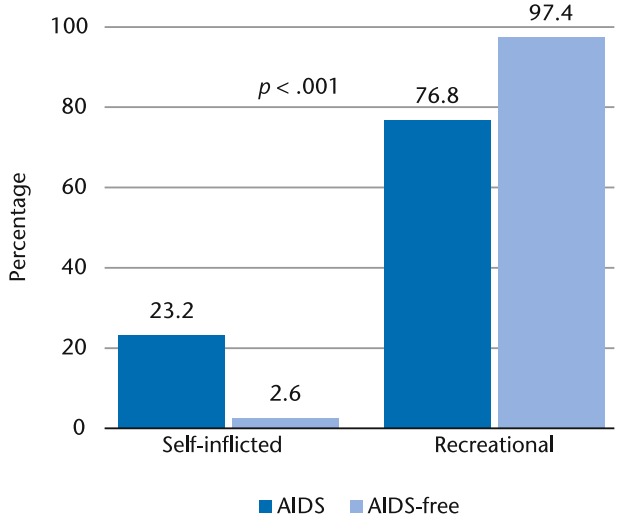

Figure 1. Intentionality of intake in HIV and non-HIV patients.

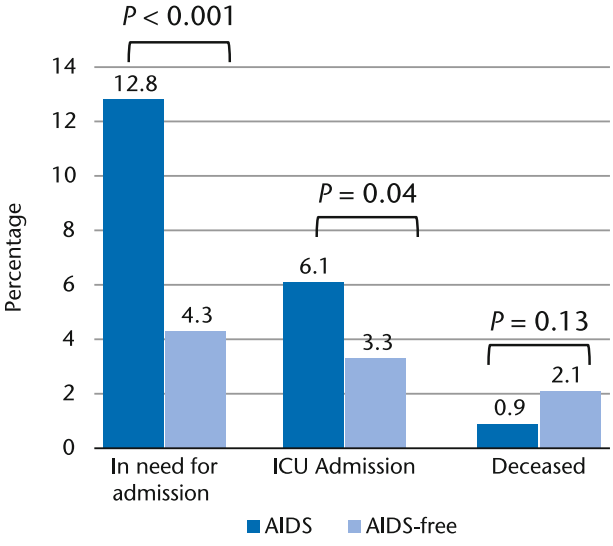

Figure 2. Patients' destination.

Table 3. Univariate analysis. Poor prognostic factors in the overall population

	Poor outcomes		Total	*P*
	No **N = 943** n (%)	**Yes** **N = 89** n (%)	**N = 1.032** n (%)	
Age				**< .001**
Mean (SD)	34.1 (10.4)	39.7 (10.6)	34.6 (10.5)	
Median (Q1, Q3)	33.0 (26.0. 41.0)	39.0 (31.0. 47.0)	34.0 (27.0. 41.0)	
Min, Max	14.0. 73.0	20.0. 73.0	14.0. 73.0	
Age ≤40	701 (74.4)	50 (56.2)	751 (72.8)	
Sex				.893
Male	768 (81.4)	73 (82.0)	841 (81.5)	
Female	175 (18.6)	16 (18.0)	191 (18.5)	
AIDS				**< .001**
No	662 (70.2)	43 (48.3)	705 (68.3)	
Yes	281 (29.8)	46 (51.7)	327 (31.7)	
Motivation				**< .001**
Self-inflicted	76 (8.1)	18 (20.2)	94 (9.1)	
Recreational	867 (91.9)	71 (79.8)	938 (90.9)	
Ethanol				.218
No	584 (61.9)	61 (68.5)	645 (62.5)	
Yes	359 (38.1)	28 (31.5)	387 (37.5)	
Cocaine				**.034**
No	537 (56.9)	61 (68.5)	598 (57.9)	
Yes	406 (43.1)	28 (31.5)	434 (42.1)	
Opiates				.612
No	833 (88.3)	77 (86.5)	910 (88.2)	
Yes	110 (11.7)	12 (13.5)	122 (11.8)	
Hashish				.224
No	674 (71.5)	69 (77.5)	743 (72.0)	
Yes	269 (28.5)	20 (22.5)	289 (28.0)	
Ecstasy				.115
No	681 (92.8)	56 (98.2)	737 (93.2)	
Yes	53 (7.2)	1 (1.8)	54 (6.8)	
Amphetamines				.314
No	693 (73.5)	61 (68.5)	754 (73.1)	
Yes	250 (26.5)	28 (31.5)	278 (26.9)	
Designer drugs				.760
Neither ecstasy nor amphetamines	661 (70.1)	61 (68.5)	722 (70.0)	
Ecstasy or amphetamines	282 (29.9)	28 (31.5)	310 (30.0)	
GHB				.593
No	804 (85.3)	74 (83.1)	878 (85.1)	
Yes	139 (14.7)	15 (16.9)	154 (14.9)	
Methadone				.297
No	694 (94.6)	52 (91.2)	746 (94.3)	
Yes	40 (5.4)	5 (8.8)	45 (5.7)	
Ketamine				.325
No	901 (95.5)	87 (97.8)	988 (95.7)	
Yes	42 (4.5)	2 (2.2)	44 (4.3)	
LSD				.375
No	723 (98.6)	57 (100.0)	780 (98.7)	
Yes	10 (1.4)	0 (0.0)	10 (1.3)	
PCP				.532
No	729 (99.3)	57 (100.0)	786 (99.4)	
Yes	5 (0.7)	0 (0.0)	5 (0.6)	
Glue				**.002**
No	724 (98.6)	53 (93.0)	777 (98.2)	
Yes	10 (1.4)	4 (7.0)	14 (1.8)	
Benzodiazepine				**< .001**
No	799 (84.7)	53 (59.6)	852 (82.6)	
Yes	144 (15.3)	36 (40.4)	180 (17.4)	
Mental disorder				**< .003**
No	652 (69.1)	48 (53.9)	700 (67.8)	
Yes	291 (30.9)	41 (46.1)	332 (32.2)	
Drug poly-consumption				.150
No	520 (55.1)	42 (47.2)	562 (54.5)	
Yes	423 (44.9)	47 (52.8)	470 (45.5)	

Bold values denote statistical significance ($P < 05$).

Table 4. Multivariate analysis. Poor prognostic factors in the overall population

	OR	95%CI	*P*
AIDS			
No	1.00	(referencia)	
Yes	2.32	1.44 (3.75)	**.001**
Age > 40 years	1.03	1.01 (10.5)	**.003**
BDZ			
No	1.00	(referencia)	
Yes	3.48	2.14 (5.66)	**.001**

BDZ: benzodiazepines; CI: confidence interval; OR: odds ratio. Values in bold denote statistical significance ($P < .05$).

The study revealed many AI due to opioids in the HIV population. It is known that in some countries, there has been an increase in the use of opiates, especially synthetic opiates,[17] which is not so important in Spain. However, an increase in non-recreational opiate intoxications in the non-HIV population has been described.[18] The present study's design does not explain the higher percentage of recreational opiate intoxications in HIV patients. However, it has already been mentioned that drug abuse use (including opiates) is more frequent in HIV patients. Also, local patterns of use may explain the high prevalence of a given drug. The importance of opioid use is that it leads to increased mortality in HIV patients.[19]

Cocaine, amphetamine, and GHB use was like a previous study by our group,[10] suggesting stability in substance use in HIV patients. Their high consumption can be explained by the high percentage of HIV patients who practice chemsex. In the non-HIV population, consumption patterns remain similar to those already described,[20-22] although the study highlights a not insignificant consumption of cocaine and alcohol. In the HIV population, alcohol was mostly associated with amphetamine and cocaine.[23]

Poly-drug use is widespread among the MSM population and, in our study, was even higher than that described by Sewell et al.[24] with 21.8%. However, it coincides with those of other large European cities such as London, Paris, and Berlin.[25] In the non-HIV population, the results are similar to those of previous studies.[26]

The study showed a higher prevalence of mental disorders in HIV patients than in non-HIV patients.[27] A high prevalence of depression, anxiety, post-traumatic stress disorder, sleep disorders (sometimes attributable to taking certain types of ART), and psychosis have been described in the HIV population.[28] In addition, HIV patients with mental health disorders often have substance use disorders and vice versa,[29] which may be associated with lower use of health services, worse prognosis, and poorer quality of life.[30] BDZ AIs were a predictor of hospital admission, probably because these AIs occurred in the context of an autolytic attempt and, therefore, patients required final psychiatric admission. Diazepam was the most used BDZ, unlike other studies in which it was clonazepam (European Euro-DEN study, conducted in the general population).[31]

Patients with psychiatric disorders are at increased risk of cardiac events in case of concomitant use of psychostimulants and psychotropic substances, such as antipsychotics, with known cardiotoxicity.[32] Chronic use of BZDs is associated with an increased risk of neurocognitive impairment in HIV patients, and it would be essential to explore therapeutic alternatives to BZDs when these patients require them to avoid prescribing them due to the risk of increased morbidity and mortality.[33]

Finally, the study showed that mortality in both population groups was similar to that previously described.[19,34] Our study has some limitations. It is a retrospective, observational study and despite being bicenter, the number of HIV patients included was small and there is a probability that, by not analyzing the presence of HIV, some HIV patients were included in the non-HIV group.

In conclusion, we believe that knowledge of the factors associated with poor outcomes in the use of drugs of abuse in HIV patients is essential for adopting the necessary measures in the emergency department. On the other hand, health professionals caring for this population should periodically monitor recreational drug use, particularly in those with mental disorders, and consider incorporating harm reduction measures to prevent intoxications related to cocaine, opiates, and amphetamines,[35] as well as their families.[36] New studies, including epidemiological surveillance studies, are needed to enable health professionals caring for these population groups to know the type of drugs in circulation, their consumption patterns, and associated pathology. We believe a multidisciplinary approach and action plans for patients with mental health disorders, substance abuse, and HIV prevention and treatment are vital.

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