

Mortality due to acute adverse drug reactions in Galicia: 1997-2011

Mortalidad por reacción aguda tras consumo de drogas en Galicia: 1997-2011

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Abstract

The aim of this research is to study all people who died in the Autonomous Community of Galicia from acute death after drug consumption (ADR) in which there was judicial intervention during the period from 1997 to 2011, according to inclusion and exclusion criteria established by the National Drug Plan for the entire national territory. Sociodemographic and clinical characteristics of deceased subjects were studied, in order to identify key risk factors and/or vulnerable populations.

A total of 805 deaths were recorded. The distribution by provinces and municipalities corresponds to the areas of greatest population, incidence of consumption and proximity to the coast. The average age of these patients was 34.34 years, with a gradual increase over years. Most of them were male (91.2%) and single (47.7). 43.5% of the deceased habitually used the parenteral route of administration and 36.4% had positive HIV serology. The most frequently-detected substances corresponded to opiates (heroin: 61.3%, methadone: 35.6%), followed by cocaine (53.7%), although the most common pattern was that of poly-consumption. ADR mortality figures remain relatively stable throughout the study period. The predominant pattern is that of males, opiates and a long history of consumption.

Keywords: Drug overdose; drug-induced deaths; mortality; epidemiology.

Resumen

Se estudian todos los sujetos fallecidos en Galicia por reacción aguda tras consumo de drogas (RAD) en los que existe intervención judicial a lo largo del periodo 1997-2011, según los criterios establecidos por el Plan Nacional sobre Drogas para todo el territorio nacional. Se recogieron y analizaron variables sociodemográficas, clínicas y toxicológicas de cada uno de los casos. El objetivo fundamental es tratar de determinar los principales factores de riesgo y/o perfil de las poblaciones vulnerables, así como sugerir medidas preventivas. En total se registran 805 fallecimientos. La edad media de los fallecidos fue de 34,34 años, con un aumento progresivo a lo largo de los años. La mayoría eran varones (91,2%) y solteros (47,7%). El 43,5% de los fallecidos utilizaban la vía de administración parenteral y un 36,4% presentaban serología positiva frente al VIH. Las sustancias detectadas con más frecuencia correspondían a opiáceos (heroína: 61,3%, metadona: 35,6%), seguidos de cocaína (53,7%), aunque el patrón más habitual era el policonsumo. Las cifras de mortalidad por RAD se mantienen relativamente estables a lo largo del periodo de estudio. El patrón predominante es el de varones, consumidores de opiáceos y con larga historia de consumo.

Palabras clave: Sobredosis de drogas; muertes inducidas por drogas; epidemiología; mortalidad

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Drug consumption is associated with a marked increase in morbidity and mortality rates which can range between 10 and 20 times those of non-consumers (Bargagli, Hickman, Davoli, Perucci, & Schifano, 2006; EMCDDA, 2013), and is related to different circumstances, among which stand out death by acute reaction after consumption, suicide, accidents, traumas, physical assaults etc. (Vicente, Giraudon, Matias, Hedrich, & Wiessing, 2009; Degenhardt, 2011; Mathers, Degenhardt, Bucello, Lemon, Wiessing, & Hickman, 2013; Waal & Gossop, 2014; Razvodovsky, 2014). It is estimated that in 2010 there were between 99,000 and 252,000 deaths worldwide related to the consumption of illicit drugs, which would represent between 0.5 and 1.3% of all deaths of persons between the ages of 15 and 64.

In Europe, it is estimated that between 10,000 and 20,000 consumers of opiates die every year, with overdose being the most frequent cause (between a third and a half of the total, which implies in the region of 7,000 to 8,000 deaths per year) (Waal et al, 2014; EMCDD, 2011), and despite prevention campaigns and therapeutic programs that are carried out with the aim of reducing the risks in the most vulnerable groups, mortality owing to acute reactions after the consumption of drugs remains stable and is even increasing in certain countries (Giraudon, Vicente, Matías, Mounteney, & Griffiths, 2012).

Mortality owing to acute reaction after drug consumption therefore constitutes the principal cause of death among drug addicts. Its etiopathogenesis (Pereiro, Bermejo, & López, 2005) may be extremely varied (overdose, anaphylactic reaction, adulterants, poly-consumption) and it is frequently difficult to determine the exact cause of death. Toxicological determinations (both qualitative and quantitative) play a fundamental role (Martínez, 2014) in the diagnosis, although the difficulty in establishing the lethal dose of each substance must be borne in mind, since the fatal outcome in each specific case is also related to individual circumstances that are not easily objectifiable (tolerance, physical condition, previous illnesses etc.).

On an epidemiological level, determining the cause of death owing to an acute reaction to drugs is one of the principal indicators of the level of consumption among the population, which is fundamental when it comes to putting in place assistance and prevention strategies for drug addiction. At the same time, it allows us to be aware of risk factors and especially vulnerable populations with the aim of drawing up specific measures aimed at those groups.

Materials and methods

This is an observational, descriptive, longitudinal and prospective study. The sample group is made up of all the deaths that occurred in the Autonomous Community of Galicia between 1997 and 2011 (including both of those years),

where there was judicial intervention and in which acute drug reaction (ADR) was the suspected cause. The same criteria of inclusion and exclusion established at a national level by the State System for Information on Drug Addiction (Sistema Estatal de Información en Toxicomanías) and specified on the Individual Registry Sheet of Death by Acute Reaction to Psychoactive Substances, drawn up by the National Drugs Plan for the whole of the Spanish State, were considered and the variables gathered are included in Table 1.

In Galicia, all cases of death by ADR were detected and notified by the forensic doctor when a death of this type was suspected. The action of the forensic doctor followed a protocol which is obligatory in all cases of death with judicial connotations, although with special reference to deaths presumably related to drug use, including the removal of the body, the autopsy on the drug addict and the collection of bodily fluids (vitreous humor, urine, bile and blood). These samples were later sent, together with all the information regarding the case, to the Toxicology Service of the Institute of Legal Medicine at the University of Santiago de Compostela, where different toxicological tests were carried out and the Mortality Indicator of the Autonomous Community was drawn up.

The toxicological techniques used included enzymoimmunoassay and fluoroenzymoimmunoassay (Engvall, 1971; Rubinstein, & Ullman, 1971; Spector, 1970), thin-layer chromatography of gases and liquids (Davidow & Quame, 1968; Blass, 1974) and mass spectrometry (Bermejo, Fernández, & Tabernero, 1998; Fernández, Bermejo, & Tabernero, 2004; Álvarez, Tabernero, López, & Fernández, 2007; Pietracci, Álvarez, Cabarcos, Balduini, & Tabernero, 2013; Di Palma, Álvarez, Cabarcos, Bacchielli, & Tabernero, 2009).

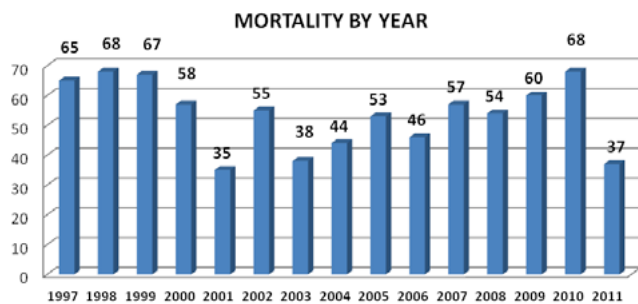
Table 1. *Collected variables*

Administrative data
Name, Surnames, ID Document N ^o
Forensic Report N ^o , Toxicological Report N ^o , Preliminary Proceedings N ^o
Institution collecting information, Courtroom (N ^o , Province, Municipality)
Sociodemographic data
Death (Date, Province, Municipality)
Sex, Marital status, Age, Birth (Date, place), Nationality
Residence (Province, Municipality)
Clinical data
Death criteria RASUPSI (recent drug use, autopsy, forensic diagnosis)
Body found in..., signs of suicide
Signs of venipuncture (needle use), aggravated previous pathology, HIV
Toxicological data
Type of biological sample
Substances detected
Quantitative result

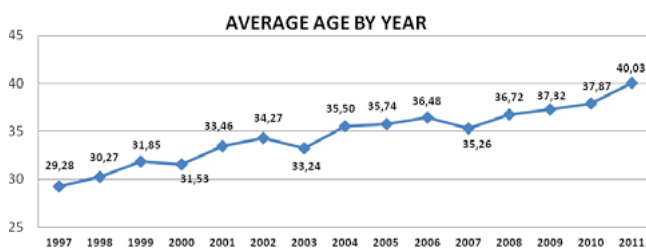
For the statistical analysis the SPSS 17.0 software package for Windows was used. A descriptive study of the different variables was made (frequency tables for qualitative variables and central tendency measures and measures of dispersion for the quantitative variables). The association between different variables was made by means of contingency tables and median comparison, attributing statistical significance to values of $p < 0.05$.

Results

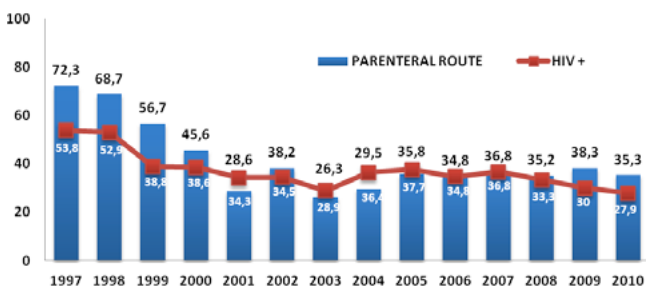
Over the 15 years of the study period (1997-2011) a total of 805 deaths by ADR were registered in Galicia in accordance with the aforementioned criteria. This represents an accumulated mortality rate for the whole period of 29.1 deaths per 100,000 inhabitants, which means an average annual rate of 1.94 per 100,000 (with the highest value being 1998, with 2.49 per 100,000 and the lowest being 2001, with 1.28 per 100,000).



Graph 1. N° of ADR deaths per year



Graph 2. Evolution of the average age (in years) by year



Graph 3. Use of intravenous injection (parenteral route of administration) (%) and HIV infection (%) by year

Tabla 2. ADR Mortality by provinces

	Total	%	Mortality rate
A Coruña	366	45,5%	29,5/100.000 hab.
Pontevedra	302	37,5%	31,6/100.000 hab.
Lugo	75	9,3%	21,7/100.000 hab.
Ourense	62	7,7%	19/100.000 hab.

The total number of deaths by ARD remained relatively stable in Galicia throughout the period studied (Graphic 1), except for a couple of years in which there seems to be a noticeable drop (2001 and 2003), and also 2011 (possibly owing to the data entered in the registry being skewed).

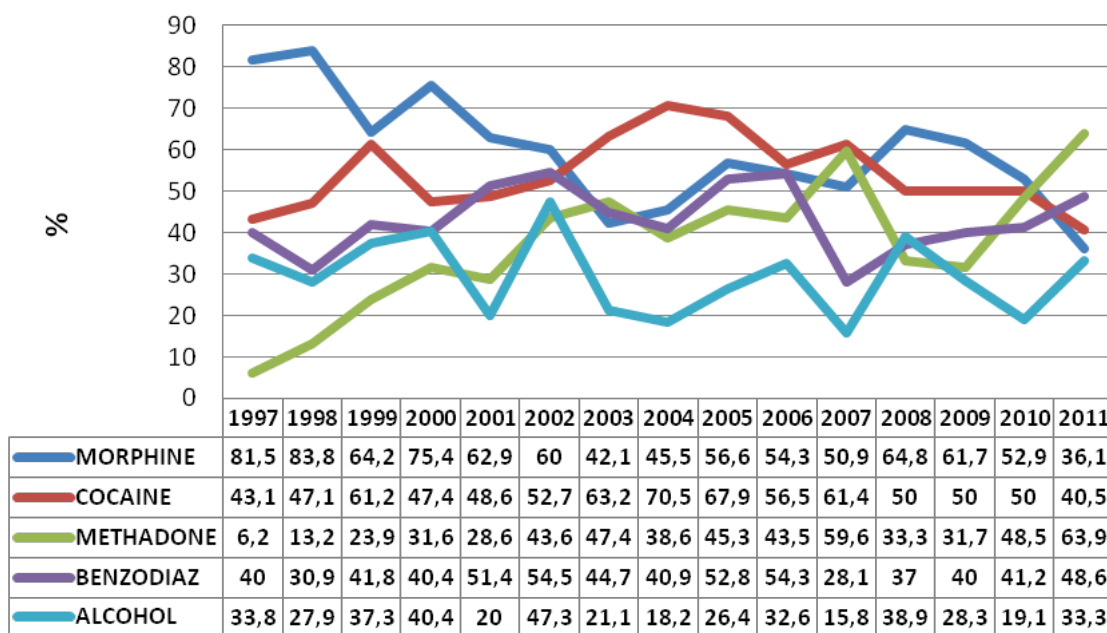
Within the sample group males predominate ($n=734$), representing 91.2% of the sample with there being no significant variation in the males/females percentage over the years of the study. The average age of the dead was 34.34 (34.8 for women and 34.3 for men), with an interval ranging from 17 to 56 years of age, and a 30-year mode. A progressive increase in age can be observed over the years of the study, rising from 29.28 in 2007 to 40.03 in 2011 (Graphic 2). Regarding the marital status (a variable that began to be registered in 2007, for which reason these data are limited to the period from 2007 to 2011), there is a predominance of unmarried persons (47.7%), followed by those who were separated or divorced (26.1%), married (25.3%) and, lastly widows/widowers (0.8%). It can also be observed that among the males the unmarried predominate (49.5%), while among the females it is married women who predominate (43.5%).

Regarding geographical location, the province in which the greatest number of deaths was registered (Table 2) was A Coruña, followed by Pontevedra, Lugo and, lastly, Ourense. Among the municipalities with the highest number of deaths are, in first place Vigo, the largest city in Galicia ($n=123$), followed by A Coruña ($n=100$), Pontevedra ($n=65$), Santiago de Compostela ($n=60$), Ferrol ($n=43$), Ourense ($n=42$), Ribeira ($n=38$), Lugo ($n=30$), Betanzos ($n=22$), Cangas ($n=14$) and Villagarcía ($n=14$).

Some 43.5% of the deceased were injecting drug users (IDUs). During the first years of the study a marked decrease in this way of administering drugs can be observed, dropping from 72.3% in 1997 to 28.6% in 2001. From that year onwards, the figures remained stable between 30 and 40% (Graphic 3). Signs of recent venipuncture (less than a week old) were found on 34.1% of the subjects who died between 2007 and 2011 (before that this was not registered), with a slightly higher, but statistically insignificant, percentage in males.

Regarding HIV serostatus, this was positive in 36.5% of the sample, negative in 58.4% and unknown in 5.1%. The analysis by gender shows very similar results in both groups, with a slightly higher prevalence among females (40.3%) than among males (38.3%). If we observe the evolution over the years (Graph 3), we see a downward trend in HIV

DETECTION OF DRUGS BY YEAR (%)



Graph 4. Variation in the type of substances detected by year

seropositivity, going from more than half of the sample in the early years (1997-1998) to lower than a third in the later years (2009-2010). There seems to be a clearly observable parallelism between the reduction if the use of syringes and HIV seropositivity.

In more than half of all cases, the dead body was found in the home (n=461, 57.1%), followed by those who were found in the street (n=190, 23.5%), penitentiary facilities (n=42, 5.2%), hotels or guesthouses (n=33, 4.1%), hospital (n=31, 3.9%) and public establishments (n=23, 2.9%), while 25 persons (3.3%) came from unspecified places. Being found in the street was much more common among males (24.8% as opposed to 9.9% in the case of females), as was the case with public establishments (3% as opposed to 1.4%), which could be related to a greater level of marginalization and/or “street living” of males.

From 2007 onwards, evidence that the death could have been self-induced or even a case of suicide began to be registered. This evidence was only found in 9% of cases, while in the great majority there were no data found that pointed in that direction. A greater prevalence is observed among females, 18.8% as opposed to 8% in the case of males, but this difference is not statistically significant owing basically to the small size of the sample in the case of females.

The distribution of deaths over the days of the week shows that the greatest number happened on Sundays (32.1%), followed by Saturdays (17.3%), Tuesdays (13.8%), Fridays (13%), Thursdays (12.3%), Wednesdays (9.9%), while only a small percentage occur on Mondays (1.8%). Therefore, the greater part was concentrated around the weekends, meaning almost half of all cases (49.4%) occurred between Saturdays and Sundays.

The substance (or combination of substances) found with the greatest frequency were opiates. Within this group morphine (a heroin metabolite) which was detected in 61.3% of cases, appeared in first place, followed by methadone (35.6%), and codeine (27.6%). In second place was cocaine, whose presence was detected in 53.7% of cases, followed by the benzodiazepines which were found in 42.4%. Alcohol consumption was determined in almost a third (29.9%) of subjects, and lastly, cannabis appeared in samples from 17.9% of the deceased persons. Over the years of the study, variations may be observed regarding the type of substances found (Graphic 4). Thus, although the opiates are the substances that were most detected throughout the period of the study, there was a progressive decline of the implication of heroin in ARD deaths, going from being found in 81.5% of the deaths in 1997 to 36.1% in the last year studied (2011). On the other hand, methadone appeared with greater frequency as the years passed, going from 6.2% in 1997 to 63.9% in 2011. Cocaine increased noticeably from the early years, going from 43.1% in 1997 to 70.5% in 2004, after which there was a steady decline to 40.1% in 2011. The benzodiazepines remained at relatively stable levels of between 30 and 50% throughout, reaching their highest level in 2002 (54.4%) and their lowest in 2007 (28.1%), but with no clear tendency that can be shown over the years. Lastly, alcohol also showed an irregular pattern between its highest value, reached in 2002 (47.3%), and its minimum, corresponding to 2007 (15.8%).

Without any doubt, poly-consumption was the most prevalent pattern and the combination of substances was the most habitual situation, with only one substance being detected in just 114 subjects (13.2% of cases), while in 361 ca-

ses (44.8%) there were two, in 240 cases (29.95) there were three, in 77 cases (9.6%) there were four, in twelve subjects (1.5%) there were five and in one case (0.1%) there were six. As far as gender is concerned, poly-consumption patterns did not show noticeable differences, although in males the highest percentage showed two substances (46%), while in females that figure corresponded to the finding of three (41.8%). Poly-consumption became more consolidated over the years. Thus, the cases in which only one substance was found went from 21.5% in 1997 to 8.1% in 2011. On the other hand, the percentage of subjects in whom three substances were detected rose from 26.2% in 2007 to 29.7% in 2011, those in which four were detected rose from 1.5% in 2007 to 18.9% in 2011, while five substances were not detected in any case in the earlier years but in the last five years that number settled at around 5%.

It is important to point out that a total of 42 deceased persons came from penitentiary centers, (5.2% of the sample). Of them, 90.5% were males with an average age of 34.95, which is in line with the general sample. The presence of HIV-positive serology was of 42.9%, higher than the median of the sample. Regarding the drugs detected in this sub-population, in order of prevalence they were: methadone (60.0%), benzodiazepines (66.7%), morphine (46.6%), cocaine (28.6%), cannabis (20.8%), codeine (16.7%) and alcohol (2.4%).

Discussion

Our study shows, in the same way as various works reviewed (Degenhardt, 2011; UNODC, 2012; Giraudon et al, 2012; Gjersing et al, 2013), that ADR constitutes one of the principal causes of death among drug addicts. At the same time, and despite the different policies aimed at reducing harm among drug users, mortality remains relatively stable, as in other countries (Giraudon et al., 2012). In any case, we are dealing with figures that are smaller than those collected in our catchment area between 1992 and 1997 (Pereiro, 2003; Pereiro, 1999), and those corresponding to other regions and neighboring countries (Bargagli, 2006; EMCD-DA, 2011; Gjersing, 2013; DGPND, 2012). We consider this fact to be related to the implementing of harm reduction strategies and the widespread use in our region of maintenance programs with agonists.

It is important to point out that the data for 2011 are less reliable as they show both a noticeable reduction in the number of deaths registered as well as having fewer data, and those being of poorer quality. This could be related to the lack of funding for the program on the part of the National and Autonomous Drug Plans owing to budgetary cut-backs affecting government spending, themselves a result of the current economic crisis.

The deaths affected the relatively young population especially (an average age of 34.3). However, the average age

in our sample was notably higher than that found in our Autonomous Community over the period from 1992 to 1997 (28.8) (Pereiro, 2003; Pereiro, 1999), and rose over the years of our study. These figures are in line with those found at a national level in this country and in other neighboring countries (DGPND, 2012). For that reason, it is clear that we can consider the ADR mortality rate shows a greater prevalence among persons with a long history of drug use, and that "experience", far from being a factor of protection, as might be supposed a priori, seems rather to be associated with greater vulnerability.

Regarding gender, males clearly predominated, with figures that remained similar over the years of the study. The progressive increase in the prevalence of substance use among females does not seem to be reflected in the figures for ADR deaths, probably because the consumption of legal drugs predominated among them, but they also continued to be far below the males in terms of illegal drugs, particularly opiates which, as we have already stated, were the main substance involved in those deaths. Other factors that might explain the greater risk of death by overdose among males, as some authors indicate, may have to do with greater levels of social marginalization and isolation (Darke, Degenhardt, & Mattick, 2007), as well as greater alcohol consumption among them (Bird & Robertson, 2011).

The majority of deceased persons who died were unmarried (47.7%), a figure that is well below that captured at national level, of around 60% (DGPND, 2012), and in second place were those who were separated or divorced. That is to say, the great majority of our sample is made up of persons who either did not live with a partner in a stable union, or whose union had broken down. Although the average age of the sample is, as we have stated, relatively young, these data are probably connected to the general psychosocial deterioration of the drug using population and its serious repercussions in their immediate circles (Darke, 2007), which makes cohabitation with anyone beyond their family of origin difficult.

As for the geographical distribution of the deaths in our Autonomous Community, in general it correlated with the areas of greatest consumption, which usually corresponds to the cities, the areas of greatest population density and the proximity to the coast (this last fact is probably related to the greater purchasing power of young people there, and the fact that those places are entry and distribution points for illegal drugs in this country).

The fact that only 43.5% of the dead were intravenous users is worthy of note, as well as the fact that those on whom signs of needle use in a period of less than a week before their death were detected was also relatively low (34.1%), showing a slight downward tendency over the period in which these data were registered (2007-2011), which seems to point to a progressive diminishing of the use of syringes as a means of administering drugs by users

in this region. These figures are in line with those found at national level (DGPND, 2012), although in this case the values are slightly higher, sitting at around 35 to 50%. This fact should also alert us to the serious risk of overdose when using other means of administration (a circumstance that many drug addicts are not always aware of and which they often play down), particularly when several substances are consumed at the same time, as was the case in most of the subjects in our sample, meaning therefore that preventive strategies must be extended to the non-IDU population who, as we have just pointed out, are at high risk of death by ADR.

HIV-positive serology accounted for 36.5% of cases. In any case, the presence of HIV seropositivity was higher than that detected in drug-dependent patients who seek treatment, for which reason there is an association of HIV with overdosing, as other studies show (Green, McGowan, Yokell, Pouget, & Rich, 2012). This association seems to be related to other circumstances that have already been mentioned, fundamentally the age (relatively high), the prolonged period of use, a greater use of intravenous administration, as well as general deterioration (both organic and psychosocial) derived from the lifestyle of drug addicts, apart from HIV infection itself (Wang et al., 2005). However, it should also be pointed out that this percentage dropped from year to year, going from the 53.8% detected at the beginning of our study (1997), to almost half (27.9%) in 2010. This drop seems to be related to the reduced use of intravenous administration (the principal cause of infection among drug addicts) (DGPND, 2012), together with the extension of maintenance programs with agonists, harm-reducing programs, safe-sex workshops etc. and other strategies aimed at preventing infection among this group.

As to the place of death, the most frequent location was the home (57.1%), followed by the street, although in a much lower percentage (23.5%). These two places were also the most frequent in the period from 1992 to 1997 (Pereiro, 2003; Pereiro, 1999), although at that time the percentage of deaths at home was significantly lower (39.2%), and that of deaths in the street was higher than in our study (30.2%), which denotes lower levels of marginalization in the period covered by our study. At a national level too, a higher percentage of deaths at home can be observed over the years, going from 54.5% in 2003 to 64.3% in 2010 (DGPND, 2012).

The fact that a greater percentage of ADR deaths occurred at home and/or in the subject's immediate circles could make it easier for family and friends to request help. In this sense, implementing preventive programs aimed at training them to recognize the symptoms of overdose, give first aid and request medical assistance where overdose is suspected (Siegler, Tuazon, Bradley O'Brien, & Paone, 2013).

Lastly, the significant percentage of subjects who die of ADR in penitentiary centers (45, 5.2% of the total) should be mentioned, as it would fully justify the existence of the-

rapeutic and risk reduction programs in these institutions with a high population of drug addicts. Studies carried out in other countries also indicate high numbers of deaths by overdose in prisons. Identifying the profile of these subjects and of the inmates who have been witnesses to cases of overdose could help to identify the target population as well as the developing of preventive policies in these institutions (Albizu-García, Hernández-Viver, Feal, & Rodríguez-Orenego, 2009; Kinner, Milloy, Wood, Qi, Zhang, & Kerr, 2012; Moore, Winter, Indig, Greenberg, & Kinner, 2013).

Signs of suicide were detected in a relatively small number of cases, although in the case of females, the percentage was considerably higher than in males, in line with data found in other studies (Cottler, Campbell, Krishna, Cunningham-Williams, & Abdallah, 2005). Of course, we are dealing here with completed suicides, so the percentage of attempts with no fatal outcome is assumed to be much higher. However, as we have already pointed out, it is not usually easy to determine whether a death by overdose was intentional or accidental (Britton, Bohnert, Wines, & Conner, 2012), so only those cases in which there was clear evidence of the intention of the subject to take his or her own life were registered as such.

As for the day of the week on which most ADR deaths occur, the weekend appears to be clearly associated, as it was when almost half of the deaths occurred, with Sundays being the day of greatest prevalence. These figures were significantly higher than those for the period from 1992 to 1997, although in that period too there was a greater frequency of weekend deaths (Pereiro, 2003; Pereiro, 1999). We believe that the tendency to engage in poly-consumption at weekends, particularly the association of CNS depressants, could explain this increase.

Regarding toxicological determinations, the most habitual situation was the detection of two or more drugs in the majority of subjects studied, while only in a small proportion was just one substance found. This is a faithful reflection of the poly-consumption that the majority of drug addicts engage in and is in line with other studies on ADR (Vicente, 2009; EMCDDA, 2011; Gjersing, 2013; DGPND, 2012), with a clear upward tendency of poly-consumption with the passing of the years over our period of study.

The most frequently-found substances were opiates and, in particular, heroin. However, a significant downward trend can be observed vis-à-vis the figures obtained for the period from 1992-1997 within our Community itself, which in that sample was as high as 84.4% (Pereiro, 2003; Pereiro, 1999), and over the years of our study. These data are in line with the drop in the consumption of heroin which was detected both in population surveys (DGPND, 2012) and among the drug addicts who seek treatment.

Within the opiates group, in second place was methadone which was found in 35.7% of the deceased. This figure was much higher than that found in the period from 1992 to

1997, which was of 8.3% (Pereiro, 2003; Pereiro, 1999). This tendency became very clear over the course of our study, in which a progressive increase of the detection of this substance can be observed. Only in 13 cases (4.5%) was methadone detected as the sole substance, while in all other cases other associated substances appeared, for which even though it may be considered as a contributor to the toxic effect of other CNS depressants, its role as the principal and/or only cause of death does not appear to be particularly relevant. It was not registered whether the patient was having methadone maintenance treatment or if the drug had been acquired on the illegal market, but the increase in the detection of this substance does reflect a greater dissemination and access of drug addict patients to these programs which without doubt do contribute to improvements in the general health and quality of life of this group, and can therefore be considered as an indicator of the quality of assistance provided. Although on first sight a certain causal responsibility in mortality could be attributed to it (and without any doubt, in combination with other CNS depressants it does contribute to the fatal outcome), the truth is that all studies point to the important role of methadone maintenance programs in the reduction of risk of ADR death (Brugal, Domingo-Salvany, Puig, Barrio, García de Olalla, & de la Fuente, 2005; Clausen, Anchersen, & Waal, 2008; Schwartz et al, 2013; Sherman, Han, Welsh, Chaulk, & Serio-Chapman, 2013; Strang, Hall, Hickman, & Bird, 2010).

Cocaine was, after the opiates, the second most frequently detected substance in ADR victims, with significant gender differences. This figure is much higher than in the period from 1992 to 1997, when it was only 22.2% (Pereiro, 2003; Pereiro, 1999). Regarding the evolution of this parameter over the period of our study, there was a notable increase in the early years, followed a period of stabilization and a certain drop later, which reflects the evolution of the consumption of this substance in recent years as detected in general population surveys (DGPND, 2012), as well as in treatment indicators.

The combination of alcohol (detected in approximately a third of the deceased) with other CNS depressants (opiates, benzodiazepines, etc.) is especially dangerous, as it enhances their effects and, therefore, increases the risk of overdose. The average concentration of alcohol was of $1,122 \pm 0,666$ gr/L, levels which were practically the same as those detected in the period from 1992 to 1997, in which they were $1,115 \pm 0,843$ g/L (Pereiro, 1999). In any case, these levels are too far below the lethal dose (Minian & Bontiette, 1989; Jones, 2003; Darke, Duflo, Torok, & Prolov, 2013; Darke, Duflo, Torok, & Prolov, 2013b) for it to be considered as a principal cause of death, although it does seem to have an important role as a contributor of the same, when combined with other depressants.

Benzodiazepines were detected in an important percentage of cases (42.4%), a figure that is significantly higher

than those found in other neighboring countries such as the United Kingdom where it was in the region of 30% (EMCDDA, 2011, Bird, 2011), but much lower than those detected by Gjersing (2013) among the deceased in Oslo, Norway, where the figure rose to 68%. On the other hand, we cannot establish a clear tendency over the period of our study, as even though there were years with a notable increase (54.5% in 2002), there were no relevant differences to be observed between the early years and the later ones. Nevertheless, the figures were notably higher than those from 1992 to 1997, in which the percentage of subjects among whom this substance was detected was of 27.5% (Pereiro, 1999).

The presence of cannabis began to be determined from 2007 onwards, for which reason we have no previous data. However, the percentage of detection (17.9%) in our sample does not seem excessively high, bearing in mind how widespread its consumption is. While it is true that, according to the profile of our sample population of ADR deaths (advanced age, long-term consumers of opiates, psychosocial deterioration...), the consumption of cannabis would very much occupy a second place, unlike in younger populations of consumers. On the other hand, the concentrations of this substance that were detected were not especially high, if we compare them with those of other studies that have been published (Karch, 2006; Hartung, Ritz-Timme, & Daldrup, 2014).

Conclusions

ARD is one of the principal causes of mortality among drug addicts, and in recent years it has not been possible to diminish its incidence despite the multiple strategies developed to reduce harm among this population and the change in consumption patterns (reduction in the use of opiates, and of intravenous drug use etc.). Males show much higher death rates than females, which is not exclusively attributable to greater levels of drug use among them, since the percentages by gender are much higher than those detected in population surveys and among drug addicts who seek treatment. The average age of the deceased, relatively high, which is going up year on year, means that deaths are not usually happening among new or inexperienced users, but rather among those with a long-term experience of consumption. More than half of all deaths were concentrated around the weekend, with Saturdays and Sundays being the days of the week with greatest prevalence, which could be related to the consumption of associated substances at those times. Regarding the place in which the dead body was found (and supposedly where death had occurred), it seems to be primarily the subject's own home, with a slight, and increasing, tendency for this to happen there, and in the street, where there is a slight downward tendency (both data sets seem to indicate a reduction in the marginalization of these subjects). But possibly the most striking fact is the continuous increase of those who die in penitentiary institu-

tions. Among these patients, as in the drug-dependent population in general, there was a reduction in intravenous use, as in the presence of HIV-seropositivity. The most frequently detected substances among the deceased in this group continued to be the opiates, especially heroin, but increasingly less, with, on the contrary, an increased presence of methadone, which indicates higher levels of accessibility to this substance and a greater level of penetration of maintenance programs using opiate agonists among the drug-dependent patients. After some years with a marked increase in cocaine amongst ADR victims, it seems that in the later years of our study this tendency was reversing. Other substances, such as alcohol or benzodiazepines remained relatively stable, with certain fluctuations from one year to another, but with no clear tendency over the study period. In the great majority of subjects, the presence of two or more substances was determined, which makes it difficult to establish a clear link between the concentrations detected of each of them and the causal attribution of the death. On the other hand, the most usual pattern of poly-consumption is reflected and had already been detected in other indicators (population surveys, treatment etc.).

Therefore, the group that is principally at risk is made up of male drug addicts with a dependency on opiates, who have been previously consuming for some years, and who usually combine several substances, particularly CNS depressants. Many of them are candidates for, or are already enrolled in maintenance programs with opiate agonists. It is on them, and their immediate circles, where strategies that allow them to avoid situations of risk should be focused, and in case of suffering an overdose, identify the signs and symptoms, give first aid and alert the health services with the aim of preventing a fatal outcome.

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Conflict of interests:

The authors state that there are no conflicts of interest to declare.

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