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Drug related deaths between 2008 and 2011. A retrospective study in 32 Romanian counties

Research Article

Dan Dermengiu[1], Sorin Hostiuc*[1], Doina Radu[2], Florina Aciu[2], Gabriel Gorun[3], Vasile Astarastoae[4], Beatrice Ioan[4], Gabriela Constantinescu[5], Alexandra Enache[6], Veronica Ciocan[6], Ioan Talos[7], George Cristian Curca[1]

1 Carol Davila University of Medicine and Pharmacy, Dept of Legal Medicine and Bioethics, National Institute of Legal Medicine, Dept of Forensic Pathology, Bucharest, Romania

2 National Institute of Legal Medicine, Dept of Forensic Toxicology, Bucharest, Romania

3 National Institute of Legal Medicine, Dept of Forensic Pathology, Bucharest, Romania

4 Iasi Institute of Legal Medicine, Dept of Forensic Pathology, Iasi, Romania

5 Iasi Institute of Legal Medicine, Dept of Forensic Toxicology, Iasi, Romania

6 Timisoara Institute of Legal Medicine, Dept of Forensic Pathology, Timisoara, Romania

7 Timisoara Institute of Legal Medicine, Dept of Forensic Toxicology, Timisoara, Romania

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Abstract: The purpose of this study is to determine the pattern of drug related deaths in Romania between 2008 and 2011 by analyzing the medical-legal cases, from a significant proportion of Romanian Counties (out of 41 plus the capital), in which the direct causal link between drug overdose and death was drug related. Material and methods. 446 forensic toxicology cases were analyzed in a four year period, obtained from more than two thirds of the counties in Romania. Results. 54.26% yielded a positive toxicological analysis, most often with benzodiazepines, opiates, barbiturates and cannabinoids. Males around 31 years old represented the most affected group. Illegal drug related deaths were more frequent in males and non-illegal drug related deaths were proportionally more frequent in females. Discussions and conclusions. The pattern of consumption is similar to the one obtained by similar studies in neighboring countries. The city capital has a very distinct pattern of consumption compared to other cities/counties.

Keywords: *Forensic science • Forensic toxicology • Drug related deaths in Romania • Opiates overdose • Benzodiazepines • Barbiturates*

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Abbreviations

DRD – drug related death
ID – illegal drugs
NID – non-illegal drugs
CNS – central nervous system
HPLC – high performance liquid cromatography
GC-MS – gas cromatography – mass-spectrometry
EMCDDA – European Monitoring Center for Drugs and Drug Addiction

* *E-mail: soraer@gmail.com*

1. Introduction

Drug related deaths are a significant health problem, especially in young adults, accounting for about 200.000 cases annually [1]. Judicially DRDs can be accidental [1], (drug overdose, body packer, body stuffer, or determined by infectious and non-infectious complications), suicidal, usually at older ages using CNS-medication [2-5] or rare, homicidal [6-10].

For the purpose of our study the definition of drug related deaths was the one given by Zwingenberger et al: "deaths where there is evidence of voluntary and recent use of drugs under circumstances that do not suggest other causes of death and reveal a causal relationship between these" [11]. DRDs are therefore considered deaths caused by overdose (including body packers or body stuffers), suicides by substance abuse, diseases directly caused by drug use or abuse, involved as an intermediary link in the thanathologic chain acute endocarditis, pneumonia, and so on, and other violent deaths in which drugs were present, and by their presence have favored the traumatic events (traffic accidents with the drivers under the influence, work-related accidents, etc.). Violent deaths in which alcohol was the only identified substance of abuse, work-related accidents in which the death was caused by non-voluntary intoxication or iatrogenic over dosage were not included. The purpose of this study is to determine the pattern of drug related deaths in Romania between 2008 and 2011, by analyzing the medical-legal cases, from a significant proportion of Romanian Counties (out of 41 plus the capital), in which the direct causal link between drug overdose and death was drug related.

2. Material and methods

The cases were obtained from 32 counties, including the capital (Romania has 41 counties plus the capital), for which a toxicological analysis was conducted in one of the three institutes (Iasi, Timisoara, Bucharest) involved in the study. Bucharest institute of legal medicine is conducting toxicological analysis for most southern counties, Iasi for eastern and north-eastern counties, and Timisoara for western counties. For illegal drugs preliminary tests were conducted using immunoassay tests (blood or urine), and confirmatory tests were conducted using GC-MS. For barbiturates, benzodiazepines and anti-psychotic medication was used HPLC. Blood and urine were mainly used as biological samples on which were conducted the toxicological tests. In particular cases were used other biological products like stomach and/or its content, kidney, liver, or bile. Toxicological tests are conducted during forensic autopsies when intoxication is suspected to be either a cause of death, involved in the death of a person or when there is no definite cause of death identified during autopsy. Each institute used its own methodology for toxicological detection, this being the main reason for the quantitative results not being reported in this presentation, leaving us to only present qualitative results. All cases were however diagnosed to be drug related deaths, the cause of death being causally linked with the substance misuse. The death was either directly determined by the acute intoxication or indirectly (e.g. traffic accidents in drivers under the influence). Cases in which another cause of death, unrelated to the drug abuse, was identified, were excluded from our analysis.

The cases were obtained from January 2008 to October 2011 and were represented by medical legal cases (cases in which the death was initially considered to be violent, suspect or determined by an unknown cause, in accordance with the Romanian legislation regarding the situations in which the medical-legal autopsy is mandatory). The results were gathered by a common reporting methodology using standardized forms and the included in a SPSS database. Statistical analysis was conducted using the SPSS v.20 for Mac OS software. The following statistical tests were used: descriptive statistics (frequencies, mean, standard deviation, range, minimum, maximum, ANOVA, p-test), crosstabulation (using the Chi2 Pearson test to test the presence of a significant correlation between descriptive data). A p value below 0.05 was considered significant.

3. Results

A total number of 446 cases were analyzed between January 2008 and October 2011, of which 204 were negative (45.74%) and 242 cases yielded positive results (54.26%). We identified illegal substances in 155 cases (34.75%) represented by morphine and related in 96 cases, methadone in 40, tramadol in 16, cannabinoids in 12, zopiclone in 8, ketamin in 7 and others (cocaine, MDMA, MDPPP, MDE, Pethidine, Oxycodone, Ergotaine, Metorphan) in 11. Legal substances considered as being involved in the physiopathologic chain leading to death were identified in 155 cases (34.75%): benzodiazepines in 103 cases, barbiturates in 58, antipsychotics in 13 cases, anti-epileptics (especially carbamasepine) in 39 cases, and other antidepressants in ten. In 68 cases (15.25%) a mix of both legal and illegal substances was identified (see Table 1 for details).

Table 1. Distribution of positive and negative cases on centers. IDs =illegal substances, NIDs = non-illegal substances

Variable	Bucharest	Iasi	Timisoara	Total
Positive (total)	179	47	16	242
Positive (IDs)	75	2	10	87
Positive (NIDs)	37	44	6	87
Positive (both)	67	1	0	68
Negative	154	9	41	204
Total	333	56	57	446

The mean age for the positive cases was 31.47 years, with a standard deviation of 11.23, a kurtosis of 3.655 and a skewness of 1.754. 78.5% of cases were males (190 cases) and 21.5% were females (52 cases). Of the 242 positive cases, data about the age was obtained for only 210 cases as the age parameter was not mandatory for reporting until 2009. Female cases had a significantly higher mean age compared to male subjects (35.85 years and 30.44 years respectively), and the kurtosis is much smaller than in males (0.873 and 4.079 respectively). Therefore the distribution of positive cases in females has an almost normal distribution whilst for males most cases have an age around the mean (see Figure 1). The difference is significant, the significance being tested using the ANOVA table, which yielded an F value of 7.730, significant at a p=0.006.

Illegal drug related deaths were more frequent in males and non-illegal drug related deaths were proportionally more frequent in females (see Table 2). The difference was significant (Pearson Chi^2 test yielded a value of 22.047, significant at a p value of 0.000016).

DRDs determined by the IDs were usually caused by the use of a single substance (106 cases, 43.80%); associations of two substances were identified in 40 cases, (16.53%), three in seven cases (2.89%) and four in two cases (0.83%). Most often illegal DRDs are associated with opiates overdose, especially in Bucharest and surrounding areas (for details see Table 3).

A single opiate was identified in 104 cases (42.98% of all DRDs), two in 24 cases (9.92), and three in two cases (0.83%). In 53.73% of all cases an opiate compound was identified.

DRDs determined by NIDs were also usually associated with the use/overuse of a single substance (131 cases, 54.13%); two substances were identified in 19 cases (7.85%), and three substances were identified in five cases (2.07%).

DRDs associated with illegal drugs tend to occur more often at younger ages whilst DRDs associated with NIDs are more heterogeneous – whilst antidepressant and antipsychotic related deaths occur as a mean at even lower ages compared to IDs, benzodiazepine and barbiturates related deaths occur at older ages (especially for benzodiazepines, which are also the most frequently identified substance category in our study). CNS-related deaths have a higher mean age (33.27 years) compared to illegal drug related deaths (28.27 years). For details see Table 4.

The distribution of cases on years reveals a slight increase in the number of cases from 2008 to 2010, followed by a severe decrease in 2011 when the number of cases is less than half the one from 2010 (32 and 79 cases respectively). The month in which most cases are identified is January with 28 cases whilst the month with the smallest number of cases in February (see Figure 2). Data for November and December 2011 was not available before the end of our study and therefore the number of cases for these months should be slightly increased. However, taking into account the yearly evolution of the DRDs the most likely the values are not as high as in January.

Figure 1. Case distribution on sex and age

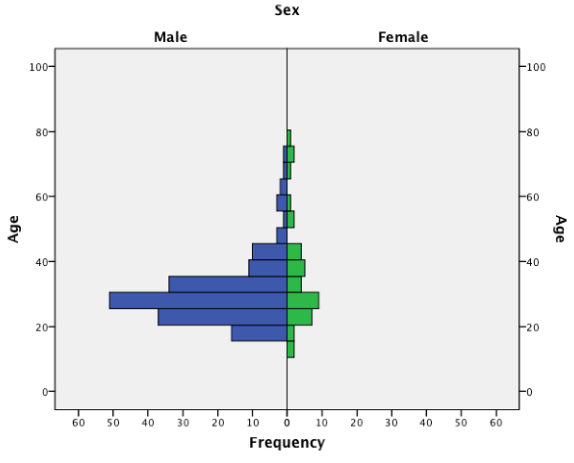

Figure 2. Cases distribution on months

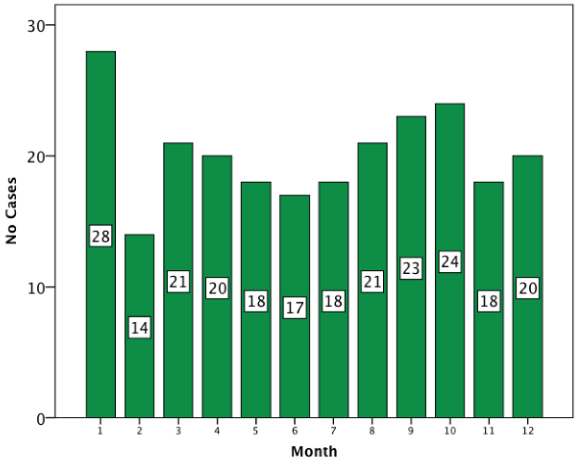

Table 2. Distribution of positive cases according to the sex of the victims.

Variable	Males			Females		
	No Cases	$\%_1$	$\%_2$	No Cases	$\%_1$	$\%_2$
Positive (IDs)	136	56.2	87.74	19	7.85	12.26
Positive (NIDs)	115	47.5	74.19	40	16.5	25.81
Positive (both)	61	25.2	89.70	7	2.89	10.30
Total	190	78.51	78.51	52	21.49	78.51

$\%_1$=(No Cases from the left neighboring cell/242)*100, %2=[(No cases from the left neighboring cell)/(No cases from the current raw)]*100

Table 3. Etiology of illegal DRDs in different centers

Drug	Center				Sex		
	Bucharest	Iasi	Timisoara	Sig	Male	Female	Sig
Morphine*)	89	0	7	0.000	83	13	0.01
Methadone	40	0	0	0.000	36	4	0.036
Cannabinoids	7	2	3	0.031	12	0	0.051
Others **)	11	0	0	n.a.	8	3	n.a
Ketamin	6	0	1	0.337	7	0	0.179
Tramadol	16	0	0	0.049	15	1	0.104
Zopiclone	7	1	0	0.62	6	2	0.542

*) In 10 cases morphine was associated with 6-monoacetil morphine, suggesting the use of heroin.
**)Cocaine, MDMA, MDPPP MOO, MDE, Pethidine, Oxycodone, Ergotamine, Metorphan, Levorphanol

Table 4. Mean age at the moment of death in various DRDs

Illegal Substances		Non-Illegal Substances	
Substance	Mean age	Substance	Mean age
Morphine	28.56	Tramadol	30.81
Methadone	27.72	Zopiclone	25.66
Cocaine	29	Benzodiazepines	31.83
Cannabinoids	28.16	Antidepressants	26.77
Ketamin	29	Antiepileptic	30.64
		Antipsychotic	26.15
		Barbiturates	37.76

4. Discussions

In Romania forensic autopsies are performed in all cases in which the cause of death is violent, suspect or unknown. As DRDs are violent deaths, in all cases a medical legal autopsy is performed, even if the patient did not die immediately after use (for example if he was in hospital, or had a complication of the drug abuse like a right heart endocarditis causing the death). The medical-legal physician is the one who determines the cause of death (whether violent or not); all cases included in the study had a violent cause of death. The manner of death (suicide, homicide, accidental) is determined by the prosecutor after analyzing the forensic report and other data; therefore, due to the confidentiality of the prosecutor's reports, we do not have objective data to determine the manner of death.

EMCDDA official reports have identified a total number of 32 directly DRDs in 2009 [12] (the last year from which the data is available), and 33 cases in 2008. Our values are much higher due to the fact that we included in the study cases of non-illegal drug related deaths and also due to the fact that EMCDDA data is mainly based on data originating from the National Institute of Legal Medicine Bucharest. A previous study, regarding DRDs in Romania has gathered data from 2001 to 2007, and has identified 12 cases in 2001, three in 2002, seven in 2003 and 2004, six in 2005, 20 in 2006 and 32 in 2007 [13]. From analyzing the data obtained from that study and from our own we can identify a significant increase in the number of cases from

2006 to 2007 and a similar increase from 2007 to 2008. The first increase was caused by the modernization of the forensic toxicology laboratories (in Bucharest, from which most of the cases were gathered for the previous study, Iasi and Timisoara) [14]. The second increase was caused by the addition of supplemental cases, from the other two medical legal institutes with their adjacent counties. In 2011 the number of cases has significantly decreased, from 79 to 32. The decrease is only partially explained by the fact that we do not have data for the last two months of the 2011. By only comparing the first ten months, the difference is also extremely high (70 cases in the last ten months of 2010). The most likely explanation is an increased use of legal highs (herbal highs, "legal" drugs) [15-18], but better preventive measures may play a part as well. DRDs associated with legal highs were not identified. However, there have been cases in which a history of legal highs use was obtained [16]. In each of these cases a "classical" illegal substance was identified during the autopsy (most often morphine, methadone or ketamine). This pattern (history of legal highs use and positive toxicology for classical drugs) may be caused by one or more of the following: (1) use of legal highs "enhanced" by the seller/producer with classical illegal drugs, (2) difficulties in the detection of most legal highs using current techniques and apparatus, (3) legal highs were added by the addicts to their usual mix of classic illegal drugs [16].

The etiology of the DRDs is highly sex and age dependent: whilst male sex and younger ages has a tendency to be associated illegal drugs, female sex and older age has a tendency to be associated with CNS-medication (especially barbiturates and benzodiazepines).

A very high number of cases associate more than one substance, either only illegal drugs, CNS-medication or both. Most likely causes for this phenomenon are the presence of impure substances on the market or the use of a substance in the treatment of other addiction (most often methadone, in opiate addiction).

Our study has identified that in 53.73% of all positive cases an opiate compound was found. The value is in accordance with most studies in Europe, which have most often associated opiates with DRDs. For example in former East Germany the percentage was 55% (in a study analyzing DRDs between 1995 and 2004). In Nordic countries, a study conducted in 2002 has identified heroin/morphine to be the most frequent cause of fatal overdose, with values ranging from 10% in Finland to 72% in Norway [19]. In Slovenia between 1997 and 2003, from 122 DRD cases were identified 89 heroine/morphine, 40 methadone, and 49 benzodiazepine overdoses[20]. The values are significantly higher for opiates than our study revealed. Also, the percentage of benzodiazepines in this study compared (40.16%) is similar to the one obtained by us (42.56%), but the ratio opiates/benzodiazepines is much higher in Slovenia.

The mean age in our study is 31.47 years, higher in females than males (35.85 and 30.44 respectively), and higher in CNS related deaths compared to illegal drug related deaths (33.27 and 28.67 years respectively). The mean age associated with illegal DRDs is higher than in the study conducted on the territory of the former Eastern Germany, where the mean age was 24 [11]. In the study conducted by Steentoft, the mean age was different between different countries, with higher values for Denmark and Norway (35-39 years), value also obtained by Toprak in Istanbul [1] and lower values for Finland and Sweden (maximum number of cases in the 20-24 years old age group). In Slovenia the most frequent affected age group is also 20-24 years old[20].

The percentage of female DRDs (21.49%) is similar to the one obtained by other studies; for example Steentoft et al [21] found the percentage of female DRD to be between 10 and 30% in Nordic countries, Seymour et al gave a percentage of 19% in Scotland [22], and Zwingenberger et al found the percentage to be 15% in former Eastern Germany [11].

A particularity of our study is the presence of a very distinct pattern in the capital compared to other counties. If in the capital opiates are very often found in the other counties cannabinoids are by far the most prevalent. The most likely cause is the fact that Bucharest is much more appealing for dealers than smaller cities.

5. Limitations

A separation between direct and indirect DRD could not be performed as the centers where the toxicological analysis were conducted did not have detailed autopsy reports in cases from neighboring counties.

The manner of death was not available, as it is determined by the prosecutors, whose reports were not available in the medical-legal system.

Age was not a mandatory field for data gathering until 2009; therefore the age parameter was not available for all cases prior to this year.

Data regarding the year 2011 was limited to the first ten months.

6. Conclusions

The pattern of consumption is similar to the one obtained by similar studies in neighboring countries. The city capital has a very distinct pattern of consumption compared to other cities/counties.

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