A five years study on drug-related deaths in Campania (Italy)

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Abstract

Objectives. The study regards n. 267 drug related deaths submitted to toxicological analyses for forensic purpose, since 2008 to 2012, at the Laboratory of Forensic Toxicology of the Second University of Napoli (SUN), Italy. Among the cases studied (94% males and 6% females) the 13.1% regards foreign citizens.

Methods. For each case autopsy findings and all drugs detected were recorded. In addition other epidemiological data such as age, race, gender, place and circumstance of death were also supplied. A systematic toxicological analysis (STA) for illicit drug, other pharmaceuticals, new psychotropic substances and ethanol has been applied on the specimens collected at autopsy and all positive results were confirmed by a quantitative analysis (GC/MS or LC-MS/MS).

Results. Toxicological results shows that simultaneous use of multiple illicit drugs was responsible of the largest mortality rate (57.7%), in both males and females. In the poly-drug use the cocaine was the most detected substance. The association of heroin/cocaine was identified in the 22.5% of deaths. The finding of only one drug was correlated with an opiate drug for the 14.2% and with cocaine for the 4.5% of cases. The distribution by age and gender demonstrates an increase in deaths among males aged over 30 years and among women older than 35 years. The territorial distribution of the deaths in the different surrounding areas and in the residential quarters of the Naples city demonstrates that the 76% of deaths occurred in a place different from the usual residence.

Conclusion. Results obtained demonstrate that prevails, at present, the need to specifically explore the changing patterns of poly-drug use among addicts, because studying the prevalence of mortality subsequent to the consumption of a single illicit drug may be insufficient to guide preventive policies in public health.

INTRODUCTION

Drug related deaths can occur in a variety of circumstances involving the acute poisonings from legal and illegal drugs, as well as the road accidents or other fatal adverse effects connected to drug abuse [1-3]. The official European data about the drug poisoning mortality, classified by the European Monitoring Center for Drugs and Drug Addiction (EMCDDA, 2012) [1] according to International Classification of Disease (ICD 10-WHO, 2010) [4] describe, in the past decade, a relatively stable rate of deaths, despite some annual fluctuations. Conversely in Italy, statistical data published in the Annual Relation to the Parliament [5] and cases recorded by Direzione Centrale per i Servizi Antidroga (DCSA) of Italian Ministry of the Interior [6] showed a progressive consistent decrease of drug related deaths since 2002 to 2011. However, it must be observed

that because these deaths were classified, by law enforcement, as deaths related to illicit drug poisoning only on the basis of circumstances suggesting a possible drug intake, in order to highlight the exact causes of deaths there is a great interest in epidemiological and toxicological studies that can clarify which are the illicit drugs that were really identified in biological specimens obtained from the autopsy, as cause of death or implicated in death. This study shows the data emerging from toxicological analyses conducted on drug related deaths observed at Second University of Naples, in the Campania Region (Italy), for forensic purpose, during a five years period (2008-2012). In addition, other epidemiological data such as age, gender, nationality and place of usual residence of the addicts *versus* the scene where they were found dead, were collected in order to study the territorial dynamics about demand and the supply of drugs.

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MATERIALS AND METHODS

The study sample was taken from n. 267 cases, submitted to toxicological analyses for forensic purpose, from 2008 to 2012, at the Laboratory of Forensic Toxicology of the School of Medicine, Second University of Naples (SUN), Italy. It should be noted that cases reported in *Table 1* and *Figure 1* refer not only to cases notified or suspected as drug related deaths by the police (n. 201 - 75.2%) but include also deaths for other causes under assessment (n. 51 - 19.1%) or deaths attributed to road traffic accidents (n. 15 - 5.6%). For each case demographic characteristics (age, race/ethnicity, gender), place and circumstance of death, borough of death were supplied. Autopsy findings and all drugs detected were also recorded. Only deaths for which, on the basis of positive results obtained by the toxicological analyses, the cause can be classified, as "accidental poisoning by drugs" (X40-X44) or "intentional self-poisoning by drugs" (X60-X64), according to the International Classification of Disease (ICD-10) were included [7]. A systematic toxicological analysis (STA) has been applied on the biological specimens routinely collected at autopsy (blood from hearth and from femoral vein, urine, bile, gastric content, liver and other relevant tissue samples):

a) immunoassay screenings for the most common drugs of abuse (amphetamines, cocaine, cannabis, opiates, methadone, buprenorphine, barbiturates, benzodiazepines) were applied on urine and bile;

b) general testing for illicit drugs, anticonvulsants, antidepressants, antipsychotics and other pharmaceuticals potentially fatal were performed on blood, urine and bile by qualitative methods using a mass spectrometry methodology coupled with gas or liquid chromatography (GC/MS or LC-MS/MS). These spectrometric analyses include also determination of new psychotropic substances (NPS), scheduled in Italy as illicit drug since 2010;

c) additional testing for ethanol and other volatile substances by gas chromatography with headspace sampling (GC/HS) methodology has been applied on the blood.

In all specimens sampled at autopsy, each positive result obtained from the STA was confirmed by a quantitative analysis performed by GC/MS or LC-MS/MS methodology.

All the above analyses were performed according to the Guidelines of the Italian Group of Forensic Toxicologists [8] that are consistent with the GTFCh Recommendations for Quality Control in Forensic Toxicological Analyses [9] and with the SOFT/AAFS Forensic Laboratory Guidelines (2006) [10].

RESULTS AN DISCUSSION

The annual trend of the drug related deaths observed at Second University of Naples, in Campania Region, over the period 2008-2012, with the male/female ratio (M/F) compared with national data, were synthesized in *Table 1*. Among the cases studied (n. 267- 94% males and 6% females) the 13.1% (n. 35) of deaths regards foreign citizens coming mainly from Eastern Europe.

Sex and age distribution

The distribution of the age and gender mortality is showed in *Table 2*.

Between 2008 to 2012 the mortality rate among younger males (years < 29) is significantly lowest compared to mortality occurred in males aged over 30 years.

The drug-related deaths among women were recorded at significantly lower level than males in every age group. However, despite the paucity of cases, it should be noted an increase in deaths in the last two years and the highest incidence among women older than 35 years.
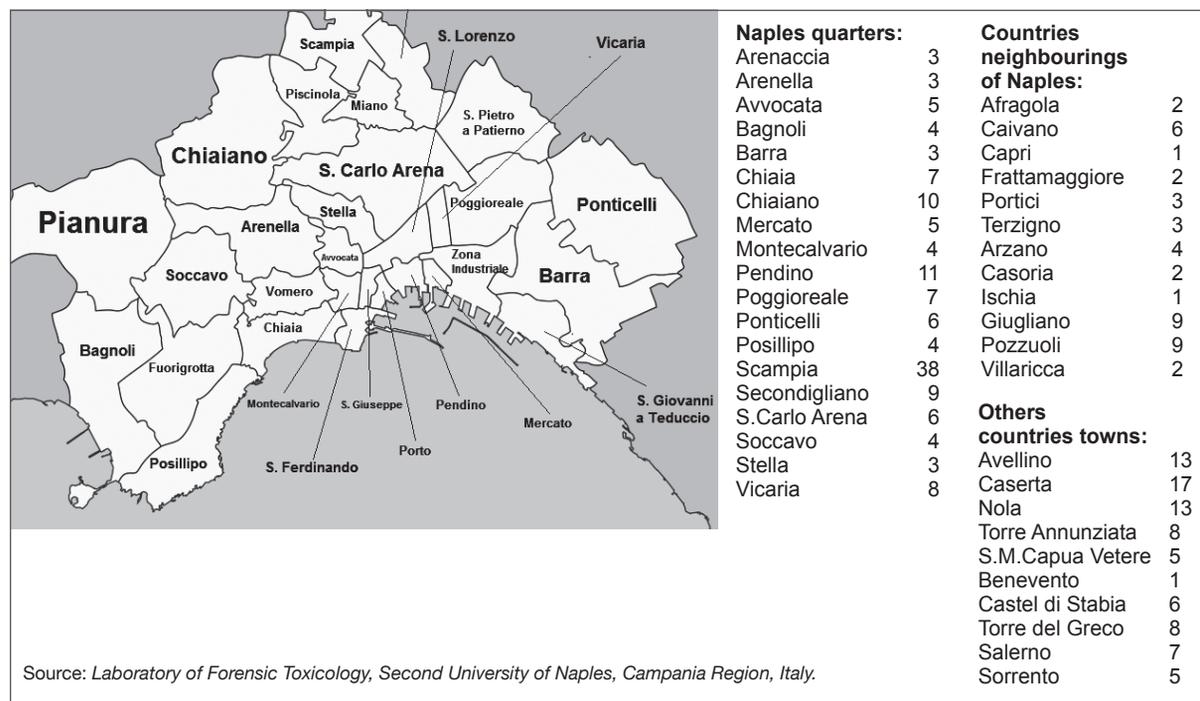
Cause of deaths

All illicit drugs involved in the drug related deaths were classified in *Figure 1* and in *Tables 3 and 4*.

Figure 1 shows that among all observed deaths (n. 267), since 2008 to 2012, the largest mortality rate in
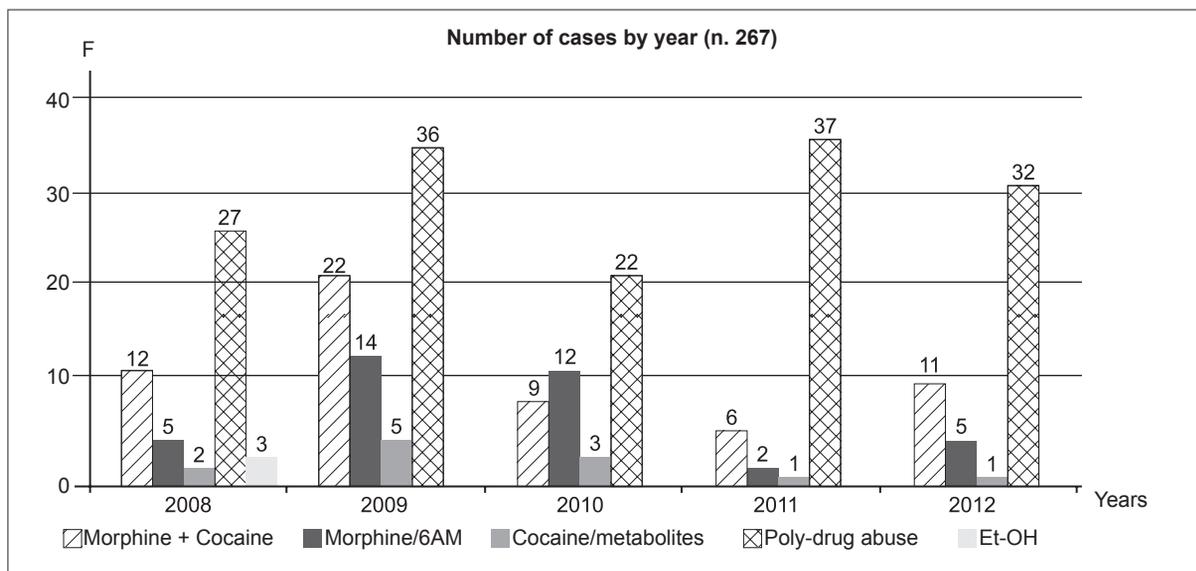
Figure 1
Frequency of illicit drug involved in drug related deaths (n. 267) in Campania Region, Italy, over the period 2008 to 2012.

Naples quarters:		Countries neighbourings of Naples:	
Arenaccia	3		
Arenella	3		
Avvocata	5	Afragola	2
Bagnoli	4	Caivano	6
Barra	3	Capri	1
Chiaia	7	Frattamaggiore	2
Chiaiano	10	Portici	3
Mercato	5	Terzigno	3
Montecalvario	4	Arzano	4
Pendino	11	Casoria	2
Poggioreale	7	Ischia	1
Ponticelli	6	Giugliano	9
Posillipo	4	Pozzuoli	9
Scampia	38	Villaricca	2
Secondigliano	9		
S.Carlo Arena	6	**Others countries towns:**	
Soccavo	4	Avellino	13
Stella	3	Caserta	17
Vicaria	8	Nola	13
		Torre Annunziata	8
		S.M.Capua Vetere	5
		Benevento	1
		Castel di Stabia	6
		Torre del Greco	8
		Salerno	7
		Sorrento	5

Source: *Laboratory of Forensic Toxicology, Second University of Naples, Campania Region, Italy.*

Figure 2
Territorial distribution of drug related deaths (n. 267) observed in Campania Region, Italy (years 2008-2012).

both males and females was connected to the simultaneous use of multiple drugs. In fact the intake of more than one drug has been responsible of the 57.7% (n. 154) of all cases. The association of heroin (morphine and/or 6-acetylmorphine (6-AM)) and cocaine together was identified in the 22.5% (n. 60) of deaths. It is interesting to note that the finding of only one drug has dropped significantly in the last years and was correlated with an opiate drug (morphine and/or 6-acetylmorphine) for the 14.2% (n. 38) and with cocaine and/or metabolites for the 4.5% (n. 12) of cases. Only the 1.1% of deaths (n. 3) were attributed to an excessive ethyl alcohol (Et-OH) intake. No one case was recognized as positive for new psychotropic substances (NPS)

In males, deaths involving the poly-drug use was observed for n. 139 of 267 studied cases. As shown in *Table 3*, in males, the finding of Δ^9tetrahydrocannabinolo (Δ^9THC and/or Δ^9THC-COOH), benzodiazepines (BDZ), methadone, ethyl alcohol (Et-OH) associated with morphine and/or cocaine occurred frequently and suggests that, in Campania Region, the increment in to the abuse of multiple illicit substance, is very significant.

The mortality and the drug misuse among females, synthesized in *Table 4*, demonstrates that more than one drug was frequently involved. Particularly the ethyl alcohol (Et-OH), among females was revealed in seven of the 16 deaths (43.7%) and into 3 cases, regarding female strangers (1 from Brazil and 2 from Ukraine), was identified as the only substance responsible of the death. On the contrary, in males the finding of Et-OH, always associated to other drugs, regards n. 26 cases (10.3%).

The identification of other cutting substances, having inherent toxicity, as the methorphan and the association of levamisole/lidocaine, never observed before, in the last

three years (2010-2012), regards respectively the presence of levamisole/lidocaine for 4.9% (n. 4 males and n. 3 females) and of methorphan for 3.5% (n. 4 males and n. 1 female) among of the 141 deaths recorded since 2010, all related to the heroin and/or cocaine abuse.

About the significance of the differences between males and females, evaluated by the Fisher test [11], was observed that with regard to cocaine, in spite of the groups' different numerousness (139 *vs* 16, *Table 3* and *Table 4*) the difference between the two percentages doesn't appear accidental (p < 0.0030, Fisher two tails).

Place of death
The territorial distribution of the deaths that occurred into the residential quarters of the Naples city and into the different country towns of the Campania Region is shown in *Figure 2*.

From data collected about circumstances surrounding the observed deaths (n. 267) it was established that only n. 64 persons (24%) were found died at own home, n. 21 (8%) at home of friends, n. 18 into hotel or other temporary addresses (7%). The deaths that occurred at the emergency room of hospitals were 10% respectively for overdose (n. 11) and for road accident (as driver or transported) (n. 15).

The maximum number of decedents (n. 136 cases) was found in a public place (51% into own car or on the road). Therefore, in our study the 76% of drug related deaths occurred in a place different from the usual residence. Particularly the distribution of deaths into different quarters of the Naples city (*Figure 2*) demonstrates that the Scampia quarter is a "zone of drug supply with elevated risk" because here the higher number of drug related deaths (n.

Table 1
Drug related deaths by male/female ratio and years. Italy and Campania Region, 2008-2012

Drug related deaths	2008 (M/F)	2009 (M/F)	2010 (M/F)	2011 (M/F)	2012 (M/F)
Italy*	462/55	440/44	332/42	316/48	343/47
Campania**	46/3	75/2	44/2	42/4	44/5

Source: *Annual Relation to the Parliament about drug use and addiction in Italy* (2012); ** *Cases analysed by the Laboratory of Forensic Toxicology, Second University of Naples, Campania Region, Italy.*

Table 2
Distribution of drug related death cases by age and gender during period 2008-2012

Males	2008 (n. 46/49)	2009 (n. 75/77)	2010 (n. 44/46)	2011 (n. 42/46)	2012 (n. 44/49)
< 25	2	4	3	2	4
25-29	7	11	14	5	5
30-34	6	18	7	9	10
35-39	14	15	13	10	11
> 40	17	27	7	16	14
Females	2008 (n. 3/49)	2009 (n. 2/77)	2010 (n. 2/46)	2011 (n. 4/46)	2012 (n. 5/49)
< 25	-	-	-	-	1
25-29	-	-	-	-	-
30-34	-	1	-	-	1
35-39	3	1	-	3	1
> 40	-	-	2	1	2

Source: *Laboratory of Forensic Toxicology, Second University of Naples, Campania Region, Italy.*

Table 3
Deaths involving poly-drug use in males (n. 139/267) in Campania Region, Italy, from 2008 to 2012

Substances	Number of deaths (M)
morphine/6AM + cocaine	52
morphine/6AM + cocaine + methadone	5
morphine/6AM + cocaine + BDZ	11
morphine/6AM + cocaine + BDZ + Et-OH	1
morphine/6AM + cocaine + BDZ + Δ^9THC	2
morphine/6AM + cocaine + Amf + Δ^9THC	1
morphine/6AM + cocaine + Δ^9THC	11
morphine/6AM + cocaine + methadone + BDZ	5
morphine/6AM + cocaine + methadone + BDZ + Δ^9THC	1
morphine/6AM + cocaine + methadone + Et-OH	8
morphine/6AM + cocaine + Δ^9THC + Et-OH	2
morphine/6AM + cocaine + Et-OH	8
morphine/6AM + Δ^9THC	4
morphine/6AM + Et-OH	2
morphine/6AM + Δ^9THC + methadone	3
morphine/6AM + Δ^9THC + Et-OH	1
morphine/6AM + BDZ, methorfan	4
morphine/6AM + BDZ + Et-OH	1
morphine/6AM + methadone	2
morphine/6AM + methadone + Δ^9THC	1
morphine/6AM + BDZ + Δ^9THC	1
cocaine + Δ^9THC	2
cocaine + BDZ, levamisole, lidocaine	4
cocaine + methadone	2
cocaine + methadone + Δ^9THC	1
cocaine + Δ^9THC + BDZ	1
cocaine +Et-OH + cocaetilene	2
cocaine + Et-OH + BDZ + cocaetilene	1

*Abbreviations: 6-acetylmorphine (6-AM), benzodiazepines (BDZ), ethyl alcohol (Et-OH), Δ^9tetrahydrocannabinolo (Δ^9THC and/or Δ^9THC-COOH)
Source: *Laboratory of Forensic Toxicology, Second University of Naples, Campania Region, Italy.*

Table 4
Substances involved as cause of death in females (n. 16/267) in Campania Region, Italy, in the years 2008-2012

Substances	Number of deaths (F)
Et-OH	3
morphine/6AM + cocaine, levamisole, lidocaine, methorfan	1
morphine/6AM + cocaine+ BDZ + Δ⁹THC	1
morphine/6AM + cocaine+ Et-OH, levamisole, lidocaine, cocaetilene	2
morphine/6AM	1
morphine/6AM + Et-OH	1
methadone	1
methadone +BDZ	2
cocaine	1
cocaine+ BDZ	2
cocaine+Et-OH, cocaetilene	1

*Abbreviations: 6-acetylmorphine (6-AM), benzodiazepines (BDZ), ethyl alcohol (Et-OH),   Δ⁹tetrahydrocannabinolo (Δ⁹THC and/or Δ⁹THC-COOH)
Source: *Laboratory of Forensic Toxicology, Second University of Naples, Campania Region, Italy.*

38) involving subjects not there resident (n. 33) or strangers (n. 5) was found.

CONCLUSION

Data emerging by our study on drug related deaths in Campania Region demonstrates that trends in overall mortality reflect considerably the diffusion of poly-drug use while overdose rates due to a single illicit drug were relatively minimized. Furthermore, cocaine was identified as the most detected substance in the poly-drug use and this can represent an indirect indicator of the spread of this drug in the general population in Campania even though the data on seizures indicate a greater prevalence of the cannabis [5, 6]. Interestingly it was observed in the last three years (2010-2012) the increase of deaths among females and the finding in biological samples of cutting substances (methorphan, levamisole and lidocaine), that potentially can increase the toxicity of the heroin and cocaine.

Consequently the criteria and the methodology for the collection of national data in this field should be reviewed with the constant association of the findings from the autopsy and toxicological analyses with circumstantial data. In particular, the need to specifically explore the changing patterns of poly-drug use among addicts prevails at present, because studying the prevalence of mortality subsequent to the consumption of a single illicit drug may be insufficient to guide preventive policies in public health [12-14].

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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