

Retrospective study of intoxication-related deaths in Republic of North Macedonia, 2010-2020

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Introduction

Use or abuse of both, licit and illicit drugs present a global public health issue (Auckloo and Davies, 2019). Combination of two or more substances at the same time can lead to serious life-threatening conditions, sometimes resulting with fatal intoxication (Akhgari et al., 2019). Whether a particular drug concentration or drug combination was responsible for the persons' death is a key question to be answered in *post-mortem* toxicology (Lahti and Vuori, 2003). Unintentional acute intoxication caused by an illicit drug is the most frequent cause of death among drug abusers, however, death may be the result of direct, indirect or long-term effects of exposure to a particular substance or group of substances (Madea and Mubhoff, 2004; Preti et al., 2002). The pattern of substances' use and abuse usually differs from country to country (Hadidi, 2004). The aim of this study was to get an overview of death cases in the Republic of North Macedonia in order to determine the pattern of fatal intoxications.

Materials and methods

Toxicological findings of autopsies performed at the Institute of Forensic Medicine, criminology and medical deontology, Medical Faculty, Ss. Cyril and Methodius University in Skopje in the period of 2010-2020, were used in the study. In this overview were included cases with intoxication as cause of death. Based on the results of toxicological analysis, the data were divided in two

categories: mono-intoxications and mixed-intoxications. Within the categories there are multiple subcategories. There are 6 divisions of mono-intoxication according to the used substance: ethyl alcohol; drugs of abuse; medicines; pesticides; corrosives and carbon monoxide. Mixed-intoxications were further grouped as: two or more medicines; medicines and ethyl alcohol (EA); two or more drugs of abuse (DOA); DOA and EA; DOA and medicines with or without EA; corrosives and medicines/EA; pesticides and medicines/EA; carbon monoxide and EA. Results presented in this study were obtained during routine toxicological analyses as a part of autopsy expertise. Toxicologically relevant substances as well as age and gender were used as variables. Statistical evaluation included descriptive statistic and Mann-Whitney-U test.

Results and discussion

In the 11-year overview of *post-mortem* data at the Institute of Forensic Medicine, criminology and medical deontology, Medical Faculty, Ss. Cyril and Methodius University in Skopje, was found that 217 death cases were due to intoxication, of which 43 (19.82%) caused by single substance, whilst 174 (80.18%) death cases were due to intoxication with more than one substance (mixed intoxication). The highest number of fatal intoxications, 29 cases, was noticed in 2018. Data analyses revealed that both genders were almost equally represented in the mono-intoxication cases (32 males and 34 females). However, male predominance was noticed in the mixed-

intoxication death cases, where only 19.54% of the cases were women. According to age, there was statistically significant difference between the groups (mono- and mix-intoxication) ($z = -3.97029$, $p = 0.00008$), observing that victims of mono-intoxication were older. There was no statistically significant difference in the age between genders in both groups.

Intoxication with ethyl alcohol (27.91%) was the most often cause of death in the group of mono-intoxications, followed by intoxication with corrosives, carbon monoxide, pesticides, and very few cases with medicines and drugs of abuse. Intoxication with carbon monoxide and corrosives was characteristic for victims with age above 55 years. Average age of the victims from ethyl alcohol intoxication was 47.92 years, while the victims of intoxication with pesticides, drugs of abuse and medications were younger.

In the mixed-intoxications the predominant group was DOA and medicine combination confirmed in 57.47% of death cases. Positive result for EA was found in 22% of the cases from the same group. Methadone and benzodiazepines were most often combination in this group (33%). Other groups were represented in the following order: pesticides and medicines/EA (12.64%); two or more medicines (8.05%); corrosives and medicines/EA (7.47%); DOA and EA (4.02%); two or more DOA and CO with EA (2.78%). Analyses of specific substances involved in mixed-intoxication shown that EA was present in 31.03% of the cases included in this group. Carbamates and organo-phosphorous substances were the most common in the pesticides related intoxications. Medicines-induced lethal intoxications were due to different combination mostly including benzodiazepines, antidepressants, verapamil and rarely beta blockers, with the highest number of cases noticed in 2020.

Conclusion

Within the long-term follow-up of the *post-mortem* toxicological analyses, it was observed that the number of mixed-intoxications is four times higher than intoxications caused by a single substance use. Mixed-intoxications are more frequent among younger's. Being the most often used, methadone and benzodiazepines are a dangerous, even lethal combination. Knowing this data, it is important to draw attention to the control and regulations of prescription medicines and substitution treatment.

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