

Deadly heroin or the death of heroin – overdoses caused by illicit drugs of abuse in Budapest, Hungary between 1994 and 2012

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Rates of illicit drug use and drug-related deaths have continuously increased in developed countries since the 1960s even though the patterns of use and thus the related mortality differ from region to region. In Europe heroin is the drug most often implicated in overdoses. The decedents are most often male, between 20 and 30 years of age and have a long history of drug use. According to the majority of available studies a concomitant use of alcohol and benzodiazepines is one of the risk factors of heroin overdose. In our study we have examined the basic demographic and toxicological features of illicit drug related death cases in Budapest, Hungary between 1994 and 2012. Drug overdose death cases have been divided into two subgroups according to the substances responsible for the death of the subjects: an opioid group and a non-opioid group. The huge majority (87.9%) of decedents died due to heroin overdose and were male (87%). There has been a significant increase in the mean age of the opioid group for the past 19 years ($p < 0.0001$, $r_2 = 0.6228$). The majority of heroin overdose cases (58%) has had no other psychopharmacocons present at the toxicological examination. We have found a slight but significant positive correlation ($p=0.0204$, $r=0.349$) between the number of heroin overdose death cases and the mean concentration of street level purity heroin. Most of the examined demographic and toxicological features of the population studied have been in concordance with data previously reported. However, in contrast to other studies we report a strikingly high proportion of “pure” heroin overdose cases where no other psychoactive substances were found. The reason for this is currently unknown; we can only speculate that it can be related to the fact that heroin is used and abused differently from other countries. The remarkable phenomenon of the “ageing” of heroin users may also support a change in the drug use habits of the youngest population. The emergence and spread of new designer drugs also change the mortality characteristics of the youngest abusers and pose a new challenge for researchers.

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Rates of illicit drug use and drug-related deaths have continuously increased in the developed world since the 1960s (Darke et al., 2007). The pattern of drug use and thus the pattern of drug-related deaths differ from country to country. According to the latest report on mortality related to drug use in Europe (EMCDDA, 2011), opioids and specifically heroin are the drugs most often implicated in overdoses and the number of reported death cases is stable or increasing in most of the reporting countries.

Heroin is a central nervous system depressant that relieves pain and induces sleep. Its use produces a dreamlike state of warmth and well-being. It may also cause a constriction of the pupils, nausea, and respiratory depression, which is in fact usually the direct cause of death in heroin overdoses. Its abuse is characterized by persistent craving for the drug, tolerance (the need for larger and larger doses to get the same result), and painful and dangerous withdrawal symptoms.

There are a number of risk factors related to heroin overdose deaths that have been highlighted in several studies from Europe (Prete et al., 2002; Morgan et al., 2006; Juel and Helweg-Larsen, 1999; Simonsen et al., 2011; Hickman et al., 2007), Australia (Hall et al., 2000) or the United States (Coffin et al., 2003; Davidson et al., 2003). For example, the majority of decedents are male and predominantly in their early to mid-thirties and have a long history of drug use. Most of the overdose deaths involve polydrug use; alcohol and benzodiazepines being frequently associated in drug-induced deaths. Interestingly, the impact of the purity of street level heroin has a yet unresolved effect on mortality due to heroin overdose. According to some authors it has no effect (Risser et al., 2007; Toprak and Cetin, 2009), while others have pointed out a decrease in heroin overdoses with decreasing purity of street level heroin (Degenhardt et al., 2005a; Degenhardt et al., 2005b).

The use of illegal substances became accelerated in Hungary after 1989 when the political changes generated the opening of the borders and an easier access to illegal drugs of abuse. Hungary was only a “transit” country at the beginning, but it soon became a “target” country, and a growing demand for drugs of abuse appeared. Hungary has been a country with no or little illicit drug-related mortality before the change of regime in 1989 as reported by the official statistics. According to the internal data system at the Department of Forensic and Insurance Medicine, which is responsible for the forensic autopsies of the Budapest region, the first illicit drug overdoses were noted in 1994.

In our study we have examined the types of illicit drugs of abuse that have caused overdoses during the past 19 years. Also, we have attempted to explore whether there is a similar interaction between heroin, benzodiazepines and alcohol, as described by other authors (Darke et al., 2000; Fugelstad et al., 2003). We have also investigated whether street level heroin purity has had any possible effect on the number of heroin overdose deaths and whether the demographic features of the population studied have shown the same characteristics as reported worldwide.

METHODS

Background

The Department of Forensic and Insurance Medicine is located in Budapest as a part of Semmelweis University. It is the primary forensic pathology centre in

Budapest and Pest country, conducting approximately 2600 autopsies a year. In Hungary the police order a forensic autopsy when a violent or unnatural death is suspected. All cases in this study have undergone a forensic autopsy with macroscopic and microscopic examination of all major organs and a quantitative toxicological examination. The blood alcohol levels have been determined at the Toxicological Laboratory of the Department of Forensic and Insurance Medicine and the detailed toxicological examinations of illegal and legal drugs of abuse and other substances have been performed at the National Institute of Forensic Toxicology (ISZKI-OTI). Cause of death has been determined by forensic pathologists on the basis of autopsy findings, toxicological analyses, circumstances of death and if necessary other medical documentation from hospitalization before death or dialog with the family of the deceased.

Selection of cases

In this retrospective study we have examined all drug-related death cases at the Department of Forensic and Insurance Medicine between 1994 and 2012. In this study we have only included acute drug overdose cases or cases where the death was attributable to the acute physical sequelae of such toxicity (e.g. crush syndrome, hypoxic brain damage), and excluded other cases of drug related deaths – suicides, accidents, homicides or natural death cases of known illicit drugs users or other causes of death when illicit drugs were found during the toxicological examination.

Case classification

We have grouped the drug overdose (OD) death cases according to the substances responsible for the death of the subjects, whether they belonged to the group of opioids (e.g. heroin, morphine, methadone, etc) or other types of illicit drugs (cocaine, amphetamine, MDMA etc). We have noted the concurrent presence of licit drugs (e.g. benzodiazepines, barbiturates, antidepressants) and the presence of blood ethanol. If more than two types of substances were found during the toxicological examination, we have grouped the cases into the opioid group even if only one opioid substance was present. Polytoxicomania has been defined as a presence of two or more psychoactive substances in bodily fluids and organs.

For the analysis of correlation between the street level purity of heroin and the number of heroin OD

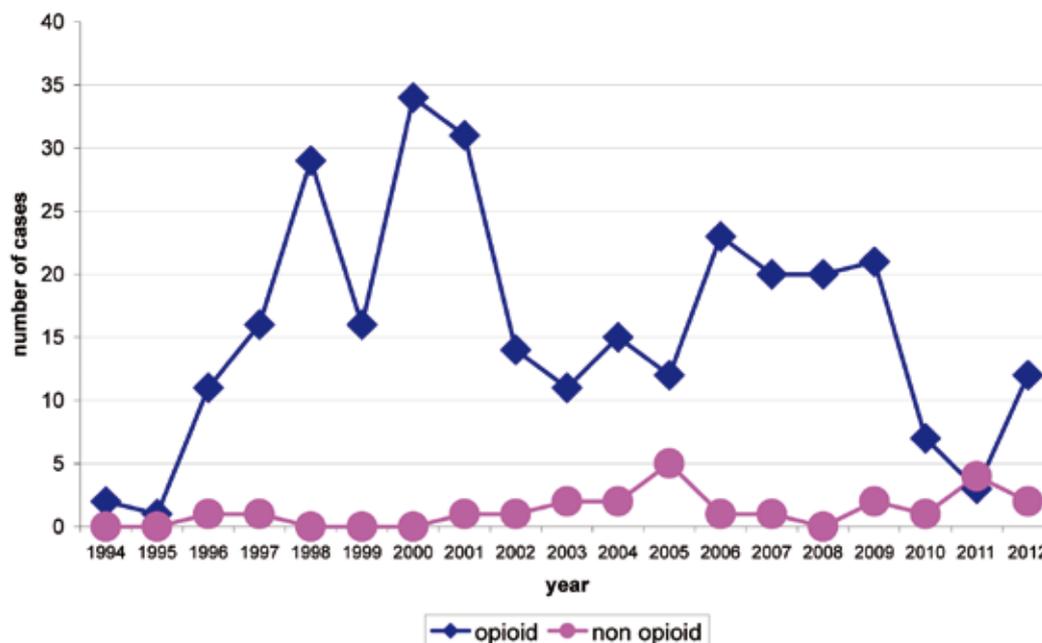


Figure 1 Yearly distribution of opioid (n=299) and non-opioid (n=24) drug overdose cases in Budapest, Hungary between 1994 and 2012

cases we have used data available online from the Drug and Arson Investigation Department at the Hungarian Institute for Forensic Sciences (Hungarian Institute for Forensic Sciences, 2012) as well as our database of all the heroin related OD death cases, irrespective of whether a detailed toxicological evaluation was available or not. As there is no available data, we have conducted our analysis with the exclusion of the years 1994, 1995, 1997 and 2011.

For the detailed analysis of the heroin OD cases we have excluded those without available blood ethanol levels (n=56). We have also excluded the cases (n=31) having no positive toxicology results due to, for instance, prolonged hospitalization prior to death or putrefaction. There was an overlap of 13 cases between the two aforementioned groups and a total of 74 cases have been excluded from the detailed analysis of heroin OD cases in regard to politoxicomania.

Statistical analysis

We have analysed the subgroups of drug overdose deaths, the subgroups of heroin OD and the gender and age divisions of drug overdose death cases in a yearly distribution with the help of GraphPad InStat version 3.10 for Windows.

RESULTS

At the Department of Forensic and Insurance Medicine, a forensic autopsy and detailed evaluation of 464 drug related death cases took place between 1994 and 2012, out of which 323 cases were acute overdoses and thus eligible for the study. 92.5% of all drug OD cases were related to opioids, while 7.5% of the cases were related to non-opioid ODs, which were attributed to amphetamine (n=13), cocaine (n=8) and MDMA (n=3). There was only one year (2011) when the number of non-opioid overdoses (three cases of amphetamine and one case of cocaine overdose) was higher than the number of opioid-related ODs. There were only two methadone ODs and one heroin OD in 2011. For the detailed distribution of the opioid and non-opioid groups during the aforementioned years see Fig. 1.

The opioid group consisted mostly of heroin OD cases (n=284), methadone OD cases (n=13) and other opioid caused OD cases (n=2). We have also examined the presence of politoxicomania. The majority of heroin OD cases (58%) had no other psychopharmacocons present at the toxicological examinations. 32% of the cases comprised of heroin OD deaths in the presence of either ethanol (26%), benzodiazepines

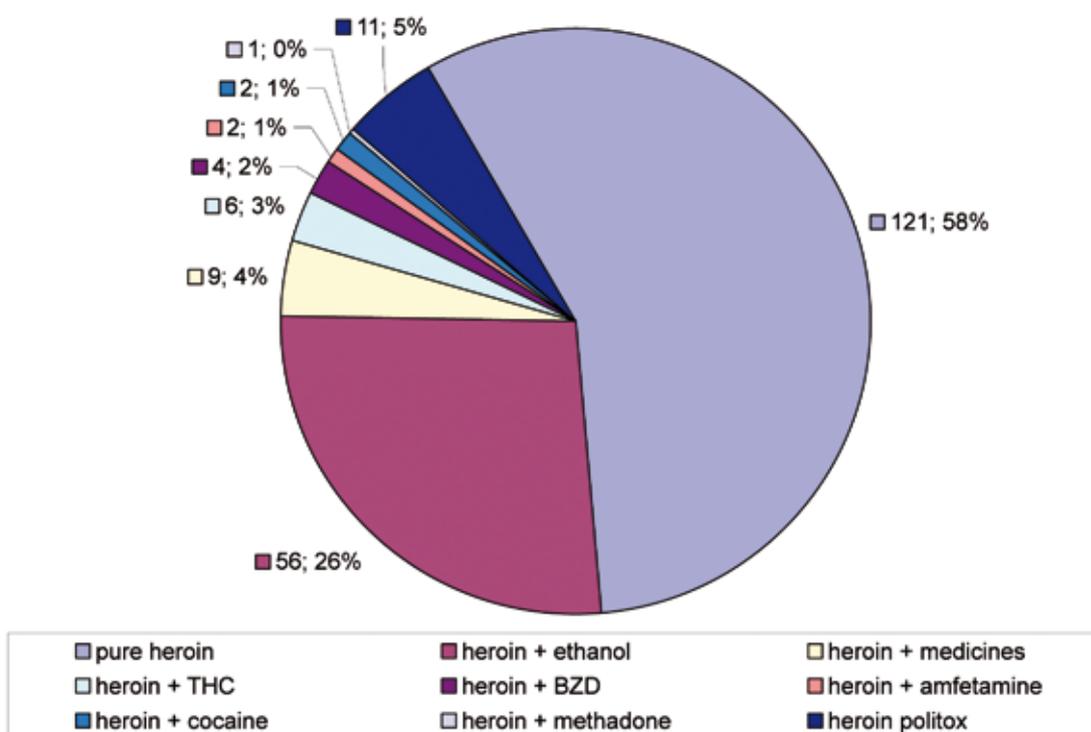


Figure 2 Distribution of heroin overdose deaths. The first number indicates the number of cases, the second the percentage of all heroin OD deaths. THC – tetrahydrocannabinol, BZD – benzodiazepine.

(1%) or other psychoactive substances, including barbiturates, glutethimide, meprobamate, tramadol and mirtazapine. For details see Fig. 2.

There was a slight but significant positive correlation ($p = 0.0204$, $r_2 = 0.349$) between the number of heroin overdose death cases and the mean concentration of street level purity heroin (Fig. 3).

There was a significant age difference between the opioid and the non-opioid group (27.15 versus 31.45 years, $p = 0.00243$). The age distribution of the opioid group is presented in Fig. 4. There has been a significant increase in mean age within the opioid group during the past 19 years ($p < 0.0001$, $r_2 = 0.6228$). The age distribution of the non-opioid group cannot be presented in a similar way due to the small number of cases in the group.

There was no significant difference between the male:female ratio between the opioid and non-opioid groups (Fishers exact test $p=1$) with a prevalence of male decedents (opioid group = 87%:13%, non-opioid group = 87.5%:12.5%).

DISCUSSION

The current study is the first one to describe the basic demographic and toxicological data related to fatalities caused by illicit drug overdoses in Budapest, Hungary between 1994 and 2012.

The gender division with the overwhelming predominance of males is characteristic of Europe and most of the previously published studies within the field. The age distribution shows a gradual increase with time, with the preponderance of cases between 20 and 30 years of age. This gradual increase is also a phenomenon described elsewhere in Europe, and is believed to be connected to an ageing population of opioid users in many EU Member States. The remarkable phenomenon of the “ageing” of heroin users may also support a change in the drug use habits of the youngest population. The emergence and spread of new designer drugs also change the mortality characteristics of the youngest abusers and pose a new challenge for researchers.

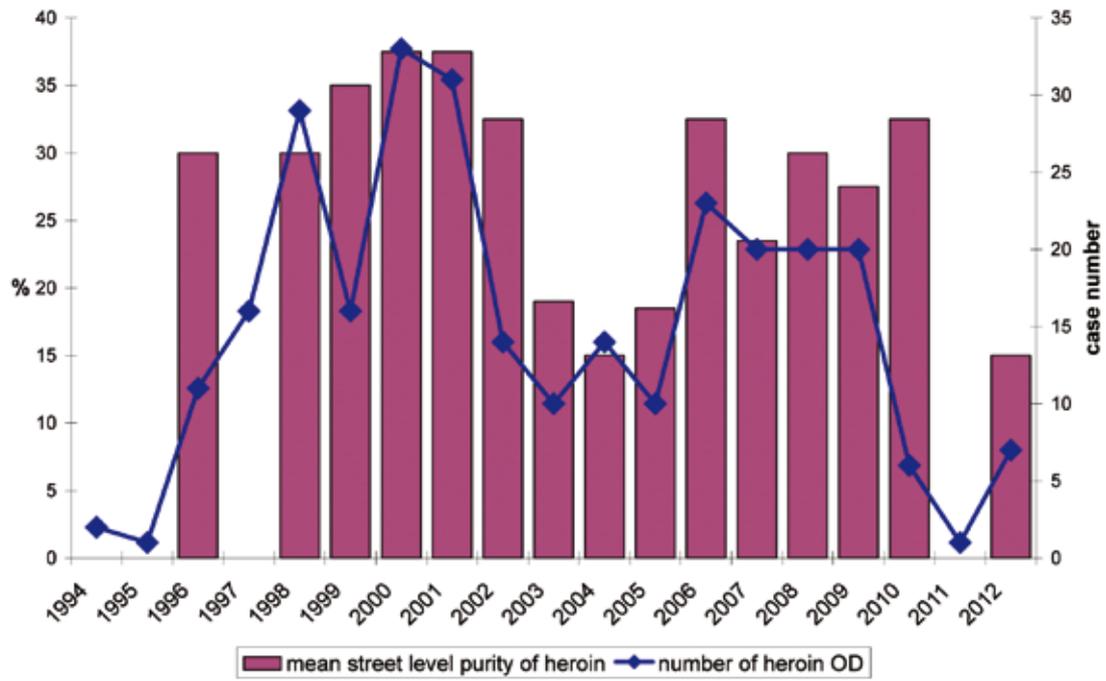


Figure 3 Correlation between the number of heroin related overdose death cases and the mean concentration of street level purity heroin. In years 1994, 1995, 1997 and 2011 no data available about the purity of street level heroin.

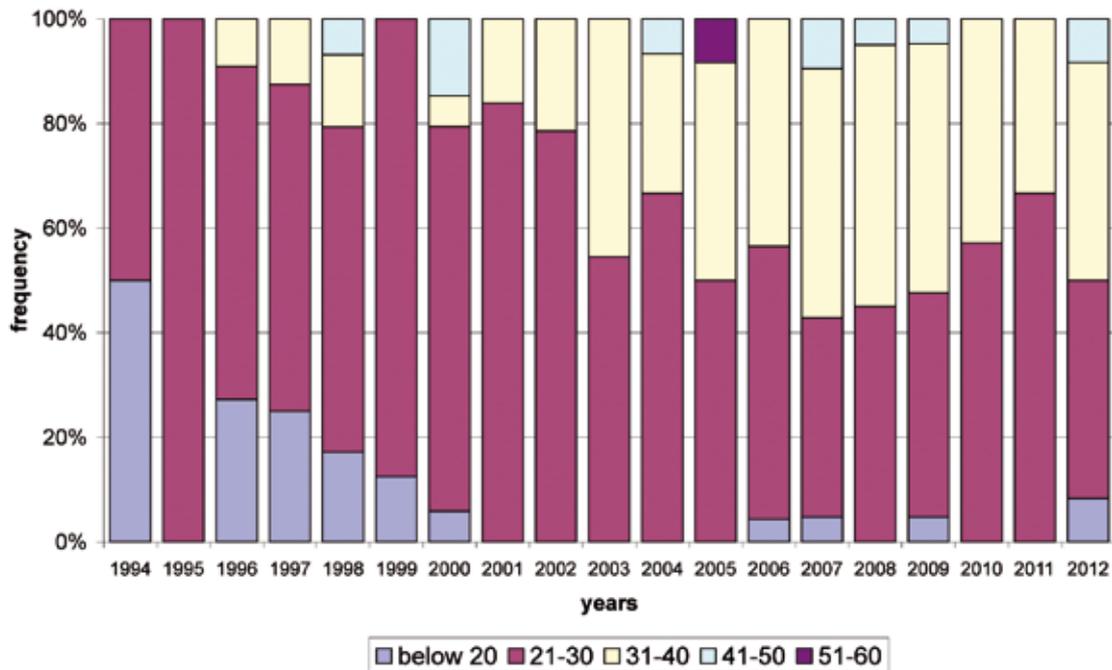


Figure 4 Yearly age distribution within the opioid group between 1994 and 2012

Interestingly there is a significant age difference between the opioid and non-opioid groups. It might be caused by the fact that heroin is relatively “cheaper” in comparison to cocaine, methamphetamine or amphetamine (EMCDDA, 2006). The latter drugs require a higher income, which is rarely associated with young people.

In concordance with the general European data, heroin is the most common illicit drug that causes overdoses in Budapest. In contrast to other studies, though, we report a strikingly high proportion of “pure” heroin overdose cases where no other psychoactive substances were found. In a review article by Warner-Smith and colleagues (Warner-Smith et al., 2001), who showed a comparison of different studies in regard to “pure” and “combined” heroin deaths, the percentage of “pure” heroin OD cases was between 13-40%. However, in our population almost 60% of all heroin related deaths occurred due to the effects of heroin without concomitant psychoactive substances being found at the toxicological examination. The reason for this is currently unknown; we can only speculate that it can be related to the fact that heroin is used and abused differently from country to country.

One can also speculate about the rapidly changing levels of opioid related deaths from one year to another, which is often very difficult to explain. Some of the decreases in heroin related deaths could be linked to sudden heroin shortages that were reported, for example, in 2001 when the cultivation of opium poppy in Afghanistan was reduced to almost zero (UNODC, 2006), or in 2011 when there was also a heroin shortage reported due to a disease of the opium poppy in Afghanistan (UNODC, 2012).

The highest numbers of heroin related deaths were reported in the years 2000-2001, when according to the Drug and Arson Investigation Department at the Hungarian Institute for Forensic Sciences the street level purity of heroin reached approximately 65% (Hungarian Institute for Forensic Sciences, 2012). Based on the previous reports, a high concentration of street level purity heroin could have had an effect on mortality rates of fatal overdoses (Darke et al., 2010). The slight but significant correlation between the amount of heroin overdose cases and the mean purity of impounded street heroin samples also strengthens the thesis that fluctuations in heroin purity can have an effect on heroin related mortality.

In summary, our data show that most of the demographic and toxicological characteristics of drug related death cases are similar to the ones previously reported worldwide. We report though an unusually

high (58%) frequency of “pure” heroin overdoses where no other psychoactive substances, including ethanol, drugs of abuses and medicines were found and where the deaths were most probably related to a single drug.

Abbreviations

BZD – benzodiazepine

MDMA – 3,4-methylenedioxy-N-methylamphetamin

OD – overdose

THC – tetrahydrocannabinol

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A halálos heroin vagy a heroin halála – budapesti kábítószer okozta túladagolások 1994 és 2012 között

A kábítószer használat és a kábítószer használattal összefüggésben kialakult halálozás folyamatosan növekedett az 1960-as évektől a fejlett országokban, ugyanakkor a kábítószer használati szokások és ennek következtében a droghalálozás régiónkénti különbségeket is mutat. Európában a legtöbb kábítószerrel kapcsolatos haláleset heroin használat miatt következik be, az elhunytak legtöbbször 20-30 év közötti férfiak, akik mögött hosszabb drogkarrier áll. A nemzetközi kutatások alapján az alkohol vagy benzodiazepin együttes használata a heroinnal növeli a halálos heroin túladagolás veszélyét. Tanulmányunkban vizsgáltuk a Budapesten 1994 és 2012 között elhalálozott kábítószerrel kapcsolatos halálesetek alapvető demográfiai és toxikológiai tulajdonságait. A kábítószer túladagolások eseteket a hatóanyagok alapján csoportosítottuk, vagyis, hogy mely hatóanyag játszott szerepet a halál beálltában. A hatóanyag tartalom alapján két csoport alakult ki, egy opioid és egy nem opioid csoport. A halálesetek túlnyomó többségét (87.9%) heroin túladagolás okozta, legfőképpen férfiak között (87%). Az opioid csoportban az elhalálozottak kora szignifikáns növekedést mutatott az elmúlt 19 évben ($P < 0.0001$, $r_2 = 0.6228$). A heroin túladagolások többségében (58%) nem volt egyéb pszichofarmakon a vegyvizsgálat során. A heroin okozta túladagolások száma és az adott évben lefoglalt heroin átlagos hatóanyag tartalma között pozitív korrelációt találtunk ($p=0.0204$, $r_2 = 0.349$). A kábítószer túladagolásban elhaltak legtöbb általunk vizsgált tulajdonsága megfelelt a korábban publikált eredményeknek, azonban a saját vizsgálati anyagunkban, ellentétben a nemzetközi trenddel, megnövekedett számú „tisza” heroin túladagolás volt a jellemző, ahol vegyvizsgálattal nem lehetett egyéb pszichofarmakonokat kimutatni. Ennek oka nem ismeretes, valószínűsíthető, hogy összefüggésben van az eltérő kábítószer használati szokásokkal. Figyelemre méltó jelenség a heroin használók „korosodása”, mely alátámasztja a kábítószerhasználó fiatalok szokásainak megváltozását. A heroin helyett az designer drogok megjelenése, s kezdődő lassú térhódítása a fiatalok korai halálozásában újabb kihívás elé állítja a kutatókat.

Kulcsszavak: heroin, túladagolás, kábítószerrel kapcsolatos halálozás, alkohol