Excess suicide mortality in Heroin Use Disorder patients seeking Opioid Agonist Treatment in Slovenia and risk factors for suicide

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Summary

Background: Heroin Use Disorder (HUD) patients are more endangered by suicide than the general population. Excess suicide mortality and the risk factor for suicide in HUD patients seeking Opioid Agonist Treatment (OAT) in Slovenia were both assessed. **Methods:** Record-linkage study of a well-defined cohort of 3,949 HUD patients seeking OAT in Slovenia in the period from 1st January 2004 to 31st December 2006, and General Mortality Register for ascertained vital status in cohort till 31st December 2011. **Results:** In the 2004-2011 period there were 31 suicides among 3,949 HUD patients seeking OAT. Standardized mortality ratio (SMR) for suicide in HUD patients was 4 (95% CI: 2.8-5.6) times higher than that of the general Slovenian population of the same age over the same period of time. SMR for male HUD patients was 3.7 (95% CI 2.6-5.4) times higher than that of Slovenian males of same age and 2.2 times higher than that of females. SMR for female HUD patients was 7 (95% CI: 2.6-18.7) times higher than that of Slovenian females of the same age. Higher age at cohort treatment entry is an important risk factor for suicide; hazard risk for suicide was significantly higher in patients entering the cohort when older (HR=1.08, 95% CI: 1.02-1.13, p=0.003), whereas those at their first OAT episode seem to be protected from suicide (HR=0.139, 95% CI: 0.019-1.036, p=0.054), while male gender, unemployment and a living alone status do not constitute a statistically significant risk factor for suicide in HUD patients seeking OAT. **Conclusions:** Specific suicide prevention interventions tailored to the needs of HUD patients are required.

Key Words: Heroin Use Disorder patients; Opioid Agonist Treatment; agonist treatment; suicide

1. Introduction

Suicide is an avoidable form of mortality and it results in a completely preventable death, but it remains in the top ten items listed for the leading causes of death in Europe [3, 26-28]. In the last 30 years suicide rates have fallen worldwide, but in the EU, turning our special attention to Slovenia, that country still has one of the highest suicide rates in the whole of the Union [26, 28].

Suicide per se is not a mental disorder, but it is related to mental health issues [26]. Over 90% of suicide victims have at least one psychiatric disorder at the moment of suicide [3, 4, 29]. According to Ber-

tolote et al. [4], a review of studies reporting diagnoses of mental disorders in suicide victims, revealed that the two most prevalent groups were mood disorders (30.2%), followed by substance abuse disorders (18%); in the most recent reports, belonging to one of these two groups Heroin Use Disorder (HUD) patients proven to be one of the strongest predictors of suicide in developed countries [7, 9, 21, 22, 27, 29].

According to Darke and Ross [7, 9] heroin users face the same major general population risk factors for suicide (gender, psychopathology, family dysfunction and social isolation), but show a higher prevalence; in addition, they face all the risk factors related to drug use [8]. Suicide is one of the principal

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causes of death among opioid users [7].

The aim of the present study has been to calculate the mortality rate for suicide in heroin addicts (HUD patients) seeking Opioid Agonist Treatment (OAT) in Slovenia, and compare that rate with members of the general population of the same age and gender at that time, while verifying the hazard risk for suicide in HUD patients who are entering OAT.

2.   Methods

The previous well-defined, first and largest national cohort study on heroin addicts seeking outpatient treatment [24] was upgraded; 3, 949 heroin addicts seeking OAT in Slovenia in the period lasting from 1st January 2004 to 31st December 2006 were followed up for their vital status till 31st December 2011. The data on mortality were obtained from the General Mortality Register (GMR). The causes of death were encoded according to the WHO International Classification of Diseases and Related Health Conditions, tenth revision (ICD-10) [36]. The codes used to identify suicide mortality included ICD-10 X60.0- X84.9 [36]. The vital status (survived, deceased) of all cohort members was ascertained through linkage of our cohort with GMR. Linkage with the GMR was updated once a year throughout the 2004-2011 period.

2.1. Statistical analysis

Datasets used for statistical analyses were made fully anonymous. Person Years (PYs) were calculated for every subject in the cohort. PYs are a summation of all cohort members' follow-up periods, from the moment of entry into the cohort until the end of the observation period for survivors and continuing to the date of death for the deceased [14, 32].

The Crude Mortality Rate (CMR) expresses the rate of deaths occurring in the cohort; in this study the calculated CMR is a measure of the number of deaths divided by PYs for the observed follow-up and then multiplied by 1000 to derive the CMR expressed as the number of deaths per 1000 PYs [14, 32].

A Standardized Mortality Ratio (SMR) compares the observed number of deaths in the cohort with the expected number of deaths for a sample of the same age and gender drawn from the general population at that time. An SMR greater than 1 indicates excess mortality in the sample compared with the general population [14, 30, 32].

By working with gender and age groups, observed deaths from suicide were compared with expected suicide mortality rates to derive SMRs. The SMRs were calculated using the age groups 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54 and 55-59 years. The expected numbers of suicides were calculated by multiplying sex- and age-specific general population suicide mortality rates by the PYs of follow-ups seen in the analysis cohort, matched by gender and age [14]. In order to generate stratified mortality rates (mortality rates for each age in the 5-year age categories ranging from 15 to 59 years and for gender categories), both the observed number of suicide deaths and observed PYs were recalculated separately for each category (stratified observation-time, number of deaths and mortality rates observed) [14].

Mortality rates were calculated within the nine five-year age groups included in the 15 to 59 year range. Rates and ratios were reported with 95% confidence intervals (95% CI) [14]. Mortality rates and ratios were calculated for suicide mortality.

The multivariate analysis related to time (suicide timing) was performed using Cox regression.

3.   Results

For 3,949 cohort members (CMs) the observed period from 1st January 2004 to 31st December 2011 was 27,659.9 PYs. For study purposes, 3,944 CMs aged between 15 and 59 years were selected; of those 3,944 members, 382 (9.7%) were followed up for 8 years, while the remaining 3,562 were followed up for an average of 6.9±1.27 years (median 7.26 years, mode 6.47 years).

Males (N=3,000) were 3.1 times better represented in the cohort than females (N=944), CMs were mostly aged between 30 and 34 years: one third of males (N=1,052) and one third of females (N=335) had an age in the 30 to 34 year range, followed by those in the 25 to 29 year range.

Among the deceased, males were 5.4 times better represented than females (N=26). 40.4% (N=67) of CMs died at an age between 25 and 34 years. 18.7% of the deceased committed suicide (N=31); of these, 38.7% (N=17) were aged between 25 and 34 years. Among suicide victims, 27 out of 31 were males. 77.4% (N=24) of suicides were registered in the first half of the observation period; female suicides did not exceed 1 case per year, and 67.7 % of all suicide victims died when less than 35 years old. Suicide victims died at a mean age of 32.3±7.3 years.

Suicide CMR/1000 PYs for CMs (15-59 years)

Table 1. Observed and expected numbers of suicides in cohort, person time spent at risk, suicide mortality rates, stratified by age (15-59 years) and diversified by gender, Slovenia, 2004-2011

	Observed suicides (N)	Person years (PYs)	Crude mortality rate (95% CI) per 1000 PYs	Expected suicides (N)	Standardized mortality ratio (95% CI)
Males	27	20,912.3	1.3 (0.9-1.9)	7.24	3.7 (2.6-5.4)
Females	4	6,705.9	0.6 (0.2-1.6)	0.57	7.0 (2.6-18.7)
Total	31	27,618.15	1.1 (0.8-1.6)	7.81	4.0 (2.8-5.6)

was more than one suicide per 1000 CMs per year, i.e. a suicide rate 4 times higher than that of the general Slovenian population of the same age. SMR for males was 3.7 times higher than that of the Slovenian population of the same age and 2.2 times that of females. SMR for females was 7 times higher than that of the Slovenian population of the same age (Table 1).

Cox model selected 3,814 cases of CMs in all, of which 436 cases had missing values. Table 2 shows hazard risk of suicide in CMs. Risk of suicide was significantly higher in patients entering the cohort at a higher age. Estimated hazard or risk of suicide increased by exp (0.07), by 1.08 times if a patient was a year older. HUD patients who were at their first OAT episode seemed to be protected from suicide (HR=0.139, 95% CI: 0.019-1.036, p=0.054), while male gender, unemployment and living alone status did not imply a statistically significant risk factor for suicide in HUD patients seeking OAT.

4. Discussion

In this study on CMs (all of them HUD patients seeking outpatient OAT), after adjusting for age and gender, suicide SMR mortality was 4 (95% CI 2.8-5.6) times higher than that of the general population. Findings in this study were similar to those of Pierce et al. [32], who reported SMR for suicides of 4.3 (95% CI 3.9 to 4.8). However, the review by Harris and Barraclough [21] reported suicide risk in opioid users up to 14 times the expected value, while meta-analysis revealed variations in studies ranging between 3 and 36 times; possible explanations include uncertainties over suicide ascertainment and HIV (high mortality attributable to HIV in some countries) [21]. One reason why suicide could be under-reported is that self-inflicted deaths by exposure to drugs are difficult to classify, so that accidental or undetermined deaths may be recorded instead of suicide [21].

Wilcox et al. [35], in their review of cohort studies on substance use disorders and suicide, confirmed their estimate of the strong association between suicide and opioid use disorders. According to Pan et al. [30], SMR for suicide mortality among HUD patients admitted to a psychiatric centre was 16.2, while suicide mortality in previous studies ranged from 6.3 to 18.4 times those in general population [6, 18, 21, 23, 30, 35]. Despite the fact that suicide rates vary across countries, all studies have reported higher suicide SMRs for heroin users than in the general population [7, 9, 18, 21, 23, 25, 30, 32, 35]. According to Fugelstad [16], however, death rates are influenced by how selection of the population sample is performed, with cohorts including inpatient drug users showing higher mortality than those including subjects in outpatient treatment; as to the duration of the follow-up, in cases with longer follow-up periods, the average age of CMs increases and the cause of death changes according to the time that HUD patients elapsed.

In interpreting these results, it should be borne in mind that the Slovenian general population has a very high suicide mortality rate, with Slovenia regularly ranked among the top EU countries in terms of the highest suicide mortality rates to be found among the general population [26, 28] – a finding that has an impact on data for SMRs in the CMs [12].

Table 2. Hazard risk of suicide in 3,378 CMs (26 suicides)

Variables	B	Exp(B)	95 % CI Exp(B)	P
Male Gender	0.82	2.28	0.68 – 7.63	0.181
Age at cohort treatment entry	0.07	1.08	1.02 – 1.13	0.003
First seeking AOT	-1, 97	0.13	0.01 – 1.03	0.054
Living alone	-1.74	0.17	0.02 – 1.31	0.091
Employed	-0.40	0.66	0.28 – 1.60	0.367
Chi-square = 22.28, df = 5, p <0.001				

In this study on suicide, CMR turned out to be 1.1/1000 PYs. For opioid users in AOT, authors reported suicide CMRs ranging from 0 to 6.1/1000 PYs [7]. Males in our cohort had a CMR that was two times higher, whereas females had a higher SMR. Several authors similarly reported a higher CMR for males than for females [2, 5, 33], and a majority of these studies report that females have higher SMRs than males [1, 15, 31, 33]. A systematic review and meta-analysis of cohort studies on the mortality of opioid users by Degenhardt et al. reported higher CMRs and lower SMRs for males than females [11]; the gender differences in SMRs reflect those to be found in the mortality of the general population [19, 34].

Suicide victims in our case were young, in their middle thirties; young heroin users run a high risk of suicide [7, 9, 10, 17]. A majority of suicide deaths in opioid users occur earlier in life; in fact, in the cohort studied by us the highest number of suicides occurred at an early age (12 cases in the 25-29 year age group, followed by 5 cases in the 30-34 year age group). According to Darke et al. [7] a lower age is a risk factor for suicide in opioid users, as suicide victims usually die in their twenties. Suicide is prevalent among younger people (teenagers and those in their twenties), when rates of illicit drug use are highest, too; another demographic peak in suicide is to be found in the elderly [7]. In a WHO study, Degenhardt et al. [13] reported that two-thirds of all suicides among illicit drug users occur in those aged between 15 to 34 years. Similarly, in the present cohort one half of all suicides occurred in those aged between 25 to 34 years, one third in those aged over 35 years and one fifth at an age under 24 years. It can be stated that those whose deaths are due to suicide are usually young [7, 9, 13], although, at the top end of the range, being elderly at cohort entry proved to be an important risk factor for suicide in this study. The fact of being at a patient's first OAT episode seemed to provide protection from suicide, while male gender, unemployment and a status of living alone did not function as a statistically significant risk factor for suicide in HUD patients seeking OAT. Longer heroin use careers are related to the risk of suicide [9]; a majority of suicide victims in this study had a previous treatment history. The natural story of heroin addiction is often accompanied by cycling or dropping out from treatment or wandering from one treatment to the next over time [20]. As in the general population, heroin users who committed suicide were predominantly males [7, 9, 21, 30, 35], but male gender did not turn out to be a significant risk factor.

4.1. Limitations and strengths

The main limitation of this study was the relatively short period of follow-up of CMs, one result being the small absolute number of suicide victims. A study involving a longer period of observation and a higher number of suicide victims would, in all probability, have given results of greater significance.

The records used could be under-reported for a variety of reasons (e.g. incomplete data, lack of resources, staff facing a work overload, administrative limitations), but this shortcoming was limited by their strengths: national coverage, continuity (databases with several decades of tradition) and a mandatory formal foundation (legally binding in these cases), international standards and comparability (due to use of ICD-10 codes). Cohort studies involving HUD patients seeking treatment allow the identification of all suicides, registered in GMR (all cases of suicide due to poisoning but also suicides due to causes of death other than poisoning), with the benefit of gaining greater insight into suicide phenomena in a population running unusually high risks.

Despite all the limitations presented here, these results provide an estimate of the national epidemiological evidence on suicide among HUD patients seeking AOT. Our cohort study reveals that the suicide issue among HUD patients seeking AOT was previously underestimated or hidden, because only the routine system applied to general mortality had been used before, whereas this study offered the opportunity to find out, not only the factual situation behind drug-induced suicides or else suicides due to overdoses, but also suicides that were due to causes other than poisoning.

5. Conclusions

The general population in Slovenia is traditionally inclined to committing suicide. HUD patients are more endangered by the risk of suicide than their peers from the general population; the excess mortality from suicide recorded for HUD patients was, in fact, 4 times greater than that calculated for the general Slovenian population of the same age. A higher age and unsuccessful previous treatment both influence the risk of suicide. Improvement in the early detection, prevention and treatment of suicidality in HUD patients seeking OAT is required. Further studies are now needed to acquire a better understanding of the phenomenon. Special emphasis is required for HUD patients currently out of treatment, as there is

evidence that mortality rates may be higher among this group [12].

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