

A comparison of the drugs taken in fatal and nonfatal self-poisoning

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The objective of this study was a) to compare patterns of drug use in fatal and nonfatal overdoses and b) to find out if toxic drugs are overrepresented in overdoses with fatal outcome. A total of 179 cases of fatal overdoses in Switzerland (population 6.6 million) were compared with 269 medically treated self-poisoners from the agglomeration of Berne (population 301,630). Because of frequent multiple drug use, all the different compounds taken singly or in combination with other drugs were recorded and grouped according to drug types. The patterns of the frequencies of drugs used were remarkably similar in both groups. The majority of the drugs were psychotropics (81% in fatal and 68% in nonfatal overdose). Twenty-nine completed suicides were the result of drug combinations specifically recommended by EXIT. In the remaining cases benzodiazepines were used most frequently in both attempted and completed suicide, often in combination with other drugs or alcohol. Barbiturates were the only drugs recorded significantly more often in fatal overdoses (9% vs 3%). No significant difference was found for tricyclic antidepressants (13% vs 10%), or other types of drugs. The results are consistent with our assumption that drugs with higher toxicity would be overrepresented in overdoses with fatal outcome. Barbiturates, which are well known to be dangerous in overdose, were clearly associated with fatal overdoses, but not tricyclic antidepressants. This, in our view, suggests that the risk of prescribing tricyclic antidepressants should not be overestimated. The frequent use of benzodiazepines in completed suicide, however, indicates that there are no truly safe drugs in overdose.

K. Michel¹, V. Waeber¹, L. Valach¹,
G. Arestegui², T. Spuhler²

¹ Psychiatrische Universitätspoliklinik, ² Swiss Federal Statistical Office, Population and Employment, Berne, Switzerland

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K. Michel, Psychiatrische Universitätspoliklinik, Murtenstrasse 21, CH-3010 Berne, Switzerland

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Overdosing is a widespread form of deliberate self-harm. Most people take overdoses on an impulse and know little about the toxicity of the drugs they take (1). We know that the availability of methods for self-harm can influence suicidal behaviour and even suicide rates (2, 3). Thus, restricted prescribing of barbiturates since the late 1960s (4, 5) resulted in an impressive drop in the number of deaths due to overdoses with this type of drug.

In recent years several authors have drawn attention to the high fatality rates of tricyclic antidepressants taken in overdose (6–8). However, there is uncertainty as to what implications these findings should have on clinical practice. It has been argued that most tricyclic substances represent an unacceptable risk for depressed patients and that their use should be restricted (9, 10). On the other hand, it appears that the problem of suicides due to non-

prescribing of antidepressants is incomparably bigger than that of suicides due to deliberate self-poisoning with these drugs. Recently, Serfaty & Masterton (11) drew attention to the so far neglected problem of the toxicity of benzodiazepines in overdoses, especially flurazepam and temazepam.

Our assumption was that, if the toxicity of a drug was a major factor for outcome in overdose – whether patients were unaware of the toxicity of a drug or deliberately chose a drug because of its toxicity – substances with high toxicity (i.e., barbiturates and tricyclic antidepressants) would be overrepresented in fatal overdoses as compared with nonfatal overdoses. Because drugs are often taken in combination, it seemed important to us to take this into consideration when investigating the potential risk of the drugs taken. The only way this could be accounted for was to record all the drugs named to

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have been taken alone or in combination and to compare the frequencies of the various drug types. We therefore collected detailed information on the drugs used in suicides due to self-poisoning in Switzerland in 1990 and on the drugs taken in medically treated nonfatal overdoses in the agglomeration of Berne.

Material and methods

Completed suicides in Switzerland (population 6.6 million) are recorded by the Federal Statistical Office based on the death certificates issued by physicians or medicolegal institutions (ICD-8 codes 950–959). During 1990 a special effort was made to record all the substances known to have been involved in drug intoxication. The trade names of the drugs, other methods involved and special circumstances of the suicides were recorded. The results of toxicological analysis were included where performed (4.5% of all fatal overdoses). In nearly half of the cases the physicians were recontacted to complete missing information.

Suicide attempts of people living within the agglomeration of Berne (population 301,630) occurring within a 12-month period (March 1989–February 1990) and leading to contact with a medical or psychiatric institution (including all inpatient and outpatient services) were recorded with a questionnaire filled in by the responsible physician. The definition used was broad and included nonserious parasuicidal acts (for definition see (12)). Medical records of all in- and outpatient institutions were checked for missing cases or missing information. The vast majority were reported from general hospitals. A sample of general practitioners (22%) reported cases of deliberate self-harm, which represented 3% of all suicide attempts. The monitoring of parasuicide was part of the WHO/EURO multicentre study on parasuicide (13), but the collection of detailed information on all the drugs involved was performed locally on our own initiative.

Comparability of the two populations

Because completed suicide in Berne is too infrequent for comparison (81 cases in 1990), we decided to use all cases of fatal overdoses in Switzerland. This is possible because the population of Berne (4.6% of the population of Switzerland) is largely representative of the whole of Switzerland. The city and agglomeration of Berne include an urban as well as a rural population and there is no difference in the distribution into different economic sectors (agriculture, industry, services) or in the levels of education to the rest of the country. Sex and age distribution are similar, but average income and the proportion

of foreigners are slightly higher in Berne. The suicide rate in the agglomeration of Berne was 26.8/100,000 in 1990, and the rate in Switzerland was 22.2/100,000; the rate of medically treated suicide attempts in Berne was 130.9/100,000 (all age groups). The rate of attempted suicide for the whole country is not known, as Berne is the only area where suicide attempts have systematically been recorded. It should be noted that the suicide attempters all had a permanent or temporary address within the geographically defined catchment area at the time of the event. Persons treated in a medical institution within the catchment area but living outside were excluded.

Statistical methods

Chi-square tests were used for comparisons. The level of significance was set at 0.05 and for multiple comparisons was adjusted according to Bonferroni (Table 1).

Results

Completed suicide

In 1990, 1467 suicides were registered in Switzerland, 1032 men and 435 women. Drug overdoses had been taken by 179 people (12%), the mean age was 53 years, 51% were female.

Attempted suicide

In 1990, 395 suicide attempts performed by 146 men and 228 women (7% being repeated attempts by the same persons) were recorded in the agglomeration of Berne. Drug overdoses had been taken in 269

Table 1. Drugs reported to have been taken in overdoses with fatal and nonfatal outcome, single or in combination with other drugs. Drugs used in EXIT suicides and all unknown drugs excluded.

	Completed suicide (n=144)	Attempted suicide (n=269)	χ^2 *	P**
Benzodiazepines	109 (44%)	172 (46%)	0.69	NS
All antidepressants	39 (16%)	47 (11%)	2.70	0.10
Tricyclics	33 (13%)	41 (10%)	1.82	NS
Neuroleptics	19 (8%)	32 (7%)	0.00	NS
Barbiturates	23 (9%)	12 (3%)	12.01	0.001
Opiates	11 (4%)	27 (6%)	0.73	NS
Nonopiate analgesics	11 (4%)	41 (10%)	5.21	0.02
Other	37 (15%)	97 (23%)	5.56	0.02
	249 (100%)	428 (100%)		

* Yates corrected. ** For comparisons a level of significance of 0.006 is assumed according to the Bonferroni correction for multiple comparisons.

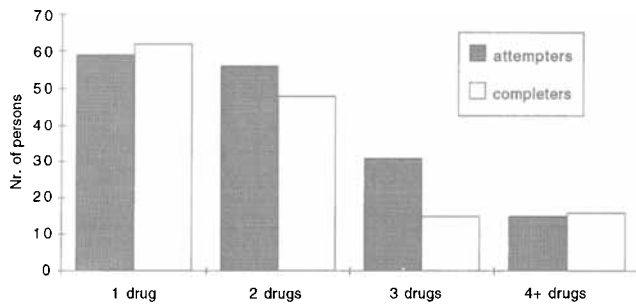


Fig. 1. Numbers of drugs taken in fatal and nonfatal overdoses. In completed suicide only identified drugs were considered.

attempts (68%), the mean age of the people was 36 years; 65% were female.

Combinations of drugs

In fatal overdose 44% and in nonfatal overdose 41% of the people took a combination of several drugs, some of them up to 5 different compounds (Fig. 1). The two groups did not differ in the numbers of drugs used. Alcohol in combination with drugs was reported in 29 (20%) of fatal and in 66 (24%) of nonfatal overdoses.

EXIT suicides

In analysing the 179 death certificates, 29 deaths were identified as EXIT suicides either by the physician's note on the death certificate (23 cases) or because of the typical drug combinations recommended by EXIT (6 cases). EXIT is an organization advocating the right to a humane death for seriously ill persons. The drug combinations recommended by EXIT are orphenadrine, an anticholinergic drug, and Vesparax®, containing hydroxyzine and two barbiturates (27 cases) or dibenzepine, a tricyclic antidepressant (2 cases). None of the suicide attempters had used such drug combinations. These drugs are not normally prescribed in this combination, and Vesparax® had even been taken off the market before the onset of the monitoring period.

Because EXIT suicides had obviously been carefully planned and carried out according to written instructions, they were considered a special group and not included in the comparison with nonfatal overdoses. Six further fatal overdoses in which neither the name nor the type of drugs was known were excluded, leaving a total of 144 fatal overdoses for comparison with the 269 nonfatal overdoses.

Types of drugs

All the drugs known to have been taken alone or in combination added up to 249 drug events for fatal

overdoses and 428 drug events for nonfatal overdoses, respectively (Table 1). Psychotropic drugs clearly were the largest group and represented 81% of all drugs in fatal overdose and 68% taken in nonfatal overdose. Benzodiazepines were recorded most often, followed by antidepressants, both with no significant difference between the two groups. Tricyclic antidepressants represented 13% and 10% respectively ($P = 0.17$). Mianserin was the only non-tricyclic compound named on death certificates. Barbiturates were used in 23 non-EXIT suicides, and the difference in frequencies between nonfatal and fatal overdoses was statistically significant (9% vs 3%; $P < 0.001$). A level of significance of 0.006 was assumed according to the Bonferroni correction for multiple comparisons (Table 1). Opiates were methadone or heroin. Nonopiate analgesics were taken rarely but more often in nonfatal overdose (4.4% vs 9.6%; $P = 0.03$). Other drugs were used in small numbers only, among them antiparkinsonian, antihistaminic and beta-blocking drugs, insulin and digoxin.

Drugs taken most frequently

Table 2 lists the drugs taken most frequently. The rank order of these drugs is very similar in nonfatal and fatal overdose. To our surprise, benzodiazepines were found as single drugs on 27 death certificates,

Table 2. Frequency order of the main substances recorded in completed and attempted suicide. Numbers of drugs are given separate for all cases and for those cases in which one drug only was recorded. The numbers are numbers of drug observations in which the trade name of the drug was known and therefore lower than in Table 1.

drug name	Completed suicide (n=118)		drug name	Attempted suicide (n=207)	
	all cases	one drug only		all cases	one drug only
Benzodiazepines					
Flunitrazepam	28	16	Flunitrazepam	28	13
Diazepam	15	1	Bromazepam	22	9
Triazolam	11	2	Diazepam	18	8
Bromazepam	8	1	Oxazepam	17	12
Midazolam	6	4			
Antidepressants					
Maprotiline	12	6	Maprotiline	11	3
Mianserin	6	1	Mianserin	6	4
Trimipramine	4	0	Trimipramine	6	4
Amitriptyline	3	1	Amitriptyline	6	0
Clomipramine	3	0	Clomipramine	3	0
Neuroleptic drugs					
Levomepromazine	4	0	Thioridazine	13	3
Chlorprothixen	3	0	Clotiapine	2	0
Barbiturates					
Phenobarbital	8	6	Phenobarbital	3	1

mainly flunitrazepam (16 suicides). Tricyclic antidepressants were involved in 29 (20%) of fatal non-EXIT overdoses (this figure is lower than in Table 1 because some people took more than one antidepressant) and appeared as single drugs on 12 death certificates, with maprotiline in first place. Mianserin, the only non-tricyclic antidepressant recorded, was taken by 6 suicide completers, usually in combination with other drugs. Two single-drug suicides were recorded with neuroleptic drugs.

Discussion

This study was carried out to compare patterns of drug use in fatal and nonfatal overdoses. Cases of fatal overdose were collected from the suicide statistics of Switzerland, and nonfatal overdoses consisted of all suicide attempts committed by people with a current address in the geographically defined agglomeration of Berne and coming to medical attention. The population of Berne and surroundings can be considered representative of Switzerland in general, as there is little difference in the important sociodemographic variables. Of course, many cases of attempted suicide not coming to medical attention cannot be recorded with this method. However, the definition used (12) was so broad as to include all nonserious cases of deliberate self-harm seen in medical institutions, thus minimizing the bias towards cases with a higher risk to life. Similarly, we must assume that a number of completed suicides have not been recognized by the examining physician. Cases of unnatural death by unknown cause (E980–989) were not included. In the reported cases, our information on drugs may not always have been complete, as it is largely based on circumstantial evidence (such as empty bottles found, interviews with relatives, etc.). However, although we have to expect that some drugs may have been missed, we can assume that this error did not specifically affect a certain group of drugs. Also, alcohol taken as concomitant substance with drugs is likely to have been undetected in a number of cases.

The percentage of suicide by intoxication (E 950) in Switzerland is relatively low compared with other countries. However, international suicide statistics show that rates of suicide by poisoning in Switzerland are not below average and that in most European countries the rates for suicide by poisoning are remarkably similar (14). Rates for other methods vary widely and in Switzerland are above average. It seems, therefore, that the relatively small percentage of suicide by intoxication in Switzerland largely reflects the high proportion of people (i.e., mainly men) using violent suicide methods.

We were surprised by the striking similarity of the drug patterns (including the frequency order of single

drugs). In our view this suggests that – apart from EXIT cases – the two populations do not basically differ in terms of numbers and types of the drugs taken. If this is true, other factors, such as the circumstances of the suicidal act, the availability of a possible helper, etc. would appear to be more important for the outcome of an overdose.

In this analysis we wanted to allow for the fact that, in overdoses, combinations of several drugs are often used. This aspect is lost in investigations into fatal toxicity indices of single drugs or in investigations based on toxicological analyses. In order to gain a picture of the potential lethality of the various drugs, we decided to use an uncommon approach in that we pooled all the different drugs reported and compared the frequencies of the different types of drugs. It could be argued that it is a limitation of our study that a toxicological analysis was not available in most cases. A toxicological analysis, however, could not give comparable results, because this method allows types of drugs to be recorded, not single drugs (such as several benzodiazepine compounds). Furthermore, it has to be considered that drugs found in a toxicological analysis are not necessarily the drugs taken in overdose (such as in patients on antidepressant medication). In that sense, our findings are of different quality and add further information to a toxicological analysis.

An unexpected finding were the 29 EXIT suicides (16% of the fatal overdoses). For the first time in Switzerland, the frequency of EXIT suicides, i.e., suicides that have been carried out according to the written guidelines distributed by EXIT to members of the organization, has been recorded. These suicides had obviously been planned according to expert advice so that there was little chance for survival. This is underlined by the fact that in none of the nonfatal overdoses in Berne had one of these typical drug combinations been used. Such suicides are a new phenomenon and it will be of interest to monitor further trends. The finding raises several medicoethical questions, among them the question of the “appropriateness” of these suicides and the ethical justifiability of recommending “effective” drug combinations for suicide.

The most interesting finding emerging from the comparison of drugs used in fatal and nonfatal overdoses is that, even after exclusion of EXIT cases, the numbers of barbiturates involved were statistically associated with completed suicide, whereas antidepressants were not. This in our view indicates that overdoses with tricyclics have a lower risk of fatal outcome than overdoses with barbiturates. We can only speculate on the reasons for this difference. Barbiturates are known to be dangerous when taken in overdose and so are tricyclic antidepressants. The most plausible explanation is that the toxicity of

tricyclics is not a major factor for the outcome in an overdose of these drugs. It may well be that one reason lies in the fast and strong sedative effect of the barbiturates, which makes it difficult to contact a potential helper after the ingestion of drugs, whereas this is not the case with antidepressants, where people have a better chance to contact another person so that they can be taken to hospital and given a gastric lavage. We know that once people are admitted to hospital they have a good chance to survive an overdose of antidepressants. Strom et al. (15) reported a case fatality rate of 3% of people admitted to hospital following an overdose with tricyclic antidepressants compared to 6% for all overdoses.

Antidepressants have been found by others to be responsible for 20–30% of fatal overdoses (8, 16), similar to our 24%. The ranking of antidepressant substances found in completed suicide is different from that of other studies where amitriptyline, dothiepin and doxepin have been associated most frequently with fatal overdoses (7, 9, 10), but there is an obvious similarity between fatal and nonfatal overdoses. In Switzerland, maprotiline, mianserin and trimipramine were used most often in completed as well as in attempted suicide. The Swiss IMS data (IMS is a market research company providing the pharmaceutical industry with information on the prescribing of Swiss doctors, based on a sample of reporting practitioners) for 1990 show that 30% of antidepressant prescriptions were for maprotiline, 14% for clomipramine, 10% for mianserin, about 10% for amitriptyline and 6% for trimipramine. The frequencies of the various compounds taken in overdose therefore largely reflect the prescribing habits in Switzerland. Maprotiline has the highest proportion of single drug deaths among the antidepressants. Of the new selective serotonin reuptake-inhibiting antidepressants, only fluvoxamine was available in 1990, but it was not found on any of the death certificates nor taken in nonfatal overdoses.

Another interesting finding was that benzodiazepines were named in a surprisingly large number of suicides, often in combination with other drugs and/or with alcohol, but also as the only substance. Only very recently has the danger of benzodiazepines in overdose been emphasized in view of the frequent combinations of benzodiazepines with other drugs and alcohol (11, 17). Although in a number of death certificates benzodiazepines were named as only cause of death, we cannot draw any further conclusions without toxicological analysis in these cases. It is likely that the concomitant use of alcohol or drugs may have been missed in these cases. Flunitrazepam, the benzodiazepine used most frequently in our fatal overdoses, is a strong hypnotic with an active metabolite with a long half-life. Although it is known to doctors that this drug is abused by drug addicts,

interestingly, it still was the most widely prescribed hypnotic in 1990 (IMS data). Obviously, in fatal overdoses in which benzodiazepines are assumed to be the only cause of death a toxicological analysis should be performed.

To our knowledge this is the first time that all the different compounds ingested alone or in combination in cases of fatal and nonfatal overdoses have been carefully recorded. In spite of a certain limitation of the reliability of this information, it adds new aspects to our knowledge of the use of drugs in overdoses. Surprisingly, the patterns of the frequencies of drugs taken in fatal and nonfatal overdose were quite similar, and only barbiturates were found to be positively associated with fatal outcome, not antidepressants or any other type of drug. Benzodiazepines were recorded most frequently and we must assume that because of the frequent combinations with other drugs they represent a considerable factor in the lethality of deliberate overdoses.

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References

1. GAZZARD BG, DAVIS M, SPOONER J, WILLIAMS R. Why do people use paracetamol for suicide? *Br Med J* 1976; 1: 212–213.
2. KREITMAN N. The coal gas story. *Br J Prev Soc Med* 1976; 30: 86–93.
3. LESTER D, FRANK ML. The use of motor vehicle exhaust for suicide and the availability of cars. *Acta Psychiatr Scand* 1989; 79: 238–240.
4. OLIVER RG, HETZEL BS. Rise and fall of suicide rates in Australia: relation to sedative availability. *Med J Aust* 1972; 2: 919–923.
5. JOHNS MW. Self-poisoning with barbiturates in England and Wales during 1959–1974. *Br Med J* 1977; 1: 1128–1130.
6. CASSIDY J, HENRY S. Fatal toxicity of antidepressant drugs in overdose. *Br Med J* 1987; 295: 1021–1024.
7. VUORI E, KLAUKKA T, LAHTI T. Fatal poisonings with antidepressants in Finland 1985–1987. *Acta Psychiatr Scand* 1989; 80 (suppl 354): 55–60.
8. WORM K, STEENTOFT A. Fatal poisoning by cyclic antidepressants. *Pharmacopsychiatry* 1990; 23: 9–13.
9. MONTGOMERY SA, BALDWIN D, GREEN M. Why do amitriptyline and dothiepin appear to be so dangerous in overdose? *Acta Psychiatr Scand* 1989; 80 (suppl 354): 47–53.
10. BEAUMONT G, HETZEL W. Patterns at risk of suicide and overdose. *Psychopharmacology* 1992; 106: 123–126.
11. SERFATY M, MASTERTON G. Fatal poisonings attributed to benzodiazepines in Britain during the 1980s. *Br J Psychiatry* 1993; 163: 386–393.
12. Working Group on Preventive Practices in Suicide and Attempted Suicide. Summary report. *Crisis* 1988; 1: 72–77.
13. PLATT S, BILLE-BRAHE U, KERKHOF A et al. Parasuicide in Europe: the WHO/EURO multicentre study on parasuicide. I. Introduction and preliminary analysis for 1989. *Acta Psychiatr Scand* 1992; 85: 97–104.

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14. LESTER D. Changes in the methods used for suicide in 16 countries from 1960 to 1980. *Acta Psychiatr Scand* 1990; 81: 260–261.
15. STROM J, THISTED B, KRANTZ T, BREDGAARD-SORENSEN M. Self-poisoning treated in an IUC: drug pattern, acute mortality and short-term survival. *Acta Anaesthesiol Scand* 1986; 30: 148–153.
16. RETTERSTOL N. Norwegian data on death due to overdose of antidepressants. *Acta Psychiatr Scand* 1989; 80 (suppl 354): 61–68.
17. MENDELSON WB, RICH CL. Sedatives and suicide: the San Diego study. *Acta Psychiatr Scand* 1993; 88: 337–341.