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Among Fatal Poisonings Dextropropoxyphene Predominates in Younger People, Antidepressants in the Middle Aged and Sedatives in the Elderly

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ABSTRACT: To compare the characteristics of dextropropoxyphene (DXP) poisoning victims with those of victims of poisonings by antidepressants and sedatives, we examined all fatal poisonings due to DXP, antidepressants or sedatives among autopsies performed at one department of forensic medicine in Sweden during the six-year period from 1992 to 1997.

In 202 cases, death was classified as fatal poisonings by DXP, antidepressants or sedatives. DXP caused death in 78 cases (39%), antidepressants in 49 (24%), and sedatives in 75 (37%). DXP as a single preparation was predominant in causing death. The second compound, flunitrazepam, caused death in 30 cases (15%).

The victims of poisonings by DXP, antidepressants, or sedatives shared a similar history of alcohol/drug abuse, depression and somatic illness. They were mostly living alone at the time of death (>60%), the majority died at home (81%), and suicide was the most frequent manner of death (73%).

Age seemed to be an important characteristic regarding the choice of drug. Younger people predominantly died of DXP (mean age 43 years, 95% confidence interval, CI 39–47), and elderly people of sedatives (mean age 59 years, CI 55–63). Antidepressants were found mainly in middle-aged victims (mean age 51 years, CI 48–54).

The predominance of sedatives among the elderly might be explained by a very high prescription rate of such drugs in older age groups, but prescription rate could not explain the DXP predominance among younger people. We hypothesize that younger people are more prone to abuse therapeutic drugs for euphoric reasons than elderly people, and that because of its high toxicity, DXP leads to accidental deaths more often than sedatives.

KEYWORDS: forensic science, forensic medicine, dextropropoxyphene, antidepressants, sedatives, fatal poisoning, characteristics

The high toxicity of the analgesic compound dextropropoxyphene (DXP), leading to intoxications and fatal poisonings, has been well documented all over the world since this drug was introduced onto the market in the beginning of the 1960s (1–8). The number of fatal poisonings where DXP has caused or contributed to death has been constantly high in Sweden since the 1970s (9–12).

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In attempts to define the characteristics of the victims of DXP poisoning, these persons have been found as a group to constitute an adult population with a marked tendency towards hypochondria, chronic minor illness, and severe psychiatric problems (13–15). In comparison with codeine deaths, among DXP-related deaths there have been fewer histories of drug addiction, more cases with mental illness and more suicides (16,17). In another study, fatal DXP intoxications have been compared with deaths caused by strong opioids; here both types of victims were found to have a history of psychiatric disease or drug/alcohol abuse, but the typical DXP victim committed suicide, whereas accidental deaths were more common among opioid victims (18).

Next to DXP, antidepressants and sedatives are the most common causes of fatal poisoning in Sweden (19). In order to analyze the characteristics of DXP victims in comparison with those of victims of poisonings due to antidepressants and sedatives, a Swedish autopsy material from the six-year period from 1992 to 1997 was examined.

Materials and Methods

The investigated population was based on the autopsies performed during the years from 1992 to 1997 at one of six departments of forensic medicine in Sweden (Uppsala). This department serves a mainly rural district with 1.1 million inhabitants. A few larger cities with populations of 50,000 to 150,000 are included in the district.

The requirement for inclusion in the study was that the primary cause of death was fatal poisoning due to DXP, antidepressants including tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitors (SSRI) or sedatives including hypnotics and anxiolytics.

The drug primarily causing the fatality was specified on the basis of the death certificate and toxicological analyses. A compilation of therapeutic and toxicological levels of the preparations was obtained from the Department of Forensic Chemistry. Alcohol was considered as a contributory cause in cases with a blood alcohol concentration (BAC) >0.1%. Since the aim was to compare the characteristics of DXP victims with those of victims due to antidepressants or sedatives cases where DXP, antidepressants or sedatives contributed to death in combination with each other or with other drugs were excluded.

In order to examine the characteristics of the deceased, with special reference to gender, age group, civil status, place of death, and manner of death, we analyzed autopsy protocols, death certificates,

police reports, toxicological findings, and additional information (e.g., hospital records), when this was kept in the medico-legal dossier. Notes on alcoholism and drug addiction, depression, psychotic disorders, other mental disorders, previous suicidal attempts, written farewell notes, and serious somatic diseases were also considered.

Statistical Methods

Means and 95% confidence intervals (CI) were calculated, and differences were considered significant at the 5% level when CI for two separate groups did not overlap. The chi–square test was also employed for comparison, using a significance level of 0.05.

Results

From 1992 to 1997, a total of 4306 autopsies were performed at the forensic medicine department under study. In 337 cases DXP, antidepressant or sedatives caused or contributed to death. Among these cases, DXP caused death in 78 cases (39%), antidepressants in 49 cases (24%), and sedatives in 75 cases (37%). In the remaining 135 cases, the drug groups contributed to death in combination with each other or with other drugs (DXP in 30 cases, antidepressants in 39 cases, and sedatives in 66 cases) why these cases were excluded.

Amitriptyline and clomipramine were the antidepressants most often found, in 18 and 16 cases respectively, while citalopram was found in 9 cases. Among the sedatives, flunitrazepam was most frequently used, in 30 cases, followed by propiomazine in 15 cases, other benzodiazepines in 13 cases, and zopiclone and alimemazine in 6 cases each.

Table 1 shows the distribution of the fatal poisonings due to DXP, antidepressants and sedatives between the study years. In 1995, the numbers of fatalities due to the three drug groups were less than half of the other years. A declining trend of antidepressant poisonings was noted, from 33% in 1992 to 26% in 1997, a decrease of 18% (Table 1).

In 111 (55%) of the 202 cases, alcohol was found in the blood, and of these, 73 (36%) had a BAC >0.1% (mean 0.21%) and were considered as cases where alcohol contributed to death. No significant differences between the drug groups were found.

The mean age, with 95% confidence interval (CI), and sex of the fatal poisoning cases are given in Table 2.

Age

The mean age of the cases of DXP fatalities (43 years, CI 39–47) was significantly lower than that of the cases of fatal poisoning due to antidepressants (51 years, CI 48–54) and sedatives (59 years, CI 55–63), and the mean age of the sedative poisoning cases was significantly higher than that of the other two drug categories (Table 2).

TABLE 1—*Fatal poisonings due to dextropropoxyphene (DXP), antidepressants and sedatives (*n*=202).*

	DXP		Antidepressants		Sedatives	
	n	%	*n*	%	*n*	%
1992	14	36	13	33	12	31
1993	12	33	10	28	14	39
1994	13	32	9	22	19	46
1995	7	37	5	26	7	37
1996	21	58	4	11	11	31
1997	11	35	8	26	12	39
Total	78	39	49	24	75	37

TABLE 2—*Mean age, with 95% confidence interval (CI), and sex of cases of fatal poisoning by dextropropoxyphene (DXP), antidepressants and sedatives.*

	Mean Age (CI)	Sex M/W in %
DXP (*n*=78)	43 (39–47)	64/36
Antidepressants (*n*=49)	51 (48–54)	46/54
Sedatives (*n*=75)	59 (55–63)	63/37
Total (*n*=202)	51 (48–53)	59/41

The age differences between the three types of drug poisoning are illustrated in Fig. 1. There was a predominance of DXP in the three younger age groups (75% of all cases), a fairly equal distribution of the three drugs in the age group 40 to 49 years, and a predominance of antidepressants and sedatives in the age group 50 to 59 years. In the older age groups the majority of the poisonings were due to sedatives (77% of all cases).

Sex

Males were in the majority among fatalities due to DXP (64%) and sedatives (63%), but were in a slight minority among those due to antidepressants (46%).

The prevalence rates of alcoholism, drug addiction, depression, psychotic disorders, unspecified mental problems, previous suicidal attempts, written farewell notes and somatic diseases among cases of fatal poisoning due to DXP, antidepressants and sedatives are shown in Table 3.

Mental Disorders

One-fifth of all the deceased suffered from alcoholism, one-tenth of drug addiction and one-third of depression. No significant differences were found between the drug groups with respect to these diagnoses, while significantly more unspecified mental problems were found among the cases of antidepressant poisoning compared with the other two groups ($p < 0.05$). Nor were any significant differences observed regarding previous suicidal attempts or written farewell notes, which were reported in 21 (10%) and 34 (17%) cases, respectively.

Somatic Illness

In one-fourth of the cases some kind of somatic illness was reported. These varied in seriousness and included malignant cancer, vertebral compressions, cardiomegaly, cardiomyopathy, nephrosclerosis, asthma, diabetes and psoriasis. The prevalence of somatic illness was independent of drug category.

No significant differences were found between the drug categories regarding place of death, civil status, or manner of death. The death occurred at home in 163 (81%) of all 202 cases, in hospital in 9 cases (4.5%), outdoors in 13 cases (6.5%) and at a residence belonging to a relative or an aquaintance in 17 cases (8%).

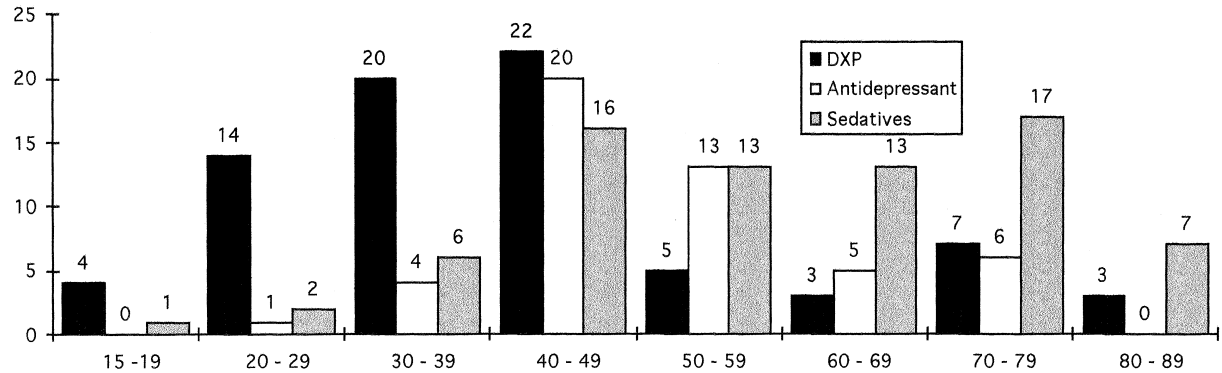

FIG. 1—*The distribution of fatal poisoning by dextropropoxyphene (DXP), sedatives and antidepressants between the different age groups (*n = *202).*

TABLE 3—*The prevalence of alcoholism, drug addiction, depression, psychosis, unspecified (US) mental problems, previous suicidal attempts, written farewell notes and somatic illness among cases of fatal poisoning by dextropropoxyphene (DXP), antidepressants, and sedatives.*

	DXP (*n*=78)		Antidepressants (*n*=75)		Sedatives (*n*=49)		Total (*n*=202)	
	n	%	*n*	%	*n*	%	*n*	%
Alcoholism	13	17	12	24	17	22	42	21
Drug addiction	11	14	2	4	8	10.5	21	10
Depression	19	24	19	38	25	33	62	31
Psychosis	0	0	1	2	1	1	2	1
US mental problems	3	4	10	20	6	8	18	9
Previous suicidal attempts	4	5	7	14	10	12	20	10
Written farewell notes	12	15	10	20	12	16	34	17
Somatic illness	14	18	11	22	28	37	53	26

Sixty-eight (34%) of the deceased were single, 63 (31%) were married or living under matrimonial-like conditions, 5 (2%) were engaged, 31 (16%) were divorced and 22 (11%) were widows/ers, while in 13 cases (6%) the civil status could not be determined from the available documents. The manner of death was classified as accidental in 4 (2%) of the 202 cases, as suicidal in 147 cases (73%) and as undetermined in 51 cases (25%).

Discussion

This study was based on data from only one of six forensic medicine districts in Sweden, and thus the conclusions drawn are mainly valid for that district, although we believe them to serve as a valid guideline concerning preventive measures in the whole of Sweden.

A possible shortage of the study was that the information of both mental disorders and somatic illnesses was limited to the information accessible in the forensic medicine dossier. This implies that some of the deceased might have had a defined illness for which he/she was on medication without any note in the death certificate. Neither did we have any possibility to investigate which individuals were on prescribed medication and which got the drugs in any other way. Anyhow, we suggest that this invalidity affects the three drug groups to the same extent, why we still expect the comparison to be valid.

Before discussing the characteristics of the victims, attention should be drawn to the fact that DXP, a single compound, was compared with groups of compounds. In comparison with other single preparations found in the blood of the deceased, DXP was considerably predominant in causing fatal poisonings. This drug was the cause of death in 78 (39%) of the 202 fatal poisonings in the period in question, as against 30 (15%) caused by the second most common compound found, flunitrazepam. As the sales of DXP and flunitrazepam during the study years were of the same magnitude, about 13.0 defined daily dose/1000 inhabitants during a 12-month period (DDD) (20), it seems that DXP was over-represented in causing fatal poisonings. This has also been found by others (21).

Age seemed to be an important characteristic when it came to the choice of drug. The mean age of the DXP cases was significantly lower, and that of sedative cases significantly higher than the mean ages of the other two drug groups. Swedish sale statistics have shown that the prescription rate of all the compounds studied increases with increasing age (20). In 1996, for instance, in the district under study the DDD of DXP increased from 2.0 in the age group 20–29 years, to 9.2 at ages 40–49 years, and to 41.7 in the group 70–79 years. The corresponding figures for antidepressants were 12.7, 44.0 and 58.0 and for benzodiazepines 4.1, 30.8 and 97.0. These figures, showing a very high prescription rate of benzodiazepines among elderly people, may explain the predominance of sedatives among the older age groups, but they do not explain the predominance of DXP among the younger people.

An analysis of the mental disorders in relation to age revealed no differences that could explain the differences in drug choice. Somatic diseases were found in significantly more cases among the elderly, giving no explanation for why DXP was used more by younger persons.

We found a BAC > 0.1% significantly more often in younger people (15–39 years) than in older (60–89 years) ($p < 0.05$), but since the distribution of the drug predominance between the age groups remained the same even when the alcohol cases were excluded, this could not explain the over-representation of DXP poisoning among younger people.

Studies have shown that DXP is abused both as a primary drug (23,24) and to potentiate the effect of alcohol or other drugs (25), especially by drug addicts but also by young people experimenting with drugs (26). In the age group 15–39 years, drug addiction was noted in 17% while among the older age groups, 60–89 years, it was reported in only 5%.

Although this difference was not significant, it may be speculated whether younger people are more prone than the elderly to abuse therapeutic drugs by reason of their euphoric effects. In order to get the kick, they might take large doses, and in the case of DXP, with its high toxicity, the overdosage might lead to accidental death. Sedatives are not as toxic as DXP, and victims of accidental overdosage of sedatives are thus more often rescued. Alsén et al. (1994), for example, showed that DXP and amitriptyline, because of their high toxicity, were involved in a strikingly higher incidence of completed suicides compared with suicide attempts (27), which was not the case with benzodiazepines.

The analyses of the characteristics of the victims showed that 20% of the deceased suffered from alcoholism, 10% of drug addiction, 31% of depression, and 9% of unspecified mental problems. Although the results confirmed earlier reports that to a high degree, victims of DXP poisoning have previous histories of alcohol/drug abuse, mental disorders and somatic illness (13–18), they showed that these characteristics were also true of victims of poisoning by antidepressants and sedatives, indicating that the choice of drug is not influenced by any of these characteristics.

The only official indication for prescription of DXP in Sweden is pain due to somatic illness, e.g., joint problems. Interestingly, however, somatic illness was not more common in this group than in the other two groups, indicating that in reality this drug must be used by the patients for other reasons than pain due to somatic disease.

The prevalence of drug intake combined with large amounts of alcohol (37%) was in accordance with findings in other studies (28,29), and confirms that alcohol plays a major role in many drug overdosages.

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