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ORIGINAL ARTICLE

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Fatal poisonings where ethylmorphine from antitussive medications contributed to death

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Abstract The hypothesis that antitussives containing ethylmorphine are abused by alcoholics and drug addicts and that this may lead to fatal poisonings where ethylmorphine causes or contributes to death was investigated. For this purpose 14 cases were analysed where a blood ethylmorphine concentration above the therapeutic level of ≥ 0.3 μg/g was found in autopsy blood samples. Alcohol was found in 8 of the 14 cases and alcoholism or drug addiction was noted on 8 of the 14 death certificates. Other drugs, mostly benzodiazepines, were found in all 14 cases. The cause of death was fatal poisoning in 8 of the 14 cases and although there were no mono-intoxications, the cause of death was specified as fatal ethylmorphine poisoning in 2 cases. Among the unspecified medicinal drug poisonings there were five cases with very high blood levels of ethylmorphine, indicating that this drug played an important contribution to the cause of death. The results indicate that deaths due to ethylmorphine in antitussive medicines may occur among drug addicts and alcoholics taking it in overdose. Physicians should therefore be restrictive in prescribing cough mixtures containing ethylmorphine to these categories of patients. Prescription of large amounts of the drug should be avoided.

Key words Ethylmorphine · Fatal poisoning · Manner of death · Drug addicts

Introduction

It is well known that drug addicts and alcoholics use medicinal drugs to potentiate the effects of the drug taken or during withdrawal. In the Nordic countries fatal poisoning due to medicinal drugs combined with alcohol and/or illegal drugs is often noted among deaths in drug addicts and opiates are among the most frequent causes of drug-related deaths [1]. In addition to overdoses of heroin and morphine, drug addicts also die from codeine and dextropropoxyphene poisoning [2].

Ethylmorphine is an opioid ingredient used in a variety of antitussive preparations mostly as a cough suppressant. Ethylmorphine is metabolised to both morphine and codeine [3] and it is often used by drug addicts in the absence of heroin, for example in France, where no prescription is needed for cough suppressants containing ethylmorphine [4]. In Sweden there are three different cough mixtures containing ethylmorphine and none of these are sold over-the-counter but require a prescription.

Although there is reason to believe that ethylmorphine is frequently used by drug addicts, deaths due to this substance are rarely reported. One case of fatal poisoning from an ethylmorphine overdose in a heroin-addicted young man was reported by Demetz et al. [5] and in 1994 Kintz et al. [4] reported another young heroin addict who died of an overdose after switching from heroin to ethylmorphine. Steentoft et al. [1] reported that six persons died of poisoning due to ethylmorphine in the Nordic countries in 1984–1985.

According to the adverse drug reaction profile reported by the pharmaceutical company producing the most frequently prescribed cough mixture containing ethylmorphine in Sweden, no fatal cases due to these mixtures were found during the years 1977–1995 (SWEDIS – Adverse drug reactions profile. Pharmacia drug company, Uppsala, Sweden, 1995).

The aim of this study was to test the hypothesis that ethylmorphine is used by drug addicts and may lead to fatal poisoning where ethylmorphine causes or contributes to death. In order to confirm or reject this hypothesis we analysed the total forensic autopsy material in Sweden during the years 1992–1995 from this aspect.

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Table 1 The 14 cases with a blood ethylmorphine concentration ≥ 0.3 μg/g: Gender, age, blood ethylmorphine concentration, blood alcohol concentration, reports in the death certificates of drug abuse or alcoholism, cause and manner of death, and other compounds found in the toxicological analyses

Case no.	Gender	Age Years	Ethyl-mor-phine μg/g	Alco-hol %	Reports of drug abuse/al-coholism	Cause of death	Manner of death	Other drugs μg/g	
1.	M	42	2.9	0.51	Yes	alcohol and medical drug poisoning	undetermined	0.14	7-amino-nitrazepam
2.	M	57	0.6	0.48	Yes	chronic alcoholism		0.10	trimipramine
								0.10	diazepam
								0.05	morphine
3.	M	20	1.6	0.00	Yes	inhalation of gastric contents due to medical drug poisoning	undetermined	0.10	diazepam
								0.10	nordiazepam
								0.03	7-amino-flunitrazepam
								0.10	morphine
								0.05	amphetamine
4.	M	36	1.0	0.01	No	ethylmorphine poisoning	undetermined	7.0	carbamazepine
								50.0	chlormezanone
								4.0	dihydropropiomazine
								0.3	diazepam
								2.2	nordiazepam
								80.0	paracetemol
								0.1	morphine
								0.2	codeine
5.	M	39	0.5	0.00	Yes	pneumonia		0.3	diazepam
								0.2	nordiazepam
								0.08	7-amino-flunitrazepam
								1.0	paracetamol
								0.08	morphine
6.	F	32	0.4	0.20	No	ethylalcohol and medical drug poisoning	suicide	30.0	carbamazepine
								0.7	moclobemid
								0.5	oxomoclobemid
								2.3	clomipramine
								0.2	desmethylclomipramine
7.	F	44	0.9	0.00	No	strangulation	homicide	1.0	paracetamol
								0.09	morphine
8.	M	36	1.1	0.00	Yes	heroin overdose	undetermined	0.3	diazepam
								1.0	nordiazepam
								0.06	7-amino-flunitrazepam
								0.12	morphine
								0.01	codeine
								0.1	amphetamine
9.	M	44	1.3	0.08	Yes	medical drug poisoning	undetermined	5.0	paracetamol
								0.1	nordiazepam
								0.002	tetrahydrocannabinol
								2.0	morphine
								0.2	codeine
10.	M	44	0.3	0.02	No	myocardial infarction		0.1	diazepam
								0.1	nordiazepam
								0.07	morphine
11.	M	28	1.7	0.00	No	medical drug poisoning	undetermined	0.2	diazepam
								0.8	nordiazepam
								0.2	7-amino-flunitrazepam
								9.0	coffeine
								2.0	paracetamol
								0.17	morphine
12.	F	50	0.4	0.00	No	pneumonia		3.8	carbamazepine
								0.2	evomepromazine
								0.1	desmethyllevomepromazine
								0.6	7-amino-nitrazepam
								0.07	nitrazepam
								0.01	morphine
								0.4	codeine
13.	M	44	1.3	0.09	Yes	polysubstance abuse		0.1	diazepam
								0.11	morphine

Table 1 (continued)

Case no.	Gender	Age Years	Ethyl-mor-phine µg/g	Alco-hol %	Reports of drug abuse/al-coholism	Cause of death	Manner of death	Other drugs µg/g	
14.	M	48	1.4	0.12	Yes	ethylmorphine poisoning	suicide	0.4	diazepam
								0.3	nordiazepam
								0.06	7-amino-nitrazepam
								0.3	diphenhydramine
								0.3	oxazepam
								0.16	morphine

Materials and methods

In Sweden there are six forensic medicine departments which examine deceased persons on behalf of the police or prosecution authorities when a death requires investigation, including all suspected fatal poisonings. Blood samples taken by the six departments are analysed at the National Laboratory. The investigated collective was the total of blood samples taken from autopsies performed at the six departments during 1992–1995. A requirement for inclusion in the study was that ethylmorphine was found to be present in a peripheral blood sample.

During the study period a total of 22,440 autopsies were performed at the 6 forensic departments and blood samples from 18,759 cases (84%) were sent to the National Laboratory for analysis. Ethylmorphine was analysed using gas chromatography-mass spectrometry, using codeine-d3 as internal standard for the quantification of ethylmorphine. The linear range was 0.005–0.4 µg/g. The limit of detection and quantification was 0.001 µg/g. Information of the recovery was not available. The method is a modification of the method described by Schuberth and Schuberth [6].

Simultaneous detection of alcohol and other drugs, reports in the death certificates of alcoholism/drug addiction and the manner of death in cases of fatal poisonings were considered in the present study. The study was based on the toxicological analyses, the death certificates and the police reports.

Results

Ethylmorphine was found in 27 out of the 18,759 peripheral blood samples analysed at the National Laboratory in 1992–1995. The blood ethylmorphine concentration was below the therapeutic level (the blood level of ethylmorphine after a therapeutic dose is < 0.3 µg/g) in 13 of these 27 cases. This study focused on the 14 cases with a blood ethylmorphine concentration ≥ 0.3 µg/g.

Table 1 shows the gender, age, blood ethylmorphine concentration, blood alcohol concentration, reports in the death certificates of drug abuse or alcoholism, cause and manner of death and other compounds found by the toxicological analyses in the 14 cases. Of the 14 cases 11 were male, three were female and the average blood ethylmorphine concentration was 1.1 µg/g (range 0.3–2.9 µg/g). Alcohol was found in the blood in 8 of the 14 cases and reports of alcoholism or drug addiction were given in 8 of the 14 death certificates. The cause of death was fatal poisoning in eight cases, two of which were specified as fatal ethylmorphine poisoning. Among the fatal poisonings the manner of death was reported to be suicide in two cases and undetermined in six. As seen in Table 1 other drugs were found in all cases and benzodiazepines, mostly diazepam, were found in 12 of the cases.

Discussion

Before discussing the results it is important to draw attention to the difficulty in assessing the primary drug causing death in poly-drug intoxications. Although some drugs found in the blood of the deceased are within therapeutic levels they might contribute to death due to synergism with other drugs. This is for instance the case for the weak opioid dextropropoxyphene, which may be lethal within therapeutic blood concentrations when combined with alcohol [7, 8]. However, we suggest that the conclusions based on the toxicological results will most probably be correct.

During the 4-year period 1992–1995, ethylmorphine was found in 14 cases at a blood concentration of ≥ 0.3 µg/g. According to the death certificates ethylmorphine was assessed by the forensic physicians as the primary cause of death in two of the cases (cases 4 and 14), although in case 4 chlormezanone was found in such a high concentration that it most certainly contributed to death. Considerably high ethylmorphine concentrations in the blood were also found in cases 1 (2.9 µg/g), 3 (1.6 µg/g), 9 (1.3 µg/g), 11 (1.7 µg/g) and 13 (1.3 µg/g) also indicating that the primary cause of death was ethylmorphine. This indicates that in all probability ethylmorphine has contributed to death in these cases.

It is stated in the drug compendium for physicians (FASS ’97 – Pharmaceutical specialities in Sweden, LINFO, Stockholm, Sweden, 1997) that there is no clinical documentation of this antitussive agent that will make an assessment of side-effects possible and it should therefore be especially important to report deaths due to this cough mixture.

Alcoholism or drug addiction was noted in 8 of the 14 cases in the study. This confirms the presumption that drug addicts are prone to use ethylmorphine as an additional drug. Although more than half of the cases were noted as alcoholics and drug addicts, there is reason to believe that alcohol abuse would be found in even more of our 14 cases as under-reporting of alcoholism in death certificates has been documented previously [9].

The finding of multiple drugs in all 14 cases confirms other reports of widespread polydrug abuse among drug addicts [1, 2]. Our results indicate that overdoses of ethylmorphine might be a problem among drug addicts but seldom among users of antitussive medicine for medical purposes.

Fatal poisoning was the cause of death in eight cases, among which six were classified as undetermined and two as suicide. No case was classified as accidental. Previous studies have shown an under-reporting of accidents as the manner of death in fatal dextropropoxyphene poisonings in Sweden [10, 11]. Although the number of ethylmorphine poisoning cases was small in the present study, a tendency to classify the manner of death as undetermined rather than as accidental was observed. The fact that fatal poisonings due to ethylmorphine seem to be classified either as suicide or as uncertain suicide may be one reason why no fatal cases due to the particular antitussive mixture mentioned in this paper have been reported earlier.

In conclusion, although the number of samples in this study was very small the conclusion may be drawn that ethylmorphine is used among Swedish drug addicts as an additional drug and may lead to fatal poisoning where ethylmorphine causes or contributes to the cause of death. This leads to the suggestion that physicians should be more restrictive in prescribing cough mixtures containing ethylmorphine to alcoholics and drug abusers. It is also recommended that the amounts prescribed be limited.

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