

Methadone and drug addicts

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Summary. Drug addicts who had died in Copenhagen City and County in 1981 and 1989 were analysed for methadone. In 1981, 94 cases were analysed of which 16% were found positive for methadone, and in 1989, 70 cases were analysed of which 37% were positive. Methadone alone was found to be the cause of death in 50% more cases in 1989 than in 1981. Only half of the drug addicts who were found positive for methadone had been under methadone treatment. Morphine and benzodiazepines were the most frequently occurring other substances in both 1981 and 1989. Alcohol was found in only about 30% of the methadone-positive cases. The median whole blood concentrations of methadone found in addicts where methadone was the cause of death was 0.3 mg/kg where no alcohol was present and 0.2 mg/kg where alcohol was present. In living persons using methadone, the median was 0.1 mg methadone/kg whole blood with or without alcohol present.

Key words: Drug fatalities – Methadone – Ethanol – Other substances

Zusammenfassung. Es wurden Drogenabhängige, die im Bereich der Stadt und des Kreises Kopenhagen in den Jahren 1981 und 1989 verstarben, hinsichtlich einer Methadoneinnahme untersucht. 1981 wurden 94 derartige Fälle untersucht, von denen 16% einen positiven Methadonbefund erbrachten. 1989 wurden 70 Fälle untersucht, von denen 37 positiv waren. Eine Methadonintoxikation als alleinige Todesursache wurde 1989 50% häufiger diagnostiziert als 1981. Nur die Hälfte der Drogenabhängigen, die Methadonpositiv waren, befanden sich in einer therapeutischen Methadonbehandlung. Morphin und Benzodiazepine waren sowohl 1981 als auch 1989 die am häufigsten nachzuweisenden weiteren Substanzen. Alkohol konnte nur in 30% der Methadon-positiven Fälle detektiert werden. Der Median der Vollblutkonzentration von Methadon betrug in jenen Fällen, in denen eine Methadonintoxikation die Todesursache war und keine zusätzliche Alkoholbeeinflussung vorlag, 0,3 mg/kg, hin-

gegen bei einer zusätzlichen Alkoholbeeinflussung nur 0,2 mg/kg. Bei lebenden Personen, welche Methadon einnahmen, betrug der Median jeweils 0,1 mg Methadon/kg Vollblut unabhängig von der Alkoholbeeinflussung.

Schlüsselwörter: Drogentodesfälle – Methadon – Ethanol – Andere Substanzen

Introduction

In Denmark the use of methadone in the treatment of drug addicts has become increasingly more common. The number of long term methadone prescriptions has increased from 897 in 1985 to 1,943 in 1989 [1]. To get an impression of the consumption and the following consequences we have made a comparison between the presence of methadone in deceased drug addicts in Copenhagen City and County in 1981 and in 1989. Methadone concentrations from drug addict fatalities from 1984–1989, where methadone was an essential contributory cause of death, were compared to the concentrations found in living drug addicts.

Materials and methods

In this survey a drug addict is defined as a person who abuses opioids and/or analeptics and/or hallucinogens. Persons, who have been prescribed the drugs primarily for the treatment of illnesses and have then become drug abusers, are not included.

All deceased drug addicts were autopsied at the Institute of Forensic Pathology in Copenhagen according to the departmental order of 1970 from the Ministry of Justice. The analysis of methadone was performed by the Institute of Forensic Chemistry in Copenhagen in each case. Generally, due to economic reasons a screening is not performed in all instances at our institute, and analyses are often not carried out when the cause of death has been established. Therefore the results will not represent the whole truth.

The concentrations of methadone in samples from living drug addicts were compared to those from deceased drug addicts from

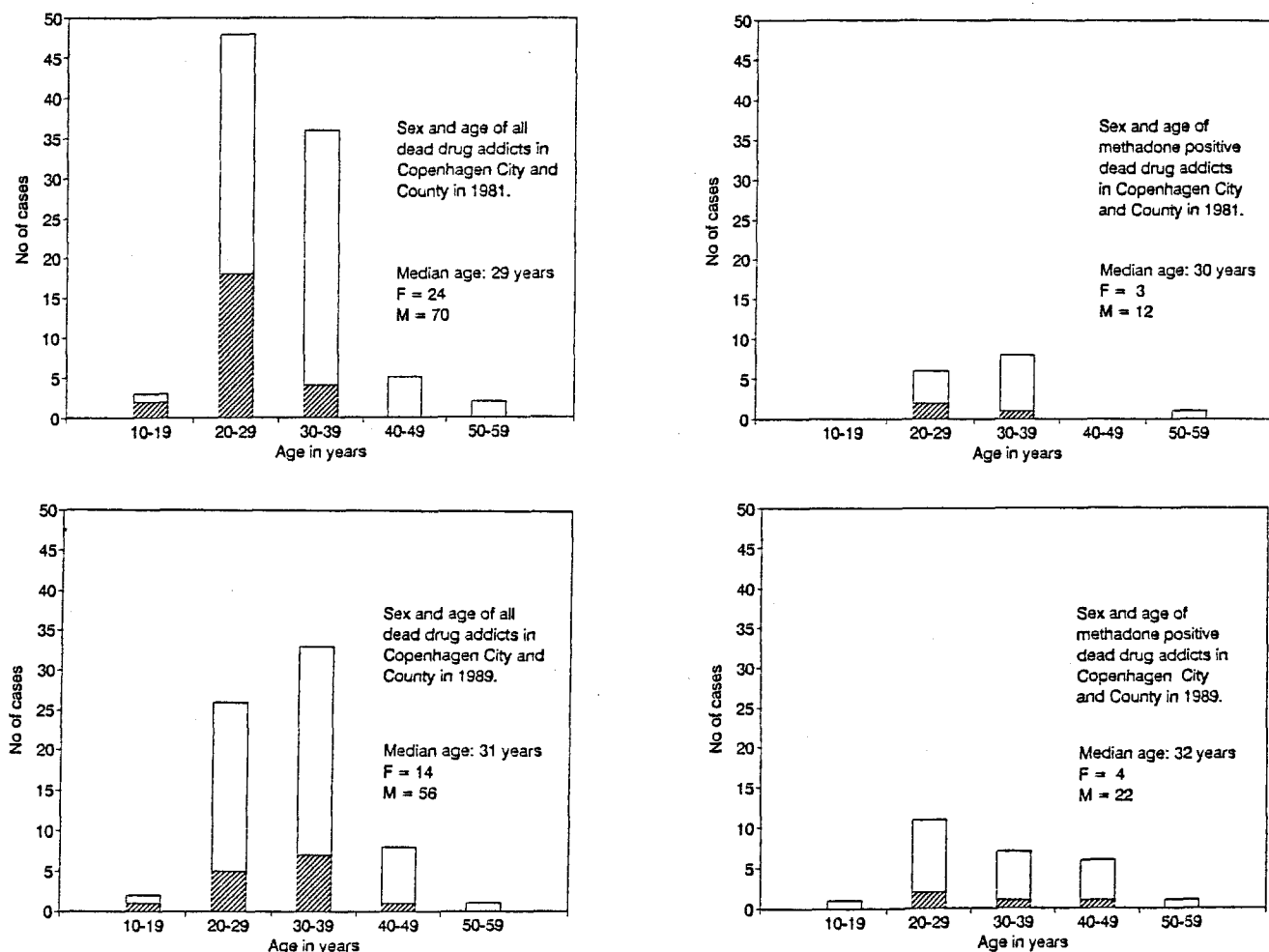


Fig. 1. Sex and age of all addicts and of addicts where methadone was found present, dying in the area of Copenhagen City and County in 1981 and in 1989, respectively. (▨) Female (F); (□) male (M)

1984–1989, where methadone was the sole or an essential contributory cause of death. This material has also been used for a comparison between concentrations of methadone in whole blood in deceased drug addicts with or without methadone treatment.

In the autopsy cases the forensic chemical analyses were performed on liver tissue and blood or muscle and in the cases from living persons on blood and urine. The methods used were capillary gas chromatography with a nitrogen-phosphorus-detector, liquid chromatography with ultraviolet and electrochemical detectors, and thin layer chromatography. The presence of methadone was confirmed by at least 2 different methods.

Results

In 1981 94 cases were analysed, of which 15 (16%) were positive for methadone, and in 1989, 70 cases were analysed, of which 26 (37%) were positive. Figure 1 shows the distribution of age, sex and median age of all deceased drug addicts and of deceased drug addicts where methadone was present in Copenhagen City and County in 1981 and 1989. The cause of death in the methadone positive cases is shown in Table 1.

Table 2 shows the blood concentrations of methadone in deceased drug addicts from 1984–1989 compared to blood concentrations from living persons from 1987–1990, derived mainly from traffic cases but also from

Table 1. Cause of death of the methadone positive dead drug addicts in Copenhagen City and Country in 1981 and 1989, respectively

Cause of death	1981 number	1989 number
Methadone	6	15
Methadone + other drugs or narcotics	3	6
Other causes of death	3	5
Unknown	3	0
Total	15	26

cases of violence. The median concentration of methadone in blood from deceased drug addicts was 0.3 mg/kg where the blood alcohol concentration (BAC) was zero and 0.2 with BAC ≥ 0.50 mg/g, while the corresponding values for living persons were 0.1 and 0.1.

Methadone blood concentrations of dead drug addicts with or without methadone treatment are shown in Table 3.

Table 4 shows the methadone concentrations in muscle and liver in deceased drug addicts, where methadone was the cause of death.

Table 2. Whole blood concentrations of methadone in living addicts and in dead addicts, where methadone was the cause of death

	Number	Whole blood concentrations of methadone in mg/kg					
		Median	1. Quartil	3. Quartil	Mean	Minimum	Maximum
<i>BAC = 0</i>							
Living addicts	62	0.11	0.06	0.19	0.14	0.03	0.56
Dead addicts	59	0.28	0.19	0.43	0.43	0.06	3.09
<i>BAC ≥ 0.50 mg/g</i>							
Living addicts	35	0.09	0.06	0.19	0.15	0.03	0.90
Dead addicts	8	0.15	0.12	0.34	0.25	0.09	0.65

BAC = Blood alcohol concentration

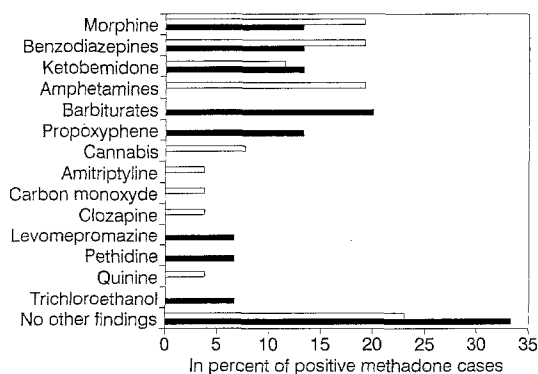
Table 3. Methadone whole blood concentrations in methadone positive dead drug addicts under or not under methadone maintenance

Methadone maintenance	Number	Whole blood concentrations of methadone in mg/kg					
		Median	1. Quartil	3. Quartil	Mean	Minimum	Maximum
Yes	11	0.43	0.19	0.59	0.47	0.03	1.24
No	11	0.22	0.06	0.37	0.27	0.03	0.99

Table 4. Methadone concentrations in muscle and liver from dead drug addicts, where methadone was the cause of death

	Number	Concentrations of methadone in mg/kg					
		Median	1. Quartil	3. Quartil	Mean	Minimum	Maximum
<i>BAC = 0</i>							
Muscle	11	0.15	0.12	0.31	0.21	0.09	0.43
Liver	71	1.92	1.27	2.72	2.40	0.59	14.5
<i>BAC ≥ 0.50 mg/g</i>							
Muscle	4	2.91	0.77	5.49	3.05	0.22	6.19
Liver	11	2.41	1.21	3.71	2.94	1.08	7.12

BAC = Blood alcohol concentration

**Fig. 2.** Other findings in percentage of the number of methadone positive dead drug addicts in Copenhagen City and County in 1981 and 1989, respectively. Ethanol not included. (■) 1981; (□) 1989

The presence of other compounds in the methadone-positive cases from 1981 and 1989 is shown in Figure 2.

Information of a methadone treatment was available in about half of the cases where methadone was the cause of death (Table 5).

Table 5. Methadone maintenance of the dead drug addicts in Copenhagen City and County in 1981 and 1989 respectively

Methadone found present	Year	Number	Methadone maintenance		
			Yes	No	Unknown
Yes as cause of death	1981	6	3	1	2
	1989	15	7	8	0
Yes but other cause of death	1981	9	6	1	2
	1989	11	5	6	0
No	1981	79	3	57	19
	1989	44	2	33	9

The blood alcohol concentrations (BAC) in the analysed cases are shown in Table 6.

Discussion

While in 1981 most deaths occurred in the age group 20–29 years in the total group of deceased drug addicts, in

Table 6. Blood alcohol concentrations (BAC) in the methadone positive and methadone negative dead drug addicts in Copenhagen City and County in 1981 and 1989 respectively

BAC mg/g	1981				1989			
	Methadone positive number	%	Methadone negative number	%	Methadone positive number	%	Methadone negative number	%
0	10	67	36	45	19	73	15	34
0 < BAC < 1.00	1	7	15	19	5	19	13	30
1.00 ≤ BAC < 2.00	2	13	16	20	1	4	11	25
2.00 ≤ BAC	0	0	6	8	0	0	5	11
Not determined	2	13	6	8	1	4	0	0
Total	15	100	79	100	26	100	44	100

1989 most deaths were seen in the age group 30–39 years (Fig. 1). However, the proportion of deaths due to methadone among the 20–29 age group was significantly higher in 1989 than in 1981 ($p < 0.01$, Fishers test). From Figure 1 it does seem, that the reverse is true with reference to the share of methadone deaths among the 30–39 age group in 1981 compared to 1989. However, this difference was not significant ($p = 1.0$, Fishers test).

In the fatal cases, where methadone was present, methadone alone was the cause of death in 50% more cases in 1989 than in 1981 (Table 1). The probable reason for this is that many more drug addicts were under methadone treatment in 1989 than in 1981. The cause of the many deaths may be that the difference between the blood concentrations seen in living persons and the blood concentrations of methadone found in deceased drug addicts is not very large. The median methadone concentration found in blood from living persons is 0.1 mg/kg and 0.3 mg/kg from dead persons, when no alcohol is present and no overlapping is seen between 3. quartil of the living and 1. quartil of the dead. The corresponding median blood concentrations in living and dead drug addicts, where alcohol was present (BAC ≥ 0.50 mg/g) are 0.1 and 0.2 mg/kg respectively, but here an overlap is seen between 3. quartil in the living and 1. quartil in the dead (Table 2).

The overlap between blood concentrations in living and dead persons is described by Segal and Catherman [2], who suggested that the cause of death could be an adverse effect of methadone. In 12 cases of death by methadone they found a methadone blood concentration of less than 0.5 mg/kg when taken orally, while in a control group of 8 cases in which the cause of death was unrelated to drugs, the blood methadone levels ranged from 0.3 to 0.6 mg/kg. Eight living addicts on methadone maintenance programs had methadone levels of 0.2 to 0.4 mg/kg.

The problem of overlap between the range of blood concentrations of victims of methadone overdosage and that of methadone maintenance subjects was also noticed by Baselt [3] who stated that it is difficult to distinguish between the two on this basis alone. For this reason a toxicological evaluation of the analytical results is not given at our institute without having the case history for support.

In 29 cases, where methadone only was evaluated to be the cause of death, Gottschalk and Cravey [5] found a methadone blood concentration range of 0.1–2.0 mg/kg. We have calculated the mean and the median of the 29 cases and found 0.5 and 0.3 respectively. Case no 511A with an exceptionally high methadone concentration in blood (33 mg/kg) was omitted. These results are in agreement with our findings where no alcohol was found. Garriott et al. [4] found methadone blood concentrations in the range of 0–1.4 mg/kg in 5 cases in which death was believed primarily to be due to methadone overdose.

It is interesting to note, that the median blood concentration of methadone in those deceased drug addicts who were known to have been under methadone treatment, was twice as high as the corresponding values in those who had not (Table 3).

Muscle and liver concentrations of methadone from cases where methadone was the cause of death are shown in Table 4. When no blood was available due to putrefaction we used muscle tissue instead, it being our experience that the concentrations in these materials are of the same magnitude [6]. According to Table 4 this is also the case for methadone when BAC = 0. When BAC ≥ 0.50 a higher value for methadone is seen in muscle tissue but this could be an artifact due to the low number of cases ($n = 4$).

Morphine and benzodiazepines were among the most frequently occurring other compounds in the methadone-positive cases. However, this is not a surprising as benzodiazepines are often prescribed in the methadone treatment. It would seem that the mixed use of morphine and benzodiazepines has risen from 1981 to 1989. Also the methadone treatment does not seem to have kept the drug addicts away from other drugs of abuse, where a change in the abuse pattern is seen. Amphetamine was among the most frequently occurring drugs in 1989, whereas it was not seen at all in 1981. In contrast, barbiturates and propoxyphene have disappeared completely in 1989 which shows that the restrictions for these compounds, which were introduced in Denmark in 1986 and 1989 respectively, has been successful (Fig. 2). Other compounds of abuse detected in deceased drug addicts who were under methadone treatment were similar to those who, according to the case stories, were not.

According to the case histories about half of the methadone-positive dead drug addicts had been under methadone treatment (Table 5), while the other half had supposedly obtained the methadone illegally. Less than 6% of the deceased drug addicts who were methadone negative had been under treatment with methadone, both in 1981 and in 1989.

Alcohol played no significant role in the death of the methadone-positive drug addicts as no alcohol was found in about 70% of the cases in both 1981 and in 1989 (Table 5).

One conclusion of this survey is that treatment with methadone does not keep drug addicts away from other compounds of abuse. Therefore drug addicts under methadone treatment should be controlled more closely than they are at present in Denmark.

References

1. Sundhedsstyrelsen (1991) Alkohol-og narkotikamisbruget 1985–1989. København, p 52
2. Segal RJ, Catherman RL (1974) Methadone – a cause of death. *J Forensic Sci* 19:64–71
3. Baselt RC (1978) Disposition of toxic drugs and chemicals in man, vol 1, centrally-acting drugs. Biomedical Publications, Canton, CO, pp 21–24
4. Garriott JC, Sturmer WQ, Mason MF (1973) Toxicologic findings in six fatalities involving methadone. *Clin Toxicol* 6 (2): 163–173
5. Gottschalk LA, Cravey RH (1980) Toxicological and pathological studies on psychoactive drug-involved deaths: Biomedical Publications Davis, CA, pp 263–279
6. Christensen H, Steentoft A, Worm K (1985) Muscle as an autopsy material for evaluation of fatal cases of drug overdose. *J Forensic Sci Soc* 25:191–206