METHADONE SUBSTITUTION THERAPY PROGRAM AND TOXICOLOGICAL STUDIES

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ABSTRACT: Methadone Substitution Therapy Program for opiate addicts at Nowowiejski Hospital in Warsaw lasted 6 years. During that time, 11424 drug of abuse analyses in urine probes were carried out by FPIA method on TDx Abbott analyser, to assess objectively methadone treatment efficacy. The results of toxicological studies indicate to a decrease of positive results (24–34% according to the drug in 1993 and 2.4–7.4% in 1997) in the first 5 years of the execution of the Program. But in the last year of the studies (1998) more opiates (9%), amphetamines (7.8%) and barbiturates (4.6%) were detected in urine of the patients.

KEY WORDS: Methadone; Drug of abuse; Opiates; Amphetamine.

Problems of Forensic Sciences, vol. XLIII, 2000, 164–170
Received 9 September 1999; accepted 16 May 2000

INTRODUCTION

Detection of drugs of abuse and their metabolites in body fluids plays a very important role in various aspects of drug abuse and drug dependence. Drug of abuse testing in urine of drug addicts is used by drug treatment facilities to:

- diagnose drug addiction,
- monitor detoxification treatment,
- evaluate objectively the success of rehabilitation and pharmacological maintenance treatment programs [6].

Methadone is a synthetic analgesic drug used as a substitution treatment for opiate addicts and in the treatment of pain. The efficacy of orally administrated methadone for opiate dependence has been demonstrated in many studies: i.e. it reduced illicit drug use, risk of HIV infection, mortality crime and unemployment [1, 3, 4].

There were several reasons for starting Methadone Treatment Programs (MTP) in Poland [10]:

1. Increasing number of HIV-infected drug users taking intravenously “compotte” (Polish “kompot”), a home-made opiate mixture.
2. Testing performed in intravenous drug users (IVDUs) showed progressive immune deficiency.

3. HIV(+) opiate addicts treated in the Infectious Diseases Unit created problems for the staff and frequency interrupted their treatment.

According to the last communication on HIV infections and AIDS cases registrationin Poland [2] the first case of HIV- seropositvity was recorded in Poland only in 1986. Since the beginning of blood testing in Poland the following data have been obtained: 5810 HIV carriers have been found and 3779 of them (65%) have been IVDU's. Among 794 cases of AIDS recorded in Poland since 1986, there were: 460 IVDU's (58%) and 334 others homosexuals and heterosexuals (42%). 442 persons with AIDS diagnosis was dead.

Since February 1, 1993 the methadone hydrohloride for both detoxification and maintenance treatment of home-made opiates dependent patients has been introduced in Nowowiejski Hospital in Warsaw.

Testing for drugs of abuse in urine of patients enrolled in Methadone Treatment Program (MTP) is required as an objective assessment of their progress toward discontinued drug use.

The purpose of this study was to present the significance of toxicological studies in scope of objective assessment of the effectiveness of methadone substitution therapy.

MATERIAL AND METHODS

Material of this study consisted of urine specimens obtained from 189 patients enrolled to MPT in Methadone Clinic at Nowowiejski hospital in Warsaw, which patients are visiting every day (except Sunday) receiving her/his maintenance dose 93 ± 22 mg/day (20–130 mg/day).

Urine specimens were collected (under nurse's supervision) and tested for drugs of abuse (DA) by fluorescence polarisation immunoassay (FPIA method) on TDx Abbott.

As positive results the values equal or greater then Minimum Allowable Threshold (factory set cut-off) were accepted [5].

Specimens of patients from MPT were taken at random, but usually once a month. Most of the specimens were tested for opiates, benzodiazepines and barbiturates. In the case of additional diagnosis of amphetamines abuse and suspicion of amphetamines or cannabinoids use appropriate drug determinations were provided. The results were compared with clinical records to estimate their utility and demonstrate the concept of their use and interpretation. In the case of too high background of the sample (Mx BKG) routine urine analyses were provided.

Data on patients enrolled into MPT at Nowowiejski Hospital in Warsaw are shown in Table I and II.

TABLE I. CHARACTERISTICS OF PATIENTS ENROLLED INTO MPT (1993–1998)

1. Number of patients enrolled:		
Total: 189 subjects	140 males	
		49 females
Age: 34.2 ± 5.4 (22–47) years		
2. Drug dependence diagnosis:		
2.1. Opiate dependence		42 subjects (22%)
2.2. Mixed drug dependence		147 subjects (78%)
(opioids, benzodiazepines and barbiturates)		
3. Additional diagnosis:		
3.1. Amphetamine abuse:		57 subjects
3.2. Alcohol abuse:		14 subjects
3.3. Endogenous psychiatric disorder:		17 subjects
3.4. Toxic liver damage (elevated GGT):	52 subjects	
3.5. History of syphilis:		20 subjects
3.6. Lung TBC:		18 subjects
4. Anti-HIV antibodies testing results:		
4.1. HIV carries		136 subjects (72%)
4.2. Negative results	53 subjects (28%)	
5. AIDS diagnosis:		
5.1.Occurrence and clinical manifestation of AIDS (HIV encephalophathy, lung TBC, Kaposi sarcoma, cerix malignancy, CNS toxoplasmosis)		41 subjects (22%)
5.2. Immunological manifestation (CD4 < 200 µl)	47 subjects (25%)	

During 6 years (1993–1998) in total 189 patients were enrolled. Only 42 subjects had opiate dependence diagnosis (22%) and remaining 78% had diagnosis of mixed drug dependence (n = 147). Additional diagnosis of drug abuse had 71 patients (among them 80% abuse amphetamines and 20% abuse alcohol). The percentage of HIV carriers (72%) and patients with AIDS diagnosis according to clinical and immunological manifestations (22% and 25%) was very high.

TABLE II. DATA ON PATIENTS PARTICIPATING IN MTP IN 1998

1. Number of patients participating in MTP:		
Total: 77 subjects	24 females	
		53 males
2. Number of new patients enrolled	28 subjects	

3. Number of discontinued patients	20 subjects
4. Duration of participation in the project (persons who did not interrupt the therapy)	
4.1. Less than 1 year	24 subjects
4.2. Over 1 year	5 subjects
4.3. Over 2 years	16 subjects
4.4. Over 3 years	32 subjects
5. HIV- seropositivity	53 subjects (69%)
AIDS diagnosis	12 subjects (16%)
6. Double psychiatric diagnosis (drug dependence + endogenous psychiatric diagnosis)	10 subjects (13%)
7. Social conditions	
Employed	38 persons (49%)
Learning at school	3 persons (4%)
Unemployed	36 persons (47%)

In the last year of the study in MPT participated 77 patients: 28 persons were enrolled for the first time and 20 persons discontinued methadone treatment. Duration of participation in the project varied from several weeks to over 5 years.

In the case of 10 patients (13%) a double psychiatric diagnosis was stated. More then 50% of MPT patients were employed or were learning at school despite of progression of HIV infection.

RESULTS

Since February 1, 1993 till December 31, 1998 the Methadone Treatment Program lasted about 6 years. During that time 11424 toxicological analyses were performed. In this number:

- 3411 (30%) were analyses of opioids,
- 2451 (21%) of benzodiazepines,
- 2581 (23%) of barbiturates,
- 2746 (24%) of amphetamines,
- 235 (2%) of cannabinoids (data from years: 1997 and 1998).

The results of the toxicological studies are shown in Table III and Figure 1.

TABLE III. ABSTINENCY CONTROL IN MTP AT NOWOWIEJSKI HOSPITAL IN WARSAW 1993–1998

Drug of abuse	Year	Positives [%]	
		All	High

Opiates	1993	26,0	13,5
	1994	16,7	9,3
	1995	6,8	2,1
	1996	3,5	1,7
	1997	2,6	1,5
	1998	9,0	4,8
Benzodiazepines	1993	34,0	6,0
	1994	21,2	3,3
	1995	6,0	0,2
	1996	3,6	0,2
	1997	3,6	0
	1998	3,7	0
Barbiturates	1993	24,3	11,8
	1994	15,4	6,7
	1995	4,9	0,8
	1996	1,9	0,7
	1997	1,4	0
	1998	4,6	1,0
Amphetamines	1993	40,0*	45,0
	1994	25,4	12,1
	1995	7,2	2,5
	1996	4,2	2,8
	1997	7,4	4,0
	1998	7,8	3,1

* Only 20 determinations.

The results of the toxicological studies indicate to a decrease of the percentage of positive results in the first 5 years of the execution of the Program [7]. It means gradual and the significant increase of MPT efficacy concerning the abstinence from opioids, benzodiazepines and barbiturates. But the amphetamines positives was on increase during last 2 years. Except of the results of benzodiazepines, the results of other analyses in the last are less satisfactory. Possible reason of this outcome may be worsening of the health state of the participants and the lack of motivation for maintaining the abstinence from drugs of abuse.

In 78 urine samples (from 42 patients) tested during 6 years observation period it was not possible to determine drugs of abuse by FPIA method because of very high background (M x BKG). Routine analyses of such urine samples showed: bilirubin – positive, URB: higher than 33 mM/l, BLD: ca 200 RBC/ml, LEU: ca 15/ml. This observation may indicate on limitation of application of immunochemical methods for drug of abuse testing in biological fluids of HIV infected drug addicts [9].

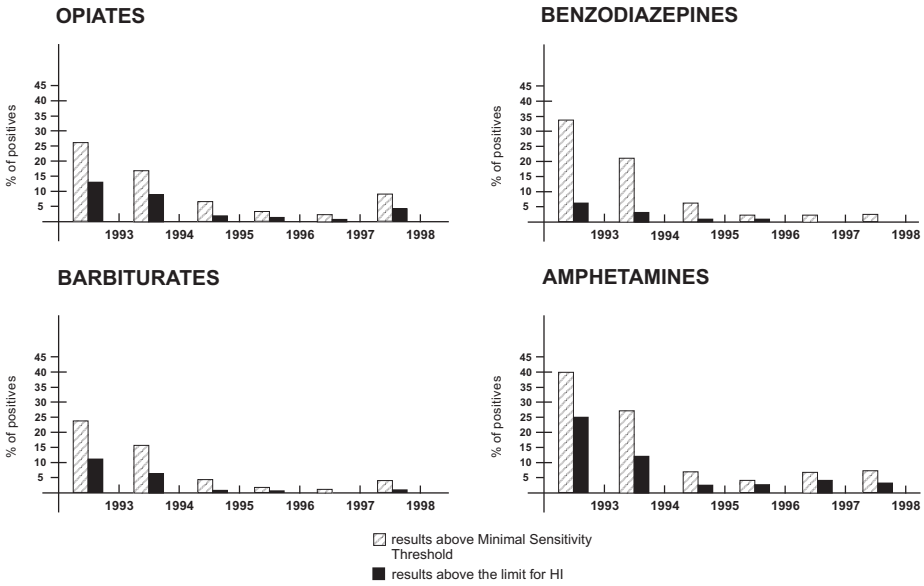

Fig. 1. Results of toxicological studies in MPT 1993–1998.

CONCLUSIONS

1. The obtained findings show that the FPIA method is very useful in the objective assessment of the efficacy of methadone treatment, on the condition that one is aware of the possibilities and limitation of this method.
2. There is an urgent need to use reference methods (GC, HPLC, GC/MS), in the clinical practice, especially in biological fluids of HIV infected patients.
3. Results of toxicological studies should be always interpretedin a wide clinical context.

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