SHORT REPORT

Predictors of adherence to tuberculosis treatment in a supervised therapy programme for prisoners before and after release

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ABSTRACT: The prison population is a high-risk group for tuberculosis (TB). This investigation aimed to study predictive factors of treatment adherence among prisoners involved in a pilot programme of supervised treatment.

The study included TB patients from the Men's Penitentiary Center of Barcelona (MPCB) in 1995. Directly observed therapy (DOT) was carried out in the infirmary or in a methadone programme. Released prisoners were referred to the municipal maintenance methadone programmes (MMP) and other social resources. Incentives and enablers were used to improve compliance (economic aid for nutritional and housing needs, methadone programmes and admittance to a sociosanitary centre). The outcome of the patients' adherence was classified as follows: completed, defaulted, dead or transferred out. Factors associated with adherence were investigated through logistic regression.

The programme included 62 patients, 43 of whom were intravenous drug users (IVDU) and 46 were infected with the human immunodeficiency virus (HIV). Nineteen had previously had TB and 32 were released from prison during TB treatment. Overall adherence was 89%; 97% among those who completed treatment in prison, and 79% among those who completed treatment outside prison ($p=0.05$). Ninety-five per cent of IVDU in an MMP completed treatment. Homeless or alcoholic ex-prisoners completed treatment only if they were admitted to sociosanitary centres. DOT throughout treatment resulted in better adherence (odds ratio (OR)= 16.80; confidence interval (CI): 2.42–116.2). Those who were incarcerated throughout treatment also showed better adherence (OR= 7.36; CI: 0.79–48.16).

Antituberculosis treatment adherence in prisoners was high even after release with adequate co-ordination among intrapenitentiary and extrapenitentiary programmes. Maintenance methadone programmes proved very useful in intravenous drug users, as did admittance to sociosanitary centres for indigent or alcoholic ex-prisoners undergoing treatment.

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The prison population is considered a high-risk group for tuberculosis (TB) disease and infection. Even in countries with low prevalences of TB, incidence rates in prisons are always much greater than in the general population [1–3].

In Spanish prisons, 40% of the incarcerated population are intravenous drug users (IVDU) [4]. IVDU were at risk for TB even before the appearance of the human immunodeficiency virus (HIV) [5] and HIV now affects 60–65% of IVDU prisoners or 25–40% of the total prison population [6]. Given the high percentage of IVDU and the frequently resulting HIV infection, there consequently is a high prevalence of *Mycobacterium tuberculosis* and HIV co-infection, estimated at around 20% in some prisons [7]. Although TB is not exclusive to Spanish inmates [1, 2, 8], it has been calculated that TB is 30 times more frequent among 15–45 yr olds in Spanish prisons than among the same age group in the population at large [4].

Both the Centers for Disease Control (CDC) [9] and, in Spain, the Conference of National Consensus for the Control of Tuberculosis have indicated the important role that prison can play in the prevention and control of TB [3]. Nevertheless, anti-TB programmes find abandonment of treatment, especially among IVDU, a major problem [10]. This is the main cause of TB relapse and resistance to the usual anti-TB drugs, a problem which is growing in the USA and is of great concern worldwide [8, 10, 11]. However, as some authors have stated [10–12], poor adherence to treatment can be modified by highly motivated health teams applying measures to ensure that medication is taken.

The objectives of this study were to determine the adherence rate to TB treatment (overall and in subgroups) and to study predictive factors of adherence to TB treatment in prisoners involved in a pilot programme based on incentives and good co-ordination among intrapenitentiary and extrapenitentiary TB programmes.

Subjects and methods

The study included all prison inmates diagnosed with TB after systematic screening upon incarceration or during their prison stay in the Men's Penitentiary Center of Barcelona (MPCB) in 1995. To guarantee follow-up and avoid case losses once the patients were released from prison, the study was restricted to residents of Barcelona. This required good co-ordination between the TB programme of MPCB and the city's prevention and control programme.

The co-ordinated activities of the health services inside and outside the prison were based on the work of a male public health nurse of the Barcelona TB Programme who visited the prison on at least 1 day per week to review and discuss the patients with the staff of the TB programme of MPCB. This nurse followed up released prisoners, visiting their homes or sociosanitary centre and finding housing for them when necessary. Each patient was individually evaluated in order to select the best incentive. Confidential linkage between several registers, such as the Barcelona TB register and the acquired immunodeficiency syndrome (AIDS), Drug Users and Mortality registers, enabled deaths to be detected.

Screening began with the tuberculin skin test upon admission to the prison. The HIV test was voluntary for all new inmates. Those with a positive result (induration ≥ 5 mm), as well as any HIV-positive patients suspected of cutaneous anergy, underwent a radiological examination at the MPCB. Where clinical evidence was found or suspicious chest radiographic images were taken, followed by a microbiological sputum examination (Ziehl-Neelsen and Lowenstein). TB diagnosis was based on standard criteria [3]. TB cases were classified according to the recommendations of the World Health Organization (WHO), based on smear and culture results [13]. HIV infection was determined by a positive enzyme-linked immunosorbent assay (ELISA) and confirmed by Western blot.

TB cases detected during screening, along with those diagnosed during the study period among those already incarcerated, were included in a programme of supervised therapy. Four-drug therapy, as recommended by the National Conference of Consensus for the Control of Tuberculosis in Spain [3], was administered for 9 months in the HIV-positive and 6 months in the HIV-negative subjects, 2 months with isoniazid, rifampin, pirazinamide and ethambutol (2HRZE) followed by 4 or 6 months with rifampin plus isoniazid (4RH or 6RH). Patients were considered to have abandoned treatment when they had stopped taking medication for more than 3 consecutive days and it was not possible to incorporate them back into the programme. Directly observed therapy (DOT) was the rule in prison. DOT was considered to be partial when the supervision of therapy was discontinued after release.

The following incentives were used to improve adherence. 1) IVDU were placed on a municipal maintenance methadone programme (MMP) in and out of prison. A place on MMP was reserved for those released during TB treatment. These patients were given TB medication before their methadone. 2) Economic aid for the nutritional and housing needs of ex-prisoners was allocated. 3) Admission to sociosanitary centres was offered to homeless and/or alcoholic ex-prisoners.

To determine the predictive factors for treatment adherence, the patients who completed the treatment were

compared with those who defaulted, while analysing the influence of sociodemographic variables (age, race or ethnic group, place of birth, indigence and alcoholism), clinical variables (TB antecedence and HIV infection) and drug-related variables (substance, method of drug use and treatment with methadone). To determine the rate of adherence to treatment in different groups (IVDU, indigents, *etc*) treatment adherence rates (completed $\times 100$ /completed + defaulted) were calculated for the total number of patients and for several subgroups.

The study was closed on 31 December 1996. Data were analysed using the statistical package SPSS (SPSS Inc., Chicago, IL, USA). Predictive factors for anti-TB treatment compliance were examined with epidemiological graphics, estimation and testing (EGRET; Statistics and Epidemiology Research Corporation, Seattle, WA, USA) [14] programme. A multivariate analysis through the logistic regression model was performed for those variables that were statistically significant ($p < 0.05$) on a univariate level (Chi-squared and Fisher exact tests), calculating odds ratios (OR) with 95% confidence intervals (CI).

Results

In total 62 TB patients were studied. They were chosen from a total of 93 cases detected from three sources: out of 3,504 prison admissions, 67 TB cases appeared (a prevalence rate of 1,912/100,000), 39 more were identified in extrapenitentiary detections and 26 TB cases were found among those already incarcerated. The 62 in question were all residents of Barcelona, and given the conditions of the correctional facility, all males, with an average age of 34 yrs (± 8). Nineteen (31%) had previously had TB. Thirty-two (51%) had been released from prison before completing TB treatment. According to WHO classification, 39% were smear-positive pulmonary, 52% smear-negative pulmonary and 10% extrapulmonary. Forty-three (69%) were IVDU, 46 (74%) HIV-positive, and 15 (24%) HIV-negative, and for one it was impossible to perform the serology test. Comparing the HIV-positive with the HIV-negative TB patients, the former were younger, more likely to be IVDU and had had extrapulmonary TB. No statistically significant differences were found for place of birth, ethnic group or TB antecedence (table 1).

Six patients (10%) defaulted from treatment, six (10%) died and three (5%) were transferred out. The overall adherence rate was 89%: 97% within prison and 79% outside prison ($p = 0.06$). Among the 31 IVDU included in MMP the adherence rate was 95% (100% inside and 90% outside prison). For the 22 non-IVDU, adherence was 81% (92% inside and 70% outside) (table 2). It is worth noting that the five patients who were either homeless or alcoholic and who were admitted to a sociosanitary centre all completed treatment, whereas the three for whom admission was impossible all abandoned treatment.

The predictive factors associated with better adherence (table 3) in the univariate analysis were incarceration throughout treatment ($p = 0.05$) and continuous supervision on DOT ($p = 0.002$). The factors that were not statistically associated were patient's origin (Spanish *versus* other), HIV infections (seropositive *versus* seronegative) and location of methadone treatment (inside *versus* outside prison). The multivariate analysis (table 3) confirmed the importance of continuous DOT, either inside or outside prison

Table 1. – Distribution of tuberculosis (TB) cases according to several variables and human immunodeficiency virus (HIV) infection*

Variable	HIV(+) (n = 46)		HIV(-) (n = 15)		OR (95% CI)	p-value
	n	%	n	%		
Average age yrs (SD)	33 (6.1)		41 (11.2)			0.001
Origin						
Spanish	40	80	10	20	3.33 (0.65–16.03)	0.11
Others	6	55	5	45		
Ethnic group						
White	39	80	10	20	279 (0.56–12.72)	0.14
Other	7	58	5	42		
IVDU						
Yes	42	100	0	0	Undefined	<0.0001
No	4	21	15	79		
Previous TB						
Yes	15	79	4	21	1.33 (0.32–6.37)	0.75
No	31	74	11	26		
TB						
Pulmonary	30	67	15	33	0.0 (0.00–0.62)	0.006
Not pulmonary	16	100	0	0		

*: In one case it was not possible to perform a HIV serology test. OR: odds ratio; CI: confidence interval; IVDU: intravenous drug user.

(OR=16.80; CI: 2.42–116.2) and the entire treatment administered during prison stay (OR = 7.36; CI: 0.79–68.16) as predictors of greater adherence to anti-TB treatment.

Discussion

TB in prisons is a serious public health problem. The present study, and similar studies [7] revealed a prison TB prevalence rate of 2,000/100,000 inmates. This study demonstrates that with good co-ordination among intrapenitentiary and extrapenitentiary programmes a high rate of adherence to TB treatment (97% in prison and 79% after release) could be achieved. Continuous DOT inside and outside prison was found to be the best predictor of compliance with TB treatment in this difficult population.

The WHO calculated that between 1990 and 1999, 90 million new cases and 30 million death, the majority in developing countries, will occur unless appropriate measures such as supervised therapy programmes [15] are put into action. In poor countries it is estimated that every year there are 400 new cases per 100,000 inhabitants. In Africa and south-east Asia, recent years have seen a serious rise in incidence [16]. Developed countries have also witnessed high incidences in pockets of large cities and in

correctional facilities [2, 9, 16, 17]. In the USA the incidence of TB had been falling until 1984, but between 1985 and 1992 there was a 20% [17] increase, due to HIV infection. Worldwide, an estimated 6 million people are co-infected with HIV and TB. In Spain, one of the European countries that is most affected by AIDS and TB [18], the incidence of TB is 40–60/100,000 [19, 20] and the situation within prisons is always much worse.

Although TB is both preventable and curable with correct therapy, it requires a prolonged treatment period, too often resulting in nonadherence. In 1994, only 53% of IVDU [20] in Barcelona (the site of the penitentiary centre chosen for this study) completed anti-TB therapy. Homeless and alcoholic subjects also had a low adherence to treatment [21]. Abandonment causes relapses and on occasion, microepidemics of drug-resistant TB, particularly among HIV-positive patients, as much in the community [22, 23] as in prisons [7, 24]. If anti-TB treatment adherence is similar to that of the general population for any other therapy (50%) [25], the situation could become extremely serious in the coming years. Therefore, it is advisable to offer incentives [21] to poor adherence groups. It has even been debated whether hospital admission [26] be required or legal action taken to detain noncompliant patients [27], so that DOT can be ensured. Both the WHO

Table 2. – Adherence rate according to risk factor and place of completion of treatment

Risk factors	In prison			Out of prison			Global AR
	Completed		AR	Completed		AR	
	Yes	No	%	Yes	No	%	
IVDU	17	0	100	12	2	86	94
In MMP	11	0	100	9	1	90	95
Not in MMP	6	0	100	3	1	75	90
Homeless	8	0	100	5	3	63	81
Resident*							
Yes				5	0	100	100
No				0	3	0	0
Others	3	1	75	2	0	100	83
Total	28	1	97	19	5	79	89

*: Sociosanitary residential centre. AR: adherence rate; IVDU: intravenous drug user; MMP: maintenance methadone programme.

Table 3. — Study of factors associated with adherence to antituberculosis treatment in inmates

Variable	Completed		Defaulted		OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
	n	%	n	%				
Origin								
Spanish	37	86	6	14	0.00 (0.00–3.75)	0.26	–	
Other	10	100	0	0				
HIV infection								
Yes	35	92	3	8	1.94 (0.14–18.95)	0.40	–	
No	12	86	2	14				
Entire treatment*								
Yes	28	97	1	3	7.37 (0.72–360.6)	0.05	7.36 (0.79–68.16)	0.07
No	19	79	5	21				
Methadone								
In prison	11	95	0	5	Undefined	0.47	–	
Out of prison	9	85	1	15				
DOT [†]								
Yes	12	100	0	0	Undefined	0.002	16.80 (2.42–116.2)	0.004
No	0	91	3	9				

*: administered during prison stay; †: continuous DOT in or outside prison. DOT: directly observed therapy; HIV: human immunodeficiency virus; OR: odds ratio; CI: confidence interval.

and the American Thoracic Society [28] recommend DOT as a demonstrated way to reduce treatment nonadherence, relapses and anti-TB drug resistance [11].

It is important to take into account that the present study dealt with typically poor-adherence groups (62% were IVDU and 28% were either homeless and/or alcoholic), and that a high percentage of patients (31%) had previously had TB and most had probably never completed treatment. There was an adherence rate of 89%, which was far higher than that for these groups in Barcelona and in line with the rate for the city as a whole (90%) [20]. Such high adherence was achieved with incentives and enablers for the affected people and, most importantly, with the collaboration of the entities attending these generally low-adherence groups (prisons, drug-dependence centres and the Barcelona TB control programme). All of these contributed to keeping patients on treatment. The study depended on workers from public assistance facilities and only US\$2,000 was needed for economic aid, a far lower cost than that calculated in other studies as the real cost incurred when treatment is abandoned [29].

Adherence within prisons, all but guaranteed with motivated health teams, was outstanding. The best incentive for IVDU was not economic, but rather inclusion in an MMP. Ninety-five per cent of users completed treatment under such conditions, a higher percentage than in New York, with a similar population [30]. For homeless or alcoholic patients, adherence was good in prison, but null upon release, except when patients were given shelter in socio-sanitary centres that could ensure DOT. Of note is that no statistically significant difference appeared in compliance between Spanish and foreign patients, thus dispensing with the need to adopt measures based on demographic factors, which could give rise to discriminatory attitudes [31].

In conclusion, tuberculosis in prison should be controlled through directly observed therapy programmes that ensure adherence, especially in low-adherence groups such as intravenous drug users, alcoholics and the homeless. Collaboration among both intrapenitentiary and extrapenitentiary tuberculosis programmes is essential in achieving high rates of adherence to antituberculosis therapy, since patients frequently are released from prison before the completion of treatment (52% in the present case). Main-

tenance methadrome programmes are highly effective for adherence among intravenous drug users, and are also very useful in preventing infection with the human immunodeficiency virus, as they break the habit of sharing injection material [32, 33]. Homeless and alcoholic tuberculosis patients must be admitted to sociosanitary centres to follow-up directly observed therapy if they are released from prison before antituberculosis treatment is completed.

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