

Efficacy of DOTS strategy in treatment of respiratory tuberculosis in Gorgan, Islamic Republic of Iran

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نجاحة استراتيجية المعالجة القصيرة الأمد تحت الإشراف المباشر في معالجة السل التنفسي في مدينة غورغان الإيرانية

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الخلاصة: أُجريت دراسة على مدى عامين، لمتابعة 260 من المرضى الأتراب الإيجابي للطاخة (178 منهم يتلقون المعالجة بحسب استراتيجية المعالجة القصيرة الأمد تحت الإشراف المباشر؛ و82 منهم لا يتلقون المعالجة بهذه الاستراتيجية)، وذلك لتقييم فعالية هذه الاستراتيجية في معالجة السل. وكان جميع المرضى قد عانوا من السعال لمدة تزيد على 3 أسابيع قبل بدء الدراسة؛ وكانت نسبة 91.9% مصابين بالحمى، و60.8% منهم يعانون من البلغم؛ وكان لدى 27.7% منهم سوابق عائلية إيجابية للإصابة بالمرض. وبلغت نسبة إخفاق المعالجة بالاستراتيجية المنقذة 9% في نهاية الشهر الثاني، و1.7% في بداية الشهر الخامس. أما المجموعة الشاهدة، فقد بلغت نسبة إخفاق المعالجة فيها 18.3% في نهاية الشهر الثاني، و7.3% في بداية الشهر الخامس. وخلصت الدراسة إلى أن استراتيجية المعالجة القصيرة الأمد للسل تحت الإشراف المباشر تعزز نسبة النجاح في معالجة السل بشكل كبير ($P < 0.05$).

ABSTRACT We carried out a follow-up cohort study of 260 smear-positive patients [178 on directly observed treatment, short-course (DOTS); 82 on non-DOTS] over a 2-year period to evaluate the efficacy of the DOTS strategy in treatment of tuberculosis (TB). All the patients had had cough for > 3 weeks; 91.9% had fever, 60.8% of them with sputum; and 27.7% had a positive family history. The rate of treatment failure with DOTS was 9.0% at the end of the 2nd month and 1.7% at the beginning of the 5th month. In the control group these rates were 18.3% and 7.3% respectively. The DOTS strategy significantly increased the success rate of TB treatment ($P < 0.05$).

Efficacité de la stratégie DOTS dans le traitement de la tuberculose pulmonaire à Gorgan en République islamique d'Iran

RÉSUMÉ Nous avons conduit une étude de cohorte portant sur 260 patients à frottis positif (178 sous traitement de brève durée sous surveillance directe [DOTS, pour *Directly Observed Treatment, Short-course*] et 82 sous traitement non-DOTS) sur une période de 2 ans afin d'évaluer l'efficacité de la stratégie DOTS dans le traitement de la tuberculose. Tous les patients toussaient depuis plus de 3 semaines, 91,9 % d'entre eux étaient fébriles, 60,8 % présentaient des expectorations et 27,7 % une histoire familiale positive. Le taux d'échec thérapeutique sous DOTS était de 9,0 % à la fin du 2^e mois de traitement et de 1,7 % au début du 5^e mois. Dans le groupe témoin, ces taux étaient respectivement de 18,3 % et de 7,3 %. La stratégie DOTS a entraîné une augmentation significative du taux de succès thérapeutique du traitement antituberculeux ($p < 0,05$).

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Introduction

Tuberculosis (TB) is the most common infectious disease worldwide, and causes the death of about 2–3 million people each year [1].

Incidence of TB has increased dramatically recently and a high prevalence of respiratory disease has been reported during recent years [2]. These reports most commonly come from developing countries. Factors involved in the increased number of TB cases include poverty, immigration, poor health facilities and drug abuse [3]. In addition, irregular use of antituberculosis drugs, incorrect dosage, poor knowledge among general physicians, improper attention of doctors, and drug resistance of *Mycobacterium tuberculosis* can be factors in treatment failure [4]. Studies done throughout the world show that by using the directly observed treatment, short-course (DOTS) strategy, the success rate of treatment is about 90%–95%, or even greater [5]. According to the same studies, even in industrialized countries and among knowledgeable and educated individuals at least 30% of patients, owing to a perception of improvement, do not take their medication properly and discontinue treatment after a while. In the DOTS strategy, in addition to direct observation of drug consumption, having a standard regimen for treatment and follow-up of patients improves the success rate. Conversely, for the reasons outlined above, treatment regimens other than DOTS have a low success rate, and may lead to TB transmission in the community and mycobacterial drug resistance [5].

Prevalence of TB in the Islamic Republic of Iran is about 39 per 100 000 [6]. Prevalence in Golestan province, where this study was carried out, is quite high, the second highest in the country [7].

The aim of this study was to evaluate the efficacy of the DOTS strategy in reducing the failure rate of TB treatment in comparison with the conventional strategy. The clinical and epidemiological features of 260 smear-positive respiratory TB patients in Gorgan were studied for a period of 2 years.

Methods

We carried out a follow-up cohort study to investigate the epidemiologic and clinical efficacy of DOTS strategy in treatment of TB patients in residential areas of Gorgan: a few areas classified as rural and one area classified as urban. All new patients (having had no prior treatment for TB) presenting to the health services during the period 1998–2000 whose respiratory specimens were smear-positive were included in the study. It should be noted that the rural area in this study was immediately adjacent to the urban area, therefore, the DOTS and the non-DOTS groups were comparable.

All the new cases of TB in the patients we studied had been diagnosed with sputum smear-positive tests using the Ziehl–Nielsen technique. The 178 patients in the rural areas were kept on the DOTS regimen (i.e. the drugs were dispensed in the health centre by a health worker, who observed the drugs being taken) in accordance with the national protocol (DOTS is obligatory in rural areas but optional in urban areas). The 82 patients in the urban areas (control group) were treated using a non-DOTS strategy, i.e. the same drug regimen was used and the drugs were dispensed in the health centres but patients consumed them at home; there was no observation of their taking the medication.

All of the new TB cases underwent a 6-month treatment regimen according to

the World Health Organization protocol: 2 months with 4 drugs (isoniazid, rifampin, pyrazinamide, ethambutol) and 4 months with 2 drugs (isoniazid, rifampin) [8]. In the DOTS group, these drugs were given to fasting patients by trained health workers in 15 health centres every morning. In the non-DOTS group, the drugs were taken by the patients themselves without any observation of consumption.

During the treatment period, sputum samples were taken at the end of the 2nd month and the beginning of the 5th month. Patients who were smear-positive after the 2nd month had an extra month on the 4-drug regimen. Those smear-positive at the beginning of the 5th month were considered treatment failures. In these cases, drug resistance was suspected and samples were sent to the Tuberculosis and Respiratory Disease Research Centre in Masih Daneshvari Hospital, Tehran for further investigation.

Results were entered into SPSS, version 11, statistical software and analysed using χ^2 and Fisher's exact tests, with $P < 0.05$ considered statistically significant. Age, sex, clinical manifestation, TB in the family and also the treatment results (sputum smear status after 2 months and at the beginning of the 5th month) were recorded.

Results

A total of 260 smear-positive patients were diagnosed during the study period. The clinical manifestations of TB are presented in Table 1. There were more females (51.5%) than males. The largest age group was females aged 15–24 years. There were no significant differences between the 2 groups with regard to age, sex, socioeconomic status or nationality.

Of the 178 patients who were under treatment using the DOTS strategy, 3 (1.7%)

Table 1 **Observed clinical manifestation of tuberculosis in patients in Gorgan (1998–2000)**

Clinical manifestation	No. (n = 260)	%
Cough	260	100.0
Fever	239	91.9
Sputum	158	60.8
Family history	72	27.7
Haemoptysis	44	16.9

were still smear-positive at the beginning of the 5th month. Of the 82 patients who were on the non-DOTS regimen, 6 (7.3%) were still smear-positive at the beginning of the 5th month (Table 2).

In the DOTS group, 91.0% were smear-negative at the end of the 2nd month and 98.3% at the beginning of the 5th month. In the non-DOTS (control) patients without direct observation, the corresponding values were 81.7% and 92.6% ($P < 0.05$).

Discussion

Through numerous studies and experience in various situations, it is now widely accepted that the most important cause of failure in TB treatment programmes is irregular drug-taking by patients, which is a direct consequence of poor motivation [5]. A successful, cost-effective, community-based programme of directly observed therapy, using volunteers, clinic staff and community health workers or trained personnel can help ensure adherence to therapy [9].

This is the first report about the efficacy of DOTS strategy in Golestan province in the Islamic Republic of Iran. The rate of negative smears at the beginning of the 5th month is an excellent index for evaluating the efficacy of TB treatment. Treatment

Table 2 Comparison of treatment failure rate in patients on the DOTS and the non-DOTS regimens

Treatment regimen	End of 2nd month				Beginning of 5th month ^a				Total
	Treatment failure		Conversion rate		Treatment failure		Conversion rate		
	No.	%	No.	%	No.	%	No.	%	
DOTS	16	9.0	162	91.6	3	1.7	175	98.3	178
Non-DOTS	15	18.3	67	81.7	6	7.3	76	92.7	82

^aP < 0.05, Fisher exact test.

failure in patients on the DOTS strategy was much lower than in the non-DOTS group. This correlates well with the results of studies done in other Asian countries [10–15].

In a study in China with a large sample population the treatment failure rate in patients under the DOTS strategy was 6.2% [12]; in our study we had better results with patients on the DOTS strategy.

In Iraq treatment failure in patients under the DOTS strategy was 2.0% and in the control group it was 5.8%, which is agreement with our findings, and emphasizes the importance of the DOTS strategy [14]. Murali and Udaya also reported a lower treatment failure rate among DOTS patients, 9% compared to 47% in the non-DOTS group, although the failure rate in our study was lower than theirs [15].

Although these differences were not statistically significant, there is a basis for further investigation. In our study, the highest rate of infection was among the younger age group, 15–24 years; in a study done in Canada, the highest rate of infection was in those > 65 years [16]. Given that in industrialized countries TB is mostly the reactivated form of primary infection [17], the high prevalence in older age groups may be a result of weaker immunity in those patients. All the patients in our study were, however, new TB cases.

The clinical syndrome in this study (sputum, cough, fever, haemoptysis) had a good

correlation with a previous study [18]. The most common clinical manifestation was cough, which was also found in other studies [13,15,16].

In accord with those of other investigations, the findings of this study demonstrate the effectiveness of the DOTS strategy in treatment of TB patients. Considering conversion rates, our study showed a better efficacy in the DOTS group compared to some studies from other countries, such as a study in India which showed a 90% success rate with the DOTS strategy compared to 81% for the control patients [11]; in a study done in Iraq, the treatment success rate with the DOTS strategy was 96.2% but 76.2% in the control group [13].

In 27.7% of cases there was a positive family history of TB. This agrees with the findings of a study from Masih Daneshvari teaching hospital in Tehran (26.9%) [18]. Therefore, family members of infected patients also need to be checked. In a study in Pakistan it was reported that only 8.5% of family members of TB patients had the disease itself. It is nevertheless an important point to be taken into consideration when managing TB patients [19].

Recommendations

The DOTS strategy is an excellent way to reduce treatment failure, therefore, the

health system authorities in our country should make every effort to get the cooperation of all the relevant organizations (both private and public sector) to implement the DOTS strategy suggested by the World

Health Organization. It is also a safe and effective way of controlling and preventing multidrug resistance in *Mycobacterium tuberculosis*.

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