THE OUTCOME OF TUBERCULOSIS TREATMENT AFTER IMPLEMENTATION OF THE NATIONAL TUBERCULOSIS CONTROL PROGRAM IN SAUDI ARABIA

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Background: Tuberculosis is an endemic disease in Saudi Arabia. Efforts to control this disease started in 1992 with the establishment of a National Tuberculosis Control Committee. Field application of a national tuberculosis control program (NTCP) was implemented in Riyadh in 1996 by the Ministry of Health, according to the guidelines of the World Health Organization (WHO). This study was aimed at evaluating the outcome of tuberculosis treatment before and after the implementation of this program.

Patients and Methods: All active tuberculosis cases admitted and treated in the Sahary Chest Hospital, Riyadh, were studied. The outcome of treatment was evaluated, and a comparison was made between 1995 (before the implementation of the NTCP) and the years 1996-1998 (after implementation).

Results: The total number of tuberculosis cases increased from 504 in 1995 to 726 (44%) in 1998. Cure rate increased from 24.4% to 36.2%, and the default rate decreased from 15% to only 1.2% during the same period. However, there was no change in the rate of completion of treatment, the rate of treatment failures, relapse or deaths.

Conclusion: Although the cure rate slightly improved and the default rate decreased, the overall outcome of the implementation of the national tuberculosis control program was not satisfactory. A recommendation for speedy application of directly observed therapy strategy (DOTS) is made to improve the control of tuberculosis in Saudi Arabia.

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Key Words: Tuberculosis, control.

Tuberculosis (TB) remains an endemic disease in Saudi Arabia.[1-3] Over the last 10 years, efforts to control the disease have been hampered by fragmented and non-systematic approaches, which have been made worse by the lack of adequate resources and personnel. Nevertheless, a National Tuberculosis Control Committee was established by the Ministry of Health in 1992, to plan and organize the implementation of a national tuberculosis control program (NTCP) throughout the Kingdom.[4] In 1996, field application of the program began with the assignment of a coordinator with the responsibility of following up and accurately reporting diagnosed cases of tuberculosis (according to WHO guidelines[5]) in each district of the Kingdom.

The aim of this study was to evaluate the outcome of treatment of tuberculosis before and after the implementation of the NTCP in the Sahary Chest Hospital, the main chest hospital in Riyadh, Saudi Arabia, where the majority of tuberculosis cases (about 70%) are treated. We further assessed the outcome of the implementation of this program on the control of tuberculosis in this area.

Patients and Methods

All cases with active pulmonary and extrapulmonary tuberculosis admitted to the Sahary Chest Hospital from January 1995 to 1998 were studied. Personal and demographic data, along with the type of tuberculosis and associated conditions of the disease were recorded. Diagnosis was made according to the WHO criteria for active tuberculosis in pulmonary and extrapulmonary cases.[6] Outcome of the management of the disease was evaluated by cure rate, completion of therapy, treatment failure, relapse, default rate, and mortality rate. Comparison was made between 1995 and 1996-1998, i.e., before and after the implementation of the NTCP.

All patients were treated with the short-course chemotherapy of rifampicin and isoniazid for six months, and pyrazinamide and ethambutol in the first two months.[7] The NTCP required an assignment of a coordinator in each district. All TB cases were reported to this coordinator, who initiated a special record for each case, which was updated frequently with follow-up data, according to the WHO recommendations.[6] After a patient was discharged, the district coordinator ensured continued outpatient clinic

TABLE 1. *Sex and nationality of patients admitted to Sahary Hospital between 1995-1998 with active tuberculosis.*

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Parameters	1995 No. %	1996 No. %	1997 No. %	1998 No. %
Sex				
Male	322 (63.9)	341 (65.1)	406 (62.4)	431 (59.4)
Female	182 (36.1)	183 (34.6)	245 (37.6)	295 (40.6)
Nationality				
Saudi	162 (32.1)	175 (33.4)	220 (33.8)	211 (29.1)
Non-Saudi	342 (67.9)	349 (66.6)	431 (66.2)	515 (70.9)
All cases	504	524	651	726

TABLE 2. *Types of tuberculosis cases admitted to Sahary hospital between 1995-1998.*

Type	1995 No. %	1996 No. %	1997 No. %	1998 No. %
PTB	362 (71.8)	376 (71.8)	454 (69.7)	481 (66.3)
Miliary	7 (1.9)	22 (5.9)	17 (3.7)	10 (2.1)
Extra–pulmonary	142 (28.2)	148 (28.2)	197 (30.3)	245 (33.7)
Pleural effusion*	34 (23.9)	73 (49.3)	71 (36)	88 (35.9)
Cases with DM	31 (6.2)	68 (13)	101 (15.5)	96 (13.2)
All cases	504	524	651	726

*Only cases where effusion was not associated with lung tuberculosis; PTB=pulmonary tuberculosis; DM=diabetes mellitus.

TABLE 3. *Outcome of tuberculosis cases admitted to Sahary hospital between 1995-1998.*

Outcome	1995 No. %	1996 No. %	1997 No. %	1998 No. %
Cured	107 (24.4)	127 (29.3)	170 (30.6)	233 (36.2)*
Completed therapy	251 (57.2)	257 (59.4)	320 (57.7)	368 (57.1)
Treatment failure	1 (0.2)	4 (0.9)	3 (0.5)	2 (0.3)
Relapse	14 (3.2)	11 (2.5)	27 (4.9)	24 (3.7)
Defaulted	66 (15)	27 (6.2)*	17 (3.1)*	8 (1.2)*
Died	– –	7 (1.6)	18 (3.2)	9 (1.4)
All cases **	439	433	555	644

*Statistically significant at 5% level, after adjustment for 3 pairwise multiple comparisons; **patients transferred to other health facilities or abroad are not included.

attendance with documentation of sputum results, x-ray studies, and other related findings. After completion of the drug treatment, patients were asked to return for follow-up visits every six months for two years so as to detect any relapse. A defaulter system was applied when a patient missed a clinic appointment. This included involvement of a social worker or a health assistant, and every effort was made to bring the patient back to the clinic for regular monthly follow-up and collection of drug prescription.

For the purpose of a uniform definition of terms used in this study, the following WHO definitions[6] were adopted:

Pulmonary TB, smear-positive: A patient with at least two sputum specimens which were positive for acid-fast bacilli (AFB) by microscopy, or a patient with only one sputum specimen which was positive for AFB by microscopy, and chest radiographic abnormalities consistent with active pulmonary TB, or a patient with only one sputum specimen which was positive for AFB by microscopy, and a culture positive for *M. tuberculosis.*

Pulmonary TB, smear-negative: A patient with symptoms suggestive of TB, with at least two sputum specimens which were negative for AFB by microscopy, and with chest radiographic abnormalities consistent with active pulmonary TB (including interstitial or miliary abnormal images), or a patient with at least two sputum specimens negative for AFB by microscopy, and a culture positive for *M. tuberculosis*, or a patient with two sets of at least two sputum specimens taken at least two weeks apart, and which were negative for AFB by microscopy, and radiographic abnormalities consistent with pulmonary TB and lack of clinical response to one week of broad-spectrum antibiotic.

Extrapulmonary TB: A patient with TB of organs other than the lungs. Pleurisy and mediastinal lymphadenopathy are classified as extrapulmonary TB.

New case: A patient who has never taken anti-TB drugs for more than one month.

Relapse: A TB patient who previously received treatment and was declared cured, and has once again developed smear-positive pulmonary TB.

Treatment failure: A TB patient who, while on treatment, remained smear-positive; or once more became smear-positive at the fifth month or later during the course of treatment, or one who was initially smear-negative before starting treatment and became smear-positive after the second month of treatment.

Return after interruption (default): A patient who completed at least one month of treatment and returned after at least two months' interruption of treatment.

Chronic case: A patient who remained smear sputum-positive after completing directly observed re-treatment regimen.

Chi-squared and Fisher's exact tests were used for statistical analysis. *P*-value less than 0.05 was considered significant.

Results

Table 1 shows the increase in tuberculosis cases over a four-year period (1995-1998), from 504 to 726 patients (44%). Male patients outnumbered female patients by a ratio of about 2:1, except for the year 1998, where the number of females slightly increased from 34.9%-37.6% in 1995-1997 to 40.6% in 1998. In 1995, Saudi nationals made up only 32.1% of all tuberculosis cases, and this ratio remained relatively unchanged over the following two years, until 1998 when it slightly decreased to 29.1%.

The types of tuberculosis are shown in Table 2, where the number of both pulmonary and extrapulmonary cases steadily increased over the four-year study period. The total

number of cases increased by only 4% in 1996 from the baseline of 504 cases in 1995 before the implementation of the NTCP. After the implementation of the program, it gradually increased by 29% and 44% in 1997 and 1998, respectively. The proportion of miliary tuberculosis cases ranged between 1.9% and 5.9%, and cases of tuberculosis in association with diabetes mellitus were 6.2% in 1995 and between 13% and 15.5% afterwards. Pleural effusion that was not associated with lung disease was seen in 23.9% and 49.3% of extrapulmonary tuberculosis cases.

The outcome of treatment of tuberculosis cases is shown in Table 3. The standard six-month short course regimen gave only a 24.4%-36.2% proven cure rate, with at least three negative consecutive sputum smear tests. However, between 57.1% and 59.4% of the patients did complete their treatment course, but were not evaluated with sputum smear test, either because they could not produce sputum, or they had a negative smear from the beginning of the course. The diagnosis of tuberculosis in this group of patients was done initially by sputum smear and/or culture, but the patients either failed to produce sputum later on, or biopsy showed non-caseating granuloma (in extrapulmonary tuberculosis cases).

Treatment failure (continued positive smear despite prolonged therapy) occurred in only a small number (0.2%-0.9%) of cases. Relapse rate slightly increased in 1997 and 1998 (4.9% and 3.7%, respectively) compared to 1995 and 1996 (3.2 and 2.5%, respectively). When only evaluable cases are considered (i.e., not calculating defaulted cases or deaths), the relapse rate was 3.8%, 2.8%, 5.2%, and 3.8% in 1995, 1996, 1997 and 1998, respectively. However, these results did not reach statistical significance. While there was a slight but statistically significant increase in the cure rate, there was no change in the percentage of patients who completed their treatment course before and after implementation of the NTCP. The most noticeable significant parameter in Table 3 is the default rate, which gradually but significantly dropped from 15.4% in 1995 to only 1.2% in 1998 ($P<0.001$).

Discussion

It is clear from the findings of this study that the implementation of the NCTP definitely had a useful impact in reducing the default rate from 15% before the organized retrieval system was applied, to only 1.2% three years later. Whether the patients who attended the outpatient clinic to obtain their drug prescription actually took the drugs prescribed is unknown. Although the proven cure rate steadily increased from 24.4% in 1995 to 36.2% in 1998 (Table 3), and the default rate definitely decreased, the total number of tuberculosis cases actually increased. Furthermore, the rate of completion of therapy, the relapse, treatment failure and death rates either increased or remained unchanged. A possible explanation is that even if patients kept their appointments and did come to the clinic for their prescription, many of them may not have actually taken the drugs. In the current NTCP, there is no system of ensuring patients' compliance with the drugs provided at the clinics.

The problem with self-administered drug therapy is clearly shown in this study. Despite a significant reduction in the default rate by bringing patients back for regular outpatient clinic visits, the outcome of the treatment was not substantially improved (Table 3). The infrastructure of the tuberculosis control program in this country is not solid enough to make the system work in a satisfactory manner. Noncompliance (NC) and drug interruptions are major obstacles to good control of tuberculosis in Saudi Arabia.[8] It is a well-known fact that compliance with prescribed drugs is the most important single factor in the success of tuberculosis treatment programs.[9-11] Even if a patient attends clinics regularly, it is still uncertain whether he/she takes the prescribed medications. Consequently, drug resistance (particularly multi-drug resistance) increases, which is another problem facing health planners.[12] Relapse also occurs as a result of drug interruptions, leading to higher rates of chronic cases. The end result of this situation is a poor control of tuberculosis and a failure of the National Tuberculosis Control Program to achieve its goals.[11,13]

Long periods of hospitalization can solve some of the problems but would be impractical and expensive. Retrieval systems (phone, letters, home visits, etc.) can bring some patients to the clinic, but it would not be possible to guarantee that they will take the prescribed drugs.[14-15] Other methods, including fixed-dose combinations, urine testing, and pill-counting, may not prevent defaulters. Twice- or thrice-weekly regimens make it easier for patients to take medications, but patients who are not willing to continue treatment will nevertheless give up.[16]

Directly observed therapy short course (DOTS), which ensures that the patient actually takes the medication under direct supervision of a nurse (or a health assistant), has emerged after many years of dealing with treatment methods as probably the best solution to the problem of noncompliance, and has been proven effective in various parts of the world.[17-19] Caminero et al. showed a relapse rate of only 3% with DOTS in extremely noncompliant patients.[20] A large Chinese study (112,842 patients) showed that with DOTS, the failure rate dropped from 17.6% to 6.2%.[21] Weis et al. also showed that drug resistance was reduced by using DOTS, in a series where primary and acquired resistance dropped from 13% and 14% to 6.7% and 2.1%, respectively. Relapse rate decreased from 20.9% to 5.5%, and relapse with multidrug resistance (MDR) decreased from 25% to 5% after applying DOTS.[22] Furthermore, DOTS has been shown to be more cost-effective in the long term than the conventional methods of managing tuberculosis.[23]

In the current setting of health services in Saudi Arabia, the application of DOTS is only possible while patients are in the hospital. This would require long periods of admission, as the first two months are the consolidation

phase of TB. We recommend a gradual application of DOTS, starting in health institutions where facilities are available. Improvement of the infrastracture of the health care system would create a suitable environment for DOTS to be a successful program. Although the application of DOTS has faced some minor difficulties in some parts of the world, we think it is the best available system to combat the problem of noncompliance in Saudi Arabia and other countries where tuberculosis is endemic.[24]

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