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ORIGINAL ARTICLE

Effect of a Hospital-based Case Management Approach on Treatment Outcome of Patients with Tuberculosis

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Background/Purpose: Tuberculosis (TB) continues to pose a heavy public health burden in Taiwan. This prospective study analyzed the factors influencing treatment outcome in patients with TB treated with and without a hospital-based case management (HBCM) approach in a referral center in Taipei.

Methods: A register-based cohort study design was used to enroll all new cases of pulmonary or extrapulmonary TB from February 2003 to January 2004. The case manager served as the coordinator among patients, physicians and public health nurses, to facilitate compliance with anti-TB treatment. Treatment outcomes were assessed according to the consensus recommendations of the World Health Organization and the International Union Against Tuberculosis and Lung Disease.

Results: Suspected or confirmed pulmonary or extrapulmonary TB was diagnosed in 524 patients in our hospital from February 2003 to January 2004. Fifty-two of these patients were excluded due to duplicate reporting, previous treatment or death before enrollment. Out of 472 patients enrolled, 103 whose original diagnosis was revised were further excluded, leaving 369 cases eligible for analysis. Patients with case management had a significantly higher rate of successful treatment (cured plus completed treatment) compared to patients without case management, (240/277, 86.6% *vs.* 67/92, 72.8%; $p = 0.002$). The overall successful treatment rate including both case and non-case management was 83.2% (307/369), which was higher than the nationwide surveillance data of 78.3% in 2002 and 69.4% in 2003.

Conclusion: Treatment of TB patients by a HBCM approach provides improved treatment outcomes compared to those without case management. [*J Formos Med Assoc* 2006;105(8):636–644]

Key Words: directly observed therapy short-course, hospital-based case management, treatment outcome, tuberculosis control, Taiwan

In 2002, the World Health Organization (WHO) estimated 8.8 million new cases of tuberculosis (TB) worldwide, with an incidence rate of 141 per 100,000 population, and 1.8 million deaths due to TB.[1] TB continues to pose a heavy public health burden in Taiwan despite rich medical resources and almost universal coverage of all people by the National Health Insurance program since 1995. The WHO introduced a five-element strategy of directly observed therapy short-course (DOTS) as the standard of care of pulmonary TB.[2,3] As Taiwan is not a member of the WHO, most of the population are not covered by this project. However, for countries with adequate health infrastructure and sufficient economic resources for TB control, adopting other management modalities in addition to the DOTS strategy may provide further benefit.[4]

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Nonadherence to treatment is one of the major causes of treatment failure and the emergence of drug-resistant TB, and is the most serious problem in the control of TB in Taiwan. The strategy of TB control should be modified according to local epidemiology, specific socioeconomic and cultural circumstances, and the type of healthcare program. Although a previous study in Taiwan found that case notification of TB was quite complete, and reported patients were followed up by public health nurses, compliance with anti-TB treatment remains unsatisfactory.[5] Public health nurses who serve as government employees at local health units are assigned the responsibility of following up compliance to anti-TB treatment. However, due to poor communication with physicians, they are usually unaware of patients' actual clinical condition and, hence, not fully trusted by patients. Health education for patients about the disease was also insufficient. We tried to address these problems by employing a hospital-based case management (HBCM) approach for the control of TB. Treatment outcomes were compared between patients with and without case management and with nationwide surveillance data. Part of the results of this study has been previously presented in the form of an abstract.[6]

Methods

Study patients

In Taiwan, suspected or confirmed diagnosis of TB, including pulmonary and extrapulmonary cases, requires notification under government regulations and registration of the case both in the database of the reporting hospital and in the Center for Disease Control in Taiwan.[7] In this study, all patients reported from February 2003 to January 2004 in our hospital were assigned to receive case management except for those with a duplicate report, previous treatment or death prior to the enrollment period. If the diagnosis was revised after enrollment, either due to nontuberculous mycobacterial (NTM) growth in culture or to diagnosis of other lung diseases, then the anti-TB regimen was discontinued and the patient withdrawn from the HBCM program. If patients changed their healthcare providers, the case manager then provided clinical information to public health nurses for further follow-up, but these patients were no longer participants in our HBCM program (Figure 1).

Case definition and diagnostic categories

The standard WHO case definition for TB[1] with modifications was adopted, requiring bacteriologic or pathologic confirmation, or diagnosis by a clinician. A smear-positive pulmonary case was defined as the finding of at least two initial sputum acid-fast bacilli smear positive (AFB+); or one sputum AFB+ and radiographic abnormalities consistent with active pulmonary TB as determined by a clinician; or one sputum AFB+ and culture positive for *Mycobacterium tuberculosis.* A smear-negative, culture-positive pulmonary case was defined based on a positive culture for *M. tuberculosis* but negative AFB sputum examinations, and radiographic abnormalities consistent with active pulmonary TB. A smear-negative, culture-negative pulmonary case was defined as a negative sputum AFB and culture for *M. tuberculosis*, or a patient whose sputum was not available for examination; radiographic abnormalities consistent with active pulmonary TB; and decision by a clinician to treat with a full course of anti-TB therapy. An extrapulmonary case was defined as a patient with TB of organs other than the lungs, proved either histologically or bacteriologically. A patient with both pulmonary and extrapulmonary TB diagnoses was classified as a pulmonary case.

Case management

A team of personnel was assigned the responsibility for continuity of care, patient follow-up, health education and reassessment. As shown in Figure 2, the HBCM approach for TB control required four types of healthcare providers in the following roles: (1) the treating physician who reported the cases and/or was responsible for treating patients; (2) the managing physician, a pulmonary

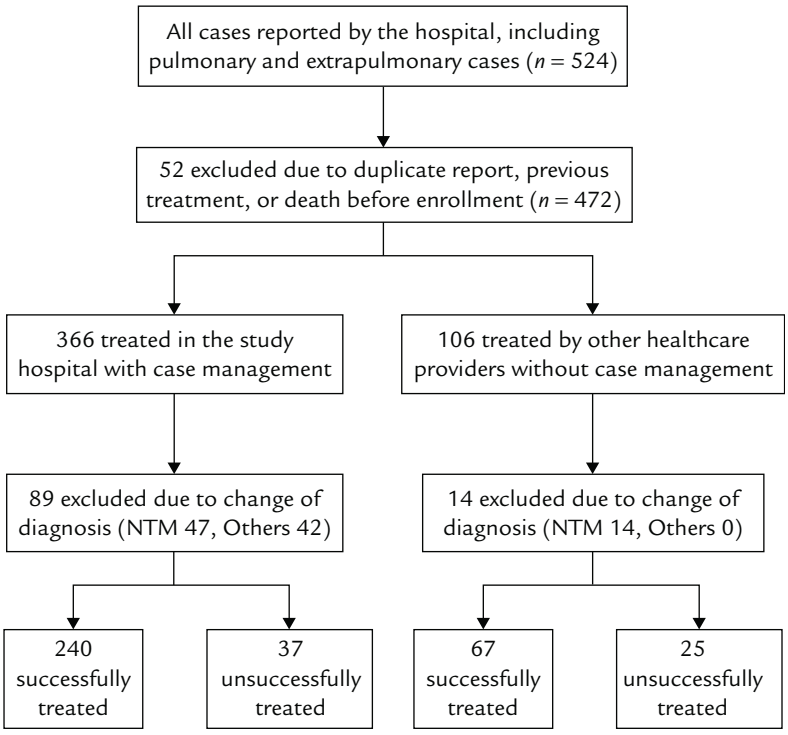

Figure 1. Study population and treatment outcomes. A total of 524 patients with suspected or confirmed pulmonary or extrapulmonary tuberculosis were reported to the Center for Disease Control. After exclusion of patients with duplicate reports, previous treatment, or death, the remaining 472 patients were enrolled. Among these patients, 366 were treated in the study hospital under case management and 106 were treated by other healthcare providers without case management. Patients whose diagnosis was subsequently changed to categories including growth of nontuberculous mycobacteria (NTM) on culture and other lung diseases were further excluded.

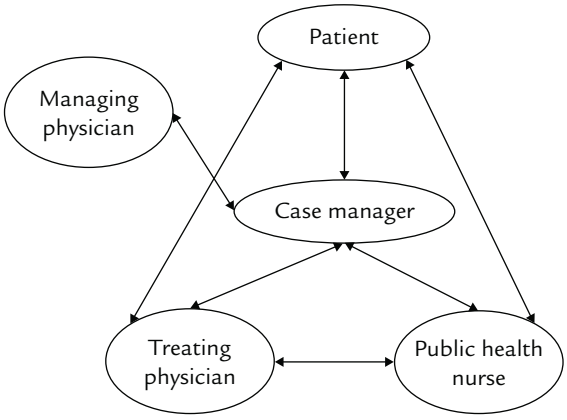

Figure 2. Components and relationships between patients and personnel involved in case management.

specialist who provided the case manager with consultation for any required information regarding the diagnosis and/or treatment of patients; (3) public health nurses who were government employees and served at the local health unit located at the corresponding patient's residence; (4) the case manager who served in the hospital in the following capacities: (a) coordinated between physicians, public health nurses and patients for better understanding of patients' clinical conditions; (b) offered health education to patients and their family members once the diagnosis was initially made; (c) contacted patients regularly to ensure compliance to treatment; (d) monitored the anti-TB drugs' side effects by telephone contact; (e) tracked for failure to keep appointments; (f) monitored the appropriateness of the anti-TB regimen by reviewing medical records.

Treatment outcomes

The definitions of the consensus-based recommendations developed by the working group of the WHO and the International Union Against Tuberculosis and Lung Disease (IUATLD) on uniform reporting of TB treatment outcomes[1,8] were adopted in this study and are briefly summarized.

Cure was defined as completion of a full course of anti-TB therapy in an initially smear- and/or culture-positive patient who was smear-negative in the last month of treatment; treatment completed was defined as completion of treatment but in a patient who did not meet the criteria for cure or failure; death was defined as a patient who died from any reason during treatment; treatment

failure was defined as a smear-positive patient who remained smear-positive at 5 months or later after the start of treatment; default was defined as treatment interruption for 2 consecutive months or more; transfer out was defined as transfer to another reporting unit in a patient for whom the treatment outcome was not known; still on treatment was defined as a patient who remained on treatment at the end of follow-up; successfully treated was defined as either cured or completion of treatment; unsuccessfully treated was defined as a treatment outcome other than successfully treated.

All patients were followed up to determine their treatment outcomes 1 year after the last patient was enrolled. Data on the treatment outcomes of patients not under HBCM were obtained from public health nurses and an online central registry database from the Center for Disease Control in Taiwan.[9]

Statistical analysis

All continuous data were expressed as mean ± SD. Differences in the means of continuous measurements were tested by Student's *t* test. χ^2 and Fisher's exact tests were used for comparison of category data. A multiple logistic regression model was used to evaluate whether case management was an independent predictor of successful treatment after adjusting for age and gender. A p value < 0.05 was considered to be statistically significant. All statistical analyses were performed on a personal computer with SPSS version 12.0 (SPSS Inc., Chicago, IL, USA) for Windows.

Results

Study population and demographic characteristics

Between February 2003 and January 2004, 524 suspected or confirmed cases of pulmonary or extrapulmonary TB were reported. Fifty-two of these cases were excluded due to either duplicate reporting, previous treatment, initiation of treatment not during the enrollment period or death before enrollment. Out of 472 patients enrolled, 366 were treated at our hospital under the HBCM program, and 106 changed their healthcare providers and were not participants in the case management program (non-HBCM). Patients whose diagnosis was revised after enrollment, including 61 with NTM growth on culture and 42 with other lung diseases, were further excluded. The remaining 369 patients comprised the population of this study including 277 participants in the HBCM program and 92 nonparticipants (Figure 1).

There were no significant differences in gender, mean age or percentage of pulmonary or extrapulmonary cases between patients with and without HBCM (Table 1). The smear-positive rate for pulmonary cases was 36.8% (85/231) in the HBCM group, 29.6% (24/81) in the non-HBCM group and 34.9% (109/312) in the overall group. Most (75%) of the patients treated at our hospital remained under HBCM throughout the treatment course. Among 92 patients who changed their healthcare providers, the median time from enrollment until change was 54 days, with 62 of them changing within the first month after enrollment.

Treatment outcomes

The rate of successful treatment was significantly higher in patients with HBCM when compared to those without HBCM (86.6% *vs.* 72.8%, $p = 0.002$) (Table 2). If the two groups were pooled together, the percentage of patients with successful treatment in the overall group was 83.2% (307/369). There was no significant difference in the treatment success rates between pulmonary and extrapulmonary cases (82.1% *vs.* 89.5%, $p = 0.168$) or by gender (males 83.1% *vs.* females 83.5%, $p = 0.920$). Patients with unsuccessful treatment outcomes had significantly older mean age than those with successful treatment (mean age, 65.9 ± 20.6 years *vs.* 51.6 ± 20.1 years, $p < 0.001$) (Table 3).

According to the standardized WHO and IUATLD recommendations for treatment outcomes, all deaths during the treatment duration

Table 1. Comparison of demographic characteristics and diagnostic findings of the 369 patients treated with or without case management

Characteristics	With case management ($n=277$)	Without case management ($n=92$)	p
Male	179 (64.6%)	57 (62.0%)	0.64
Mean age ± SD (yr)	54.7 ± 20.3	52.0 ± 22.4	0.28
Age distribution (yr)			
< 15	2	0	
15–39	69	34	
40–64	101	22	
> 64	105	36	
Pulmonary cases	231 (83.4%)	81 (88.0%)	0.28
Smear (+)	85	24	
Smear (–), culture (+)	57	29	
Smear (–), culture (–)	89	28	
Extrapulmonary cases	46 (16.6%)	11 (12.0%)	
Lymph node	17	4	
Pleural	21	6	
Urogenital	4	0	
Meningeal	2	0	
Bone	1	0	
Peritoneal	1	0	
Pericardial	0	1	

SD = standard deviation.

Table 2. Comparison of treatment outcomes in patients who received case management ($n=277$) and non-case management ($n=92$)

Characteristics	Case management, *n* (%)	Non-case management, *n* (%)
Successfully treated	240 (86.6)	67 (72.8)
Cure	109 (39.4)	N/A*
Treatment completed	131 (47.3)	67 (72.8)
Unsuccessfully treated	37 (13.4)	25 (27.2)
Still on treatment	1 (0.4)	3 (3.3)
Treatment failure	0 (0.0)	1 (1.1)
Default	9 (3.2)	2 (2.2)
Transfer out	1 (0.4)	3 (3.3)
Died	26 (9.4)	16 (17.4)

**In non-hospital-based case management patients with successful treatment, follow-up bacteriologic results before treatment completion were not available to the case manager. Hence, we classified all of these patients' treatment outcomes as having treatment completed. N/A = not available.*

irrespective of cause were counted in the analysis.[1,8] Among patients with unsuccessful treatment outcomes, 26 (9.4%) in the HBCM group and 16 (17.4%) in the non-HBCM group died, which comprised the majority of patients with unsuccessful treatment (Table 2). Further analysis of treatment outcomes excluding all patients who died showed a significantly higher treatment success rate in the HBCM group when compared with the non-HBCM group (95.6% *vs.* 88.2%, $p=0.027$) (Table 4). Multiple logistic regression analysis of predictors of treatment outcome showed that HBCM was the single independent predictor of successful treatment

Table 3. Univariate analysis of association of management approach and patient characteristics with successful treatment outcome including patients who died during treatment

	Successfully treated	Unsuccessfully treated	*p*
Case management (*n* = 277), *n* (%)	240 (86.6)	37 (13.4)	0.002
Non-case management (*n* = 92), *n* (%)	67 (72.8)	25 (27.2)	
Pulmonary cases (*n* = 312), *n* (%)	256 (82.1)	56 (17.9)	0.17
Extrapulmonary cases (*n* = 57), *n* (%)	51 (89.5)	6 (10.5)	
Male (*n* = 236), *n* (%)	196 (83.1)	40 (16.9)	0.92
Female (*n* = 133), *n* (%)	111 (83.5)	22 (16.5)	
Mean age, mean ± SD (yr)	51.6 ± 20.1	65.9 ± 20.6	< 0.001

SD = standard deviation.

Table 4. Univariate analysis of association of management approach and patient characteristics with successful treatment outcome excluding patients who died during treatment

	Successfully treated	Unsuccessfully treated	*p*
Case management (*n* = 251), *n* (%)	240 (95.6)	11 (4.4)	0.027
Non-case management (*n* = 76), *n* (%)	67 (88.2)	9 (11.8)	
Pulmonary cases (*n* = 272), *n* (%)	256 (94.1)	16 (5.9)	0.70
Extrapulmonary cases (*n* = 55), *n* (%)	51 (92.7)	4 (7.3)	
Male (*n* = 204), *n* (%)	196 (96.1)	8 (3.9)	0.033
Female (*n* = 123), *n* (%)	111 (90.2)	12 (9.8)	
Mean age, mean ± SD (yr)	51.6 ± 20.1	45.5 ± 20.3	0.19

SD = standard deviation.

Table 5. Multiple logistic regression of association of case management, gender and age as predictors of successful treatment outcome including and excluding patients who died during treatment

Outcomes	β	*p*	Relative risk	95% CI
Including patients who died				
Case management	1.035	0.001	2.82	1.53–5.19
Age	−0.039	< 0.001	0.96	0.95–0.98
Excluding patients who died				
Case management	1.019	0.032	2.77	1.09–7.02
Gender	0.919	0.053	2.51	0.99–6.37

CI = confidence interval.

either including (relative risk [RR], 2.82; 95% confidence interval [CI], 1.53–5.19) or excluding patients who died (RR, 2.77; 95% CI, 1.09–7.02) (Table 5).

Discussion

This study showed that patients with TB treated with a HBCM approach had a significantly higher rate of successful treatment outcome compared to those without HBCM. Patients who died comprised the majority of patients with unsuccessful treatment outcomes, although the causes of death in these patients were not necessarily due to TB and were often difficult to discern due to the presence of comorbidities. Further analysis of treatment outcomes after excluding those patients who died still showed a significantly better treatment outcome in HBCM patients. Deaths during the treatment

period were due to delay in diagnosis and/or comorbidities rather than due to the treatment. In the evaluation of treatment outcomes, exclusion of patients who died might more accurately reflect the efficacy of a control strategy. This study found an improved treatment success rate compared with both the previous data with non-HBCM reported from the same hospital in 1982–1983 as well as nationwide surveillance data in 2003.[9,10]

This study included consecutively reported TB cases in a single referral center. This cohort had comparable demographic characteristics to the nationwide surveillance data including gender ratio, mean age, rate of open pulmonary TB (smear-positive plus smear-negative, culture-positive) and rate of extrapulmonary TB.[9] In 1997, the Bureau of National Health Insurance in Taiwan introduced the following two policies related to TB notification: (1) the no-notification-no-reimbursement policy, and (2) the notification-fee policy, which substantially improved completeness of reporting.[5] In addition, according to the Communicable Disease Control Act in Taiwan, only the reporting of TB is required but reporting the change of diagnosis is not required.[7] Out of 524 cases reported in our hospital during the study period, 369 (70.4%) were eventually confirmed to have either pulmonary or extrapulmonary TB, a percentage comparable to the nationwide rate in 2003 (22,362 reported of which 15,042 confirmed, 67.3%). Since TB can mimic many other lung diseases and other lung diseases also mimic TB, diagnosis presents a challenge. Under the HBCM approach in this study, once patients were reported to have TB, public health nurses who served the health unit located at patients' residence began to follow up the patients. However, it should be noted that under the current system, public health nurses face many difficulties in contacting the responsible physicians or obtaining the required clinical information in a timely manner. Intervention by the case manager is thus required to help reduce the burden placed on public health nurses. Studies that show the effect of such coordinated efforts on treatment outcomes are required.

In this study, about one-fourth of patients changed their care providers and dropped out of case management after enrollment. The reasons for why patients were not managed at the same hospital are multifactorial. First, patients are able to choose care providers freely under the National Health Insurance program; second, patients changed care providers if they moved or changed their work; third, the epidemic of severe acute respiratory syndrome (SARS) occurred during the study period and led to the evacuation of all TB isolation wards in order to care for SARS patients. The case manager continued to follow up those patients who changed care providers and facilitated continuity of care at the institution to which these patients were transferred and by working with public health nurses. This intensive follow-up explains the overall successful treatment rate of 83.2%, which is an improvement when compared to the nationwide rate of 78.3% in 2002 and 69.4% in 2003 for surveillance data.[9]

DOTS, an international standard of TB control, contains five elements: (1) political commitment to support TB treatment; (2) the passive detection of active TB by sputum microscopy; (3) ensuring drug supply; (4) standardized recording and reporting system; (5) direct observation of treatment (ingestion of anti-TB medications directly supervised by a healthcare worker) during at least the first 2 months.[2] By combining the aspects of government regulation, universal health insurance coverage, and a case management approach for TB control, the strategy reported in this study is more comprehensive than DOTS, except for direct observation of therapy. To achieve direct observation, patients must either go to the healthcare provider or the healthcare worker must visit them. Implementation of required patient visits to observe treatment has been challenged by considerations of patients' willingness, and home visits by healthcare workers would require enormous resources. Nevertheless, the impact of not implementing this aspect of DOTS may also be great. By the time of completion of the first 2 months of treatment, most patients will have

clinical improvement and are likely to interrupt their treatment if direct observation of treatment is discontinued. The possibility of nonadherence and interruption if direct observation of treatment is implemented only during the first 2 months would thus be far greater. Although the HBCM approach does not directly observe treatment, it may be reasonable to assume compliance in most cases based on the patient's willingness to treat, their clinical response, roentgenographic improvement and bacteriologic conversion. The case manager should seek to earn the trust of patients as this may be more important than just watching them take the drugs.

A limitation of DOTS is the inadequate attention to smear-negative cases who can also transmit the disease.[11,12] The broad coverage of the HBCM approach in this study to all TB patients could further reduce transmission early after the diagnosis. Another drawback of DOTS is patients' concern about the stigma of TB infection recognized by their neighbors when healthcare workers visit them for direct observation of treatment. In contrast, the HBCM approach does not infringe on patients' right to privacy.

Several randomized control studies suggested that DOTS may not be better than self-administered therapy for treatment completion.[13–16] Although no controlled cost-effective study comparing case management and DOTS has been reported, data showed that DOTS would generate cost savings only in settings with high default and relapse rates.[17,18] A case management control strategy to cover all TB patients followed by selective DOTS for patients with high risk of nonadherence may be more cost-effective than DOTS alone. Collaboration of case managers between different healthcare providers, with sharing of patient information and continuity of care if patients move or require transfer, will constitute a network of care that reduces the default rate.

This study was limited by lack of randomized group assignment and the inclusion of patients who changed to various healthcare providers. It is difficult to conduct such a randomized control study under the infrastructure of an open system health insurance program. In conclusion, this study supports that HBCM results in improved treatment outcomes in newly diagnosed patients with pulmonary or extrapulmonary TB.

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