MAJOR ARTICLE

Intermittent Directly Observed Therapy for Abdominal Tuberculosis: A Multicenter Randomized Controlled Trial Comparing 6 Months Versus 9 Months of Therapy

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Background. The duration of treatment of gastrointestinal tuberculosis continues to be a matter of debate. The World Health Organization advocates intermittent directly observed short-course therapy (DOTs), but there is a lack of data of its efficacy in abdominal tuberculosis. We therefore conducted a multicenter randomized controlled trial to compare 6 months and 9 months of antituberculosis therapy using DOTs.

Methods. One hundred ninety-seven patients with abdominal tuberculosis (gastrointestinal, 154; peritoneal, 40; mixed, 3) were randomized to receive 6 months (n = 104) or 9 months (n = 93) of antituberculosis therapy using intermittent directly observed therapy. Patients were followed up 1 year after completion of treatment to assess recurrence. Patients were evaluated for primary endpoint (complete clinical response, partial response, and no response) and secondary endpoint (recurrence of the disease at the end of 1 year of follow-up).

Results. Baseline characteristics were similar between the 2 randomized groups. There was no difference between the 6-month group and 9-month group in the complete clinical response rate on per-protocol analysis (91.5% vs 90.8%; $P = .88$) or intent-to-treat analysis (75% vs 75.8%; $P = .89$). Only 1 patient in the 9-month group and no patients in the 6-month group had recurrence of disease. Side effects occurred in 21 (21.3%) and 16 (18.2%) patients in the 6-month and 9-month groups, respectively.

Conclusions. There was no difference in efficacy of antituberculosis therapy delivered for either 6 months or 9 months in either gastrointestinal or peritoneal tuberculosis, confirming the efficacy of intermittent directly observed therapy.

Clinical Trials Registration. NCT01124929.

Keywords. duration of treatment; peritoneal tuberculosis; intestinal tuberculosis.

A 6-month antituberculosis drug regimen using a combination of rifampicin, isoniazid, ethambutol, and pyrazinamide for 2 months, followed by rifampicin and isoniazid for 4 months, cures approximately 90% of tuberculosis patients among human immunodeficiency virus (HIV)–uninfected individuals and is the globally accepted treatment for drug-susceptible, active tuberculosis [1, 2]. However, poor compliance and irrational prescribing increase the risk of selection of drug-resistant strains of *Mycobacterium tuberculosis*, which are more difficult to treat [3–5].

The exact duration and compliance to treatment are 2 major issues in managing abdominal tuberculosis. The duration of treatment of gastrointestinal (GI)

Received 15 January 2015; accepted 29 April 2015; electronically published 12 May 2015.

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Clinical Infectious Diseases® 2015;61(5):750–7

DOI: 10.1093/cid/civ376

tuberculosis, whether 6 months or longer, continues to be a matter of debate [6–8]. Although most guidelines recommend 6 months of treatment, evidence to support such recommendation is weak [9, 10]. Furthermore, despite the recommended 6-month treatment duration, many physicians treat such patients for a longer duration [11]. In a recent Korean study including 90 patients with intestinal tuberculosis, Park et al showed comparable efficacy (93.3% vs 91.1%; $P = 1.00$) and recurrence rate (2.4% vs 0%; $P = 1.00$) between 6 and 9 months of treatment [7].

Poor compliance may cause prolonged infectiousness, drug resistance, relapse, or even death. Incomplete treatment poses risk to the community as well [11–13]. To achieve good compliance, the World Health Organization has adopted a strategy of providing antituberculosis therapy under directly observed short-course therapy (DOTs) [14]. DOTs has also been adopted by the government of India under the Revised National Tuberculosis Control Programme (RNTCP) [15]. The DOTs strategy in India was piloted in 1993 and expanded nationally in 1997 [16]. In the intermittent thrice-weekly regimen of antituberculosis therapy, higher doses of the standard antituberculosis drugs, except for rifampicin, are recommended [3].

The efficacy of therapy for pulmonary tuberculosis using the DOTs strategy is well established [17]. There, however, is lack of data on its efficacy in treatment of abdominal tuberculosis except for a small pilot study from southern India, which showed comparable efficacy of antituberculosis therapy administered for 6 months and 9 months [18].

We therefore conducted a randomized controlled trial (RCT) to determine the efficacy of an intermittent short-course antituberculosis drug regimen for 6 months and 9 months under the DOTs strategy for treatment of abdominal tuberculosis. A secondary objective was to determine the differences in the recurrence rate at 1 year of follow-up after completion of primary treatment in the 2 groups.

PATIENTS AND METHODS

This was a multicenter (3 Indian tertiary centers), prospective RCT (between September 2008 and April 2014) and was approved by the ethics committees of the respective centers. Consecutive newly diagnosed patients (aged 15–65 years) with either GI or peritoneal tuberculosis or both were recruited after obtaining their informed written consent.

Patients who took antituberculosis medication during the past 5 years; those with HIV/AIDS, chronic liver disease, peritoneal carcinomatosis, Crohn's disease, or associated significant comorbidities; those with history of drug sensitivity; and those not willing to provide consent were excluded. Patients who had received any investigational agents during the past 6 months, as well as pregnant women or lactating mothers, were also excluded.

Clinical Data Collection

Patients underwent a detailed clinical and laboratory evaluation, including hematological and biochemical tests, Mantoux test, and chest radiography. They also underwent colonoscopy and retrograde ileoscopy (wherever feasible) using a videocolonoscope after adequate preparation. During colonoscopy, segment-wise involvement and type of lesions were recorded, and multiple biopsies obtained from the edge of lesions were sent for histologic and microbiologic testing. For histology, biopsies were fixed in 10% buffered formal-saline, and for microbiological tests (culture, staining for acid-fast bacilli [AFB], and AFB polymerase chain reaction [PCR]), biopsies were collected in sterile normal saline. Small intestine was evaluated using computed tomography (CT) enteroclysis/enterography or magnetic resonance enterography or barium enteroclysis.

Patients suspected to have peritoneal tuberculosis underwent the following tests: ascitic fluid analysis including cell counts, total and differential; biochemical tests including protein, sugar, and adenosine deaminase; and microbiological tests (AFB stain, culture). They also underwent ultrasonography and/or contrast-enhanced CT for assessment of peritoneal involvement.

Microbiological Tests

The biopsy and fluid (after centrifugation) were stained using Ziehl–Neelsen staining and scanned for AFB. The *M. tuberculosis* cultures were done using either the BACTEC (Becton Dickinson, East Rutherford, New Jersey) or mycobacteria growth indicator tube (MGIT) (Becton Dickinson, East Rutherford, New Jersey) systems. The AFB DNA PCR was performed for the *mpt*64 gene.

Diagnostic Criteria for GI and Peritoneal Tuberculosis

A "definite" diagnosis of tuberculosis was considered in the presence of ≥2 of the following: (1) clinical, imaging, or endoscopic evidence of GI involvement; (2) AFB on smear or culture of biopsies; and/or (3) caseating granuloma. A presumptive diagnosis was made if there was strong clinical suspicion based on clinical, endoscopic, and histological features and confirmed if there was persistent response to treatment.

Peritoneal tuberculosis was diagnosed based on presence of high-protein (>2.5 g/dL) ascites containing >250 white blood cells/mm^3 (predominantly lymphocytes) along with at least 1 of the following: evidence of peritoneal inflammation on ultrasound, CT, or demonstration of *M. tuberculosis* in the ascitic fluid either by direct smear, culture, or caseating granuloma in the peritoneal biopsies.

Randomization

The randomization was done for each center separately using computer-generated tables by a person not involved in the study. The randomized treatment allocation (ie, 6 or 9 months)

was printed and concealed in sealed envelopes bearing the serial number of the patient (separately for each site).

Intervention

Patients meeting inclusion and exclusion criteria were randomized into 2 groups: Group I and group II received RNTCP category I treatment for 6 months and 9 months, respectively. In this regimen, the intensive phase included 4 drugs (rifampicin 450 mg, isoniazid 600 mg, pyrazinamide 1500 mg, and ethambutol 1200 mg) 3 times weekly for 2 months. The continuation phase included rifampicin and isoniazid for an additional 4 months in those randomized to 6 months, and for 7 months in those randomized to receive 9 months of therapy. Patients weighing ≥60 kg received an additional 150 mg of rifampicin. All the drugs were administered under supervision [19].

Patients were registered with the DOTs clinics at their respective centers, and DOTs was administered at the DOTs center closest to their home. All the patients were followed up at the clinics of their respective centers at regular intervals.

Follow-up and Management of Side Effects

All side effects were recorded. Liver function tests (LFTs) were done at regular intervals. Drug-induced hepatitis was managed by replacing hepatotoxic drugs (isoniazid, rifampicin, pyrazinamide) by quinolones and streptomycin. While monitoring LFT closely, first-line drugs were reintroduced after resolution of hepatitis. The total duration of interruption due to hepatitis was compensated by prolongation of the treatment duration.

Adherence to Treatment

Patients received treatment under direct supervision through the network of DOTs centers. They were requested to report to the enrolling center at every 2 months. Nodal officers and medical social workers kept track of patients for compliance. The drug intake was recorded in a diary, and a compliance of >80% of days of drug intake was considered compliant. Poorly compliant (patients taking drugs <80% of intended days) patients received further counseling, and noncompliant patients were excluded from the study.

Assessment at End of Treatment

Randomized patients were clinically evaluated for symptom resolution. Depending on the site of pretreatment lesions, patients underwent repeat colonoscopy and retrograde ileoscopy, upper GI endoscopy and/or evaluation of the small intestine using barium meal follow through/enteroclysis, and CT/magnetic resonance enteroclysis for evaluation of resolution of lesions. Patients with peritoneal tuberculosis underwent clinical evaluation and imaging to demonstrate healing of lesions.

Follow-up for 1 Year for Recurrence of Tuberculosis

Patients were followed up every 3 months for 1 year after completion of the primary treatment. Those who failed to visit the clinics were contacted by telephone and interviewed regarding recurrence.

Outcome Measures

"Complete clinical response" was defined as complete symptomatic response with normalization of biochemical and hematological tests at end of therapy (EOT). A partial response was defined as resolution of clinical manifestations and partial healing of lesions at EOT. Nonresponse was defined as persistent clinical symptoms and inflammatory lesions at EOT. Among patients agreeing to undergo end-of-treatment evaluation, healing of lesions at colonoscopy or resolution of inflammatory features, including thickening of the intestinal wall or peritoneum on imaging, at end of primary therapy was also assessed.

Statistical Analysis

The study was designed to test the hypothesis that 9 months of antituberculosis therapy is more efficacious than a 6-month regimen (using the DOTs strategy). To demonstrate a difference in the complete clinical response rate of 15% between 9 months and 6 months of treatment and considering a power of 80% and 5% significance, 172 patients (86 patients in each group) were required. With expected loss to follow-up of 10% of patients and 10% requiring surgery, which could not be considered for calculation of efficacy and recurrence of disease, 206 patients were required. Statistical analysis was conducted using Stata software, version 12.1. Comparisons between 2 groups were performed using χ^2 test for categorical variables and Student *t* test for continuous variables. Primary analysis was done as intent-to-treat (ITT) followed by per-protocol analysis. A *P* value of <.05 was considered significant.

RESULTS

Study Cohort

Of 499 patients who were screened, 302 were excluded and 197 were included in the study (Figure 1). Of 197 eligible patients, 104 and 93 patients were randomized to a 6-month (group A) or a 9-month regimen (group B), respectively. Four patients in group A and 2 patients in group B were ultimately found to have an alternative diagnosis (Crohn's disease in 5 and adenocarcinoma in 1) on follow-up and thus were excluded.

Characteristics of the Patients and the Disease at Baseline

There was no difference in the clinical, hematological, and biochemical parameters at baseline between the 2 groups (Table 1). The site of primary disease as established by colonoscopy and/or contrast enhanced computerized tomography/CT enteroclysis/enterography is summarized in Table 2. Colonoscopic examination at the baseline was performed in 73 (73%) patients in the 6-month group and 66 (72.5%) in the 9-month group.

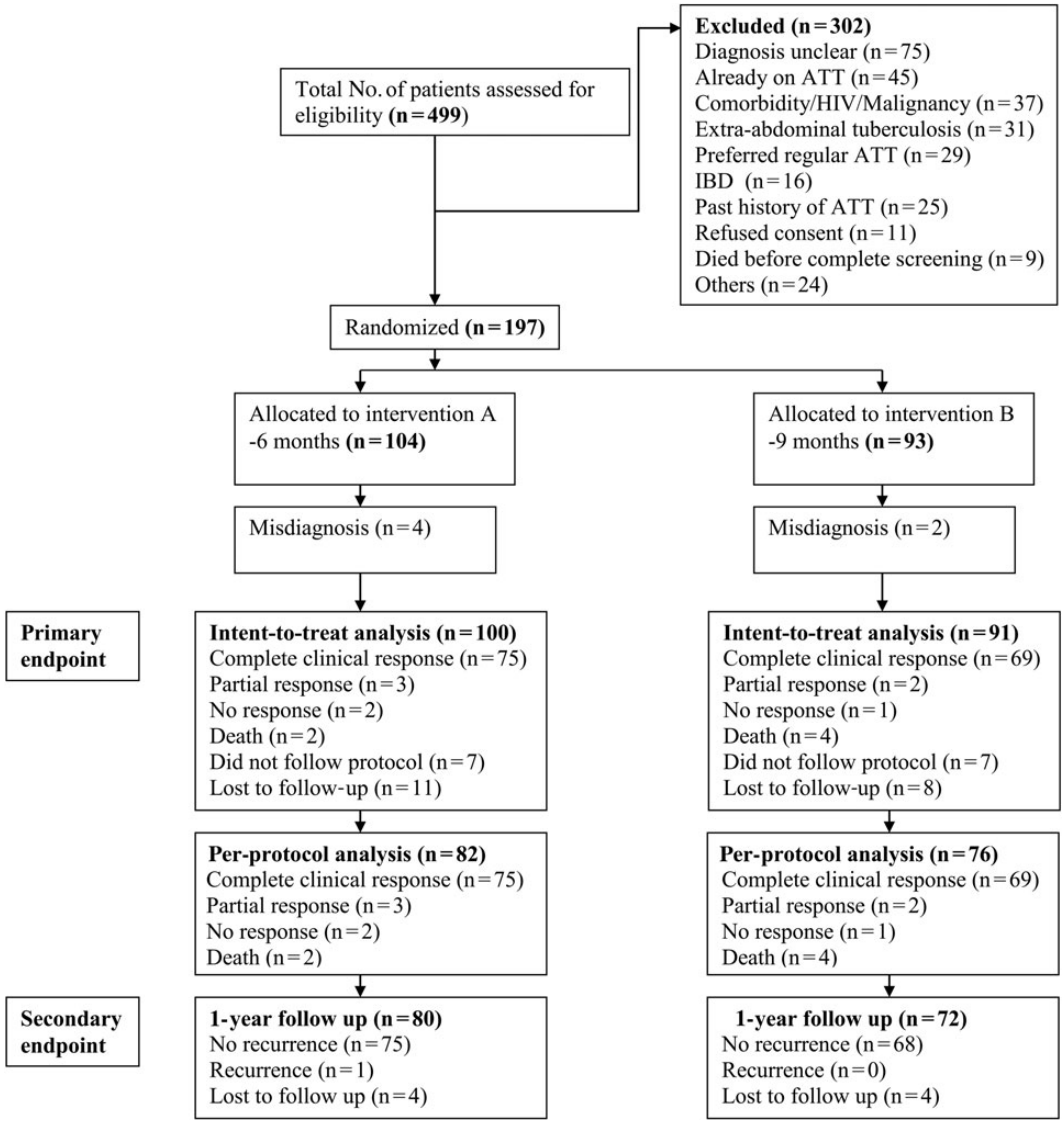

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flowchart. Abbreviations: ATT, antituberculosis; HIV, human immunodeficiency virus; IBD, inflammatory bowel disease.

Basis of Diagnosis and Site of Predominant Disease

Presence of any of the 3 features, such as caseating granulomas on histology, a positive culture, or tissue/fluid staining for AFB, were considered to be diagnostic of tuberculosis. Tuberculosis PCR alone was not considered to be sufficient for a definitive diagnosis of tuberculosis (Table 3).

On the basis of any of the 3 criteria mentioned above, 54 (54%) patients in the 6-month group and 57 (62.6%) in the 9-month group had a definitive diagnosis of tuberculosis. In others, the diagnosis remained presumptive and was based on a combination of strong clinical suspicion, colonoscopy, and/or imaging findings. Of 100 patients in the 6-month group, 76 (76%) had GI tuberculosis, 22 (22%) had peritoneal tuberculosis, and 2 (2%) had features of both. Of 91 patients in the 9-month group, 72 (79.1%) had GI tuberculosis, 18 (19.8%) had peritoneal tuberculosis, and 1 (1.1%) had features of both. Patients described as having GI tuberculosis included 3 with duodenal, 3 with gastric, and 2 with esophageal tuberculosis.

End-of-Treatment Response

ITT Analysis

Eleven (11%) patients in the 6-month group and 8 (8.8%) in the 9-month group were lost to follow-up (Figure 1). On ITT analysis, complete clinical response was seen in 75 (75%) patients in the 6-month group and 69 (75.8%) in the 9-month group ($P = .89$; Table 4). Three (3%) and 2 (2.2%) patients showed

Table 1. Demographic and Clinical Characteristics at Baseline

Characteristics	Patients Randomized to 6-mo Group (n = 100)	Patients Randomized to 9-mo Group (n = 91)	*P* Value
Age, mean ± SD	34 ± 14.2	34.9 ± 13.9	.56
Sex			
Male	53 (53)	52 (57.1)	.67
Female	47 (47)	39 (42.9)	
BMI, kg/m^2	(n = 80)	(n = 71)	.25
Underweight (<18.5)	40 (47.6)	41 (57.7)	
Normal weight (18.5–24.9)	33 (49.3)	28 (39.4)	
Overweight (25–29.9)	3 (3.6)	2 (2.8)	
Obese (≥30)	4 (4.8)	0	
Clinical features			
Abdominal pain	79 (79)	71 (78.0)	.86
Weight loss	79 (79)	69 (75.8)	.60
Loss of appetite	68 (68)	56 (61.5)	.35
Fever	57 (57)	50 (54.9)	.77
Symptoms of intestinal obstruction	41 (41)	39 (42.9)	.79
Recurrent/chronic diarrhea	29 (29)	35 (38.5)	.16
Blood in stool	9 (9)	11 (12.1)	.48
Dyspepsia	36 (36)	37 (40.7)	.50
Arthralgia	23 (23)	30 (33.0)	.12
Chronic cough	12 (12.0)	19 (20.9)	.09
Laboratory investigations			
Anemia (Hb <12 in women and <13 g/dL in men)	74/96 (77.1)	67/88 (76.1)	.87
Raised ESR	54/65 (83.1)	56/67 (83.6)	.93
Low albumin (<3.5 g/dL)	30/90 (33.3)	37/83 (44.6)	.12

Data are presented as No. (%) unless otherwise specified.

Abbreviations: BMI, body mass index; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; SD, standard deviation.

partial response in the 6- and 9-month groups, respectively. Two (2%) patients in the 6-month group and 1 (1.1%) patient in the 9-month group showed no response.

Per-Protocol Analysis

Excluding patients not following DOTs or lost to follow-up, 75 (91.5%) in the 6-month group and 69 (90.8%) in the 9-month group showed complete clinical response; there was no difference in outcomes between the 2 groups ($P = .88$; Table 5).

Demonstration of Healing of Lesions in Patients With GI Tuberculosis

Of 62 evaluable patients with GI tuberculosis randomized to 6 months of therapy, 54 had predominant ileocolonic involvement and were eligible for colonoscopic reevaluation for demonstration of mucosal healing; all 31 (57.4%) patients agreeing to colonoscopy showed mucosal healing. Overall, of 62 patients, 38 (61.3%) showed healing of lesions on either colonoscopy or imaging.

In patients randomized to 9 months of therapy, 57 patients with GI tuberculosis showed either complete, partial, or no response. Of these, 47 were eligible for repeat colonoscopy; all 24 (51.1%) patients agreeing to colonoscopy showed mucosal healing. Overall, of 57 patients, 31 (54.4%) showed healing of lesions on either colonoscopy or imaging.

Table 2. Predominant Site of the Disease

Site	Patients Randomized to 6-mo Group (n = 100)	Patients Randomized to 9-mo Group (n = 91)	*P* Value
Peritoneum	23 (23)	18 (19.8)	.58
Gastrointestinal tract			
Rectum	1 (1)	0	.33
Colon	13 (13)	8 (8.8)	.35
Ileocolonic/terminal ileum	47 (47)	47 (51.6)	.52
Small intestine	6 (6)	10 (11)	.21
Duodenum	1 (1)	2 (2.2)	.50
Stomach	2 (2)	0	.17
Esophagus	2 (2)	0	.17
Multicentric	5 (5)	6 (6.6)	.63

Data are presented as No. (%).

Demonstration of Healing of Lesions in Patients With Peritoneal Tuberculosis

In the 6-month group, all 18 patients showed complete clinical response. Of them, all 11 (61.1%) undergoing imaging at EOT showed resolution of lesions. In the 9-month group, 15 patients showed either complete, partial, or no response. Of them, all 3 (20%) undergoing EOT imaging showed resolution of lesions.

Outcome of Patients Having No Clinical Response

Three patients showed no response to treatment. One patient with peritoneal tuberculosis in the 9-month group who had persistent ascites responded to additional treatment for 3 months.

Table 3. Yield of Diagnostic Tests

Diagnostic Test	6-mo Group (n = 100)	9-mo Group (n = 91)
Granulomas	42/77 (54.5)	41/75 (54.7)
BACTEC culture	10/57 (17.5)	12/59 (20.3)
AFB stain	12/70 (17.1)	15/64 (23.4)
AFB PCR	25/45 (55.6)	18/40 (45.0)

Data are presented as No. of positive tests/No. of tests performed (%).

Abbreviations: AFB, acid-fast bacilli; PCR, polymerase chain reaction.

Table 4. Results of Efficacy at End of Treatment: Intent-to-Treat Analysis

Outcome	6-mo Group (n = 100)	9-mo Group (n = 91)	*P* Value
Complete clinical response	75 (75)	69 (75.8)	*P* = .89
Partial response	3 (3)	2 (2.2)	
No response	2 (2)	1 (1.1)	
Lost to follow-up	11 (11)	8 (8.8)	
Death	2 (2)	4 (4.4)	
Did not follow protocol	7 (7)	7 (7.7)	

Data are presented as No. (%).

The other 2 patients, in the 6-month group, had to undergo surgical intervention for intestinal obstruction (at 5 and 6 months from baseline, respectively) during treatment. Antituberculosis therapy was completed in these patients; 1 of them preferred to take a daily drug regimen. All 3 nonresponders were doing well after 1 year of follow-up.

Mortality

Six patients died during the treatment period; the time of death and possible reasons are described in Table 6.

Outcome of Patients Who Did Not Follow Protocol

Fourteen patients who did not follow the DOTs protocol and took treatment elsewhere were followed up separately through telephone conversation or by mail. Of them, 12 (85.7%) showed complete clinical response, whereas 2 could not be followed up.

Subgroup Analysis

A complete clinical response was observed in 109 (73.7%) patients with GI tuberculosis and 33 (82.5%) with peritoneal tuberculosis on ITT analysis ($P = .24$). On per-protocol analysis, 109 (89.3%) with GI tuberculosis and 33 (97.1%) with peritoneal tuberculosis showed complete clinical response ($P = .16$). Among patients with peritoneal tuberculosis, there was no significant difference in response rate between 6-month and 9-month group on ITT analysis (81.8% vs 83.3%; $P = .90$) and per-protocol analysis (100% vs 93.75%; $P = .28$).

Table 5. Results of Efficacy at End of Treatment: Per-Protocol Analysis

Outcome	6-mo Group (n = 82)	9-mo Group (n = 76)	*P* Value
Complete clinical response	75 (91.5)	69 (90.8)	*P* = .88
Partial response	3 (3.7)	2 (2.6)	
No response	2 (2.4)	1 (1.3)	
Death	2 (2.4)	4 (5.3)	

Data are presented as No. (%).

Table 6. Profile of Patients Who Died During Treatment

Group	Age/ Sex	Time to Death After Initiation of Antituberculosis Therapy	Comments
6 mo	33/M	1 mo	Ileocolonic tuberculosis, malnourished
9 mo	43/F	2 mo	Ileocolonic tuberculosis, developed intestinal obstruction, underwent surgery but developed sepsis and died
6 mo	22/M	3 mo	Ileocolonic tuberculosis, malnourished
9 mo	25/F	4 mo	Ileocolonic tuberculosis, developed intestinal obstruction, died after presentation in the emergency department
9 mo	26/M	2 mo	Ileocolonic tuberculosis developed ileal perforation, underwent surgery, developed peritonitis with septicemia, died in the postoperative period
9 mo	16/F	3 mo	Peritoneal tuberculosis, failed to follow up after 1 month of randomization; when contacted at 4 mo, it was found that patient died 3 mo after treatment was started

Adherence to Treatment

Among patients following the protocol, 82 and 76 in the 6-month and 9-month groups, respectively, were compliant with treatment. One patient in the 9-month group missing treatment for 1 month was treated with an additional month of treatment.

Side Effects

Twenty (21.3%) and 16 (18.2%) patients in the 6- and 9-month groups, respectively, developed 1 or more side effects (Table 7). Three and 5 patients in the 6- and 9-month groups, respectively, developed drug-induced hepatitis and were managed as described in the "Patients and Methods" section. All of them were followed up closely; after resolution of hepatitis, first-line drugs were reintroduced. All of them recovered.

Table 7. Side Effects

Side Effect	6-mo Group (n = 94)	9-mo Group (n = 88)	*P* Value
Vomiting	13 (13.8)	16 (18.2)	.42
Epigastric pain	6 (6.4)	12 (13.6)	.10
Hepatitis	3 (3.2)	5 (5.7)	.41
Anorexia	4 (4.3)	6 (6.7)	.46
Any single side effect	20 (21.3)	16 (18.2)	.60

Data are presented as No. (%).

Secondary Outcome: 1-Year of Follow-up for Recurrence

After completion of primary treatment as per randomization, evaluable patients (ie, 80 in the 6-month group and 72 in the 9-month group) were followed up for recurrence. Four patients from each group were lost to follow-up; 1 patient in the 6-month group developed recurrence of tuberculosis at 11 months of follow-up. The patient developed a new cervical lymph node; fine-needle aspiration showed caseation and AFB. The tuberculosis culture, however, was negative. His intestinal disease was evaluated again at this stage, which showed healed lesions. The patient was treated with DOTs category II treatment for 9 months, and he responded. No recurrence of the disease was observed in the rest of the patients at the end of 1 year of follow-up.

DISCUSSION

The present study included 3 major findings. First, there was no difference in the complete response, partial response, or mucosal healing rate between the 6 months and 9 months of antituberculosis regimens in treatment of GI and peritoneal tuberculosis. Second, antituberculosis drugs given intermittently using the DOTs strategy were efficacious. Finally, there was no difference in the recurrence of tuberculosis after 1 year of follow-up.

Because treatment of tuberculosis is prolonged, adherence to treatment is a major problem in many parts of the world including India [20, 21]. To increase the rate of adherence to treatment and reduction in the duration of exposure of potentially toxic drugs, efforts are being made to decrease the duration of treatment. The ideal duration of antituberculosis therapy among patients with GI and peritoneal tuberculosis is a still a debatable issue and has policy implications for several countries, including India [6–8]. Tuberculosis of pleura, which is a paucibacillary disease, is now treated with antituberculosis drugs given for 4 months only [22, 23]. Furthermore, even ultra-short treatment (4 months) along with spinal surgery has been tried for patients with spinal tuberculosis [23]. In a study of 90 patients with intestinal tuberculosis, Park et al from Korea showed a comparable efficacy of regimens spanning 6 months and 9 months (93.3% vs 91.1%; $P = 1.00$) [7]. The present study, which was adequately powered, further confirms that even 6 months of treatment has an efficacy of 91.5% vs that of 90.8% with 9 months of treatment on per-protocol analysis.

Recurrence of the disease remains a concern with short-course therapies. Several retrospective cohort analyses have documented higher recurrence rates with rifampicin-containing regimens of <6 months' duration and when antituberculosis drugs are given intermittently during the intensive phase [24, 25]. In the present study, 1 patient developed recurrence of the disease 11 months after completion of primary treatment during the follow-up phase of the study. Furthermore, in the Korean study, the recurrence rate at 1 year of follow-up was also similar between the 6-month and 9-month treatment groups [7].

Although a numerically higher percentage of patients with peritoneal tuberculosis achieved complete clinical response than those with GI tuberculosis, both on per-protocol (97.1 vs 89.3%; $P = .16$) and ITT analyses (82.5% vs 73.7%; $P = .24$), there was no statistically significant difference. There is a lack of efficacy studies on tubercular peritonitis except for a report of 47 patients almost 45 years ago [26]. The present study, although including a small number of patients, confirms a high cure rate of >90% by both 6 months and 9 months of intermittent therapy.

This study had much strength, but a few weaknesses need mention. Although a follow-up of at least 1 year is desirable for recurrence of the disease, late recurrence of the disease after 1 year was not evaluated.

The results of the present study not only provide evidence for existing recommendations on the duration of treatment for patients with GI tuberculosis, but also provide evidence to policy makers for recommendation of intermittent therapy using the DOTs strategy for patients with GI tuberculosis in those countries where adherence to treatment is a barrier to effective treatment for tuberculosis.

In conclusion, these findings show that short-course intermittent treatment for 6 months was as effective as 9 months in the management of abdominal tuberculosis. There was no difference in the recurrence rate at 1 year of follow-up.

Notes

Acknowledgments. We acknowledge the contribution of all the patients for participating in this study. The contribution of all the directly observed short-course therapy (DOTs) centers and DOTs officers is deeply appreciated. We appreciate the efforts of Dr Deepak Gupta in helping to coordinate the various DOTs centers.

Financial support. This work was supported by the Central Tuberculosis Division, Ministry of Health and Family Welfare, government of India.

Potential conflicts of interest. S. K. S. has served as a member of the National Research Committee on Operational Research in Tuberculosis and as an advisor to the National Task Force on the Involvement of Medical Colleges in the Revised National Tuberculosis Control Programme, and has received research grants from the Indian Council of Medical Research, New Delhi. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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