Research Article

Abdominal tuberculosis: experience with RNTCP category III antitubercular therapy

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Abstract

Background: Abdominal tuberculosis as such has been put in seriously ill category III regimen because the therapy of abdominal tuberculosis throws up many challenges, especially those presenting with immune compromised and malnourished state. To accommodate all the accompanying challenges, it is prudent to keep the regimen flexible.

Objective: To study the 30- and 60-day efficacy of daily versus alternate-day self-administered therapy of abdominal tuberculosis in young adults with ileocecal tuberculosis (IC) and mesenteric tubercular lymphadenitis (ML).

Materials and Methods: This study was conducted for a duration of 2 years, starting June 2013, in an outpatient setting of a tertiary referral center in north India. Patients identified during a study of causes of functional abdominal pain syndrome (FAPS) or "only pain" presentation in gastroenterology (GI) outpatient and diagnosed as IC or ML on the basis of contrast-enhanced computerized tomography (CECT) and/or colonoscopy with ileoscopy were given daily (weight based) versus alternate-day revised national tuberculosis control program (RNTCP) category III regimen therapy in a nonrandom manner.

Result: Twelve patients of abdominal tuberculosis were identified: eight cases had IC with varying degrees of gastrointestinal disturbances whereas four had ML with no other organic disease explaining the symptoms. Groups prescribed daily versus alternate-day therapy did not differ significantly because of the presentation as FAPS in young adults. All patients received clinically significant improvement with antitubercular therapy. Four patients prescribed RNTCP category III regimen showed excellent clinical relief. Dyspepsia occurred significantly more with alternate-day therapy.

Conclusion: Self-administered DOTS alternate-day therapy according to RNTCP category III regimen is equally efficacious to daily-weight-based regimen in young adults with abdominal tuberculosis.

KEY WORDS: Abdominal, tuberculosis, DOTS, functional abdominal pain syndrome

Introduction

Abdominal tuberculosis, a type of extrapulmonary tuberculosis (EPTB), presents in a variety of forms.[1] Abdominal tuberculosis as a whole is more difficult to treat because it spreads contiguously and produces distortion of lumen and peristaltic activity that can permanently affect gastrointestinal function, predisposing the patient to lifelong strictures and small intestinal bacterial overgrowth. Abdominal tuberculosis as such has been put in seriously ill category III regimen because the therapy of abdominal tuberculosis throws up many challenges, especially those presenting with immune compromised and malnourished state. To accommodate all the accompanying challenges, it is prudent to keep the regimen flexible. Poor nutrition and phytosanitary standards are two such challenges in southeast Asian countries. Cost of therapy and compliance are the other important variables in

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treatment of abdominal tuberculosis because of its disturbingly symptomatic and prolonged course.

Short-course alternate-day antitubercular therapy (ATT) in this group of primarily infected young patients is an attractive option for both reducing cost and increasing compliance.

The purpose of this study was to study the 30- and 60-day efficacy of alternate-day therapy (with higher dose per person; weight immaterial between 30 and 60 kg) to daily regimen (with per kg based doses) in a selected group of patients with abdominal tuberculosis.

Materials and Methods

Patients presenting to gastroenterology (GI) outpatient department (OPD) with complaints of abdominal pain without GI symptoms were enrolled in a study to determine the cause of pain as functional or organic. Study duration was of 2 year from June 2013 onwards. Following investigations, colonoscopy with ileoscopy with biopsy and contrast-enhanced computerized tomography (CECT) of abdomen, ascitic fluid examination (where available), and X-ray chest (where supportive evidence required) were performed. Mantoux skin sensitivity test, tubercular culture, polymerase chain reaction (PCR) for tuberculosis, and GeneXpert tests were mostly not performed due to low sensitivity and high cost. Diagnosis was based on clinical inputs and a CECT of abdomen and/or colonoscopy evidence. Histopathology was performed on identified lesions. Normal mucosa of ileum was biopsied routinely.

Patients were divided to receive alternate-day therapy [H: isoniazid (600 mg), R: rifampicin (450 mg), Z: pyrazinamide (1500 mg), E: ethambutol (1200 mg)] or daily-weight-based regimen (H, 5 mg/kg/day; R, 10 mg/kg/day; Z, 20 mg/kg/day; E, 15 mg/kg/day) nonrandomly. Patients who weigh 60 kg or more received additional rifampicin (150 g) as per RNTCP guidelines. Weight-based daily regimen was given to patients with low body mass index, anemia, malnutrition, or an antecedent immunocompromised state. Alternate-day therapy was given mostly to those where identification of ileocecal tuberculosis/tubercular mesenteric lymphadenitis (IC/ML) seemed to be incidental or non-resolution of radiological evidence. A paired two-tailed *z*-value was calculated from the proportions of response to two regimens on a Web-based calculator (http://www.socscistatistics.com).

Result

During the study period, 54 patients were diagnosed with abdominal tuberculosis: 17 had tubercular ascites with cirrhosis of liver; 7 had military tuberculosis with pleural effusion with tubercular enteritis and/or tubercular ascites; 14 had tubercular ascites alone; 3 had tubercular colitis; 15 with tubercular enteritis presented with other comorbidities such as diabetes mellitus type II (6 patients), hypothyroidism (3 patients), pancytopenia (2 patients), seizure disorder (1 patient), acute renal failure with congestive cardiac failure (1 patient), and chronic diarrhea (2 patients).

Twelve patients with IC and ML tuberculosis were identified during the study period. Patients with ML tuberculosis were younger than those with IC tuberculosis. Eleven patients were identified with mesenteric lymphadenitis. Five patients had nonspecific lymphadenitis and responded to conservative treatment. Three patients were lost to follow-up. Four patients were prescribed daily antitubercular treatment because of their low weight. Three patients with IC tuberculosis with mild features of intestinal obstruction were found to have multiple ileal strictures. Most other patients with IC tuberculosis presented with right lower quadrant pain and did not respond to conventional analgesic and anti-infective treatment. These patients were then advised a CECT of abdomen wherein the diagnosis was confirmed.

Discussion

Functional abdominal pain syndrome (FAPS) or “only pain abdomen” is a common clinical presentation in young patients presenting to a GI OPD. Tuberculosis was found to be one of the foremost organic pathologies detected in this group of patients in a typically southeast Asian nation tertiary referral center OPD of Gastroenterology. Other diagnoses detected were liver hemangioma (2 patients), ureteric calculi (7 patients), diverticulosis (3 patients), urinary tract infection (10 patients), and gynecological conditions (6 patients).

Because of an abundance of patients with pulmonary tuberculosis in southeast Asian subcontinent, abdominal tuberculosis is found accompanying diseases such as chronic pancreatitis, extrahepatic portal hypertension, diabetes mellitus, hypothyroidism, and chronic renal disease. This latter situation causes considerable confusion as to the primary diagnosis and contribution of tuberculosis in morbidity. Considerable number of colonoscopies performed for diseases such as irritable bowel syndrome and irritable bowel disease also throws up a subset of patients where tuberculosis is incidentally detected. Hepatobiliary and pancreatic tuberculosis are the other types of enigmatic abdominal tuberculosis.

Moreover, it is often seen that EPTB especially abdominal tuberculosis is seen in immunocompromised states such as cirrhosis of liver, pancytopenia, malnutrition, diabetes mellitus, and alcoholism. Overall, abdominal tuberculosis especially gastrointestinal tuberculosis can affect the well-being of the patient and quality of life by affecting GI function and coping functions.

A characteristic of abdominal tuberculosis is its low diagnostic yield. Best estimates are for laparoscopic biopsy, approaching a healthy 60–80% in different series. In all the other modalities of investigation, the best estimates of PPV are 20–40%. Diagnostic laparoscopy is not a widely practiced diagnostic modality in southeast Asian nations, partly because of the extra workload it puts on the busy schedule of the attending surgeon. A study of abdominal tuberculosis from reputed hospital in a metro city could provide a histological or bacteriological evidence in only 64% patients with best available tools.[2] A combination of radiology such as CECT

and endoscopy such as ileocolonoscopy coupled with few supporting clinical or lab evidences may be an acceptable strategy of identifying ileocecal and lymph node abdominal tuberculosis when other possibilities have been suitably (mostly clinically) excluded.[3,4] Cost of confirmatory evidence such as AFB positivity, caseating granuloma, or other ELISA or PCR tests is very high and time-consuming. Low sensitivity of these tests also proscribes its extensive reliance.

A therapeutic trial of ATT for 2–3 months has been an acceptable strategy of differentiating circumstantial evidence of abdominal tuberculosis from other differentials. Ultrashort ATT regimen of 3 months is often prescribed by gynecologist in tubo-ovarian mass or dysmenorrhea or lower abdominal pain patient to delineate the etiology in resource constrained settings.

Ileocecal tuberculosis (mural involvement as identified with CECT) is often accompanied with tubercular lymph adenitis. Isolated mesenteric tubercular lymphadenitis of differing patterns such as para-aortic, mesenteric, and peripancreatic and periappendiceal is mostly seen in younger patients without much mural involvement.[6] The types of involvement change with age of the patient and age of exposure. Both primary and post-primary abdominal tuberculosis can occur although post-primary tuberculosis is more common in young adult patients.

Very often, it is seen that nonspecific therapy with good nutrition also "cures" the condition in this group of patients. Usefulness of a short therapeutic nontubercular anti-infective challenge cannot be ignored before prescribing more decisive ATT.

Reported rate of drug-induced hepatitis in our study are fortuitously low. One reason for this may be relatively young age of patients. Hospitalized drug-induced liver injury due to ATT patients are usually those with multiple comorbidities. Average age of patients in this study population was 30 years whereas those with comorbidities admitted to GE ward was 44 years.

The apparent high response rate in alternate day therapy may be due to low number of patients and need to be confirmed with a larger longer study, which is ongoing. High overall symptom response rate may have to do to the rigorous clinical approach with which patients were clinically screened for abdominal tuberculosis. Probably only those with pathology of abdominal tuberculosis were being treated. A thorough counseling for dietary measures along with an adequate and productive follow-up before treatment to rule out nontubercular etiologies also contributed to the success.

One drawback of the study was that the patients could not be randomized between ileocecal and lymph node groups

Table 1: Demographic profile of patients with IC and ML tuberculosis

Parameter	IC TB	ML TB
Number	8	4
Age (years)	29 (15–45)	19 (12–26)
M/F	4:5	2:1
Presenting complaints		
Predominantly pain	8	4
Bloating/dyspepsia	6	3
Features of SAIO	3	0
Weight loss	3	1
Physical finding		
Pallor	3	1
Tenderness over abdomen	7	2
Carnett's test	3	1
Lump	4	0
Mean weight (kg)	47	34
Signs of weight loss	4	0
Investigations		
Hb (g%)	10.5	11.2
ESR (mm Hg)	34	20
CRP	All < 3	All < 1
Histopathology +	6	0
Colonoscopy +	4/6	-
CECT diagnosis	8/8	4/4

CECT, contrast-enhanced computerized tomography.

Table 2: Comparison of 30- and 60-day efficacy of daily vs. alternate-day ATT

Parameters	Treatment response, 30 day		*p*-value	Treatment response, 60 day		*p*-value
	Daily ($n = 8$)	Alternate day ($n = 4$)		Daily ($n = 8$)	Alternate day ($n = 4$)	
Response to therapy*	7/8	3/4	0.60	8/8	4/4	1
Improvement in pain	4/8	2/4	1.0	8/8	3/4	0.13
Significant weight gain	3/8	2/4	0.66	6/8	2/4	0.38
Reduction of lump	3/4	-		4/4	-	
Adverse events						
Dyspepsia	2	2	0.38	3	3	0.0375*
Hepatitis	0	0	0.0	1	0	0.47

*$p < 0.05$.

as per Table 1. The reason was that most patients with ML tuberculosis were adolescents with body weight less than 30 kg and thus not suitable to alternate day higher dose therapy.

Another drawback was that commercially available formulations were prescribed and thus it was not possible to assure exact dosing in each case. High-dose alternate-day therapy produced symptoms of gastritis in significant number of cases (Table2). Another study from a teaching hospital found similar incidence of dyspepsia in patients receiving fixed-dose alternate-day DOTS regimen.[7] It can be argued that formulations appropriately reducing the number of tablets in given case can further improve compliance and efficacy.

An offshoot of the alternate-day therapy was the realization by the patient that the abdominal discomfort was drug related so had to be tolerated. This also assured of better compliance due to better knowledge.

Thus, this study demonstrates that alternate-day high-dose ATT was as efficacious as daily-weight-based ATT in a special subset of young adult patients of abdominal tuberculosis without significant comorbidities.

Conclusion

Self-administered DOTS alternate-day therapy according to RNTCP category III regimen is equally efficacious to daily-weight-based regimen in young adults with abdominal tuberculosis.

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