

bronchiectasis must be ruled out.² Histologically, the cavities consist of an area of central necrosis coated with a wall of converging conglomerated sarcoid granulomas.^{1,2} The cavities may be present from onset, or develop months or years later. They can remain stable for a time, but they can also disappear and new cavities can form.³

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Treatment of Latent Tuberculosis Infection in a Tuberculosis Clinic^{*}



Tratamiento de la infección tuberculosa latente en una unidad clínica de tuberculosis

To the Editor:

Tuberculosis (TB) is still a major worldwide public health problem. Individuals with latent tuberculosis infection (LTI) are at risk of developing the disease, and this risk is associated with their immune status. The development of TB can be avoided by the use of preventive treatment - treatment of latent tuberculosis infection or TLTI.¹ The effectiveness of TLTI depends on the efficacy of the regimens used² and on compliance with these regimens.³

We conducted an observational retrospective study to evaluate TLTI compliance and factors associated with dropout.

Subjects with a diagnosis of LTI who began TLTI in the Unidad Clínica de Tuberculosis Vall d'Hebron-Drassanes between January 2011 and December 2016 were studied. The diagnosis of LTI was established on the basis of a positive tuberculin test and/or IGRA with a normal chest X-ray. The TLTI regimen was indicated according to the guidelines of the Spanish Society of Pulmonology and Thoracic Surgery.⁴

All cases were followed up with monthly clinical and laboratory evaluations, and whenever the patient presented intolerance. Adherence was assessed through interview and determination of isoniazid metabolites in urine,⁵ and compliance was defined as administration of more than 80% of the prescribed doses.

In total, 1113 patients with a mean age of 29 years were included consecutively; 713 were men (64%). A total of 793 (71%) were immigrants from more than 50 countries (Table 1). Seventy percent of African patients were from the Maghreb countries (primarily Morocco), and the rest were sub-Saharan. In total, 71.5% of Asians were from the Indian subcontinent, the majority from Pakistan. In the group of Latin American patients, most were from Bolivia (23%), Ecuador (21%), Peru (14%), Dominican Republic (11%), and Colombia (9%). Fifty-five percent of patients from eastern Europe were Romanian.

TLTI was indicated as a result of contact tracing in 675 (61%) individuals, and screening of the at-risk population in 438 (39%).

The TLTI regimen of choice was the combination of isoniazid and rifampicin for 3 months, which was indicated in 1017 patients (91%). The 6-month isoniazid regimen was reserved for patients in whom rifampicin was contraindicated to avoid interactions with their regular medication. Monotherapy with rifampin for 4 months was used in patients with TLTI indicated due to contact with patients with active TB known to be isoniazid-resistant, and as a rescue drug when isoniazid was withdrawn for liver toxicity.

In total, 920 patients (83%) completed treatment and 150 (13%) dropped out. Adverse effects (AE) were recorded in 274 patients (24%), the most common being raised liver enzymes (106; 10%). TLTI was withdrawn in only 43 patients who reported AE (4%). In 42 (4%) cases, the initially indicated regimen was switched; of these, 98% completed the TLTI.

Variables related to dropout in the logistic regression analysis were: diagnosis by screening of at-risk population (OR 2.06; 95% CI 1.45–2.93), male sex (OR 1.79; 95% CI 1.20–2.65), age less than 35 years (OR 1.76; 95% CI 1.14–2.73), not living with family (OR 3.2; 95% CI 2.19–4.80), low educational level (OR 5.11; 95% CI 1.83–14.13), unemployment (OR 3.09; 95% CI 2.04–4.68), smoking (OR 1.62; 95% CI 1.12–2.35), alcoholism (OR 1.96; 95% CI 1.26–3.06), and immigration (OR 3.2; 95% CI 1.92–5.35). Among the subgroup of immigrants, worse compliance was observed in those who had resided for less than 2 years in Spain (OR 1.86; 95% CI 1.27–2.72).

We believe that 3-month course of combined isoniazid and rifampicin usually used in our hospital is the main factor contributing to the TLTI completion rates that we observed. The use of short regimens based on rifampicin alone or in combination with other drugs has been shown to improve TLTI completion rates compared to long regimens with treatments of 6–9 months, and this is considered a fundamental strategy for improving adherence, while maintaining the same efficacy as the traditional regimens.^{3,6} In a clinical trial conducted by our group, the use of a combination of isoniazid and rifampicin during 3 months showed a rate of compliance (72%) significantly higher than the 6-month isoniazid regimen (52%), with no differences in AE incidence, liver toxicity or efficacy.⁷

The diagnosis of LTI also influences subsequent compliance with the TLTI. Patients who are prescribed TLTI as the result of contact tracing adhere better to treatment (86%) than those in whom TLTI was prescribed as a result of at-risk population screening (78%). A recently published review that collected TLTI completion rates from 13 prospective studies shows that compliance among recent contacts of active TB cases was 53%–82% compared with 25%–71% of individuals detected in screening programs. This behavior was attributed to the lack of perception of risk in the latter group.⁸

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Table 1
Factors Associated with Treatment of Latent Tuberculosis Infection Compliance.

	Total	%	Correct TLTI Compliance	%	TLTI Dropout	%	OR (95% CI)	P
<i>Years</i>								
<i>Sex</i>								
Women	400	36	342	86	37	9	Ref	
Men	713	64	578	81	112	16	1.79 (1.20–2.65)	.003
<i>Age group, years</i>								
Less than 35	777	70	631	81	120	15	1.76 (1.14–2.73)	.009
35–50	302	27	260	86	28	9	Ref	
Over 50	34	3	29	85	1	3	0.32 (0.04–2.44)	.49
<i>Regimen</i>								
Others	48	4	43	90	5	10	Ref	
3RH	1017	91	842	83	134	13	1.32 (0.53–3.51)	.66
6H	48	4	35	73	10	21	2.45 (0.76–7.85)	.16
<i>LTI diagnosis</i>								
TB contact tracing	675	61	578	86	67	10	Ref	
At-risk population screening	438	39	342	78	82	19	2.06 (1.45–2.93)	<.001
<i>Immigration</i>								
No	320	29	280	88	18	6	Ref	
Yes	793	71	640	81	131	17	3.2 (1.92–5.35)	<.001
<i>Geographical origin</i>								
Africa	245	31	188	77	50	20	2.9 (1.77–4.85)	<.001
Asia	274	35	237	86	29	11	1.3 (0.77–2.34)	.32
Eastern Europe and Romania	56	7	35	63	9	16	2.8 (1.23–6.51)	.025
Latin America	193	24	164	85	22	11	1.4 (0.81–2.68)	.21
Spain and EU	349	31	298	86	27	7	Ref	
<i>Years of residence in the Spain (immigrants)</i>								
2	509	64	424	83	68	13	Ref	
<2	284	36	214	75	64	23	1.86 (1.27–2.72)	<.001
<i>Educational level</i>								
Low	590		474	80	97	16	5.11 (1.83–14.23)	.0002
Mean	289		244	84	32	11	3.2 (1.13–9.51)	.019
High	110		100	91	4	4	Ref	
<i>Family situation</i>								
Living in a family	674		623	92	51	8	Ref	
Not living in a family	319		252	79	67	21	3.2 (2.19–4.80)	<.001
<i>Working situation</i>								
Active	518		449	87	46	9	Ref	
Unemployed	279		205	73	65	23	3.09 (2.04–4.67)	<.001
Others	303		253	83	35	12	1.35 (0.84–2.15)	.22
<i>Alcohol consumption (> 60 g/day)</i>								
No	962		810	84	116	12	Ref	
Yes	149		110	74	31	21	1.96 (1.26–3.06)	.003
<i>Smoking</i>								
No	793		669	84	92	12	Ref	
Yes	305		241	79	54	18	1.62 (1.12–2.35)	.009
<i>Drug use</i>								
No	1083		898	83	142	13	Ref	
Yes	29		21	72	7	24	2.1 (0.88–5.04)	.09
<i>Adverse effects</i>								
No	830		775	93	43	5	Ref	
Yes	172		141	82	6	3	0.76 (0.32–1.83)	.6
<i>Liver toxicity</i>								
No	889		823	93	46	5	Ref	
Yes	106		89	84	1	1	0.2 (0.02–1.47)	.11

95% CI: 95% confidence interval; OR: odds ratio; TLTI: treatment of latent tuberculosis infection; 3RH: rifampicin + isoniazid for 3 months; 6H: isoniazid for 6 months; Ref: reference population.

In our review, AE and liver toxicity were not associated with TLTI dropout, in contrast to the findings of other authors.⁹ During the study, around 25% of patients reported some type of AE, although the monthly visits and easy access to the tuberculosis clinic whenever symptoms appeared helped us to initiate measures to resolve problems, thus avoiding dropout. Elevated transaminases were the most common AE: 89% of cases were asymptomatic,

and only 12 patients were classified as severe (1%), figures similar to other studies.^{10,11} Analytical monitoring, temporary suspension of treatment and/or a change in regimen usually ensured successful completion of treatment.

The most important sociodemographic factors associated with lack of compliance were young age, worse social situation, such as not living in a family, low educational level, unemployment, and

immigration. These factors have been described previously by other authors as predictors of compliance failure.^{12,13}

In conclusion, TLTI compliance in our center was satisfactory. Although the appearance of AEs was very common, these were easily resolved with close monitoring by expert personnel and easy access to the clinic, facilitating completion of the TLTI.

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Cardiorespiratory Side Effects in the Clipping Technique for the Treatment of Axillary and Palmar Hyperhidrosis[☆]



Efectos secundarios cardiorrespiratorios en la técnica del pinzamiento para el tratamiento de la hiperhidrosis palmar y axilar

To the Editor:

The surgical treatment of primary palmar and axillary hyperhidrosis (HH) consists of interruption of the thoracic sympathetic nerve. The most common intervention is sympathetic chain lysis or sympathectomy.^{1,2} The clipping technique was designed to allow reversal of the intervention in the case of severe adverse effects, primarily compensatory HH.³ The main aim of this study was to evaluate the effects of this technique on cardiopulmonary function.

This was a prospective study, approved by the Clinical Research Ethics Committee of Hospital Universitario de Gran Canaria Dr. Negrín Centro. All patients signed an informed consent form before participation. The study variables were respiratory and cardiovascular side effects. Patients aged between the ages of 14 and 40 years, with palmar or palmoaxillary HH and no history of smoking or cardiorespiratory disease were included.

Study patients were treated with a surgical technique of clipping at the T3 (palmar HH) or T3–T4 (palmoaxillary HH) level. Cardiopulmonary function was studied before and 6 months after the intervention. The following tests were performed: forced spirometry, measurement of lung volumes and airway resistance,

calculation of CO diffusion, and a maximum incremental cardiorespiratory exercise test and stress test using a cycle ergometer.

Quantitative variables were analyzed using the t test for paired data and repeated measurements using analysis of variance. Categorical variables were compared with the Chi-square or Fisher's exact test. The SPSS 15.0 statistical package (SPSS Inc., Chicago, IL, USA) was used. Differences with a *P* value <.05 were considered statistically significant.

We analyzed 31 patients with an average age of 21.81±4.87 years who underwent surgery between 2013 and 2015. There were no postoperative complications. Six months after surgery, a significant decrease was observed in FEF_{25%–75%} (–5.6%), and no differences were found in FVC, FEV₁, lung volumes and airway resistance. CO diffusion decreased significantly (–6.4%). The stress test showed a significant decrease in maximum minute ventilation (–12.2%), and in heart rate at peak effort (–3.9%) and at 2 min during recovery (–6.2%). No significant differences were found in oxygen consumption. Systolic and diastolic arterial pressures were reduced at peak effort (–11.5% and –7.1%, respectively), as was diastolic blood pressure at rest (–8.1%). All patients completed the pre- and post-clipping exercise tests with no significant symptoms. These data are summarized in Table 1.

Similarly to other sympathectomy techniques,^{4–6} this study showed that clipping the sympathetic chain at the T3 and T3–T4 level causes significant changes in cardiopulmonary function. We found a decrease in FEF_{25%–75%}, probably reflecting an increase in bronchomotor tone due to the altered balance between sympathetic and parasympathetic innervations. However, in previous studies,^{4,5} we found a decrease in FEV₁ and FEF_{25%–75%}, in line with the results of other authors,⁷ showing that changes in spirometry are less significant with clipping than with conventional sympathectomy. We did not note any changes in lung volumes, although the non-significant increase in airway resistance would support the hypothesis of an increase in bronchomotor tone. The decline

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