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Sputum induction is a safe procedure to use in prisoners and MGIT is the best culture method to diagnose tuberculosis in prisons: a cohort study

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SUMMARY

Objectives: To evaluate the concordance and safety of induced sputum (IS) and spontaneous sputum (SS), and estimate concordance and time to detection of *M. tuberculosis* between Lowenstein–Jensen (LJ), thin-layer agar (TLA), and the Mycobacteria Growth Indicator Tube system (MGIT).
Methods: This was a cohort study. Prisoners with pulmonary tuberculosis (PTB) were followed for 2 years. At baseline and every follow-up visit, three sputum samples were taken on consecutive days (one IS and two SS) and adverse events occurring before, during, and 30 min after IS were registered. All sputum samples were stained with auramine and cultured in LJ, TLA (to test resistance), and MGIT.
Results: Five hundred eighty-six IS and 532 SS were performed on 64 PTB patients. Breathlessness (1.6%), cough (1.2%), hemoptysis (0.3%), and cyanosis (0.2%) were the only complications. Concordance between IS and SS was 0.78 (95% confidence interval 0.69–0.87); 11 positive cultures from IS samples were negative in SS, and 11 positive cultures from SS samples were negative in IS. One hundred seventy-eight cultures were positive by any technique: MGIT 95%, LJ 73%, and TLA 57%. Time to detection of *M. tuberculosis* in LJ, TLA, and MGIT was 31, 18, and 11 days, respectively.
Conclusions: The IS procedure is safe in prisons. The MGIT system is better and faster than LJ and TLA in the diagnosis of *M. tuberculosis*.

1. Introduction

Tuberculosis (TB) is a public health threat, particularly in prisons where the incidence of TB and latent TB infection is high.[1] The second element of the directly observed therapy strategy (DOTS) is case detection through quality-assured bacteriology, and includes bacteriology for diagnosis (sputum smear microscopy, culture, and drug susceptibility testing) and strengthened laboratory networks.

In Colombia, guidelines published by the Ministry of Health state that culture of a sputum sample is mandatory for prisoners with suspected TB.[2] This policy is not adhered to due to the lack of a well-implemented TB program in the country and, with regard to prisons, a lack of political commitment, inadequate financing for diagnostic laboratories, and a lack of awareness of the magnitude of TB incidence in prisons. This situation is similar in other prisons around the world.[3]

Sputum smear microscopy remains the cornerstone of TB diagnosis in developing countries and in prisons; however, it is hampered by low sensitivity ranging from 50% to 80% for active pulmonary TB cases, decreasing to 20% in HIV-infected individuals. There must be 5000 to 10 000 bacilli per milliliter of specimen to allow the detection of bacteria in stained smears, whereas culture is able to detect as few as 10 bacteria per milliliter.[4] Also, there are factors that influence the sensitivity, such as the staining technique, centrifugation speed, reader experience, and the prevalence of TB in the population being tested.[4] The inadequate sensitivity of sputum smear microscopy leads to misdiagnosis in

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up to a half of patients with active TB, which means that, on average, a person with active TB will infect between 10 and 15 people every year unless he/she receives adequate treatment. Furthermore, overcrowding and poor ventilation in prisons provide optimal conditions for the transmission of TB. Therefore, it is important to use culture. However, conventional cultures (Ogawa–Kudoh and Lowenstein–Jensen (LJ)) require a protracted incubation period (mean range from 25.6 to 32.6 ± 11.8 days[5–10]) due to the slow growth rate of TB bacilli. A good alternative to decrease the time to detection of *Mycobacterium tuberculosis* is the use of liquid cultures. In Colombia, there are two alternatives: the Mycobacteria Growth Indicator Tube system (MGIT) and thin-layer agar (TLA). These methods have been shown to decrease the mean time to detection of growth to 11–15.1 days.[5,6,9,11–14]

The method of obtaining a respiratory sample is also critical. In prisons, it is important to employ alternative strategies to obtain a specimen when the patient cannot expectorate or has inadequate sputum (HIV patients or those with a dry cough), during follow-up to confirm that the patient is cured, or for people who are sputum smear-negative. Although bronchoscopy for bronchoalveolar lavage (BAL) is an alternative, this procedure is invasive, expensive, and requires specialized personnel and equipment that is not available in prisons. The lack of available resources necessitates the transport of prisoners to a hospital in order to obtain a BAL sample, which may not be feasible due to safety issues or limited resources. Sputum induction could, therefore, be an option in prisons. Recent studies have reported that the overall success of sputum induction is high (76.4–100%), while adverse events associated with induced sputum (IS) are infrequent and mild.[15] Also, the diagnostic yield of IS has been found to range from 35% to 95% and there are no differences in the yield according to HIV prevalence or age.[16]

The objectives of this study were (1) to evaluate the safety of the IS procedure; (2) to compare the quality of IS and spontaneous sputum (SS) samples and estimate the concordance between them; and (3) to estimate the concordance and the time to detection of *M. tuberculosis* in three cultures: LJ, TLA, and MGIT.

2. Materials and methods

2.1. Study design and setting

This prospective cohort study was carried out in four prisons (two male and two female) in two cities in Colombia (Medellín and Bucaramanga). These prisons have middle and high security block cells, and there are sentenced individuals and others awaiting sentencing. The percentage of overcrowding in three of the prisons is 147.5%, 95%, and 33%, respectively.[17] One prison was recently constructed and divided into male and female prisons and there is no overcrowding at present.

2.2. Participants, procedures, and follow-up

All prisoners older than 18 years of age and diagnosed with active pulmonary TB were eligible for inclusion in the study.

People diagnosed with active pulmonary TB by sputum smear or culture were followed for 2 years or until the end of the study, from April 30, 2010 to December 23, 2012 in Medellín, and from April 30, 2010 to June 30, 2011 in Bucaramanga, as described previously.[17] Follow-up visits were done monthly for 6 months after starting anti-TB treatment, or 9 months in the setting of HIV or monoresistance. Subsequent follow-up was carried out on a bimonthly basis for the next 6 months, and quarterly during the second year. During each follow-up, one sample of SS was taken followed by one sample of IS an hour after the SS on the first day, and one SS sample was taken the next day.

The day prior to sputum induction, patients were instructed not to brush their teeth with toothpaste before the procedure. Each patient received detailed information and clear instructions about the sputum induction. Patients who agreed to the procedure were asked about any contraindication to the procedure, such as a history of massive epistaxis necessitating an emergency room visit, history of bleeding disorders, history of heart failure, chest tube drainage for pneumothorax, recent eye surgery, and history of severe asthma requiring treatment in the intensive care unit. In the absence of a contraindication, participants were asked for the presence of the following symptoms in the last 48 h: persistent cough, hemoptysis, dyspnea, and pleuritic chest pain. The same symptoms were sought during and 30 min after the IS procedure. A physical examination was performed before, during, and after the IS procedure. Due to the lack of negative pressure isolation rooms in prisons, the procedures were conducted in sports fields within the prisons. These places were chosen because they are far from other individuals and they are well-ventilated areas.

The procedure was carried out by trained personnel (a physician and a nurse or a physical therapist). During sputum induction, the personnel kept a distance of 5 m from the participant, while observing the patient at all times. Supplemental oxygen and full resuscitation were available during the procedure. Before sputum induction, the patients rinsed their mouth with water. The field team instructed patients to spit into the container when they felt the urge to cough. Pretreatment with salbutamol 200 μg (two puffs from a standard metered-dose inhaler) was given. The nebulization started with hypertonic saline solution (5%) 15–20 min after bronchodilator pretreatment using a model 1121 MEDI-PUMP nebulizer. The field team stopped the procedure 10 min after the nebulization was started to perform a physical examination, after which nebulization was restarted until the patient completed 15 to 20 min. All sputum samples were taken under direct supervision by the field team.

All sputum samples were processed using the conventional sodium hydroxide–*N*-acetyl-L-cysteine method, decontamination, and concentration methods. A smear was prepared for auramine–rhodamine staining to visualize acid-fast bacilli (AFB). The first sample of SS and the IS sample of each person was inoculated in LJ medium, in MGIT incubated in an MGIT 960 BACTEC instrument (BD Diagnostics, Sparks, MD, USA), and in TLA for the detection of resistance to rifampicin and isoniazid, as reported previously.[18] *M. tuberculosis* was identified by standard biochemical tests. All procedures were done as described previously.[18–20] All contaminated cultures for all three media (LJ, TLA, and MGIT) were considered negative.

2.3. Study variables

The following information was collected: persistent cough, hemoptysis, dyspnea, pleuritic chest pain, heart rate, blood pressure, respiratory rate, temperature, breathlessness, abnormal breath sounds on lung auscultation, epistaxis, and cyanosis. The consistency, presence of mucus and blood, and volume of sputum samples were recorded. The presence of *M. tuberculosis* in each culture, the date of TB treatment initiation, the date on which the sputum samples were taken, and the date when each culture was positive were also noted.

2.4. Definitions

A patient without any clinical signs before sputum induction, who presented breathlessness, cyanosis, hemoptysis, or cough during and/or after the sputum induction, was considered to have experienced an adverse event.