Induced sputum versus gastric aspirate for microbiological confirmation of pulmonary tuberculosis in infants and young children: A prospective cohort study

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ABSTRACT

Introduction: The diagnosis of tuberculosis (TB) is challenging in children due to the paucibacillary nature of disease and difficulty in sample collection. Gastric lavage (GL) is recommended in children because children tend to swallow sputum and do not expectorate; however, it is invasive, stressful and requires admission. **Objective:** The objective of this study was to compare the yield of GL samples with that of induced sputum, which is a non-invasive method and can be done on an outpatient basis. **Methods:** A prospective cohort study was done on 55 children, who were <6 years of age, admitted for suspected pulmonary TB (PTB) in Medical College, Aligarh, from December 2011 to December 2013. Sputum induction and GL were done on 3 consecutive days according to the standard procedure. All samples were stained for acid-fast bacilli and each sample was cultured for *Mycobacterium tuberculosis*. **Results:** The median age of the children in the study group was 28 months. A positive smear and culture were positive for *M. tuberculosis* in 7.2% and 20% of children, respectively. There was no significant difference in smear positivity from induced sputum samples compared to gastric aspirate samples. However, the culture positivity for *M. tuberculosis* was better with induced sputum than gastric aspirate and the difference was statistically significant ($p<0.05$). Sputum induction procedures were well tolerated; minor side effects were vomiting, mild epistaxis, coughing, or transient wheezing. **Conclusion:** Sputum induction is safe and useful for microbiological confirmation of TB in young children. This technique is preferable to GL for diagnosis of PTB.

Key words: *Children, Gastric aspirate, Induced sputum, Pulmonary tuberculosis*

Tuberculosis (TB) is a global public health problem with India heading the 22 highest burden countries in the world. The epidemic of HIV has further compounded the problem and has led to the need for intensification of TB control programs [1]. However, overburdened health systems in developing countries traditionally have low priority attributed largely to the non-infectious TB cases among children. Apart from the paucibacillary nature of the disease, difficulty in the sample collection is a major problem faced while evaluating TB in a child. Failure to confirm the presence of *Mycobacterium tuberculosis* at the first presentation may contribute to on-going disease transmission. It follows that various strategies to improve the bacteriologic confirmation of pulmonary TB (TB) by the optimization of sample collection are of great importance for the control of the epidemic.

The two commonly used methods for isolation of tubercular bacilli are the gastric aspirate and induced sputum. For microbiological confirmation of the diagnoses of PTB in young children, sequential gastric lavage (GL) is done because children swallow their sputum and do not expectorate. However, GL is invasive, stressful for both child and health worker, usually, requires the admission of children and overnight fasting. Induced sputum is less invasive than GL, takes less time, and can be performed on outpatients or resource-poor settings. Hence, this study was conducted with the aim of comparing repeated specimens from induced sputum with repeated GLs for a yield of *M. tuberculosis* in infants and young children with suspected PTB in a high burden area.

METHODS

This was a prospective cohort study conducted between December 2011 and December 2013, at general pediatric ward and pulmonology and infectious disease clinic of the department of pediatrics, in a medical college and hospital, Aligarh. The study was approved by the institutional ethics committee and written informed consent was obtained from the parents before recruitment.

During the study period, children <6 years of age presenting with cough >2 weeks or any of the following symptoms were

taken as a TB suspect (presumptive TB) and were enrolled in the study: Fever >2 weeks, significant weight loss (loss of >5% of highest weight recorded in the past 3 months), hemoptysis, abnormalities of chest radiograph (parenchymal infiltrate, atelectasis, pleural effusion, or lymphadenopathy), and contact of TB case. The children over 6 years of age, children taking treatment or prophylaxis for TB, children showing signs of upper airway obstruction, children with severe respiratory distress, unconscious children (GCS <8) or convulsions, children with bleeding tendency, patients in whom consent could not be obtained, or in whom the procedure could not be completed, were excluded from the study.

All consecutive cases satisfying the inclusion criteria were included in the study. A total of 66 cases were included, while the sampling was completed in 56 cases as 10 patients dropped out of the study. After admission, history was taken and physical examination was done. Baseline vitals were undertaken in all children; monitoring was done throughout the procedures. Children were clinically monitored for the duration of their stay in the hospital. HIV testing was done for all the children included in the study. These children were admitted and subjected to both induced sputum and gastric aspirate for 3 consecutive days.

For gastric aspirate, children were made to fast in the night for at least 4 h and a nasogastric tube was placed. In the early morning, at least 20 ml of gastric aspirate was obtained, and if the sample was less than that 5–10 ml of normal saline was instilled and aspirate obtained. The aspirate was placed in a sterile vial containing sodium bicarbonate to prevent the bacilli from dying due to acidic gastric secretions. Pulse oximetry was done throughout the procedure to stop the procedure if the saturation falls <93% for >5 s, which did not happen in any of the cases of our study. The specimen was labeled and was transported to the laboratory for processing within 4 h, and if it was likely to take more time than 4 h, then the sample was stored in the refrigerator at 4–8° centigrade.

Sputum induction was done the same day 3 h later to GL as the child was comfortable. The child was nebulized with 200 mcg salbutamol through metered dose inhaler with attached spacer and mask or 0.15 mg/kg of levosalbutamol was given through a jet nebulizer with oxygen at a flow rate of 5 L/min mixed with normal saline. The child was then nebulized with 5 ml of 3% saline for 15 min. Chest physiotherapy was done and was instructed to take two deep breaths followed by holding the breath for a few seconds and then exhaling slowly. The 3rd time, the child was asked to breathe in and then forcefully blow out air. Then, the child was asked to cough and sputum sample, if any, was collected in a wide-mouthed sterile plastic container. Most children who were either unable to expectorate or follow instructions, nasal or nasopharyngeal suction was done by a mucus sucker to obtain the sample and a 3 ml sample was considered adequate.

This sequence was repeated for 3 consecutive days and all the samples collected were sent for smear examination, which was done by Ziehl–Neelsen method and was cultured separately on Lowenstein-Jensen media. TB was diagnosed when a stain for acid-fast bacilli (AFB) was positive, or *M. tuberculosis* was cultured from induced sputum or GL specimens. Spacers and nebulizer equipment were sterilized after use in every patient.

The yield of *M. tuberculosis* from induced sputum and GL was compared with the two-sided McNemar test and odds ratios and 95%. Confidence intervals were calculated for paired data.

RESULTS

A total of 55 children underwent the procedure of gastric aspiration and sputum induction for 3 consecutive days; of which, 61% were male while the mean age was 28 months. 11 children were confirmed for PTB based on positive culture and/or AFB positivity. The youngest child in whom sputum induction was done, was 5 months old, the other 5 children (10%) were 6 months or younger, and 12 (22%) were less than a year old. The mean respiratory rate was 40 (33–46/min).

In our study, 68% of the children belonged to the lower socioeconomic group. Among the study population, 90% of the children were undernourished at the time of enrolment. The most common symptom was associated with fever in 98% (54) of the patients followed by cough in 61% (34) of cases. The results showed that 61% (34) had a history of contact and 11% (6) of children were tested positive for HIV. The most common radiological finding was bilateral hilar lymphadenopathy in 90% of cases, with effusion in 2% (1) and generalized reticulonodular shadows in 2% of cases.

The total number of gastric aspirates was 165 and 165 induced sputum samples. No serious adverse reactions attributable to sputum induction or gastric aspirate occurred during or after the procedure; the most common adverse events were episodes of vomiting in 14 procedures (4.5%) with 2.5 episodes per patient and 1.5 episodes per patient in gastric aspirate and induced sputum, respectively. Mild epistaxis in 8 (2.5%) cases, and wheezing that was responsive to an inhaled bronchodilator in one (0.03%) case. Median oxygen saturation during the procedure was 95%. A total of 8 (2.5%) episodes of transient hypoxia were recorded during sputum induction in which the arterial oxygen saturation dropped <92%.

Hence, on smear examination, 4 of 55 patients turned out positive for AFB, and all four, who were positive on smear-induced sputum examination, were also positive on gastric aspirate. A positive culture for *M. tuberculosis* was obtained in 11 of 55 cases. With induced sputum, culture for *M. tuberculosis* was positive in 10 patients, while eight patients had culture positivity in gastric aspirate. Three patients who were positive on sputum culture were negative on gastric aspirate and one patient positive on gastric aspirate was negative on sputum culture.

M. tuberculosis was identified from the first sample of induced sputum in 9 (81.8%) of diagnosed children and subsequent two samples increased the yield by only one case, increasing the yield to 90.9% (Table1). The first sample from GL was positive in 5 children (45.5%); the second and third samples identified an additional three cases, increasing diagnostic yield to 72.2%

Table 1: Cumulative yield of *Mycobacterium tuberculosis* from repeated sputum examinations

Patients (n=55)	Culture positive	Smear positive	Culture or smear positive	Cumulative yield (%)
1st specimen	09	04	09	81.8
2nd specimen	08	04	08	90.9
3rd specimen	08	03	08	90.9
Total	10	04	10	90.9

Table 2: Cumulative yield of *Mycobacterium tuberculosis* from repeated GL

Patient (n=55)	Culture positive	Smear positive	Culture and smear positive67	Cumulative yield (%)
1st specimen	05	02	05	45.5
2nd specimen	04	02	04	63.6
3rd specimen	04	02	04	72.2
Total	08	04	08	72.2

GL: Gastric lavage

(Table 2). The yield of all three samples of induced sputum for culture was better than all three samples of gastric aspirate for culture by 18.7% (odds ratio 1.30 [0.47–3.60], p=0.61). The yield from the first sample of induced sputum was similar to that from three consecutive samples from GL (odds ratio 1.1 [0.39–3.10], p=0.85). However, the first sample yield of induced sputum was significantly higher than that from one sample from GL (odds ratio 1.91 [0.60–6.11], p=0.27).

Overall, smear positivity was 10.3% while smear positivity was 6.67% by induced sputum and 3.63% by gastric aspirate. Thus, smear positivity by induced sputum was better than gastric aspirate, but the difference was not statistically significant. Overall, culture positivity was 23% of the samples analyzed. 15% of samples of induced sputum were culture for Mycobacterium tuberculosis while 8% samples of gastric aspirate were positive. The culture positivity for *M. tuberculosis* was better with induced sputum than gastric aspirate and the difference was statistically significant ($p<0.05$). The occurrence of culture or smear-positive TB among HIV-infected children was 2 of 6 (33.33%), whereas children who were HIV negative or did not have clinical signs of HIV infection, 9 of 49 (18.37%) were culture positivity (odds ratio 2.22).

DISCUSSION

In this study, it was found that the diagnostic yield from sputum induction was better than that from GL in infants and young children admitted for suspected PTB. The yield from any sample from induced sputum was more than that from GLs, which has been the usual practice for microbiological confirmation in infants and young children. Furthermore, the cumulative yield for *M. tuberculosis* from induced sputum was higher than that from GLs. Contrary to the accepted practice, sputum samples could be induced even in very young infants, and sputum induction was well tolerated and could be effectively and safely done in infants and young children.

Pediatric TB is an increasingly important problem, especially in developing countries with high HIV prevalence. The smear and culture confirmation of PTB in children has relied on sequential GL specimens because sputum induction has not been regarded as feasible in young children who do not expectorate but swallow their secretions [2]. Gastric aspiration is a tedious process because the child needs to be hospitalized, time consuming, needs fasting beforehand, and is invasive as well as distressing to child and health worker. Even under ideal circumstances, isolation rates for *M. tuberculosis* from GL range from 28% to 40% in children with suspected TB although rates can rise to 75% in infants [3-6]. On the contrary, sputum induction is a less invasive procedure, can be done as an outpatient procedure and easier to do than GL.

The GLs gave lesser yield as compared to induced sputum. The order of the procedures might have influenced the yield; a study of adults found the yield to be equivalent when induced sputum was done immediately before GL, but higher from sputum when lavage was done first [7]. However, the substantial time period between induced sputum and GL in our study makes it unlikely that the first procedure could change the yield from the second.

It is thought that young children with pulmonary TB have paucibaccilary disease and therefore less contagious. However, in this study, we found that almost half of the culture-positive sputum samples were also smeared positive. Sputum induction has been an effective and useful technique for improvement of the smear-positive case detection rate in adults in TB control programs in developing countries, and smear microscopy is widely used for diagnosis [8-10]. However, careful environmental control should be undertaken to prevent nosocomial transmission of TB to patients or health care workers. Sputum induction should be done in a room with adequate ventilation and personal respiratory protection should be worn by health care workers [11]. However, in many areas in developing countries, where the prevalence of TB is high and such resources are unavailable, examination of sputum is usually done at primary health-care settings with rudimentary facilities [8-10,12]. It is recommended that induction can be done when spontaneous production of sputum is not possible; sputum collection areas should be well ventilated and protective masks should be worn by health care workers. The risk of nosocomial transmission is lower in children than in adults, who have higher bacillary loads; nevertheless, adequate precautions should still be taken.

CONCLUSION

In this study, the yield from any sample from induced sputum was more than that from GLs. Furthermore, the cumulative yield for *M. tuberculosis* from induced sputum was higher than that from GLs. Contrary to the accepted practice, sputum samples could be induced even in very young infants and sputum induction was well tolerated.

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