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YIELD OF SPUTUM INDUCTION WITH 3 % HYPERTONIC SALINE IN SMEAR NEGATIVE PULMONARY TUBERCULOSIS

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ABSTRACT

Tuberculosis continues as a major health problem all over the world. Sputum AFB is still the initial diagnostic strategy in Pulmonary Tuberculosis (TB) as it is cost effective, non invasive and easily accessible. But due to the lack of a proper specimen lot of suspected cases remain misdiagnosed and wrongly treated leading to unnecessary cost and side effects. Here we are trying to produce good quality of sputum to increase the yield of AFB smear for TB diagnosis by inducing sputum with 3% hypertonic saline.100 patients who had clinico-radiological suspicion of pulmonary tuberculosis having either initial sputum smear negative or inadequate sputum were included in the study. 91 patients produced adequate amount of sputum (>2 ml) after induction procedure.37 patients were found to be smear AFB positive after induction. Sputum induction with hypertonic saline produces good quality and adequate amount of sputum for smear examination thereby increasing the yield for smear positive pulmonary tuberculosis

KEY WORDS: **Sputum induction, hypertonic Saline, adequate sputum, smear AFB, Ziehl- Neelson**

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INTRODUCTION

Conventionally Pulmonary Tuberculosis is diagnosed by Smear AFB, AFB culture, radiology and mantoux in most part of the world. In Pulmonary TB the best method of diagnosis is the identification of organism in sputum. This is usually done by smear microscopy by Ziehl- Neelson staining method. Radiology and Tuberculin sensitivity tests are corroboratory evidences but sensitivity and specificity is very low. So the detection of bacilli is very much essential and helpful for diagnosis of Tuberculosis. Sensitivity of conventional microscopy ranges from 20%-80%[1,2].Fairly good number of strongly suspected cases of Tuberculosis are not confirmed bacteriologically due to poor quality or amount of sputum. The *sine qua non* of success in obtaining bacteriological confirmation of active pulmonary tuberculosis is the collection of adequate lung secretions[3]. But sometimes it may be difficult to obtain a good specimen for smear microscopy. Several techniques have been developed to obtain good respiratory specimen like bronchial lavage , gastric aspiration etc. Sputum Induction is one of the techniques which is easier, cost effective and non invasive and has revived recently due to these aspects and lower chance of nosocomial transmission compared to fiberoptic bronchoscopy[4]. Present study was to determine the efficacy in increasing the diagnostic yield of smear AFB by inhalation of 3% hypertonic saline using an ultrasonic nebuliser.

MATERIALS AND METHODS

Inclusion criteria

1) All cases of Spontaneous smear negative suspected pulmonary tuberculosis
2) Patients having dry or productive cough more than 2 weeks with radiological opacities suggestive of Tuberculosis
3) Patient having normal chest X ray with strong clinical suspicion of Tuberculosis especially in HIV cases

Exclusion criteria

1) Lack of Consent
2) Patients who are unable to follow instructions
3) History of hypersensitivity to hypertonic saline
4) Recent haemoptysis
5) Unstable cardiac status
6) Severe dyspnoea
7) History of epilepsy
8) Pneumothorax
9) Fracture ribs
10)Recent eye surgery
11)Thoracic,abdominal,or cerebral aneurysm
12)Pulmonary embolism

This is a cross sectional study conducted on patients admitted to TB ward of the department of pulmonary medicine, SCB Medical College, Cuttack, India. It was conducted on one hundred patients from September 2008 to August 2010.Ethical committee clearance obtained for the study on 24/2/2011. The study population included all patients of both sexes more than the age of 15 years, irrespective of their HIV status, who were having clinico radiological suspicion of pulmonary tuberculosis. A clinical suspect of pulmonary tuberculosis is defined by RNTCP(Revised national tuberculosis control program) criteria as(a) individual having cough 2 weeks or more(b)contacts of TB patients having cough of any duration (c)suspected or confirmed extra pulmonary TB having cough of any duration (d) HIV patients having cough of any duration with or without other symptoms such as evening rise of temperature, loss of weight, anorexia .A radiological suspect is defined by chest X ray finding which are suggestive of active TB defined by CDC (Centres for disease control and prevention) guidelines along with physician's judgement. These include infiltration or consolidation, cavitations, nodule with poorly defined margins, pleural effusion, hilar or mediastinal lymphadenopathy, miliary TB. Radiological extent of severity is defined by classification of national Tuberculosis association of USA. Minimal-Slight to moderate density with no cavitation. May involve a small part of one or both lung but should not exceed the volume of lung on one side that occupies the space above the second chondrosternal junction and the spine of fourth or body of fifth vertebra. Moderately advanced- Total extend should not exceed following limits: disseminated lesions of slight to moderate density that may extend throughout the total volume of one lung; total diameter of cavitations must be less than 4 cm Far advanced- lesions more extensive than moderately advanced Those patients who were excluded from the study are (a) recent haemoptysis (b) unstable cardiac status (c) history of epilepsy (d) Acute respiratory distress (e) known hypersensitivity to hypertonic saline. A patient was considered to have dry cough when no expectoration produced. Patient producing only saliva or volume of expectoration less than 2 ml was defined as having scanty sputum. Quality of sputum is assessed by RNTCP classification for visual appearance as M (mucoid) B (Blood) Saliva(S) Ethical clearance for the Study obtained from institutional ethical committee. Informed consent was taken from all patients prior to the procedure. All the patient's details were recorded including past medical history. Prior to the procedure, clinical examination, routine blood investigations, chest radiology, direct sputum smear microscopy were done. PEFR before and after the procedure were done in cases susceptible for bronchospasm.200 µg salbutamol MDI 2 puff were given with spacer prior to the procedure in such cases. Procedure was conducted in a well ventilated room. Patients were asked to rinse their mouth and gargle with water before the procedure. Patients were asked to sit upright ,straight head, and nebulisation mask fitted to face and nebuliser turned on. Patients were asked not to begin the procedure until staff member has left the room and closed the door. 7 ml of 3% hypertonic saline was used with ultrasonic nebuliser (LUPINEB palm – flow rate 0.4- 0.5ml/minutes; particle size 5µ) and they were asked to take forceful deep inhalation via mouth. Procedure was interrupted every 5 minutes for collecting sputum. Procedure was continued until 2 ml of respiratory secretion collected or 20 minutes of procedure elapsed. Expectorated Sputum was collected in a sterile container. Observed for complications and stopped the procedure accordingly. After the procedure, container labelled

properly. Smear AFB examination were done in designated microscopy centre (DMC) by Ziehl Neelson staining. Recording of results of sputum smear recorded as for grading as per RNTCP guidelines as negative, scanty, 1+, 2+, 3+

RESULTS

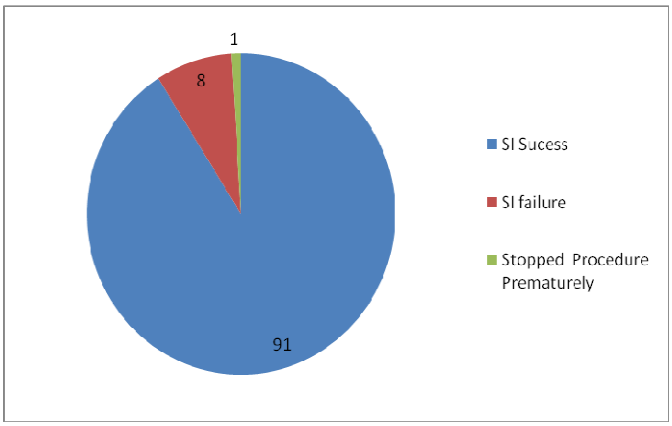
We conducted study on 100 people (74 males and 26 females). Mean age was 40.14.

Table 1
Demography of Study Population

Age	Male	Female	Total	%
15-34	25	16	41	41%
35-54	32	6	38	38%
55-74	12	4	16	16%
≥75	5	0	5	5%

57% patients had productive cough, 21% had dry cough and 28% had no cough at the time of presentation.78% patients had non cavitary lesions and 16% had cavitary lesions in chest X ray. 6 patients had normal Chest X ray. 46 patients had minimal lesions, 22 patients had moderate and 22 patients had far advanced lesions in the chest X ray. 31% had upper zone involvement, 10% had mid zone, 8% had lower zone and 45% had multiple zone involvement. In 91% cases sputum induction was successful in obtaining adequate amount of sputum (>2 ml) and in 8% it failed to produce sputum. One patient had to stop the procedure prematurely due to complication.

Figure 1
Success Of Sputum induction(SI) in Obtaining adequate sputum sample



Smear for AFB was positive in 37% of cases after sputum induction. In those cases with dry cough there was a yield of 48.3%(15/31) after induction and in those with productive cough the yield was 44.68% (21/44).

Figure 2
Extra yield after Sputum Induction

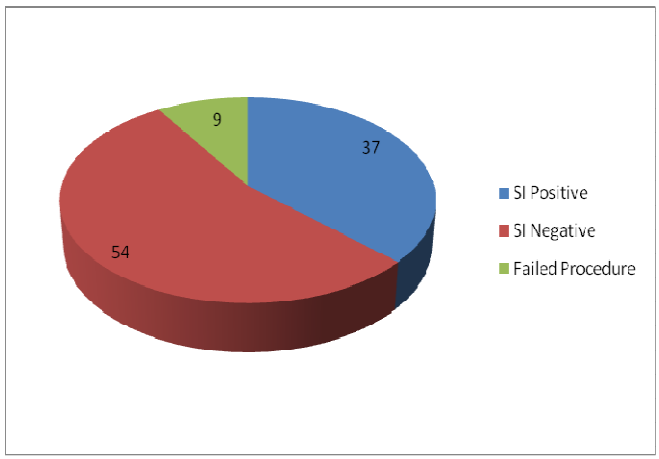


Table 2
Induced Sputum positivity compared to spontaneous sputum

Initial Sputum negative n(%)	Smear AFB report not available n(%)	Induced sputum negative n(%)	Induced sputum positive n(%)	Failed induction n(%)
88 (88%)	12 (12%)	54(54%)	37(37%)	9(9%)

78 cases (85.17%) provided adequate sample with mucoid appearance. 13 cases provided saliva after induction. 31 patients(39.74%) of mucoid samples and 6 patients(46.15%) of saliva sample were smear positive after SI procedure

Table 3
Visual appearance of induced sputum samples and smear positivity

Visual appearance	SI negative n(%)	SI Positive n(%)	Total
M(mucous)	47(60.26%)	31(39.74%)	78
S(Saliva)	7(53.85%)	6(46.15%)	13

In HIV cases sputum induction yielded smear positivity in 7.7%of cases. Sputum induction had best yield in cavitary cases (75%) ie 12/16 cases. Moderate or far advanced lesions yielded more smear positivity after induction 50% (22/44**).**

Figure 3

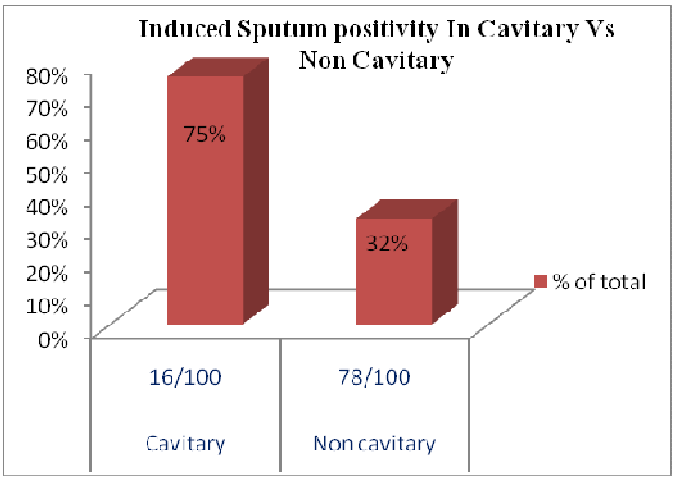


Table 4
Radiological extent of severity in induced cases

Radiological extent of severity	Total No: of cases	SI negative n(%)	SI positive n(%)	% of total
Minimal	46	26	15	32.61
Moderate	22	6	14	63.63
Far advanced	22	12	8	36.36

Good quality of specimen after sputum induction yielded higher grades. It is observed in this study that all the high grades (3+) are from 'Mucous' samples after induction.

Table 5
Grading Vs Quality Of Sputum In Induced Sputum

Grading	M(mucous) n(%)	S(Saliva) n(%)	Total n(%)
Scanty	1(25%)	3(75%)	4(10.8%)
1+	14(87.5%)	2(12.5%)	16(43.24%)
2+	6(86.71%)	1(14.29%)	7(16.22%)
3+	10(100%)	0(0%)	10(27.2%)

17% patients had complications which were mild .

Table 6
Complications of The Procedure

Complications	During procedure	Immediately after procedure	Total
Dizziness	2	4	6
Hemoptysis	1	2	3
Chest tightness	0	2	2
Breathlessness	0	2	2
Wheeze	0	1	1
Cough	0	2	2
Vomiting	1	0	0

DISCUSSION

Direct sputum smear examination is the basic approach to diagnose pulmonary tuberculosis[5]. Smear negative disease (patient with clinical and radiological evidence of pulmonary tuberculosis but repeatedly spontaneously negative sputum for AFB) is complicating diagnostic dilemma especially in elderly patients and immuno compromised like HIV due to atypical presentation and multiple differential diagnosis and lack of production of adequate amount of respiratory secretions. A good quality sample should be thick, or semisolid, purulent or yellowish mucous and of sufficient quantity (at least 2 ml). A good sample increases the detection chance of AFB in Microbiological examination[6]. A sample >5 ml of sputum increases sensitivity for Mycobacterium tuberculosis [7]. So every effort should be made to obtain adequate amount of sputum to detect active disease. Several methods like gastric washing, trans tracheal aspirate, bronchoscopy are used to collect specimen in cases of lack of expectoration but are invasive procedures and requires minimum level of expertise. It has been found out that induced sputum appears to be better than gastric washing in diagnostic point of view[8]. Sputum induction with 3% hypertonic saline delivered through an ultrasonic nebuliser is a non invasive but effective method to obtain respiratory secretions for detection of pulmonary TB. Inhalation of an aerosol of hypertonic saline to produce sputum was firstly used by Bickerman et al. in 1958 for cytology of lung cancer[9].It is suggested that hypertonicity of the deposited saline draws interstitial fluid into the lower airways by osmosis and also it causes bronchial irritation which stimulate coughing.[10,11]In this study procedure was successfully completed in 91% persons in obtaining adequate sample. It has been reported that 97% success of procedure in obtaining sputum by Marcus Conde etal.[12] and K.B.Gupta[5]. Here 37% became positive after sputum induction which is an extra yield.

Table 7
Comparison among previous studies in yield of induced sputum

Study	Induced Sputum positivity (%)
Marcus Conde etal.(2000)[12]	35%
K.B.Gupta& Seema Garg(2005)[5]	38%
Li etal.(1999)[14]	33.86%
Hartung etal.(2002)[15]	29%
Present study*	**37%**

The yield of procedure for smear AFB positivity for those who had initial spontaneous smear negative report was 35.22% (31/88).K.B. Gupta and Seema Garg reported 38%[5]. Quantity of sputum is important as inadequate sputum give low yield for smear positivity. In this study there is an extra yield of 37% for smear positivity who had either initial smear negative or no report due to inadequate sample or no expectoration. Sputum induction is found to increase the quality of sputum along with quantity of sputum. Though the visual appearance of sputum is an important factor for assessing the quality of sputum, a good number of induced sputum samples resembling saliva were smear positive. In this study percentage of induced sputum positivity is more in 'saliva' which is due to less absolute number of saliva samples. It can be concluded that no sample should be discarded after induction just on the basis of visual appearance. Usually sputum after induction is clear and watery. At the same time after induction 'Mucous' (M) sample by visual appearance yielded more higher grades which indicates high bacillary load. Quality of sputum is important for smear positivity and at the same time saliva can also yield sputum positivity. In cavitary cases it is highly necessary to obtain specimen for diagnostic purpose as it is usually active, carries high bacillary load leading to high infectivity, more chance of relapse and drug resistance if not properly treated. In this study 75% of cavitary cases in comparison with 32% non cavitary cases became sputum positive after induction. K. B. Gupta reported 50% Sputum positivity in cavitary and 38.15% in non cavitary cases after induction[9].Sputum Induction procedure is a safe procedure. In Our Study 17% patient reported mild complications which are comparable with other studies. K.B.Gupta & Seema Garg reported 13% of cases having distressing cough[5] .Dick menzies reported bronchospasm during induction in cases with pre existing Asthma[3].Marcus B Conde etal. reported 3 % side effects and Anderson reported no side effects during the procedure[12]. Donald C .Vinh stated that SI procedure is having extremely low side effects that include headache, bronchospasm and cough[13] .

CONCLUSION

Present study shows that sputum induction is safe, easy, cost effective,non invasive method of obtaining

respiratory secretion in patients suspected with pulmonary tuberculosis with no cough or scanty expectoration especially in resource poor country like India with increasing incidence of HIV-TB coinfection.

CONFLICT OF INTEREST
Conflict of interest declared none

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