# COMPARISON BETWEEN THE RESULTS OF ACID FAST BACILLI OBTAINED FROM SPONTANEOUS SPUTUM WITH SPUTUM INDUCTION BY SALINE 0.9 % AND BY SALBUTAMOL NEBULES IN THE DIAGNOSIS OF SPUTUM SMEAR NEGATIVE PULMONARY TUBERCULOSIS

### Kusdiantoro, M Jusuf Wibisono

Department of Pulmonology, Faculty of Medicine, Airlangga University Dr Soetomo General Hospital, Surabaya

#### **ABSTRACT**

The aim this study was to evaluate Sputum induction with Saline 0.9% and Salbutamol nebules in comparison with spontaneous sputum in the diagnosis of sputum smear negative, X-ray positive pulmonary tuberculosis. The design used in this study was Experimental Quasy, time series before and after design to all patients hospitalized with sputum smear negative, X-ray positive pulmonary tuberculosis during periode 3 months in the Department of Pulmonology, Dr Soetomo Hospital. In all, a total of the 29 patients were enrolled in the study, of these 2 patients exclude for reasons: 1 drop out and 1 dead et caused asphyxia. They are divided in 2 groups at random with system randomized permuted block use random statistic table. Each patient undergoing sputum smear examination and compared between spontaneous sputum by education effective cough and chest physiotherapy with sputum induction by Saline 0.9 % and by Salbutamol nebulas. Among Saline 0.9 % induction and Salbutamol induction performed wash out for 48 hours. Before and after sputum induction performed PEFR examination has been done and compared the result of it. During induction with Salbutamol nebules is performed heart rate and oxygen saturation monitoring by Oxymetri. There is significant difference PEFR before and after Saline 0.9 % induction and Salbutamol nebules induction ( p= 0,000 and p= 0,000 each for Saline 0.9 % and Salbutamol nebules respectively. The results of induction Saline0.9% and Salbutamol nebules in compared with spontaneous sputum there is no significant difference ( p=1,000 and p=0,317, each for Saline 0.9 % and Salbutamol nebules respectively ). In conclusion, there is no increase significant between spontaneous sputum by effective cough education and chest physiotherapy with induction Saline 0.9% and Salbutamol nebules to patients of pulmonary tuberculosis with sputum smear negative and X-ray positive. Effective cough education and chest physiotherapy can be obtained proper sputum.

Keywords: sputum induction, Saline 0.9%, Salbutamol, pulmonary tuberculosis

**Correspondence:** Kusdiantoro, Department of Pulmonology, Faculty of Medicine, Airlangga University, Dr Soetomo General Hospital, Surabaya

## INTRODUCTION

Tuberculosis is still a world problem, both the Morbidity and Mortality and become global threats. The disease is mostly found in the productive age (15-50 years). WHO estimates there are 8 million new cases and 2 million deaths due to TB every year (Blanc et al 2003). According to this global health organization, in 1996, Indonesia ranks third in the number of TB sufferers in the world after India and China with an estimated number of consecutive patients as much as 1761 .000, 1.45 million and 557.000.32 While the Household Health Survey (SKRT) in 1995 by Indonesian's Ministry of Health show that TB disease is the third cause of death after cardiovascular disease and respiratory disease in all age groups, and number one

from group infectious diseases. Figures for the growth of pulmonary tuberculosis in Indonesia amounted to 8 per 10 000 population per year. This amount is expected to continue meningkat (Depkes RI, 2002)

TB diagnosis in the TB reduction program was made through direct sputum examination and adequate sputum is important but for people that can not be issued a sputum or just slightly out sputum is a problem in TB pulmonary diagnosis (Brodie & Schluger 2005)

One of the efforts used to obtain an adequate sputum was by induction with Saline through the effects of increased airway lining fluid, which can increase mucosal permeability and induce bronchial mucous by glands submucosal secretion (Paggiaro et al 2002). In

2001, Yazdani et al. perform sputum induction by giving oral salbutamol in subjects with symptomatic pulmonary TB and get a 86% (255 of 289 subjects) positive of AFB (Yazdani et al 2002)

Lafortuna & Fazio in research on chronic bronchitis patients and healthy individuals who were given salbutamol nebules and get an average increase in clearance is significant compared to controls who received placebo (Lafortuna & Fazio 1984) But not yet known whether giving through nebules salbutamol can induce sputum and give better results than the specimens from sputum spontaneously and through saline induction.

#### MATERIALS AND METHODS

This research design is the Design Control Group Pretest. All patients who meet the full study is taught how to cough effectively to facilitate the discharge of phlegm. After doing chest physiotherapy, the patient asked to cough up sputum into a sterile pot that has been provided for the inspection of AFB (AFB sputum spontaneously 1). Prior to sputum induction measured PEFR three times as much and taken the best results. induction was done by nebulization physiological saline solution 0.9% for 15-25, then performed chest physiotherapy and patient asked to cough up sputum into a sterile pot that has been provided for the inspection of AFB (AFB sputum induction saline 0.9%). Completed induction PEFR measurements were taken three times and the best results, subsequently washed out for 48 hours.

Performed beginning with chest physiotherapy, the same patient asked to cough up sputum into a sterile pot that has been provided for the inspection of AFB (AFB sputum 2). Having done as much as three times PEFR measurements and taken the best results, sputum induction was done by salbutamol nebulization with a dose of 1 mg over 15-25 minutes, then the patient asked to cough up sputum into a sterile pot that has been provided for inspection AFB (AFB sputum induction salbutamol), PEFR measurements were then performed three times and taken the best results. Nebulization performed using ultra-sonic nebulizer Comfort II, the speed 0,25-0.75 ml / min.

The population was divided into two groups: group A given treatment as above, and group B point d and f is done in reverse. Election randomized group with a randomized permuted block system using random numbers table. The statistical analysis used was signet Wilcoxon rank test to test differences in sputum smear results before and after treatment, and Mann Whitney

test (Wilcoxon rank sum test) to test the results of sputum smear sputum induction Nebulization way saline solution 0.9% with salbutamol Nebulization. Signet Wilcoxon rank test used to test semikwantitatif ordinal scale data, two observations in one sample, while Mann Whitney test for ordinal scale semi-quantitative test data, inter-sample (2) independent.

#### RESULTS

There were no significant differences in gender distribution, age, and Relative Body Weight (RBW) in group A and group B. Most patients in the age group 25-34 years to reach nine people (33.3%), this results in accordance with the WHO report states that 75% of TB patients in developing countries about the productive ages of 15-50 years (Depkes RI 2002). Complaints and clinical symptoms found were: cough (85.2%), came out of sputum (74.1%), fever (66.7%), decreased appetite and weight loss (96.3%), night sweat (88.9%), breathlessness and chest pain (29.7%). Complaints are usually found in patients with pulmonary tuberculosis (Garay 2004).

Results of laboratory examination complete blood between the two groups did not differ significantly in levels of hemoglobin, leukocyte, erythrocyte sedimentation rate of blood and platelets. Platelet count in patients with pulmonary TB can vary, thrombocytosis in pulmonary tuberculosis patients because of acute phase reaction (Oyer & Schlosberg, 1999). Increased rate of blood crept in both groups because of the inflammatory process. In patients with pulmonary TB are usually increasing (Garay 2004). Accompanying diseases on the subject of most research is pleura effusion (55.6%) while the second is diabetes mellitus (7.4%).

Photo piston which are based on the extent of lesions in both groups according to the American Thoracic Society is currently at least 12 patients and 15 patients, the lesions are not widely available. Clinical diagnosis of pulmonary tuberculosis based on complaints, clinical symptoms, laboratory and photos piston.

Inspection PEFR before and after induction was done to see whether there is airway obstruction during sputum induction. In this study, PEFR measurements therefore easier, practical, and faster than the use of measuring instruments FEV1. Sputum induction should be discontinued if there is a complaint or a decrease in shortness of FEV 1 or PEFR  $\geq 20\%$ .

During this study, there were no shortness of breath in both the Saline or Salbutamol. PEFR increased significantly after induction induction Saline 0.9% and salbutamol. Increased PEFR between induction Saline 0.9% with salbutamol nebules didapatkaan induction a significant difference where the increase in PEFR in the induction of salbutamol greater than the induction Saline 0.9%, due to the existence bronkodilatasi effects of salbutamol.

In granting a nebulizer salbutamol should be considered signs of adverse effect, Heart rate and rhythm apex beat regularly and saturation monitoring oxygen (Rowley et al 1996). In this study, during induction with salbutamol nebules found no significant difference in heart rate at the beginning and end of induction in both groups. Oxygen saturation during induction with salbutamol was not significant difference (table 9.10). Leigh (1994): Oxygen saturation change in sputum induction never exceeds 4% (Leigh et al 1994)

Expectorated sputum has a sensitivity range of between 34-80%, the sensitivity tends to increase in patients with cavities, and lowest in patients who cough is weak and has not advanced disease (Brodie 2005). Based on the extent of piston images showed lesions in 12 patients with minimal lesions (44.4%) and 15 patients with lesions of moderate (55.6%), lesion area and the cavity can not be found in both groups of subjects.

The average duration to obtain adequate sputum specimens for smear examination is 18 minutes (group A) and 17 minutes (group B) for Saline 0.9%, 15 minutes (group A) and 16 minutes (group B) for salbutamol nebules . Between the two groups showed no significant. Sputum were successfully induced either by Saline 0.9% or salbutamol nebules.

### The results of sputum smear examination

Table 1. Comparisons between two groups of sputum smear

Group	Sputum -	BTA examination		
		Negative (%)	+1 Positive (%)	- Σ
A	Spontaneous I	10(83.3)	2(16.7)	12
	Induced by Saline 0.9 %	10(83.3)	2(16.7)	12
	Spontaneous II	11(91.7)	1(8.3)	12
В	Induced by Salbutamol	11(91.7)	1(8.3)	12
	Spontaneous I	15(100)	0(0)	15
	Induced by Salbutamol	14(93.3)	1(6.7)	15
	Spontaneous II	15(100)	0(0)	15
	Induced by Saline 0.9 %	15(100)	0(0)	15

Table 2. Comparison of spontaneous and induced sputum AFB

	AFB examination		Σ
Way the sputum taken	Negativ +1 Positive (%)		
Spontaneous I	25( 92.6)	2(16.7)	27
Spontaneous II	26(96.3)	1(3.7)	27
$\sum$ Spontaneous sputum	51(94.4)	3(5.6)	54
Induced by Saline 0.9 % I	10(83.3)	2(16.7)	12
Induced by Saline 0.9 % II	15(100)	0(0)	15
∑ Sputum induced by Saline 0.9 %	25(92.6)	2(7.4)	27
Induced Salbutamol I	11(91.7)	1(8.3)	12
Induced Salbutamol II	14(93.3)	1(6.7)	15
∑ Sputum induced by Salbutamol	25(92.6)	2(7.4)	27
∑ Sputum induced	50(92.6)	4(7.4)	54

### Comparison of sputum smear before induction

With the Wilcoxon Signed Ranks test statistic test showed no significant difference between spontaneous sputum smear AFB I and II of spontaneous sputum (p = 0.564), from 27 sputum smear examination showed two positive sputum AFB smear examination of sputum spontaneously at first and a positive sputum smear spontaneous sputum smear examination II, but this difference was not significant.

# Comparison of sputum smear before and after induction

Signet Wilcoxon statistical test Rank test did not showed significant difference between spontaneous sputum smear AFB sputum induction I and Saline 0.9% (p = 1.00).

Signet Wilcoxon statistical test Rank test did not showed significant difference between spontaneous sputum smear AFB sputum induction II and salbutamol (p = 1.00).

Signet Wilcoxon statistical test Rank test did not showed significant difference between spontaneous sputum smear AFB sputum induction I and salbutamol (p = 0.317).

Signet Wilcoxon statistical test Rank test did not showed significant difference between spontaneous sputum smear and AFB sputum induction Second Saline 0.9% (p = 1.00).

# Comparison of sputum smear after induction Saline 0.9% vs salbutamol

With a statistical test Mann Whitney test in both groups showed no significant difference in positivity.

# DISCUSSION

On sputum smear examination in group A showed spontaneous sputum smear positive samples of I 2 (1 +) and AFB 2 Induction Saline 0.9% positive samples (1 +), spontaneous BTA II, the first positive sample (1 +) and induction of salbutamol nebules one positive sample (1 +). In treatment group B, a positive sputum smear (1 +), only one sample was found in AFB sputum induction salbutamol nebules being spontaneous I, II and spontaneous sputum sputum induction results Saline 0.9%, all negative. There were no significant difference between spontaneous sputum smear examination results with the educational effective cough and chest physiotherapy with results of sputum smear examination

results of induction Saline 0.9%, p=1 ( $p \le 0.05$ ), in treatment group A and group B and between the results with spontaneous sputum smear and chest physiotherapy education with AFB sputum induction results salbutamol nebules p=1 ( $p \le 0.05$ ) in group A and p=0.317 ( $p \le 0.05$ ) in group B.

From all the results of sputum smear examination spontaneous and induced sputum samples obtained 7 (6.48%) are positive which consists of two spontaneous sputum samples I and two samples of sputum induction saline 0.9%, one sample II and a sample of spontaneous sputum induction salbutamol (group A) and a sample induction of salbutamol (group B) were 101 samples (93.52%) negative (Fig. 11). In most of the negative results are false negative possibilities, since microscopically to obtain the necessary 10 000 Mycobacterium tuberculosis Mycobacterium each milliliter of sputum, in contrast to the culture examination takes only 10 -100 Mycobacterium each milliliter sputum (Kent & Kubica 1985). In this study, no complications occurred bronchospasm or coughing up blood during or after induction, either by induction Saline 0.9%, or by induction of salbutamol nebules.

The limitation of this study were (1) results of sputum induction in this study was not done homogenization and concentration (centrifuge) before sputum smear was made; (2) the result of spontaneous or induced sputum in this study was not done culture examination.

## **CONCLUSIONS**

From the results of this study did not obtain a significant increase in sensitivity between spontaneous sputum AFB smear examination with chest physiotherapy education and induction saline 0.9% and salbutamol nebules induction in pulmonary tuberculosis patients with smear negative and positive radiological picture in the living room and male lung lung women. By educating how effective cough and chest physiotherapy can be obtained by proper sputum examined.

Sputum induction with 0.9% saline and salbutamol nebules does not cause bronchospasm or coughing up blood complications during and after induction. Induction procedures should be interpreted correctly so that the spread of executor can be prevented. Negative results of sputum smear examination can be a spontaneous or induced false negative culture examination that is required to increase the sensitivity of the results of the examination. Induction of sputum is an alternative way that is easy, safe and cheap and can be accepted by patients.

Educate how effective cough and chest physiotherapy on sputum of patients will be checked to be done to get a proper sputum examined. Sputum induction can be performed on patients who had difficulty of expectorate the sputum.

#### REFERENCES

- American Thoracic Soecity (1990). Diagnostic and classification tuberculosis. Am Rev Respir Dis; 142: 723-35.
- American Thoracic Soecity (1994). Treatment of Tuberculosis in Adult and Childreen. Am J Resp Crit Care Med. 1994; 149: 1349-74.
- Blanc L, Chaulet P, Espinal M, et al. (2003). Treatment of tuberculosis. Guidelines for national programmes 3<sup>rd</sup> ed. World Health Organization, Geneva.
- Brodie D, Schluger NW (2005). The diagnosis of Tuberculosis. Clin Chest Med; 26: 247-71
- Conde MB, Soares SL,Mello FC et al (2000). Comparison of sputum induction with fiberoptic bronchoscopy in the diagnosis of Tuberculosis.Am J Respir Crit Care Med; 162: 2238-40.
- Departeman Kesehatan Republik Indonesia (2002).Pedoman Nasional Penanggulangan Tuberculosis, Jakarta :1-56
- Fernandes LB, Henry PJ, Goldie RG (2003). Beta-2 adrenoreceptor. Available from : rgoldie@receptor.pharm.uwa.edu.au.
- Ferron GA (1994). Aerosol properties and lung deposition. Eur Respir J;7:1392-4.
- Fireman E (2003). Induced as diagnostic tactic in pulmonary diseases. IMAJ;5: 524-7.
- Fourie B(2002) Specimen collection In: Tuberculosis clearing house. Available from: http://www.sahealthinfo.org/tb/micrcollection.htm.
- Friedman LN (1997). Mycobacterium tuberculosis. In: Bone RC ed. Pulmonary and Critical care,1<sup>st</sup> Ed. Mosby Year Book inc: 1-44.
- Garay SM (2004). Pulmonary Tuberculosis.In: Rom WN, Garay SM (Eds).Tuberculosis, 2<sup>nd</sup> ed.Philadelphia; Lippincott William&Wilkins: 345-394.
- Glassroth J, Crnich CJ et al, (2004). Pulmonary infection Mycobacterial spesies. In: Baum's Textbook of pulmonary diseases, 7<sup>th</sup> ed. Lippincott Williams and Wilkins Company, Philadelphia: 373-404.
- Guleria R, Singh TR, Sinha S et al(2003). Effect of single inhalation of a salbutamol, ipratropium bromide and beclomethasone on mucociliary clearance in patients with chronic obstructive airway disease. Indian J Chest Dis Allied Sci;45:241-6.
- Helfets LB, Good RC (1994). Current laboratory methods for the diagnosis of tuberculosis. In: Bloom

- BR ed. Tuberculosis pathogenesis, protection, and control. ASM press, Washington: 85-98.
- Higgenbottam T (1997). Key issues in nebulized drug delivery to adults. Eur Respir J;7: 378-9.
- Hopewell PC (1995). A clinical view of tuberculosis. In: Goodman PC, Jinkins JR, eds. The radiologic clinics of north America Imaging of tuberculosis and craniospinal tuberculosis; 3:641-53.
- Hopewell PC (2001). Tuberculosis and other mycobacterial diseases. In: Murray JF, Nadel JA, Mason RJ eds. Textbook of respiratory medicine 3<sup>rd</sup> Ed. WB Saunders company, Philadelphia: 1043-49.
- Houtmeyers E,Gosselink R, Ramirez GG et al. (1999). Regulation of mucocilliary clearance in health and disease. Eur Respir J;13:1177-88.
- Kent PT, Kubica GP. Public Helth Mycobacteriology, Aguide for the Level III Laboratory. U.S. Dept. of Health and Human services, Center for Disease Control Atlanta, Georgia.1985.
- Kim S, Shao M X G, Nadel JA (2005). Mucus production, secretion, and Clearance. In :Moser RJ, Bradeus VS, Murray JF, Nadel JA eds.Textbook of respiratory medicine, 4<sup>th</sup> Ed.WB Saunders-company, Philadelphia: 330-54.
- Kim WD (1977). Lung mucus : a clinician's view.Eur Respir J;10: 1914-7.
- Kishioka C, Okamoto K, Kim JS, et al (2003). Hyperosmolar solutions stimulate mucus secretion in the ferret trachea. Chest; 124: 306-13.
- Lafortuna CL, Fazio F (1984). Acute effect of inhaled salbutamol on mucociliary clearance in health and chronic bronchitis. Respiration;45:111-23.
- Leigh TR, Kirby K, Gazzard BG(1994). Effect of sputum induction on arterial oxygen saturation and spirometry in HIVinfected patients. EurRespir J;7:453-58
- Li LM, Bai LQ, Yang HL et al (1999). Sputum Induction to improve the diagnostic yield in patients with suspected pulmonary tuberculosis. Int J Tuberc Lung Dis; 12: 1137-39.
- Lobue PA (2001). Tuberculosis: Syndrome, In: Bordow RA, Ries AL, Morris TA, eds. Manual of clinical problem in pulmonary medicine, 5<sup>th</sup> Ed. Lippincort Williams and Wilkins, Philadelphia: 159-63.
- Luelmo F (2004). What is the role of sputum microscopy in patients Attending health facilities?.In: Toman's tuberculosiscase detection, treatment, and monitoring questions and answers 2<sup>nd</sup>.Ed: Frieden T,World Health Organization,Geneva: 7-10.
- Luna JA (2004). ATuberculosis Guide for Specialist Physicians.International Union Agains tuberculosis and Lung Disease, Paris: 81-2.
- McAdams HP, Erasmus J, Winter JA(1995). Radiologic manifestations of pulmonary tuberculosis. The Radiologic Clinics of North America 1995;33:655-78

- Menzies D (2003). Sputum induction: Simpler, cheaper, and safer- but is it better? Am J Respir Crit Care Med; 167: 676-7.
- Moher D, Raviglione M,(2003).Global epidemiology of Tuberculosis. Clin Chest Med; 26: 167-82.
- Molloy A, Kaplan G (1996). Cell-mediated Immune response, In: Rom WN, Garay SM,eds. Tuberculosis, 1<sup>st</sup> ed. Little brown and Company, Boston: 305.
- Moulding T (1999). Pathogenesis, pathology, and immunology: Clinical Orientations. In: Schlossberg D ed. Tuberculosis and nontuberculosis mycobacterial infections, 4<sup>th</sup> ed. WB Saunders Company, Philadelphia:48-56.
- Ormerod LP (1994). Respiratory tuberculosis. In: Davies PDO ed.Clinical Tuberculosis, 1<sup>st</sup> ed Chapman and Hall Medicall, London: 74-91.
- Oyer RA, Schlosberg D (1999). Hematologic changes in tuberculosis. In: Schlosberg D ed. Tuberculosis and non tuberculosis mycobacterial infection, 4<sup>th</sup> ed. WB Saunders company, Philadelphia: 296-302.
- Paggiaro PL, Chanez P, Holt O, et al (2002). Sputum Induction. Eur Respir J; 20 : 3 S-8S.
- Phipps PR, Gonda I, Anderson SD, et al (1994). Regional deposition of saline aerosols of different in normal and ashmatics subjects. Eur Respir J;7:1474-82
- Pizzichini E, Pizzichini MMM, Leigh R, et al (2002). Safety of sputum Induction. Eur Respir J; 20: 9S-18S.
- Pudjiharjo WJ (1993). Penentuan sampel. Dalam: Poerwadi T, Joesoef AA, Widjaja L.ed. Metode penelitian dan statistic terapan. Airlangga University Press, Surabaya: 49-59.

- Rowley S, Asher I,Cooper D,(1996). Management of Adminitration of nebulised salbutamol. Available from:www.adhb.govt.nz/newborn/drug
- protocols/salbutamol pharmacology.htm [Acceessed 4 August ,2005].
- Soedarsono (2000). Diagnosis dan pengobatan tuberculosis paru dalam : Pendidikkan Berkelanjutan Paru IV, Lab-SMF Penyakit Paru FK Unair/RSUD dr Soetomo, Surabaya:49-60.
- Stanford JL(2000).Mycobacteria: Biology and epidemiology. In: Medicine International Far east edition.Respiratory disorder part 2of 2: 102-4.
- Stokes TE, Hocking GC,(2001).On the optimal inner tube shape for an ultrasonic nebulizer. Anziam J;43:E37-77.
- Triyono KSP (2002). Radiology of tuberculosis. Dalam: Palilingan JF, Maranatha D, Winariani ed. Simposium nasional TB update 2002, Surabaya.
- William TM, Wells AU, Harrison AC et al (2002). Induced sputum and brochoscopy in the diagnosis of pulmonary tuberculosis. Thorax;57:1010 14.
- Woods GL (2002). The Mycobacteriology laboratory and news diagnostic techniques Mycobacterial infectious. Infect Dis; 16: 127-44.
- Yazdani A, Kiran AL, Murty KJR (2002). Sputum induction by oral salbutamol. Ind J. Tub.;49:221-23.
- Zheng X, Robert GD (1999). Diagnosis and susceptibility testing. In : Schlossberg D, ed. Tuberculosis and non tuberculosis mycobacterial infection,4<sup>th</sup> ed. WB saunders Company, Philadelphia: 57-64.