FEASIBILITY OF INDUCED SPUTUM FOR DIAGNOSIS OF RESPIRATORY DISEASE AMONG HOSPITALISED CHILDREN AT UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

Original Article

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The use of Induced Sputum (IS) for diagnosis of lower respiratory tract infection has the potential to produce diagnostic samples that are micro-biologically representative of the site of infection among children who cannot expectorate sputum. While IS has become an accepted technique for collecting pediatric respiratory samples in some settings (ref: PMID:28575360 – Murdoch, Morpeth, et al., 2017), this procedure is not routine at the University Teaching Hospital (UTH) in Lusaka, Zambia.

Introduction

Induced Sputum is a technique that plays an important role today in the diagnosis and management of a wide range of respiratory diseases, including tuberculosis,4 lung cancer,1 asthma, 5 COPD,6 and pneumonia,7. It can produce samples for culture, TB smear, and PCR amplification to detect pathogens in the lower airway,8 or for cytology to identify abnormalities of the airway itself. 1,5 The procedure produces these samples by mobilising typically viscous mucus in the lower airway, facilitating its movement up and out of the lungs to be expelled as sputum.

In children, IS is preferred over other techniques for sampling the microbiology of the airway because it is low risk, 6, 15 non-invasive, 10 and produces samples of consistent quality, even in patients as young as 1 month of age,3. IS is also of particular utility in low-resource settings 3 because it is easily performed with minimal training, 3, 10 and at low cost. 13, 14 Thus, in low-resource settings where childhood respiratory diseases are a major concern, we should expect IS to be embraced and widely utilised. To the best of our knowledge, induced sputum is not a routine procedure anywhere in the government healthcare system. Even at the Ministry of Health's flagship institution, UTH in Lusaka, IS was not a procedure that staff were trained or equipped to perform until it was introduced as part of the standard operating procedures for the PERCH project11 in 2011.

Our data show that despite their lack of prior experience with the IS procedure, healthcare workers at UTH were able to safely collect samples with a high standard of quality for PERCH, as evidenced by consistently high Bartlett scores. Thus, introducing IS testing in Zambia would be practical as well as useful.

We feel that IS is an important diagnostic procedure that can and should become routine in health facilities throughout Zambia.

Methods

UTH is one of seven sites of the Pneumonia Etiology Research for Child Heath (PERCH), a multi-country study designed to determine the causes of pneumonia in children under five. Children admitted to UTH with WHO-defined severe or very severe pneumonia were enrolled from October 2011 through October 2013. Children with no contraindications (i.e. hypoxia or bronchospasm) had IS performed within 24 hours of admission. Oxygen saturation and vital signs were monitored throughout and for 4 hours after the procedure. Aerosolized salbutamol was administered for bronchodilation and nebulized hypertonic saline pretreatment along with gentle chest physical therapy (PT) was used to improve mobilisation of sputum. Pulmonary excretions were suctioned out of the nasopharynx using a foot pump and samples were collected into a sterile trap and sent immediately to the microbiology lab for processing.

Methodology

Over a period of 24 months beginning in October 2011, the Zambian PERCH site enrolled children at UTH between the ages of 1 and 59 months who presented with severe or very severe pneumonia, as defined by the WHO.19

IS testing was required for all pneumonia cases in the PERCH project, unless contraindicated because: 1) the patient had oxygen saturation less than 92% on oxygen; 2) the patient was unable to protect their airway; or 3) the patient presented with severe bronchospasm. Clinicians had discretion to exclude patients for other reasons as well. IS was performed within 24 hours of admission in a well-ventilated area under strict droplet infection control, and O2 saturation was monitored by pulse oximetry throughout the procedure and for 4 hours afterwards.

Initially, the clinician cleared the anterior nasal secretions using a tissue or suction device that was then discarded.

With the nose cleared of mucus, subjects were administered salbutamol to prevent bronchospasm during the procedure. This was administered using a spacer device in two 100µg puffs of a metered dose inhaler, ten seconds apart.

After waiting for five minutes for the bronchodilator to take effect, the clinician nebulised the patient with 5mL of 5% saline solution, sometimes in conjunction with oxygen at a flow rate of 5 to 8L/min as appropriate. Nebulisation continued for 10 minutes or until the 5mL of saline was exhausted. Gentle chest percussion aided in the mobilisation of sputum.

Once the child began to cough, a sterile mucus extractor cannula was inserted through the nose into the nasopharynx to aspirate the expectorated sputum.

Once a minimum of 1mL of sputum was collected, the clinician removed the extractor (with suction off to avoid anterior nasal contamination), then aspirated an additional 5mL of sterile, isotonic saline to flush the tube, finishing the procedure.

For the next four hours, patients were monitored for SAEs, which were defined by: 1) a 5% drop in oxygen saturation for 15 minutes; 2) new onset of unconsciousness; 3) a new or increased requirement for bronchodilation; 4) a clinically significant increase in respiratory rate, work of breathing, or oxygen demand, sustained for 15 minutes; or 5) death. In cases of suspected TB, IS was performed a second time, 4 to 32 hours after the initial procedure.

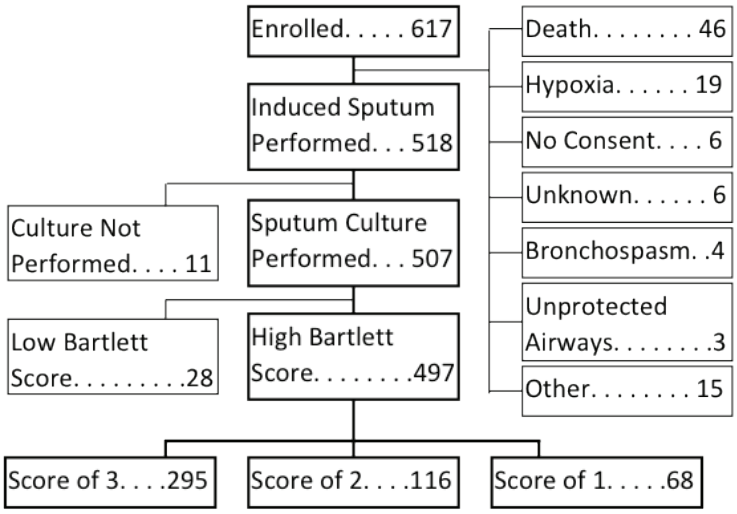
Samples were sent immediately to the lab for processing, where they were subjected to TB testing (via culture and microscopy), bacterial culture and susceptibility testing, and multiplex PCR for 30 respiratory pathogens. To assess the quality of the specimens, Bartlett scores20 were assigned during routine gram stain microscopy based on the number of neutrophils and epithelial cells per field, and the presence or absence of mucus. Samples with more than 25 neutrophils per field, fewer than 10 epithelial cells per field, and mucus were assigned perfect Bartlett scores of 3, while those with fewer than 10 neutrophils per field, more than 25 epithelial cells per field, and no mucus were assigned the lowest score of -2. Specimens with Bartlett scores greater than 0 were considered of high quality, while those with scores less than or equal to 0 were considered of low quality.

Results

617 children were enrolled over a 24-month period. 518/617 (84%) had IS procedures performed, and 507/518 (98%) samples were cultured. 479/507 (94%) of cultured samples were of good quality as determined by a Bartlett score greater than 0. Only 2/518 (0.4%) patients had a serious adverse event (SAE) reported within 4 hours
as a routine procedure in Zambia.

As summarized in Figure 1, 617 pneumonia patients between 1 and 59 months of age were enrolled in the PERCH study over a

Figure 1. Induced Sputum Patient Flow Chart



24-month period in 2011-2013. Of these, 518 (84%) underwent sputum induction. Of the 99 patients that did not undergo sputum induction, 46 (46%) died before the procedure, 19 (19%) were hypoxic, 6 (6%) refused consent, 6 (6%) declined for unknown reasons, 4 (4%) presented with bronchospasm, 3 (3%) had unprotected airways, and 15 (15%) were excluded for other reasons. After the procedure, only 2 of 518 patients (0.4%) recorded an SAE that was possibly related to the sputum induction. Both of these patients had oxygen saturations that dropped below 92%.2/518 (0.4%) patients had a serious adverse event (SAE) reported within 4 hours
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Table 1. Breakdown of Induced Sputum samples by Bartlett score quality rating

Bartlett Score		n	%	Subtotal (n)	Subtotal (%)
Low Quality	-2 -1 0	2 4 22	0.4% 0.8% 4.3%	28	5.5%
High Quality	1 2 3	68 116 295	13.4% 22.9% 58.2%	479	94.5%
Total		507	100.0%	507	100.0%

Results

As presented in Figure 1, 507 of the 518 IS samples (98%) were cultured, of which 383 (76%) produced at least one bacterial isolate. There were 537 bacterial isolates in total.

All of the samples that were cultured were also evaluated for quality by assigning them Bartlett scores. Of the 507, 479 (94%) were of high quality as indicated by a Bartlett score of 1 to 3, and 28 (6%) were of low quality as indicated by a Bartlett score of 0 to -2. Results are summarized in Table 1.

Conclusion

Induced sputum is a safe procedure that can easily be employed in a low income setting with minimal training. IS could be valuable in the diagnosis and management of community acquired pneumonia, pulmonary TB, asthma, COPD, lung cancers, and opportunistic infections, in Zambian children. IS should be introduced.

We were able to safely and successfully perform IS in a challenging pediatric population. Few patients were unable to undergo sputum induction. Of the 617 in our study, all of whom were challenging subjects for the procedure, given that they presented with severe or very severe pneumonia, only 99 (16%) were excluded. If we set aside the patients that died before their sputum induction time, only 53 of 571 patients (9%) met the exclusion criteria for sputum induction.

Sputum induction in our trial was extremely safe. Even fewer patients had adverse reactions to the procedure: 2 of the 518 that underwent sputum induction (0.4%) met the criteria for a SAE. Both of these patients recorded temporary drops in their oxygen saturation within the 4 hour timeframe, and both eventually recovered.

The IS samples produced in our study were also of very high quality. Bartlett scoring indicated that 94% of samples were high quality, and 58% were of the highest quality. 0.4% of samples were of the lowest quality. IS is an important, low-cost diagnostic technique for pediatric respiratory disease, and yet it has been overlooked in Zambia's respiratory-disease-burdened government hospitals. Our results show that Zambian healthcare workers are capable of learning and executing sputum induction safely, and with high standards of quality specimen collection, it isuseful in pediatric pulmonary tuberculosis and pneumonia aetiology diagnosis, even in a challenging pediatric population. In light of this new information, we recommend the introduction of IS as a routine procedure in the Zambian healthcare system, especially for the treatment of pediatric respiratory disease.

LIST OF REFERENCES

1. Bickerman, HA et al. (1958). “An aerosol method of producing bronchial secretions in human subjects: a clinical technic for the detection of lung cancer.” Diseases of the Chest, 13:4.
2. Gupta, KB & Garg, S (2006). “Induced Sputum - a useful tool in diagnosis of respiratory diseases.” Lung India, 23:82-86.
3. Moore, HA et al. (2011). “Induced Sputum for microbiological diagnosis of childhood pulmonary tuberculosis in a community setting.” International Journal of Tubercular Lung Disease, 15(9):1185–1190.
4. Iriso, R et al. (2005). “The diagnosis of childhood tuberculosis in an HIV-endemic setting and the use of induced sputum.” International Journal of Tubercular lung disease, 9(7):716–726.
5. Wilson, NM et al. (2000). “Induced sputum in children: feasibility, repeatability, and relation of findings to asthma severity.” Thorax, 55:768–774.
6. Pizzichini, E et al. (2002). “Safety of induced sputum.” European Respiratory journal, 20: Suppl. 37, 9s–18s.
7. Lahti, E et al. (2009). “Induced sputum in the diagnosis of childhood community-aquired pneumonia.” Thorax, 64:252–257.
8. al Zahrani, K et al. (2001). “Yield of smear, culture and amplification tests from repeated induced sputum for the diagnosis of pulmonary tuberculosis.” International Journal of Tubercular Lung Disease, 5(9):855–860.
9. Fishman, JA et al. (1994). “Use of Induced Sputum Specimens for Microbiologic Diagnosis of Infections Due to Organisms Other than Pneumocystis carinii.” Journal of Clinical Microbiology, 131-134.
10. Henderson, AJW (1994). “Bronchoalveolar Lavage.” Archives of Disease in Childhood, 70: 167-169.
11. Levine, OS et al. (2012). “The Pneumonia Etiology Research for Child Health Project: A 21st Century Childhood Pneumonia Etiology Study.” Clinical Infectious Disease, 54 (suppl. 2):S93-S101.
12. Bandyopadhyay, T et al. (2000). “A Comparison of Induced and Expectorated Sputum for the Microbiological Diagnosis of Community Acquired Pneumonia.” Respiration, 67:173-176.
13. McWilliams, T et al. (2002). “Induced sputum and bronchoscopy in the diagnosis of pulmonary tuberculosis.” Thorax, 57:1010–1014.
14. Chouaid, C et al. (1993). “Cost effectiveness of the induced sputum technique for the diagnosis of Pneumocystis carinii pneumonia (PCP) in HIV-infected patients.” European Respiratory Journal, 6:248-252.
15. Loh, LC et al. (2005). “Induced Sputum in Corticosteroid-Dependant Asthmatics: Risks and Airway Cellular Profile.” asian pacific journal of allergy and immunology, 23:189-196.
16. Beck, JM et al. (2012). “The Microbiome of the Lung.” Translational research, 160(4): 258–266.
17. Mandell, LA et al. (2007). “Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults.” Clinical Infectious Diseases, 44:527-72.
18. Garcia-Vazquez, E et al. (2004). “Assessment of the Usefulness of Sputum Culture for Diagnosis of Community-Acquired Pneumonia Using the PORT Predictive Scoring System.” archives of internal medicine, 164:1807-1811.
19. Scott, JA et al. (2012). “The definition of pneumonia, the assessment of severity, and clinical standardization in the Pneumonia Etiology Research for Child Health study.” Clinical Infectious Disease, 54(suppl 2):S109-16.
20. Deris, ZZ et al. (2008). “Implementation of Routine Sputum Rejection Criteria to Improve the Outcome of Sputum Culture Results.” International Medical Journal,