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Original Article

Microbiological yield from induced sputum compared to oropharyngeal swab in young children with cystic fibrosis

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Abstract

Background: Standard respiratory sampling in young children with cystic fibrosis (CF) is by oropharyngeal swab (OPS) as they cannot spontaneously expectorate. Sputum induction (IS) has been poorly investigated in this population. We aimed to compare the bacteriological yield of OPS vs. IS in young children with CF.

Methods: Sequentially paired OPS followed by IS samples was collected in children < 5 years of age attending a CF clinic in Cape Town, South Africa.

Results: IS was successfully paired with OPS in 98/113 (85%) attempts in 32 children (mean ± SD 19 ± 16 months), with no serious adverse events. IS culture yield for any CF-associated bacteria from IS was 46% vs. 28% from OPS ($p = 0.01$). The sensitivity, specificity, PPV and NPV of OPS compared to IS in isolating CF-associated bacteria were 56%, 96%, 93%, and 72% respectively.

Conclusion: Sputum induction is feasible, safe and superior to OPS for detecting CF-associated bacteria in young children with CF.

Keywords: Induced sputum; Oropharyngeal swab; Cystic fibrosis; Young children

1. Background

Early lung disease in cystic fibrosis (CF) is characterized by airway infection and inflammation and may be asymptomatic in infants and young children [1,2]. Targeted antimicrobial therapy against airway pathogens is the cornerstone of managing CF lung disease. Identification of lower airway pathogens through culture of lower respiratory tract samples is therefore important in routine care of children with CF.

Bronchoalveolar lavage (BAL) is considered the most reliable sampling method in infants and young children with CF who are unable to expectorate. Serial bronchoscopy in young children is, however, not feasible in routine CF care in most settings owing to its invasive nature, cost and the requirement for skilled expertise and general anaesthesia. Furthermore, BAL-directed therapy in young children has not been shown to improve outcomes compared to oropharyngeal (OP) swab-directed therapy [3]. Culture of OP swabs thus remains standard practice in many CF centres in young children [4]. A positive OP swab culture,

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however, lacks sensitivity when compared to BAL. Negative OP swab cultures may therefore be more helpful to "rule out" rather than "rule in" the presence of lower airway pathogens [5].

Sputum induction (IS) with hypertonic saline has consistently been shown to be safe and the microbiological yield either similar or superior to conventional sampling techniques in expectorating and non-expectorating children with CF [6–11]. However, most children included in these studies were old enough to voluntarily expectorate. Induced sputum has been shown to be useful in infants and young children for microbiological confirmation of pulmonary tuberculosis and for detecting pathogens in pneumonia [12,13]. There is little data on the utility and feasibility of IS in very young children with cystic fibrosis. The aim of this study was to compare the microbiological yield and safety of IS and OP swabs in children less than 5 years of age with CF.

2. Methods

2.1. Study participants

A prospective study was conducted between January 2011 and April 2014 in children with CF who were less than 5 years of age at Red Cross War Memorial Children's Hospital, a paediatric referral hospital in Cape Town, South Africa. CF was diagnosed by two positive sweat tests (sweat chloride > 60 mmol/L) and/or identification of two known cystic fibrosis transmembrane regulator (CFTR) mutations. Children were consecutively enrolled at routine multidisciplinary CF clinic visits. Informed consent was obtained for repeated sampling throughout the study period or until children reached 5 years of age. Respiratory samples were obtained either for surveillance or for investigation of an acute pulmonary exacerbation.

2.2. Clinical information and procedures

Demographic and genotype information was recorded for each participant at study entry. Patients were classified as pancreatic insufficient (PS) if the faecal elastase level was <200 μg/ml.

The indication for individual sampling episodes was classified as surveillance if children were well or as symptomatic if children presented with new respiratory symptoms or a pulmonary exacerbation as determined by the attending clinician. For surveillance purposes, routine sampling was done at 6 monthly intervals in individual participants. Any change in clinical management as a direct consequence of an OP swab or IS culture result was documented. Samples were collected by the same physiotherapist throughout the study period using a standardized methodology.

Children with newly acquired *Pseudomonas aeruginosa* infection received three months eradication therapy according to South African guidelines [14]. Sampling was repeated after three months of therapy to determine *P. aeruginosa* infection status. Sputum induction was not attempted in children hospitalized with severe pulmonary exacerbations in whom oxygen haemoglobin saturation could not be maintained higher than 90% on nasal cannula oxygen using 100% oxygen at a flow rate of 1 L/min. Children known to have severe airway hyperreactivity following nebulised hypertonic saline were excluded.

OP swab: After gently opening the mouth (with the aid of a tongue depressor in uncooperative children), a cotton-tipped swab was passed to sample the posterior pharynx or induce a cough. The swab was immediately placed in a culture medium and sent to the laboratory for processing.

Sputum induction: After obtaining the OP swab, sputum induction was performed with 5% saline solution as previously described [12,15]. Thereafter, samples were collected by expectoration or, in those who could not expectorate, by nasopharyngeal suction (NPS), oropharyngeal suction or post-induction swab in those who refused suctioning or were uncooperative with the procedure (Fig. 1). Adverse events as observed by clinical observation and pulse oximetry monitoring during IS collection were documented. Sputum induction was performed with standard infection control precautions in a dedicated well-ventilated IS room away from the clinic area.

2.3. Microbiological investigations

Induced sputum samples and OP swabs were inoculated into the following culture media: chocolate agar; Columbia-gentamicin agar (plus optochin disc); MacConkey agar; mannitol salt agar; pseudomonas cepacia agar; oxidation/fermentation-polymyxin-bacitracin-lactose; and sabouraud dextrose agar + amikacin. Positive cultures were reported semi-quantitatively. Any positive culture was included. In addition, IS samples were submitted (if sufficient sample volume) for fungal culture and mycobacterial microscopy and liquid culture as previously described [15].

2.4. Sputum quality assessment

To determine if IS samples were representative of lower respiratory tract secretions, sputum collected by expectoration or NPS was examined on fixed slides by a histopathologist to identify alveolar macrophages using the Papanicolaou stain method [16]. In difficult cases, the acid phosphatase method was used to highlight macrophages which appear bright orange compared to the background reactive epithelial cells [17].

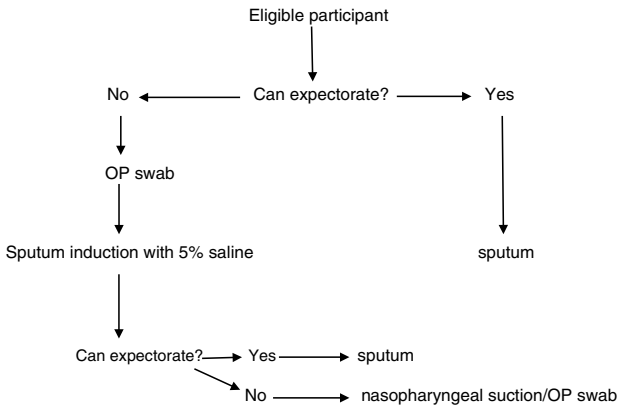

Fig. 1. Sputum collection procedures.