RESPIRATORY CARE Paper in Press. Published on September 15, 2020 as DOI: 10.4187/respcare.07890

Airway Microbiology in Tracheostomized Children

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BACKGROUND: Potentially pathogenic microorganisms are frequently isolated from tracheostomized children, although evidence for empirical therapy of respiratory exacerbation is limited. We aimed to describe upper airway microbiology as found on endotracheal aspirate (ETA) in tracheostomized children and to correlate it with lower airway microbiology through bronchoalveolar lavage fluid. METHODS: We retrospectively reviewed records and airway microbiology of all tracheostomized children under the follow-up care of Queensland Children's Hospital. Subanalysis was based on ventilatory and multidrug-resistant organism status. Sensitivity and specificity of ETA for predicting *Pseudomonas aeruginosa* and *Staphylococcus aureus* lower airway isolation were calculated using concomitant bronchoalveolar lavage fluid culture as the accepted standard. RESULTS: From 43 children (18 female, median [interquartile range (IQR)] age 68 (41–115) months, 14 ventilated), 15 different potentially pathogenic microorganisms were isolated (mean ± SD: 3.30 ± 2.23), with *S. aureus* (n = 33, 77%) and *P. aeruginosa* (n = 29, 67%) predominating. Significantly more types of potentially pathogenic microorganisms were isolated from ventilated children (median 4.00 [IQR 3.25–5.75]) than from nonventilated children (median 2.00 [IQR 1.00–4.00] (P = .007), with 93% of ventilated children isolating *S. aureus* and 86% *P. aeruginosa*. Multidrug-resistant organisms were present in 12 (28%) children, of whom 8 were ventilated. Methicillin-resistant *S. aureus* (MRSA) was isolated in 9 (21%) children, of whom 6 were ventilated. For *P. aeruginosa* and *S. aureus* isolation, ETA had high sensitivity (95% and 100%, respectively) but low specificity (64.7% and 33.3%, respectively) when compared with bronchoalveolar lavage fluid. CONCLUSIONS: In children with tracheostomy, the predominant respiratory bacterial pathogens were *S. aureus* and *P. aeruginosa*, with MRSA being isolated less frequently than previously described. Multidrug-resistant organisms are isolated more frequently from ventilated children. ETA microbiology is a good screening modality, with negative ETA potentially ruling out lower airway *S. aureus* and *P. aeruginosa*. Adequately powered prospective studies with quantitative cultures could enhance understanding and guide therapy. *Key words: tracheostomy; bronchoalveolar lavage fluid; Pseudomonas aeruginosa; airway microbiology; respiratory system; child.* [Respir Care 0;0(0):1–●. © 0 Daedalus Enterprises]

Introduction

Tracheostomy is a surgical procedure dating back more than 2,000 years whereby a cannula is passed from the external environment into the trachea to maintain airway patency.[1] Its use is increasing in complex pediatric populations with the improvements seen in modern

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Dr Kapur presented a version of this paper at the ERS International Congress 2019, held September 28 to October 2, 2019, in Madrid, Spain. Dr McLaren presented a version of this paper at TSANZSRS 2019, held March 29 to April 2, 2019, in Gold Coast, Australia.

The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.07890

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pediatric care.[2] In children, it is most commonly indicated in cases of severe congenital or acquired airway lesions causing airway obstruction and in neurologic conditions requiring long-term ventilation or pulmonary toilet.[3,4] Potentially pathogenic microorganisms are frequently isolated from the airways of children with tracheostomy.[5,6] Tracheostomy is associated with increased infection rates, due to the bypassing of the protective oronasal passage, increased secretions, decreased clearance of these secretions, and aspiration risk.[5,7] The tracheobronchial tree of patients with long-term tracheostomy is prone to bacterial colonization, predisposing them to more frequent symptomatic infections. Moreover, long-term tracheostomy tube placement may lead to irritation of tracheal mucosa and necrosis, further increasing the risk for infection and complication.[8] It appears that children who have long-term tracheostomy due to airway malformations have higher risk of chronic pulmonary suppuration.[9-11]

There are limited data available describing the lower respiratory microbiology in tracheostomized children, and consequently limited evidence to guide empirical therapy in the event of respiratory exacerbation in this cohort.[12,13] Studies comparing upper and lower airway pathogens in children with cystic fibrosis and those with intercurrent lower respiratory tract infections indicate that upper airway microbiology has high sensitivity and negative predictive values, but poor positive predictive values, for lower airway microbiology.[14-17] To our knowledge, there are limited data of this kind in tracheostomized children. To address this, we aimed to describe the spectrum of potentially pathogenic microorganisms in the airway of children with tracheostomy and the effect of long-term ventilation on this. In addition, using concomitant bronchoalveolar lavage fluid (BALF) as the accepted standard, we assessed the utility of endotracheal aspirate (ETA) in predicting the presence of lower airway potentially pathogenic microorganisms.

QUICK LOOK

Current knowledge

Children with tracheostomy frequently isolate potentially pathogenic microorganisms from the airway. There are limited published data to guide empirical therapy in the event of a respiratory exacerbation.

What this paper contributes to our knowledge

We described the airway microbiology as found on simple tracheal aspirate in a cohort of children and correlated this to more invasive bronchoalveolar lavage fluid to determine colonization of the lower airway. We found a predominance of *S. aureus* and *P. aeruginosa*, with methicillin-resistant *S. aureus* less common than previously reported. Ventilated children have larger quantities of bacteria isolated than their nonventilated counterparts, with more frequent colonization of multidrug-resistant organisms. Tracheal aspirate microbiology may be a useful tool to rule out lower airway infection, hence reducing reliance on bronchoscopy.

Methods

All children with tracheostomy under follow-up care at the Queensland Children's Hospital at the time of the review (April–June 2018) were considered eligible. A retrospective review of electronic medical records and airway microbiology was conducted for all eligible children. Patients with no microbiology results available were excluded. Data were extracted on subject demographics, underlying diagnosis, and indication for tracheostomy. Microbiology results were accessed to identify all potentially pathogenic microorganisms isolated after tracheostomy via ETA and concurrent BALF ($\geq 10^3$ colony-forming units considered significant). Analysis was conducted using descriptive statistics. The Student *t* test was used to calculate differences in means for normally distributed data, and the Mann-Whitney *U* test was used for differences in medians of non-normally distributed data. Subgroup analyses included description of differences in isolates based on ventilatory status and multidrug-resistant organism status. Using standard microbiology culture techniques, concurrent BALF and ETA cultures were used to calculate the sensitivity and specificity of ETA for *P. aeruginosa* and *S. aureus* lower airway isolation. Where concurrent BALF cultures were not available, ETA cultures within 6 months of the BALF were used. Flexible bronchoscopy in our unit is done under general anesthesia with the child spontaneously breathing. The bronchoscope is introduced through the nose and suction is avoided until the bronchoscope is beyond the vocal cords. The scope is further progressed to the lower airway on the side of the tracheostomy tube, not through the tracheostomy tube. A protective sleeve is not usually used for the procedure. Ethics approval for this human study was granted by Queensland Children's Hospital Human Research Ethics Committee.

Results

A total of 44 children with tracheostomy were identified, with 1 subject excluded due to a lack of microbiology data. The median (IQR) age of the 43 included children was 68 (41–115) months; 18 subjects were female, and 14 (33%) subjects were on long-term invasive ventilation. The underlying causes for tracheostomy are outlined in Table 1. Many of the subjects had multiple underlying comorbidities.

Fifteen different types of potentially pathogenic microorganisms were isolated from the ETA cultures in this group,

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Table 1. Underlying Conditions of Children With Tracheostomy

Underlying Condition	Ventilated ($n = 14$)	Nonventilated ($n = 29$)
Congenital central hypoventilation syndrome	7	0
Cervical spinal cord injury	2	0
Transverse myelitis	2	0
Congenital diaphragmatic hernia with pulmonary hypoplasia	1	0
Unilateral pulmonary artery and airway hypoplasia	1	0
Craniofacial syndrome	1*	11†
Bilateral vocal cord palsy	0	6
Subglottic stenosis	0	5
Thyroid cartilage injury	0	1
Plexiform neurofibromatosis	0	1
Lymphatic malformation	0	1
Others	0	5

* Beare-Stevenson syndrome.
† CHARGE syndrome ($n = 3$); Pfeiffer syndrome ($n = 2$); Treacher Collins syndrome ($n = 2$); Crouzon syndrome ($n = 1$); Di George syndrome ($n = 1$); Moebius syndrome ($n = 2$; 1 child with Moebius syndrome also had bilateral vocal cord palsy).

Table 2. Potentially Pathogenic Microorganism in ETA Culture

Isolates	Ventilated ($n = 14$)	Nonventilated ($n = 29$)	Total ($N = 43$)
S. aureus (MRSA)	13 (6)	20 (3)	33 (9)
P. aeruginosa	12	17	29
H. influenzae	7	13	20
S. pneumoniae	5	6	11
M. catarrhalis	5	5	10
K. pneumoniae	4	6	10
S. pyogenes	3	6	9
S. marcescens	4	2	6
S. maltophilia	5	0	5
A. baumannii complex	2	2	4
E. cloacae	2	1	3
K. oxytoca	1	2	3
A. lwoffii	1	0	1
Achromobacter sp.	0	1	1
E. aerogenes	1	0	1

MRSA = methicillin-resistant *S. aureus*
ETA = endotracheal aspirate

with a mean ± SD of 3.30 ± 2.23 different potentially pathogenic microorganisms isolated per subject (Table 2). *S. aureus* and *P. aeruginosa* were the most common potentially pathogenic microorganisms with 33 (77%) and 29 (67%) subjects infected with these organisms, respectively. Thirteen (93%) of the ventilated children cultured *S. aureus* and 12 (86%) cultured *P. aeruginosa* (Table 2).

Of the 12 children with multidrug-resistant organisms, 8 (86%) were ventilated (Table 3). Methicillin-resistant *S. aureus* (MRSA) was the most common multidrug-resistant organism isolated, being present in 9 (21%) of subjects, 6 of whom were ventilated. Four children had multiple multidrug-resistant organisms, and all of these subjects were ventilated. Ventilated children isolated significantly more types of potentially pathogenic microorganisms per child (median 4.00 [interquartile range (IQR) 3.25–5.75]) than nonventilated children (median 2.00 [IQR 1.00–4.00]) ($U = 99, P = .007$).

We analyzed 37 BALF samples with concomitant ETA in 20 subjects. Because most children had multiple ETAs, the ETA closest to the BALF was chosen for this analysis. For *P. aeruginosa* and *S. aureus*, ETA had high sensitivity (95%, 100%, respectively) but low specificity (64.7%, 33.3%, respectively) when compared with BALF (Table 4).

Discussion

It has long been established that tracheostomy placement changes the histology of the trachea, making it more prone to infection.[18] Since the introduction of vaccinations, indication for placement has shifted from acute infection to more complex and chronic conditions involving upper airway anomalies or respiratory failure.[2,19,20] Children with these conditions typically require long-term tracheostomy, thus increasing their risk of complications, including respiratory infections and exacerbations of chronic pulmonary suppuration.[2,21] The respiratory microbiology and etiology of these infections has not been well studied, with limited guidance on empirical treatment of respiratory exacerbations.

Our findings support those of other recent studies investigating the respiratory microbiology of tracheostomized children, which suggest a predominance of *P. aeruginosa* at 90% and other Gram-negative organisms and *S. aureus* at 46%.[12,13] Notably, we had a much lower incidence of MRSA in our cohort at 21% than previously reported, where MRSA was a predominant organism with a reported incidence of 56%. Our findings were in keeping with nationally decreasing rates of MRSA in Australia, particularly hospital-acquired MRSA.[22,23] This is perhaps a reflection of improving infection control measures in hospitals, the decreasing virulence of some strains of MRSA, or, more likely, a combination of these and other factors.[24] This could also be due to a lower proportion of children in our cohort being preterm with bronchopulmonary dysplasia compared to previous cohorts, thus affecting the microbiota.[25]

Ventilated children had significantly more types of potentially pathogenic microorganisms isolated in their cultures than their nonventilated counterparts, with more frequent colonization of multidrug-resistant organisms. Poly-microbial infection was common in the ventilated group, especially with multidrug-resistant organisms. Ventilated patients

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Table 3. Multidrug-Resistant Organism Status

	Nonventilated	Ventilated	Total
MRSA	3	2	5
ESBL	0	1	1
CRP	1	0	1
VRE	0	1	1
MRSA + CRP	0	1	1
MRSA + ESBL	0	2	2
MRSA + CRP + ESBL	0	1	1

$n = 12$.
ESBL = extended spectrum β-lactamase
CRP = carbapenem-resistant *Pseudomonas*
VRE = vancomycin-resistant *Enterococcus*
MRSA = methicillin-resistant *S. aureus*

Table 4. ETA as a Surrogate for BALF for the Detection of *P. aeruginosa* and *S. aureus*

	BALF Positive	BALF Negative
*P. aeruginosa**		
ETA positive	19	6
ETA negative	1	11
S. aureus†		
ETA positive	7	20
ETA negative	0	10

* Sensitivity = 95.0%, specificity = 64.7%, positive predictive value = 76.0%, negative predictive value = 91.7%.
† Sensitivity = 100%, specificity = 33.3%, positive predictive value = 25.9%, negative predictive value = 100%.
BALF = bronchoalveolar lavage fluid
ETA = endotracheal aspirate

are more likely to have extended stays in ICU, and it is likely that the isolation of multidrug-resistant organisms in this group reflects colonization during ICU stay rather than being directly caused by the process of home ventilation.[26] Humidification of the ventilator may be another source of infection.[27,28] This is usually less relevant in tracheostomized children not on home ventilation because they typically use heat-and-moisture exchangers to maintain airway humidification.

Identification and treatment of lower airway pathogens is often guided by upper airway cultures in children and adults with cystic fibrosis.[15,29] This extrapolation to cohorts that do not have cystic fibrosis is debatable. Our finding of high sensitivity but low specificity indicates that ETA is not diagnostic but may be an appropriate screening tool for bacterial colonization, which may precede and predict lower airway infection.[30,31] Afolabi-Brown et al[32] reported a moderate correlation between ETA and BALF for the detection of bronchitis in tracheostomized children, but the correlation was considered excellent for the detection of *S. aureus* and *P. aeruginosa* specifically. Our findings of ETA microbiology being a useful surrogate for lower airway microbiology is in contrast with findings by Cline et al,[5] who reported different antimicrobial susceptibility patterns between the isolates, suggesting acquisition of new strains or new resistance capacities. However, they used "surveillance" aspirates during an exacerbation, whereas our BALF samples were collected when the children were relatively well, given that bronchoscopy was usually done for suspected granuloma, peritubal bleed, prior to decannulation for lower airway assessment or lower airway sample for excessive secretions.

Our study had some limitations. Being a retrospective analysis, the correlation between BALF and ETA was opportunistic, samples were not all collected concurrently, and some data were missing. There is a possibility of upper airway contamination during the bronchoscopy procedure, as our bronchoscopy protocol in tracheostomized children is to cannulate on the side of the tracheostomy through the nose, not through the tracheostomy. We also did not look at the lower airway cellularity on BALF to segregate infection from possible colonization. Nonetheless, our findings are novel; to our knowledge, no other study has analyzed the airway microbiology in children with tracheostomy on the basis of long-term ventilation status or correlated it with BALF microbiology. Our finding that ETA is potentially a good surrogate for lower airway microbiology could be helpful in dictating empirical antibiotic therapy for respiratory exacerbations, which is currently guided by ETA findings with no evidence of whether this is indicative of lower airway findings.

Conclusions

In children with long-term tracheostomy, predominant respiratory bacterial microbes isolated were *S. aureus* and *P. aeruginosa*, with MRSA being less common than previously reported. Ventilated children have a higher number of bacteria isolated than their nonventilated counterparts, with more frequent colonization of multidrug-resistant organisms. Tracheal aspirate microbiology is a useful tool to rule out lower airway infection, hence reducing reliance on the bronchoscopy. Prospective studies with longitudinal data would help understand the role of these isolates in the long-term pulmonary outcomes in this cohort of children.

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