ORIGINAL STUDY

Tracheostomy tube infection in children: a systematic review of the literature

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ABSTRACT

BACKGROUND. Currently, health professionals face the management of artificial airways in paediatric groups. This action requires delicate care and a lot of attention to detect, establish and manage pressing situations, in these cases being a greater risk of tracheopulmonary bacterial infections.

OBJECTIVE. To identify and evaluate the scientific publications on infections in paediatric patients with tracheostomy tubes.

MATERIAL AND METHODS. A systematic review of the years 2015-2020 was carried out, using the Elsevier, PubMed, Google Academic and Scielo databases, considering the population aged between 0-20 years who used a tracheostomy tube.

RESULTS. From 322 articles distributed in the databases, 13 articles that met the inclusion criteria were selected. Comorbidities that were described as most frequently associated with infection of the tracheostomy tube in children were: neuromuscular disease, prematurity, ventilator use, congenital anomalies, chronic lung disease, obstruction airway, cystic fibrosis, and heart disease. The factors associated with length of stay (LOS) were the age from 30 days to 12 months, with a greater probability of re-entering the hospital and the presence of 4 or more complex chronic diseases. Regarding respiratory infections in patients with tracheostomy, P. aeruginosa was the most frequent bacteria present in cultures (90%), followed by Staphylococcus aureus.

CONCLUSION. Although there are currently clinical criteria, risk factors and laboratory tests associated with infections of the post-tracheostomy tube in paediatric patients, further research is required to define clinical guidelines for the management in medical decision-making cases.

KEYWORDS: tracheostomy, infections, paediatrics, child.

INTRODUCTION

The tracheostomy can provide access to the airway for mechanical ventilation. It is a surgical procedure whereby a cannula is passed from the external environment into the trachea to maintain the airway patency[1]. It was initially used to relieve the acute airway obstruction, being considered a measure of last resort. Asclepiades is credited with performing the first tracheostomy in Rome, in the second century BC[2]. Requiring a tracheostomy will be a life-changing event, impacting the child and their family[3]. Children with tracheostomy tubes are at risk for ventilator-associated pneumonia[4]. The optimal timing for the transition to tracheostomy is unclear, and the decision should be individualized according to the evaluation of the patient's progress[5]. Tracheostomy rates varies per region; in the weighted analysis of paediatric discharges in 2012 in the United

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States, 7 million hospitalizations are estimated, with 0.6% of these related to tracheostomy[6]. Studies have shown that the time for insertion of a tracheostomy tube is, on average, 14.4 days. Many doctors believe that patients should not be ventilated through an endotracheal tube for longer, unless they are unstable or do not benefit from the tracheostomy. This opinion is based on the observation that tracheostomy improves nursing care, patient comfort, patient communication and reduces the need for sedation[7].

It is necessary to clarify the following terms: "tracheobronchitis" versus "tracheitis"; these are often used interchangeably to describe infections associated with artificial airways. We will use the term "tracheobronchitis". Other concepts are "ventilator-associated tracheobronchitis", which has been proposed as a distinct clinical entity and possibly a precursor to ventilator-associated pneumonia generally characterized by clinical signs of respiratory tract infection (e.g., cough, fever, increased sputum production) without radiographic evidence of pneumonia and artificial airway-associated tracheobronchitis. Children with laryngeal shunt and tracheostoma without a tracheostomy tube can also develop bacterial tracheitis[4,8]. A separate term, "bacterial tracheitis", is used to describe thick purulent exudates and tracheal pseudomembranes, which can cause acute airway obstruction and respiratory arrest in previously healthy children (for example, croup and epiglottitis). The artificial airways are commonly colonized by *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter* spp, *Escherichia coli*, *Serratia marcescens*, and other *Enterobacterial* and *Stenotrophomonas* species[9]. Most cases of ventilator-associated tracheobronchitis are due to a single organism, most commonly *Pseudomonas aeruginosa*. Cases of *Candida* and *Aspergillus* have been reported in the cultures of children with artificial airways, but the role of fungal pathogens is still unclear[10]. In the study of 69 children who underwent tracheostomy, 53% of them were found to have positive tracheal cultures within 30 days after surgery[11].

There are few published reports on respiratory tract infections in children chronically dependent on tracheostomy. In our experience, most of these children recover from a single episode of tracheobronchitis without lasting sequelae. However, frequent or recurrent respiratory tract infections probably contribute to morbidity and mortality in this population. For this reason, cases of recurrent pneumonia play a more critical role than tracheal infections[7,12].

MATERIAL AND METHODS

We performed a systematic review of the literature using the Elsevier, PubMed, Google Academic and Scielo databases of health sciences, to locate articles with the terms "paediatric tracheostomy infection", "tracheostomy infection in paediatrics". The papers were independently evaluated by two of the authors according to quantitative outcome criteria.

The inclusion criteria for selecting articles were: articles written in English or Spanish language, retrospective reviews or case-control studies, articles published between 2015-2020, with participants aged between 0 to 20 years who benefited from a tracheostomy tube. Those articles which did not contained sufficient data about the infectious complications of tracheostomy tubes, clinical cases and adult patients' groups were excluded.

Data was organized including authors, study sample, design and results. From each selected article we extracted information regarding the age and gender of the patients, the reason for the existence of the tracheostomy tube along with the comorbidities and the associated tracheostomy tube infections.

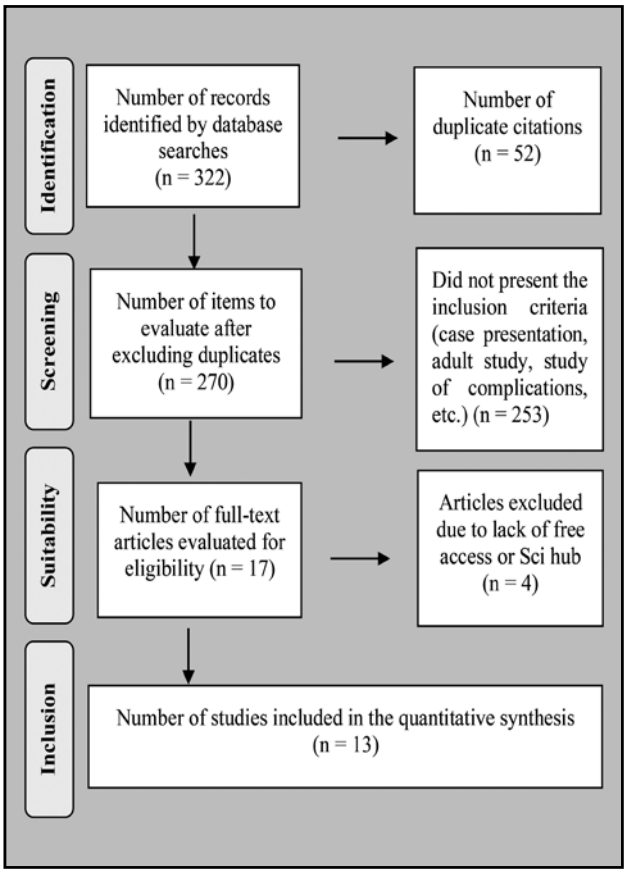

Figure 1. Flow diagram of the selection of studies for the systematic review of the literature on tracheostomy

Table 1. Summary of characteristics of the studies (authors, year of publication, type of the study, number of patients included in the study, patients' age, length of stay).

Author	Year of publication	Study	Number of patients	Age	Mean length of stay
Ni JS et al.[8]	2020	Retrospective review	2,394	0 - 20 years	6.37 days
Wheeler DS et al.[10]	2015	Retrospective case-control study	77	<30days, 30days-1year, 1-12years, >12years	21.5 days for the study group
Grønhøj C et al.[11]	2017	Retrospective review	69	4 months - 17 years .	No data
Sanders CD et al.[13]	2018	Retrospective review	185	0 - 18 years	No data
Ginderdeuren FV et al.[14]	2017	Randomized controlled trial	103	0 - 2 years	4.5 ± 1.9 days for the control group 3.6 ± 1.4 days assisted autogenic drainage group 3.5 ± 1.3 days for the intrapulmonary percussive ventilation group
Russell CJ et al.[15]	2018	Multicenter, etrospective cohort study	7355	30 days - 17 years	4 days
Tan CY et al.[16]	2018	Retrospective study	90	0 - 20 years	8.83±5.59 days patients with bacterial pneumoniae 5.67±2.55 days patients with non-bacterial pneumoniae
Cade SHA et al.[17]	2020	Retrospective review	108	0 - 12 years	No data
Kun SS et al.[18]	2012	Retrospective cohort study	109	0 - 10 years	99 days
Russell CJ et al.[19]	2019	Retrospective cohort study	210	0 - 18 years	34 days
Russell CJ et al.[20]	2017	Retrospective cohort study	240	0 - 18 years	73 days
Cline JM et al.[21]	2012	Retrospective study	189	3 - 7 years	No data
McCaleb R et al.[22]	2016	Retrospective chart review	93	0 - 4 years	No data

RESULTS

The analyse of the four databases revealed the existence of 322 articles (Figure 1). After eliminating the duplicate citations (n = 52), 253 articles which did not fulfil the inclusion criteria, only 17 full-text articles were evaluated for eligibility. Four articles were excluded due to lack of free access or Sci hub. In the end, 13 articles were included in the present systematic review. In Table 1, the summary of characteristics of the analysed articles is presented.

Regarding respiratory infections in patients with tracheostomy, from the total 11,222 paediatric patients, 6718, representing 59.86%, presented an infection pathogen associated with the tracheostomy. The evaluation of the articles revealed that *Pseudomonas aeruginosa* was the highest infection present in cultures (86.81%%), followed by *Staphylococcus aureus* (4.48%), *Strenotrophomonas maltophilia* (1.94%), *Serratia marcescens* (1.64%) and *Moraxella catarrhalis* (1.32%) (Table 2). There were cases in whom the association of different germs was present[10,11,13]. Recently, increased resistance by these bacteria to multiple drugs such as Ciprofloxacin has been found, limiting post-tracheostomy treatment. These data indicate that new therapies and techniques are required to prevent infections[10,11,13,16,17,20,21].

According to the results (Table 3) of the selected articles, the comorbidities that were described as most frequently associated with infection of the tracheostomy tube in children were: neuromuscular disease[10-15], prematurity[13,19,21], congenital anomalies[11,13,16,18], and others, less frequently, such as chronic lung disease[19,20], obstruction airway[15,19], cystic fibrosis[16], heart disease[18], and acquired ab-

Table 2. Identified bacteria in tracheostomy tube infection of the patients included in the review.

Pathology	Number	Percent
Pseudomonas aeruginosa	5832	86.81%
Staphylococcus aureus	301	4.48%
Strenotrophomonas maltophilia	130	1.94%
Serratia marcescens	110	1.64%
Moraxella catarrhalis	89	1.32%
Acinetobacter baumannii	53	0.79%
Haemophilus influenzae	41	0.61%
Group beta Streptococcus	32	0.48%
Streptococcus pneumoniae	29	0.43%
Klebsiella pneumoniae	27	0.4%
Mycobacterium	16	0.24%
Acinetobacter calcoaceticus	13	0.19%
Serratia liquefacieus	9	0.13%
Haemophilus parainfluenzae	7	0.10%
Enterococcus faecium	6	0.09%
Coagulase negative Staphylococcus	6	0.09%
Escherichia Coli	4	0.06%
Proteus mirabilis	3	0.044%
Providencia species	2	0.03%
Enterococcus	1	0.015%
Ralstonia mannitolilytica	1	0.015%
Ralstonia picketti	1	0.015%
Chryseobacterium indologenes	1	0.015%
Chryseobacterium menigosepticum	1	0.015%
Pseudomonas putida	1	0.015%
Citrobacter diversus	1	0.015%
Raoultella planticola	1	0.015%

Table 3. Tracheotomy-associated comorbidities.

Comorbidity	Number	Percent
Neuromuscular diseases	4143	39.91%
Congenital anomalies	2548	24.54%
Cardiovascular diseases	1235	11.9%
Metabolic disorders	532	5.12%
Renal	486	4.68%
Hematologic	273	2.63%
Prematurity	242	2.33%
Upper airways anomalies	222	2.13%
Malignancy	174	1.67%
Chronic lung disease	141	1.35%
Neurodevelopmental delay	94	0.9%
Neurological conditions	83	0.79%
Cerebral palsy	60	0.57%
Chromosomal anomalies	37	0.35%
Cardiac surgery	28	0.26%
Central nervous system disease	26	0.25%
Trauma	23	0.22%
Spina bifida	6	0.05%
Diaphragmatic hernia or paralysis	4	0.03%
Vocal cord palsy	4	0.03%
Central hypoventilation syndrome	3	0.02%
Other	16	0.15%

normalities[11,13]. There also existed an association of different comorbidities in the same patients. Analysing the articles, we found no significant relationship between a certain comorbidity and tracheostomy tube infection. The factors associated with length of stay (LOS) were the age from 30 days to 12 months, with a greater probability of

re-entering the hospital, and the presence of 4 or more complex chronic diseases (adding a greater possibility of readmission). Concerning a longer LOS, the following were considered: the principal diagnosis of aspiration pneumonia and admission to the ICU at some point during hospitalization[15].

Although there are currently clinical criteria, risk factors and laboratory tests associated with infections of the post-tracheostomy tube in paediatric patients, further research is required to define clinical guidelines for the management in medical decision-making cases.

DISCUSSIONS

Children with a tracheostomy tube have an increased risk for tracheopulmonary infections because the tracheostomy tube avoids the natural protector of the nasal and oral airways, providing an open portal for bacteria's entry into the lower respiratory tract[21]. Likewise, the tracheostomy tube's plastic material predisposes to a higher colonization of pathogenic microorganisms due to the formation of biofilms by *Pseudomonas aeruginosa* and *Staphylococcus aureus*, thus increasing the probability of developing exacerbations of respiratory symptoms[12,16,22].

This procedure is performed in approximately 2% of paediatric patients[23]. To the extent that good outpatient management is provided, future hospitalizations can be reduced or prevented, considering that it is associated with better survival[12,20].

There is a limited amount of literature on the subject. However, multiple studies point to the relevance of tracheostomy tube infections in the paediatric population due to their prevalence, vulnerability and characteristics[23]. During the literature research, a discrepancy was found in different studies regarding empirical antibiotic treatment for respiratory tract infections associated with a tracheostomy[12,22]. A significant finding in the review was the difficulty of identifying the etiology of infections in the tracheostomy because the bacterial culture sampling varies depending on the protocol of each institution and each study[12]. Besides, a culture of tracheal secretions showed multiple colonizing bacteria[22]. It should be noted that the most prevalent microorganism associated with this clinical picture reported in the literature was *Pseudomonas aeruginosa*, which was present in all the studies reviewed. Seeing as risk factors Hispanic ethnicity and male gender associated with the readmission and the development of chronic positive cultures of *Pseudomonas aeruginosa* respectively, these are considered with caution because these results vary around the sample size and the amount of male-female, the proportion and demography according to the studies' characteristics.

Tracheobronchitis is common in children chronically dependent on tracheostomy. In studies of children with newly placed tracheostomy tubes, approximately 30% to 40% were readmitted to the hospital within the first 12 months for lower respiratory tract infections (tracheobronchitis and pneumonia)[18,20]. Pneumonia accounted for most readmissions, but many additional tracheobronchitis episodes that did not require hospital admission likely occurred.

Tracheobronchitis in children with artificial airways can be difficult to distinguish from associated lung infection. Some aspects that suggest a possible tracheal infection include: new fever or elevation above the most recent baseline of daily maximum temperature elevation; change in colour, viscosity, and/or odour of tracheal secretions; increased need for airway suction (suggesting increased production or volume of secretions or exudate from the airway); more remarkable work of breathing, new crackles, rhonchi and/or wheezing on auscultation of the chest. The evaluation of suspected bacterial etiology includes: chest X-ray to distinguish ventilator-associated pneumonia; complete blood count with differential, peripheral blood with white blood cell count[24]; Gram stain and culture of tracheal aspirate which should be compared with previous cultures if there are any available. The presence of microbes with a different morphology from those identified in recent samples, a positive Gram stain alone, with no other clinical data, can only reflect colonization. Quantitative cultures that produce $\geq 10^4$ufc/mL of a single bacterial species are indicative of infection rather than colonization[10-13]. Although it is rarely required for routine evaluation in children with artificial airways, bronchoscopy can confirm or exclude other diagnoses. If bronchoscopy is performed, bronchoalveolar lavage specimens should be sent for culture.

In the diagnosis of tracheobronchitis in children with artificial airways, a clinical diagnosis is poorly defined. No single test confirms the diagnosis. Tracheobronchitis is usually diagnosed clinically based on fever and new-onset purulent tracheal discharge in children chronically dependent on tracheostomy, in the absence of other causes for these findings. Sputum cultures are helpful in the management, but positive sputum cultures alone are insufficient to make the diagnosis. Inflammatory biomarkers such as C-reactive protein and procalcitonin have not been validated as diagnostic aids in children.

Oral antimicrobial therapy is appropriate for treating tracheobronchitis in chronically tracheostomy-dependent children who do not appear to have systemic disease. Intravenous antibiotic therapy is generally indicated for patients with artificial airway-associated bacterial tracheobronchitis who appear to be systemically diseased. After initiating treatment for artificial airway-associated tracheobronchitis, a reevaluation of the diagnosis within 48 to 72 hours is recommended, based on ongoing clinical courses and available laboratory data[8].

Considering all the above, we think it is essential to continue the research on this topic since there is a great deal of discrepancy in the treatment of tracheostomy tube infections in children and identifying the determining risk factors for the readmission. Precision and reduction of infection risk are of great importance in tracheostomy care for children. This is a population with higher morbidity and mortality than the general population.

CONCLUSIONS

Children who require artificial airways have an increased risk of tracheopulmonary bacterial infections due to bacterial colonization of the artificial airways and cannulation mucosal lesions. This entity has clinical signs such as fever, cough, increased sputum production without radiographic evidence of pneumonia. The paraclinical evaluation include a chest X-ray, complete blood count with differential, Gram stain and tracheal aspirate culture. Viral studies are helpful in some circumstances.

The diagnostic criteria commonly used include: the absence of clinical or radiographic evidence of pneumonia, a positive culture obtained by deep tracheal aspiration or bronchoscopy, and two or more of the following signs or symptoms with no other recognized cause: fever> 38°C, cough, production of sputum, rales and/or wheezing. In infants less than one year old: respiratory distress, apnea, and/or high bradycardia, should be a diagnostic criterion for airway infections.

Initial empirical antimicrobial therapy aims to provide coverage for the most likely pathogens and is individualized according to the severity of the disease.

It is necessary to emphasize a significant difference between colonization of the artificial airway and a clinical picture of acute infection. The last one presents diagnostic criteria, while colonization is represented by the finding of the artificial airway cultures with a high degree of controversy in antibiotics use.

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Contribution of authors: All the authors have equally contributed to this work.

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