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Contents

COVID-19 in Children: Treat Now and Stop with Vaccines in Future

Since December 2019, COVID-19 has infected more than 1 billion people and killed more than 2 million people worldwide. Although the World Health Organization and all countries have made efforts to control COVID-19, a third and more serious infection surge is currently ongoing. Some medications have been used to treat the disease; however, it is believed that vaccines are the only effective way to stop this pandemic. With the close cooperation of scientists and regulatory agencies, several COVID-19 vaccines have been approved and used in many countries since December 2020. However, none of these vaccines have yet been authorized for use in children. Children usually suffer mild to moderate symptoms, and the treatment strategies are different from those in adults including home isolation and being cared for by their parents/caregivers. The current issue includes two excellent review articles on COVID-19. The first article reviews the current SARS-CoV-2 vaccines used in adults and addresses their potential use in children. The second article reviews when to identify SARS-CoV-2 infection in children, and how to treat children with mild-to-moderate COVID-19 disease. In addition, a third article discusses the diagnostic role of computed tomography (CT) and flexible bronchoscopy (FB) in children with suspected foreign-body aspiration (FBA) and the therapeutic role of FB.

SARS-CoV-2 vaccines are an urgent and important topic. Chatani and Ng[1] reviewed the currently available SARS-CoV-2 vaccines including mRNA vaccines, inactivated viral vaccines, and vector-based vaccines. In this article, the author compares these vaccines and provides a table that includes the manufacturer (name of product), mechanism of action, and reported side effects. Several vaccines have been approved by the regulatory agencies and been rapidly deployed in adults in many countries. Two vaccines are currently being tested in ongoing trials for children as young as 12 years old. Dr. Chatani and Ng discusses the administration and use of vaccines in the pediatric population, as well as potential pitfalls such as the historical background of respiratory syncytial vaccine and dengue virus vaccine. We hope that the results of the vaccine trials in children will show their safety and efficacy. After being approved by appropriate regulatory agencies, vaccines will protect children and help to attenuate the pandemic.

Children infected with SARS-CoV-2 usually less severe illness. Kabra[2] reviewed the treatment of mild to moderate COVID-19 including the role of physicians in identifying and managing these patients. The findings of this review will help to elucidate when and whom to test for SARS-CoV-2 based on influenza-like symptoms, underlying conditions, family history, and contact history. The author also clarifies how to treat mild, moderate, and severe patients according to clinical features and the corresponding management. The treatment strategies include isolation at home or COVID-19 care facilities, monitoring by the parents/caregivers, teleconsultation, and admission to a ward or pediatric intensive care unit if indicated. The article also updates information about the use of medicines in children.

FBA in children is still an important diagnostic and therapeutic challenge, especially in cases without a history of aspiration of foreign body. Recently, the role of CT in the diagnosis of FBA and the role of FB in the treatment of FBA have gained increasing attention.[3] Bhat *et al*.[4] conducted a prospective study to evaluate the role of CT and FB in the diagnosis of suspected trachea-bronchial FBA in children and found that the sensitivity and specificity rates for chest CT were lower than those for FB. They also reported that FB is a good therapeutic tool to retrieve airway foreign bodies, and that it is a safe procedure with minimum complication rate.

I would also like to remind the readers that the current issue is labeled April–June 2020 although it is in fact published in February 2021 because of the delay in publication. My sincerest apologies for any inconvenience caused to the authors.

The SARS-CoV-2 vaccines are already helping to combat the COVID-19 pandemic. I hope you are safe and well!

Yu-Tsun Su

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Review Article

SARS-CoV-2 Vaccines: A Brief Review

Brandon Chatani[1], Daniel K. Ng[2]

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Abstract

SARS-CoV-2 has immensely changed the landscape in how vaccines are researched and developed. The timeline truncated for the propose of meeting the grave demand. Children stand to benefit from herd immunity for multiple reasons. Protection from SARS-CoV-2 would not only protect children from COVID but also a unique entity called Multisystem Inflammatory Syndrome in Children (MISC). Thus, it is vital that general pediatricians and practitioners who care for children to have foundational knowledge regarding the ever-expanding array of soon to be available COVID19 vaccines along with the potential pitfalls of their rushed development and implementation. This article seeks to provide a brief review of the most prominent COVID19 vaccines under development with intention for Pediatric use as well as recall historical knowledge regarding rushed development of respiratory viral vaccines that resulted in unintended consequences.

Keywords: SARS-CoV-2, Vaccine, COVID, Pediatric, Corona virus, RSV

Introduction

The climate of the COVID19 Pandemic has put vaccine development to rush order. Several manufacturers moved products through early research and development at outstanding paces. By early August 2020, there were at least eight vaccines in large-scale efficacy tests, primarily focused on the adult population. From the laboratory to clinic, a vaccine passes through several trials to become approved and available for commercial use. The start for COVID19 was in January 2020, virologist sought to decode the genomic contents of the virus. By identifying the bevy of possible antigen targets, trials could begin to test which would elicit an immune response. The production of antibodies isn't enough, the antibodies which the host produces must have an activity to prevent infection. Animal testing is moved to human testing in small groups, then larger groups to ensure safety of proposed vaccine products. The greatest hurdle then is being the large-scale efficacy trials which would need to show that the vaccine provides protection to at least 50% of vaccinated people to be approved by agencies such as the United States Federal Drug Administration (FDA) and the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom.

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Vaccines

Companies such as ModernaTX, Inc. and Pfizer, Inc. own some of the vaccine products that have passed through Phase 3 trials, as seen on ClinicalTrials.gov. They have chosen products based on nucleoside-modified messenger RNA (mRNA).[1] Their teams identified mRNA in COVID19 which could be modified to allow perfusion into the human body and instigate an immunologic response. The sites for targeting antibodies against the virus can vary, however, the large majority of vaccine products under investigation, the site of focus is a protein on the viral envelope (spike protein).[2] As of December 2, 2020, both the FDA and the MHRA have approved the product developed by Pfizer/BioNTech. The two regulatory agencies conducted independent reviews of data from the laboratory pre-clinical studies, clinical trials, and manufacturing quality controls, in addition to their own

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laboratory testing of the product to ensure stringent safety and quality standards are met in every batch. Both regulatory agencies are globally recognized for their mechanisms by which safety and efficacy of vaccine products are ensured. It is certainly no small feat to gain approval from both in the time which it was achieved.

In a different approach, Sinovac Biotech Ltd. produced a vaccine by a more traditional route via an inactivated viral strain, similar to the way the inactivate poliovirus vaccine was produced.[3] Although in this case, the vaccine involves the CN2 strain of SARS-Cov2 isolated from a COVID19 positive patient, augmented in cell culture, and inactivated by beta-propiolactone.[4]

Yet, another approach to confer immunity to COVID19 with a vectored vaccine which has gained much attention is truly on the cutting edge of science and modern medicine. Few manufacturers based their vaccine on vectored delivery of the immunogenic vaccine components via a recombinant adenovirus. A few of the companies that have utilized a vector-based vaccine approach include CanSino Biological/ Beijing Institute of Biotechnology (China), Johnson and Johnson (USA), and AstraZeneca (UK).[5] From a publication on September 4, 2020, the results from Logunov *et al*. indicate a promising candidate from Russia, vaccine rAd26-S and rAd5-S.[6] This heterologous COVID-19 vaccine utilizes two-recombinant adenoviral vectors (type 26 and type 5) to carry the gene for SARS-CoV-2 spike glycoprotein. Investigators studied the system as a two-dose series at day 0 and day 28. They identified a reported 100% seroconversion rate after the second dose with the most common adverse events not unlike the other vaccine trials currently ongoing, including pain at the injection site, hyperthermia, headache, asthenia, and muscle and joint pain. Of note, the preliminary results published in Lancet include a very small sample size of 38 volunteers. The majority of volunteers were white males, who were confirmed seronegative for SARS-CoV-2 and of normal height and weight.[6] Although a high serologic conversion rate is published in their findings, there remains the question of efficacy to prevent infection. Similarly, there are preliminary results for the product of AstraZeneca which are comparable to the Logunov *et al*.[7] A unique finding found among recipients of AZD1222 was decreased adverse events among individuals older than 56 years old.[8] The adenoviral components of the vaccine may prompt an immune response targeting adenovirus types 26 and 5, rather than the COVID19 spike protein. It is too soon to tell in what ways this will alter the efficacy of the cellular and humoral responses, whether to produce an efficacious mode of prevention or possibly deleterious mode of promotion. An overview comparing each of the aforementioned vaccines is provided in Figure 1. Whether based on an inactivated viral strain or a modified mRNA or viral-based vector, each approach has benefits and risks associated with administration into the human body that only further study and careful analysis will discover.

Considerations for Pediatric Population

A special population to consider in the administration and utilization of vaccines is the pediatric population. Initial vaccine approvals have been for young adults and older; for example, Pfizer's vaccine has been authorized for ages 16 and up, while Moderna's vaccine is currently authorized for ages 19 and up. Both have ongoing trials for younger children as young as 12 years old. This age group is of particular interest because of the known increased rate of transmission and disease severity found among them. Bunyavanich *et al*.[9] first described the possible link between angiotensin-converting enzyme 2 in the nasal epithelium as a mode by which the attenuation of transmission and disease occurs with younger ages. Of the 305 individuals tested, aged 4 years to 60 years, there was a logarithmic correlation of age with the quantity of ACE2 gene expression in the nasal epithelium. In each age bracket, <10 years old, 10–17 years, 18–24 years, and >25 years old, there was an increase in present ACE2 found to be statistically significant (P = 0.1, <0.001, =0.001, respectively). The role of ACE2 in SARS-CoV-2 host entry is a major difference compared to SARS-CoV-1, which augments its ability to transmit from one human to another in the pandemic.[10] Within the USA, the return to in-person school was met with many outbreaks, especially among the 12–18-year-old population. From March to September of 2020, the Centers for Disease Control and Prevention in the USA noted among adolescents aged 12–17 years, the number of COVID19 cases was twice the amount compared to children aged 5–11 years old.[11] Pediatric advocacy groups should urge for teachers and adolescents who qualify for the vaccine to be placed on the priority list for public safety. As for the younger aged children, more time will be necessary for appropriate testing to validate safety and efficacy.

Potential Pitfalls

Although the call to control COVID19 has been powerful, it could potentially lure investigators and clinicians to rushing to a product that does more harm than good. The ultimate benefit of administrating a vaccine is the stimulation of neutralizing antibodies which protect the individual from developing disease after exposure to the virus. However, the level of this benefit of immune protection is limited by a variety of factors, such as the level of response, type of response, and sustainability of response. Respiratory syncytial virus (RSV) provides us with a historical background for previous pitfalls and limitations of vaccines targeting respiratory viruses.[12] From autoimmune disease to variable immune response, the legacy of RSV immunization tests dating from the 1960s outlines possibilities which may be seen on the path to eradicating COVID19. In some cases, RSV vaccines elicited a hyperimmune response at the time of natural infection causing more severe disease.[13] In the initial trials, almost 80% of the formalin-inactivated RSV vaccine recipients required hospitalization and a handful died.[14,15] Already, some research trials identify COVID19 vaccines resulting in an increased eosinophilic proinflammatory pulmonary response.[16] Dengue virus, another well sought after

Figure 1: Comparison of COVID 19 vaccines

Manufacturer (name of product)	Mechanism of action	Reported side effects (%)
Pfizer/BioNTech (COVID-19 mRNA vaccine BNT162b2 concentrate for solution for injection)	Formulated in lipid nanoparticles Delivery of the RNA into host cells to allow expression of the SARSCoV-2 Spike antigen	Pain at the injection site (>80) Fatigue (>60) Headache (>50) Myalgia (>30) Chills (>30) Arthralgia (>20) Pyrexia (>10)
Moderna	mRNA-1273 vaccine encodes the S-2P antigen, consisting of the SARS-CoV-2 glycoprotein with a transmembrane anchor and an intact S1-S2 cleavage site The mRNA is held in a lipid nanoparticle capsule composed of four lipids	First injection Pain at the injection site (13-80) Fatigue (13-20) Chills (6-13) Headache (20-26) Second injection Pain at the injection site (69-73) Fatigue (14-40) Fever (33-35) Chills (7-53) Headache (15-64) Nausea (7-40)
AstraZeneca (AZD1222, previously referred to as ChAdOx1 nCoV-19)	recombinant replication-defective chimpanzee adenovirus expressing the SARS-CoV-2 S surface glycoprotein	Injection site pain (5-50) Fatigue (5-75) Headache (2-60) Fever (1-40) Myalgia (2-50)
SinoPharm (BBIBP-CorV)	Inactivated whole virus, alum adjuvanted	Injection site pain (13-38) Fever (4-25) Fatigue (3-13)

vaccine candidate, initially had a vaccine in the 1980s which produced more severe infections when a vaccinated individual was infected with another serotype due to the enhancement of viral uptake by the vaccine-induced antibodies.[17] Whether a heightened immune response or promotion of viral infection, there remains the possibility of the same adverse events occurring with COVID19 vaccines. SARS-Cov2 is becoming well known for its related multisystem inflammatory syndrome in children as an illness stemmed in a type of immune response. Although not yet seen among clinical vaccine trials involving adult aged patients, there is still a risk when these vaccines against COVID19 are brought over to children. At the other end of the spectrum of a potential vaccine, responses are limited, unreliable response. When scientists attempted to produce a live, attenuated RSV vaccine, some recipients obtained prolonged viral shedding with little to no protection against the wild type virus.[18] Shedding of SARS-Cov2 for prolonged periods of time could potentially produce local outbreaks and the exposure of some of the most vulnerable patients. Although the path to a safe and effective vaccine appears clearer for adults, it remains not the case for children, pregnant women, and immunocompromised people.

Conclusion

With such a variety of vaccine products being studied and all utilizing a gamut of scientific mechanisms, there is hope that at least one, if not many, will help attenuate the ongoing pandemic. Physicians should continue to look to the leading regulatory agencies for guidance around vaccine safety and efficacy with appropriate comparison trials upcoming.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Treatment of Mild to Moderate COVID-19 in Children

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Abstract

Children as such have less infection and less severe covid 19 illness. Majority will be asymptomatic or mildly symptomatic. Symptoms are nonspecific and suspect in children presenting with influenza-like illness (ILI) or children presenting with respiratory difficulty. Children with definite contact with COVID-positive patients or those who had severe illness (irrespective of COVID status) in the past 2 weeks should be subjected to test. The rest of the children may be tested if any of the following are present: 1. The presence of high-risk factor in child such as immunocompromised condition (long-term steroids, cancer chemotherapy, biological agents, and primary or secondary immune deficiency) or chronic illnesses including chronic respiratory illnesses 2. Any person in family who is at risk of developing serious illness (elderly, immunocompromised, diabetic, hypertensive, etc.,). Majority of mild to moderate illness can be managed at home with symptomatic treatment ensuring monitoring for worsening of symptoms. There is no proven benefit of antibiotics, antiviral agents, steroids, hydroxychloroquine or other anti-inflammatory agents.

Keywords: COVID-19, dexamethasone, hydroxychloroquine, remdisavir

COVID-19 pandemic is ongoing since December 2019, it is unclear, what will be its course. However, we can definitely say that COVID-19 infection is going to stay with us for months to year.[1] As of now, most countries have developed separate COVID care teams for testing and managing different severity of cases. Once the pandemic gets flattened, sporadic cases or localized outbreaks in different geographic regions will continue to occur. Children as such have less infection and less severe illness. Majority will be asymptomatic or mildly symptomatic. Majority can be treated with home isolation and supportive care.[2] Therefore, pediatricians and general practitioners will play an important role in the identification and management of such patients.

When to Suspect

COVID-19 is no more a restricted disease to particular continent. As the symptoms are similar to any viral respiratory tract infection, it is very difficult to identify COVID infection on the basis of clinical symptoms alone. Therefore, keeping a high index of suspicion is important. It may not be exaggeration to suggest that all children presenting with influenza-like illness (ILI) like symptoms may have COVID-19 infection. With time when panic goes down and we are more confident, approach will change. Most children with mild-to-moderate illness can be managed at home with precautions for high-risk groups.

Approach to Children Presenting with Influenza-Like Illness

Any child presenting with ILI for <10 days duration may be assessed for likelihood of COVID infection and severity of illness.

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Table 1: Assessment of severity

Severity of illness	Clinical features	Management
Mild disease	ILI with cold cough, no respiratory difficulty, feeding well	Assess for feasibility of home isolation and ambulatory treatment If feasible: Home isolation, symptomatic treatment and education of parents about monitoring at home, when to bring child to health care facility If not feasible; management in COVID care facility (if available) in nearby house
Moderate disease	ILI with difficulty in respiration RR >60/min in <2 months of age RR >50/min in 2–12 months of age RR >40/min in 12–60 months of age RR >30/min in >5 years of age Lower chest in drawing Oxygen saturation in room air >92% Respiratory rate more, mild chest indrawing and SaO_2 >92%, feeding well Respiratory rate more, severe chest indrawing and SaO_2 >92%, feeding less	Home isolation and treatment or treatment at covid care facility Admission in ward
Severe disease	ILI with pneumonia with at least one of the following central cyanosis or SpO_2 <90%; severe respiratory distress (e.g., fast breathing, grunting, very severe chest indrawing); general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions	Admit in PICU and treat accordingly

ILI=Influenza-like illness, RR=Respiratory rate, PICU=Pediatric intensive care unit

Likelihood of COVID

Children who come from a family or definite contact with COVID-infected adults are considered to have COVID infection. As the infection can be transmitted by individuals with asymptomatic infection or presymptomatic (still not developed symptoms), it is very difficult to identify contact with COVID infection.

Whom to Test

It is difficult to decide whom to test and isolate. All children with definite contact with COVID-positive patients or those who had severe illness (irrespective of COVID status) in the past 2 weeks should be subjected to test. The rest of the children may be tested if any of the following are present:

1. The presence of high-risk factor in child such as immunocompromised condition (long-term steroids, cancer chemotherapy, biological agents, and primary or secondary immune deficiency) or chronic illnesses including chronic respiratory illnesses
2. Any person in family who is at risk of developing serious illness (elderly, immunocompromised, diabetic, hypertensive, etc.,).

If none of these are present, child may be treated with home isolation unless has moderate or severe illness.

Pathways to Follow for Children with Influenza-Like Symptoms

All children presenting with ILI should be assessed by asking mother about, oral intake, difficulty in respiration. Child should be examined for the respiratory rate counting for full minutes, look for lower chest indrawing, and check oxygen saturation. Based on the above observations, may be classified as mild/moderate or severe illness.[3]

Management of Mild and Moderate Illness without Hypoxia

These children have no respiratory difficulty, or mild lower chest in-drawing, feeding well, have SpO2 >92% and feasibility of monitoring home can be managed at home isolation facility. For home isolation, need to assess feasibility (availability of room, with wash room, no adult with high risk, possibility of monitoring/teleconsultation at home, and taking child to health-care facility immediately to health-care facility). If feasible, may be treated at home. If this is not feasible, then the child should be managed in COVID care facility (if available).

Antibiotics

No role routinely.

Antiviral agents

There is no role of antiviral agents such as lopenavir-Retinovir and Interferon alfa). There are no studies of benefits of remdisavir in mild-to-moderate illness in children. Studies in adults suggest some beneficial role in moderate-to-severe illness [Table 1].

Dexamethasone

Studies in adults suggest the survival benefit in severe illness, but no significant improvement in mild illness. There are no randomized controlled trials in children.

Other medications

Hydroxychloroquine was advocated in the beginning of pandemic, now randomized controlled trials have shown that

there is no role of hydroxychloroquine. In some patients with severe illness secondary to cytokine storm, anti-interleukin 6 Tocilizumab and human plasma infusion has shown some improvement. However, as of now, there is no conclusive evidence of beneficial roles of these medications in mild-to-moderate illness in children.

Supportive Care

Control of fever using paracetamol (10–15 mg/kg/dose SOS/q 4–6 hourly if required). Regarding the use of nonsteroidal anti-inflammatory drugs (NSAIDs), indirect evidence suggests no evidence of severe adverse effect in viral respiratory infection.[4] There is no direct evidence for adverse effect of NSAIDs in COVID-19 infection. Therefore, may be used if indicated.

Ensure adequate hydration by asking parents to give the plenty of liquids to child.

Monitoring at Home

Children being managed in home isolation require good monitoring to identify deterioration early and seek medical advice. Monitoring consist of observing for the development of respiratory difficulty (rapid respiration and chest indrawing), reduced feeding, development of lethargy, dull sensorium, seizures, cold extremities, reduced urine output, and if feasible fall in oxygen saturation of <92%. It is desirable that mother or any other person in family is trained in monitoring and keeping records at least twice a day. It is also desirable that doctor contacts the family at least once a day to family telephonically or by video to assess the status till child is afebrile and complete recovery.

When to take the child to health care facility

If child develops any of the above parameters, family should contact treating doctor and act as per the advice of doctor. If not able to contact doctor should take the child to nearest health-care facility for assessment.

Precautions for Parents

The parent/caregiver should take the necessary precautions and use appropriate PPE including a mask. Frequent washing of hands or use of sanitizer, frequent washing, or cleaning of toys of child. Keeping child isolated from other members of household. If any other member of household develops ILI symptoms, to get their test for COVID-19 infection.

Duration of Isolation

Child should be afebrile for 72 h and at least 7 d after symptom resolution OR negative samples (if done earlier). Virus shedding can last up to 4 weeks in symptomatic children and infection control measures such as wearing mask and stringent hand hygiene should be practised. Repeat test is indicated only in children who have underlying illness.

Children with moderate illness with hypoxia and severe illness

These children need hospitalization and appropriate supportive care.

A new manifestation of COVID 19 infection

A new syndrome called "Multisystem inflammatory syndrome temporally related to COVID-19" has been described recently. Children may present with fever >3 days, rash/nonpurulent conjunctivitis/mucocutaneous signs, hypotension, myocardial dysfunction, coagulopathy, acute GI problems, elevated markers of inflammation, evidence of COVID-19 (antigen or serology)/likely contact with positive patient, and no obvious bacterial cause. These children may need treatment in pediatric intensive care unit, supportive care such as systemic steroids with or without IV IgG infusion.[5]

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Conflicts of interest

There are no conflicts of interest.

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Comparative Analysis of Computed Tomography Scan and Flexible Bronchoscopy in the Evaluation of Suspected Foreign Body Aspiration in Children and the Role of Later in its Removal

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Abstract

Background: Foreign body aspiration (FBA) in children is considered one of the most important diagnostic and therapeutic challenges for physicians. Often there is no history of aspiration of foreign body in this population and these children present with a wide range of nonspecific signs and symptoms. The objective of the study was to study the diagnostic utility of chest computed tomography (CT) scan in children with suspected FBA in comparison to flexible bronchoscopy (FB) and the role of later as a therapeutic tool in the removal of airway foreign bodies. **Methods:** This was a prospective observational study conducted from January 2015 to August 2019. Children admitted for persistent respiratory symptoms underwent CT chest and FB for confirmation of the diagnosis and retrieval of the foreign body if present. **Results:** A total of 101 patients of both genders were enrolled in the study. Fifty-three participants were boys and 48 were girls. FBA was diagnosed in 53 patients on chest CT. On FB, FBA was confirmed in 55 patients. The sensitivity and specificity of chest CT in our study were 85% and 87% respectively. In 25 of these patients, removal was successfully done by the FB. **Conclusion:** We conclude that a Chest CT scan is inferior to FB in the diagnosis of suspected trachea-bronchial foreign bodies in children. FB as a therapeutic tool has an excellent safety record in the retrieval of airway foreign bodies in this population.

Keywords: Bronchoscopy, foreign bodies, tomography

Introduction

Foreign body aspiration (FBA) into the tracheobronchial tree is an important cause of childhood mortality especially in young children between six months to 3 years of age.[1] According to the National Safety Council of USA, the rate of fatal choking in American children <5 years of age is 0.43/100,000 of the general population.[2] The majority of times there is no history of FBA especially in toddlers, these patients usually present with nonspecific symptoms of persistent cough, hemoptysis, collapse, asymmetrical air entry, and nonresolving pneumonia.[3] Delayed diagnosis is associated with increased complication rate,[4,5] hence early diagnosis is essential to reduce complication rate and overall mortality in these patients.

Chest X-ray is the initial investigation in children evaluated for persistent respiratory symptoms; however, X-ray findings especially in the case of radiolucent FBA are usually nonspecific, which may include unilateral hyperlucency, persistent collapse, mediastinal shift, etc. In about 30% of patients, there may be no abnormality on chest X-ray.[6] Computed tomography (CT) scan chest with or without virtual bronchoscopy is being increasingly used as a diagnostic tool in suspected FBA in children. It has excellent sensitivity in picking up radio-opaque foreign bodies; however, sensitivity is variable in the case of radiolucent foreign bodies, which is the commonest one in children.[7] In contemporary Pulmonology, flexible bronchoscopy (FB) has found an important place in the initial evaluation of children with suspected FBA. It is a very

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safe procedure in expert hands with nearly 100% sensitivity and specificity in diagnosing FBA.[8-10] Besides diagnosis, it is now increasingly used for the removal of foreign bodies from the trachea-bronchial tree with an established safety profile.[11] FB is especially useful in removing foreign bodies at difficult locations like upper lobe bronchus, deep lower lobe bronchus. The present study was conducted to study the diagnostic utility of chest CT scan in children with suspected FBA in comparison to FB and the role of the later as a therapeutic tool in the removal of airway foreign bodies.

Methods

This was a 56-month prospective observational study from January 2015 to August 2019 conducted in the department of pediatrics of a tertiary care hospital of northern India. The study material consisted of Children admitted or referred to or hospital as suspected FBA. Suspected FBA was defined by "a child with persistent respiratory symptoms like chronic cough and/or indirect radiological evidence of trachea-bronchial foreign body like unilateral hyperinflation, persistent collapse, non-resolving pneumonia or soft tissue shadow in the trachea-bronchial tree with no definite history of FBA/chocking." Patients, with X-ray chest and/or CT chest documented radio-opaque foreign bodies were excluded from the study, and these patients were directly subjected to the rigid bronchoscopy for its removal. A standardized data extraction form was used to obtain the demographic and clinical data including age, sex, weight, and the duration of the symptoms. Chest CT scan findings were documented in all the enrolled patients. FB (Olympus video bronchoscope) was done in all the enrolled patients. The authors used a BF-XP160F™ scope with channel size 1.2 mm in children <4 years of age and BF-MP-160F™ scope with a channel diameter of 2 mm in children above 4 years of age. Written informed consent was taken from all the patients before undertaking the procedure. All procedures were performed in a bronchoscopy suite which is close to the pediatric intensive care unit. Bronchoscopy team comprised of two bronchoscopists, one pediatric resident, one bronchoscopy technologist, and one nurse. During the procedure blood pressure, ECG, and oxygen saturation were continuously monitored using multi-channel Nelcor™ Monitor. All patients received supplemental oxygen via nasal cannula during the procedure. Nasal mucosa was anesthetized by using lidocaine gel locally. 2% lidocaine in 1 mL aliquots in 1:1 dilution with normal saline was instilled in the tracheobronchial tree by the "spray-as-you-go" technique. Supplemental local anesthesia was given as per requirement. All patients received midazolam bolus at the dose of 0.1 mg/kg over 1 min. In addition to midazolam bolus, the majority of our patients received intravenous (IV) ketamine bolus at the dose of 1 mg/kg over 2 min diluted in normal saline. Signs of pain or discomfort, agitation, persistent cough, and inadequate motor or verbal response to manipulation were considered indicators for insufficient sedation, leading to the administration of additional doses of IV ketamine bolus at 1 mg/kg/dose. Patients, who received ketamine, were also given IV glycopyrrolate 5 μg/kg to reduce ketamine-induced increased respiratory secretions. Bronchoscopy findings were recorded in a standard format, which included all anatomic and functional details, presence of foreign body if any and its location, type of foreign body, any granulation tissue, purulent secretions, and bleeding tissue surrounding the foreign body. Complications if any during or postprocedure were recorded in a standard format.

Statistical analysis was performed using SPSS 20, IBM; Armonk, United states. The normality of the data was checked by using the Shapiro–Wilk test. Parametric data are expressed as mean ± standard deviation and nonparametric tests as median (interquartile range). Categorical variables are presented as percentages. The study was cleared by the ethical committee.

Results

During the 56 months of the study period, 143 patients were fulfilling the inclusion criteria. In 20 patients, CT chest could not be done; these were excluded from the study. Twenty-two patients couldn't be enrolled due to the refusal of consent for a bronchoscopy. So a total of 101 patients were enrolled in the study. Fifty-three participants were boys and 48 were girls. The baseline characteristics of the study population are shown in Table 1. On CT chest FBA was diagnosed in 53 patients. It was seen in a right bronchus in 38 patients and left bronchus in 15 patients. Among 53 patients with CT diagnosis of FBA, a second differential diagnosis of thick mucus plug was given in 23 patients [Figure 1].

FB was done in all 101 patients. FBA was confirmed in 55 patients with 41 foreign bodies visualized in right bronchus and 14 in the left bronchus. In 25 patients, removal was successfully done with the help of the flexible scope. Removal was done by Dormia basket, loop, or forceps [Figure 2]. Success in foreign body retrieval was inversely related to the duration of symptoms. Table 2 shows the characteristics of the two groups. The most frequently aspirated foreign body was nut and kernel (52.7%) followed by bean (30.9%). Plastic foreign bodies were seen in 7 (12.7%) patients and two patients had aspirated chewing

Table 1: The baselines characteristics of the study populations (*n*=101)

Characteristics	Value
Age in months (IQR)	17 (15)
Weight in kg (mean±SD)	13.8±3.8
Height (cm) (IQR)	95.0 (35.0)
Duration of symptoms in days (mean±SD)	17.3±7.3
Male (%)	53 (52.4)
Oxygen saturation (mean±SD)	93.0±12.6
Respiratory rate (mean±SD)	36.0±8.0

SD=Standard deviation, IQR=Interquartile range

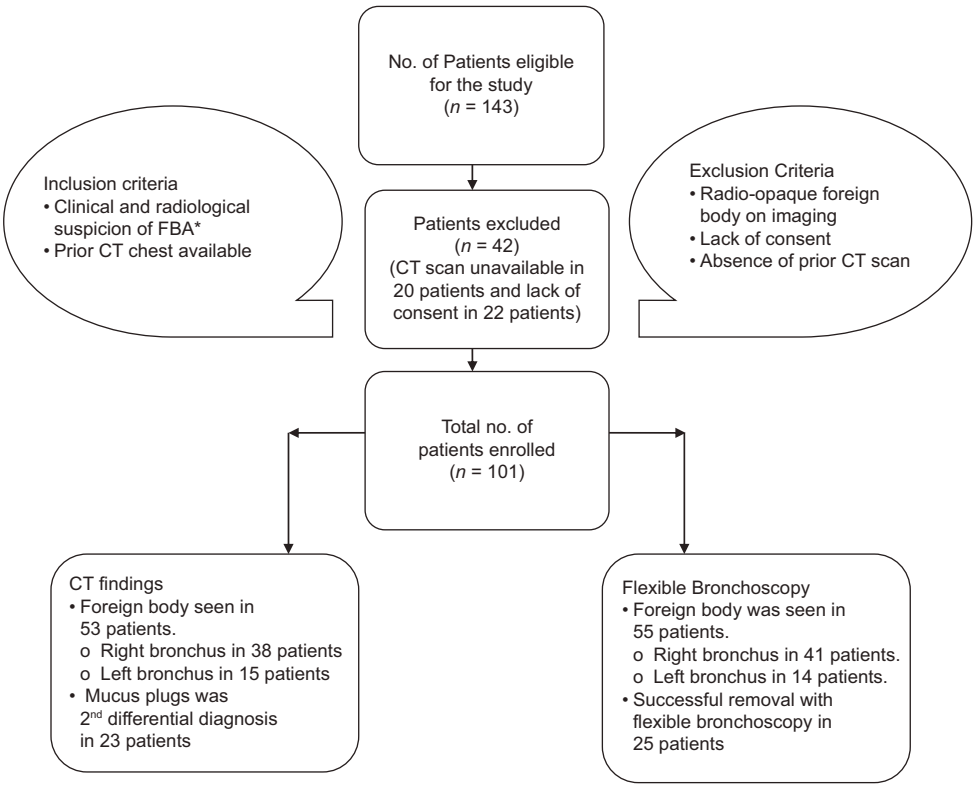

Figure 1: The flow chart showing the patients enrolled and their computed tomography scan and bronchoscopic findings. FBA = Foreign body aspiration.

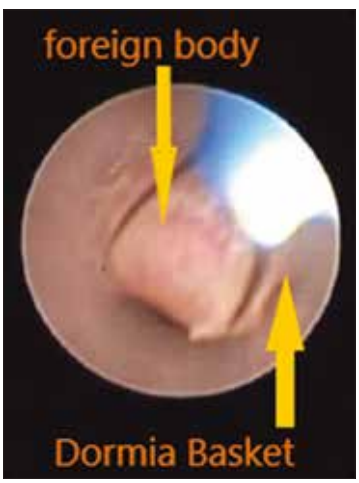

Figure 2: The Dormia basket holding the foreign body (a peanut) in the right main bronchus.

gum. There was no statistically significant difference between the type of foreign body and the success of removal with the flexible scope. Among 53 patients with CT diagnosis of FBA, six patients had no foreign body visualized in the tracheobronchial tree on FB (thick mucus plug in four patients, granulation tissue in two patients). Similarly, in eight patients CT chest was reported as normal, however, FBA was detected on FB. The sensitivity and specificity of chest CT scan in our study were 85% and 87% respectively. No major adverse event was noticed during the procedure. Minor adverse events like transient desaturation were seen in five patients (11%), apnea in two patients (4.7%), and post bronchoscopy wheeze in one patient (2.5%) requiring salbutamol nebulization.

Table 2: The characteristics of patients in foreign body removal and non-removal groups

Characteristics	Foreign body removal group (*n*=25)	Foreign body nonremoval group (*n*=30)	*P*
Age in months (mean±SD)	22.4±12.7	19.8±9.4	0.24
Weight in Kg (mean±SD)	13.7±3.9	14.0±3.1	0.41
Duration of symptoms in days. (mean±SD)	13.4±4.2	20.4±6.5	0.03*
Male (%)	17 (68.0)	14 (46.6)	0.11
Right tracheobronchial tree (%)	17 (47.2)	19 (52.8)	0.33

*P<0.05 statistically significant values; SD=Standard deviation

Discussion

In this 56-months prospective study, we found that the CT scan is 85% sensitive and 87% specific in diagnosing suspected airway foreign bodies. FB not only helped us in confirming the presence of a foreign body but also enabled us to identify its position and attempt its removal in the case of a small and recently aspirated foreign body. We encountered a very few minor procedural side effects during the removal.

Aspiration of foreign body in the tracheobronchial tree is a common and life-threatening situation in children. Up to 50%

of patients especially toddlers have no history of aspiration. These patients present with non-specific respiratory symptoms in the form of cough, wheeze, recurrent/non-resolving pneumonia, persistent collapse, and decreased air entry.[3,12] The complication rate is highest in this subgroup of patients. Chest X-ray is the first investigation for the evaluation of persistent respiratory symptoms in children; however, its role in the evaluation of FBA is controversial. In a study by Mallick[6] chest X-ray was normal in 32.2% of patients. CT scan chest with or without virtual bronchoscopy has gained importance in the evaluation of suspected FBA in children because of its ease of availability and non-invasive nature of the investigation. CT scan chest may reveal the impacted foreign body directly as a hyperdensity in the lumen of the airway or from ancillary findings like lobar/unilateral emphysema, atelectasis, consolidation, and bronchiectasis.[13] Three-dimensional CT has excellent sensitivity in detecting radio-opaque foreign bodies, however, in the case of radiolucent foreign body, sensitivity is variable. We found an overall sensitivity of 85% in our study cohort. In a study by Applegate *et al*.[7] on a cadaveric model using a spiral CT scan, they reported a combined sensitivity and specificity of 83% and 89% respectively in the detection of aspiration of LEGO foreign bodies. However, sensitivity was only 34% in the case of peanut aspiration. As the majority of FBA in children are due to organic foreign bodies, the chance of false-negative rate is high, making this investigation less useful in the investigation of radiolucent FBA in children. CT scan also exposes a child to a high radiation dose. The radiation dose from a typical chest CT scan in a child is about 250–300 times higher than a chest X-ray.[14] Mathews *et al*.[15] in their study on a large cohort of patients found an increase in cancer incidence by 24%, and the risk was greater for persons exposed at a younger age.

FB is increasingly being used for the evaluation of persistent/recurrent respiratory symptoms in children. This procedure helps us to obtain the detailed anatomic and functional information of the tracheobronchial tree. In the case of FBA, it can provide us information about the foreign body's nature, its orientation, and associated changes in the airway mucosa as well as attempts its extraction in the same setting.[16] FB has proven an excellent and safe tool for the removal of foreign bodies from the tracheobronchial tree in children. In our study, about 50% of foreign bodies were successfully removed with a flexible scope. Swanson *et al*.[17] published 8 years of experience of foreign body retrieval through FB. In their series, all airway foreign bodies were successfully removed with a fiberoptic bronchoscope. Tang *et al*.[18] in their study successfully removed airway foreign bodies by FB in 91.3% of the patients without any major complications. The reason for the less retrieval rate in our series was because our study was done in patients with no clear cut history of FBA. All patients in our study had non-specific chest problems like persistent lobar/segmental collapse, non-resolving consolidation, unilateral emphysema, with a mean duration of the symptoms of 17.35 ± 7.3 days. The vegetative foreign body swells and gets stuck-up with time, making its retrieval difficult with the flexible scope, this might be the reason for less extraction rate in our patients.

FB in children is a very safe procedure.[9,19] The authors also did not find any major complications during the procedure. Minor adverse events like transient desaturation were seen in five patients (11%), apnea in two patients (4.7%), and post bronchoscopy wheeze in one patient (2.5%) requiring salbutamol nebulization making this procedure very safe.

The limitation of our study is that it is an observational study; a well-controlled RCT comparing FB with rigid bronchoscopy would be more accurate and will be helpful in further assessing the clinical utility of the FB in suspected FBA.

Conclusion

We conclude that a Chest CT scan is inferior to FB in the diagnosis of suspected FBA in children. FB is a good therapeutic tool for retrieval of airway foreign bodies. Besides, it is a safe procedure with minimum complication rate and can be done as a daycare procedure under conscious sedation.

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Conflicts of interest

There are no conflicts of interest.

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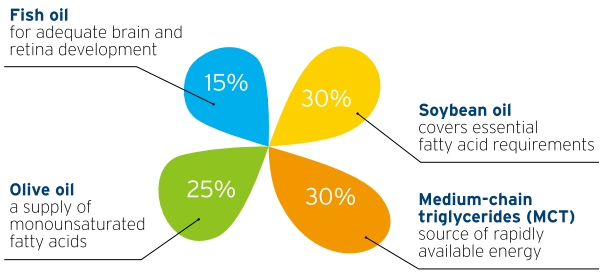

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