Volume VIII, Issue III
July 2020

PediaNews

The Official Newsletter of RxPups – Student Society of Pediatric Advocates

A Historical Moment in Pediatric Pharmacy

The American Geriatrics Society (AGS) is well-known for the Beers Criteria, a list of potentially inappropriate medications that are typically best avoided by older adults.

The Pediatric Pharmacy Association (PPA) has recently published a resource about drugs that are potentially harmful and inappropriate for use in the pediatric population: The KIDs List.

The KIDs List consists of 67 drugs and/or drug classes and 10 excipients that should be avoided or used with caution in all or subsets of the pediatric population. This resource is an essential steppingstone to enhancing medication safety. It is a reference tool to identify medications that are associated with adverse drug reactions. This tool could be used to assess and improve quality of care, decrease costs, and identify areas for needed research in the pediatric population.

To read this special resource, you can find it at the following website: https://www.jppt.org/doi/full/10.5863/1551-6776-25.3.175

INSIDE THIS ISSUE

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KAWASAKI-LIKE DISEASE IN COVID-19 PEDIATRIC PATIENTS

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The onset of the global COVID-19 pandemic represents an unprecedented occurrence in this generation. Since the declaration of the first pandemic outbreak in China in late 2019, most of the globe has been affected by the Sudden Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Although, pandemic responses worldwide are working to elucidate the characteristics of the virus and its effects on those infected, little is known about how COVID-19 affects infants, children, and young adults.

Notably, pediatric patients have been a minimal medical burden during the outbreak. In the United States, as of April 2020, only 1.7% of COVID-19 cases are made up of children under the age of 18[1]. Symptoms in children are generally similar to that of adults, including those characteristic of upper respiratory tract infections such as fever, fatigue, sore throat, cough, and shortness of breath. Severe cases can present with respiratory failure, shock, coagulopathy, and renal injury. However, several studies have shown that the coronavirus disease in children is generally milder than in adults. In an epidemiologic report of over 700 confirmed pediatric cases, researchers characterized over 90% of the population as asymptomatic or mild to moderate severity of disease[2]. Despite this, and in light of recent reports, new concerns are being raised for a possible Kawasaki-like syndrome found in children that may be associated with COVID-19. Reports from the United Kingdom, Italy, and now the United States suggest that a possible link exists between coronavirus infection, asymptomatic or otherwise, and a delayed inflammatory response. With many countries, including the US, re-opening school systems, it is important for healthcare providers to understand these manifestations and treatment options.

In the 1960s, Dr. Tomisaku Kawasaki was the first to describe the inflammatory disease that would later be his namesake. He described the phenomenon as an “acute febrile, mucocutaneous syndrome with lymphoid involvement specific desquamation of the fingers and toes.” It is a rare, but possibly severe vasculitis, or inflammation of the blood vessel walls, that predominantly affects children younger than five years of age with the median age being 10 months[3, 4]. The purveying concept is that Kawasaki disease is the manifestation of immunologic responses to some exposure in the GI tract or respiratory system. Since the highest rates of occurrence are recorded in Japan and China, there is also a suspected genetic factor that predisposes to susceptibility. Cases peak during the winter and spring months, suggesting that an infectious involvement. However, the exact etiology remains unknown. According to the American Heart Association, the diagnostic criteria include a fever that lasts at least five days with four of five diagnostic symptoms: extremity changes with erythema and edema in the palms and soles, diffuse polymorphic rash, bilateral non-exudative conjunctivitis, oral mucosal changes with cracked lips or oral erythema, and typically unilateral cervical lymphadenopathy that is 1.5 cm or greater in diameter. Complications can occur in severe cases, with the most common being coronary artery aneurysm which can occur in up to 20% of cases. Coronary aneurysms can rupture which can pose a significant risk for thrombosis or myocardial infarction later in life. In fact, Kawasaki disease is the most common cause of acquired heart disease in children in the US and other developed countries. Treatment of Kawasaki disease usually

consists of intravenous immunoglobulin (IVIG) and moderate to high doses of aspirin (30-50 mg/kg/day up to 80-100 mg/kg/day). The goal of treatment is to limit the inflammatory process and prevent the onset of coronary artery aneurysms, with aspirin being used for its antithrombotic effects. Other anti-inflammatory treatments such as corticosteroids, cyclosporine, and biologics like tumor necrosis factor alpha (TNFα) inhibitors are used in refractory cases[4].

In April of 2020, an alert was issued by the UK's National Health Service regarding a cluster of eight children showing a Kawasaki-like disease[4]. In a case series reported by the South Thames Retrieval Service in London, the children were previously healthy, and each presented with vasoplegic shock and some degree of myocardial dysfunction. All of them had unrelenting fever along with symptoms typically seen in Kawasaki disease, such as rash, conjunctivitis, and peripheral edema. Unlike what is typically seen in Kawasaki disease, they also presented with non-bloody diarrhea, vomiting, abdominal pain, ascites, and ileitis. One child developed coronary aneurysm and one died of refractory shock and cerebrovascular infarction. Most of the children's polymerase light chain (PCR) nasal swabs were negative for COVID-19. However, although the majority of these children did not have preceding COVID-19 symptoms, they had positive serology tests for SARS-CoV-2 antibodies. This indicates that they may have recovered from a previous infection. This is further supported by the fact that the surge of cases occurred 2-3 weeks after the peak of COVID-19 infections in the area. Because of these, the authors speculated that the hyperinflammatory syndrome they were witnessing was the result of uninhibited immune response occurring post-COVID-19 infection and encouraged vigilance and further study from the greater pediatric community[5]. Due to these observations and others seen within the country, pediatricians in the UK named the condition pediatric inflammatory multisystem syndrome temporarily associated with SARS-CoV-2, or PIMS-TS[6].

After the initial observations seen in the UK, another cohort of 10 cases was published from Italy. These cases were centered in the city of Bergamo in Lombardy, the epicenter of the COVID-19 outbreak in the country. The authors detail the ten cases seen from February 18 to April 20, a monthly incidence of 30-fold higher than observed in the previous five years in the region[6]. Of the 10, five children presented with features diagnostic of Kawasaki disease with the other five presenting with fewer than three of the five criteria. Five children presented with hypotension requiring fluid resuscitation. Two of these required further inotropic support. Most of the patients presented with either polymorphic rash or conjunctivitis and two showed coronary aneurysm on echocardiography[7]. Although most children with Kawasaki disease respond well to treatment with IVIG, the majority in this cohort required intravenous corticosteroid treatment as well[6, 7]. This possibly suggests that the authors were not witnessing an outbreak of Kawasaki disease but a separate ailment with similar presentation. Only two of the children were found to have active SARS-CoV-2 infection through PCR swab. However, eight showed the presence of antibodies with serology testing, somewhat mirroring the observations seen in the UK publication[7]. This suggests that COVID-19 may be the primary trigger for the hyperinflammatory state observed in these cohorts.

As reports of a new multisystem inflammatory process brought on by COVID-19 emerged, retrospective observational studies have been inspired. One such study was conducted in Paris, France regarding 21 children and adolescents admitted to Necker Hospital for Sick Children between April 27 and May 11. The population was chosen to include only patients who met criteria for Kawasaki disease. Coronary abnormalities were seen in eight patients, with none showing coronary artery aneurysm. However, all had elevated markers for inflammation including C reactive protein, procalcitonin, and interleukin-6. Interestingly, most of the patients had signs of cardiac myopathy including 17 with elevated troponin I and 18 with high B-type natriuretic peptide. Nineteen patients also had high D-dimer indicating possible coagulopathy[8]. This represents a much higher rate of cardiac myopathy and coagulopathy that is typically seen with Kawasaki disease[9]. Of the 21 patients, eight had positive nasal swabs for COVID-19, although only one was found to be symptomatic. Strikingly, 19 had positive serology tests. In order to exclude the possibility of nosocomial acquired infection, the nasal swabs were performed within three days of hospitalization. In order to rule out possible viral etiology from viruses other than SARS-CoV-2, multiplex PCR was performed for rhinovirus, seasonal coronaviruses, influenza, metapneumovirus, and human respiratory syncytial virus. Nineteen of these were negative. Urine, cerebrospinal fluid, and blood cultures were drawn for all patients to rule out bacterial cause. None of these resulted in bacterial growth. Seventeen patients were treated for hemodynamic instability in critical care units and received IV fluid resuscitation or inotropic support along with classical treatment of Kawasaki disease. All patients received IVIG and aspirin. Like in the UK and Italian cohorts, the surge of Kawasaki-like disease coincided temporally with the outbreak of COVID-19 in the area[8]. Because over 90% of the patients in the analysis had positive serology tests with only 38% showing a positive PCR test, the authors concluded that the pandemic may have caused the Kawasaki-like symptoms seen in these patients.

Case definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

An individual < 21 years presenting with

- Fever,[a] laboratory evidence of inflammation,[b] and evidence of clinically severe illness requiring hospitalization, with multisystem (> 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

Additional comments

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

[a]Fever > 38.0°C for ≥ 24 hours, or report of subjective fever lasting ≥ 24 hours.
[b]Including, but not limited to, 1 or more of the following: an elevated C-reactive protein, erythrocyte sedimentation rate, fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase, or interleukin 6, elevated neutrophils, reduced lymphocytes and low albumin.
RT-PCR = reverse transcription polymerase chain reaction

Figure 1. https://emergency.cdc.gov/han/2020/han00432.asp

Pediatric cutaneous inflammation in the setting of COVID-19 has not solely affected Europe. On May 4, New York City Department of Health announced that 15 cases of Kawasaki-like inflammatory syndromes had been treated in New York hospitals from April 17 to May 1. Time magazine reports that since then, over 100 children have presented with the affliction, resulting in 5 deaths[4, 10]. On May 12, the Center for Disease Control and Prevention named the phenomenon multisystem inflammatory syndrome in children (MIS-C)[11]. However, they were

unable to provide treatment recommendations or pinpoint an etiology for the disease. It appears likely that the novel coronavirus outbreak may serve as a delayed trigger for MIS-C. Kawasaki disease has long been hypothesized to have viral etiology, including other coronaviruses. Although the two diseases have differences, namely the dramatic markers for cardiac myopathy and greater instances of gastrointestinal symptoms seen in MIS-C, similar treatment has seen some success[9]. This includes IVIG with or without corticosteroids. However, the extent of the similarities is unknown, or if MIS-C can also result in coronary aneurysms. This is an important aspect as many areas are under "stay-at-home" orders and parents may be hesitant to seek treatment for fear of COVID-19 exposure[3]. Furthermore, as other parts of the nation are re-opening, this raises further concern for the impact MIS-C and COVID-19 may have in pediatrics[6]. Going forward, worldwide collaboration will be necessary to recognize what association COVID-19 has with MIS-C and to determine the best prevention and treatment options for our patients.

References

1. Coronavirus Disease 2019 in Children - United States, February 12–April 2, 2020. (2020, April 09). Retrieved June 7, 2020, from https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm
2. Dong, Y., Mo, X., Hu, Y., Qi, X., Jiang, F., Jiang, Z., & Tong, S. (2020). Epidemiology of COVID-19 Among Children in China. *Pediatrics, 145*(6). doi:10.1542/peds.2020-0702
3. Xu, S., Chen, M., & Weng, J. (2020). COVID-19 and Kawasaki disease in children. *Pharmacological Research, 159*, 104951. doi:10.1016/j.phrs.2020.104951
4. Panupattanapong, S., & Brooks, E. B. (2020). New spectrum of COVID-19 manifestations in children: Kawasaki-like syndrome and hyperinflammatory response. *Cleveland Clinic Journal of Medicine*. doi:10.3949/ccjm.87a.ccc039
5. Riphagen, S., Gomez, X., Gonzalez-Martinez, C., Wilkinson, N., & Theocharis, P. (2020). Hyperinflammatory shock in children during COVID-19 pandemic. *The Lancet, 395*(10237), 1607-1608. doi:10.1016/s0140-6736(20)31094-1
6. Viner, R. M., & Whittaker, E. (2020). Kawasaki-like disease: Emerging complication during the COVID-19 pandemic. *The Lancet, 395*(10239), 1741-1743. doi:10.1016/s0140-6736(20)31129-6
7. Verdoni, L., Mazza, A., Gervasoni, A., Martelli, L., Ruggeri, M., Ciuffreda, M., . . . D'antiga, L. (2020). An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: An observational cohort study. *The Lancet, 395*(10239), 1771-1778. doi:10.1016/s0140-6736(20)31103-x
8. Grimaud, M., Starck, J., Levy, M., Marais, C., Chareyre, J., Khraiche, D., . . . Oualha, M. (2020). Acute myocarditis and multisystem inflammatory emerging disease following SARS-CoV-2 infection in critically ill children. *Annals of Intensive Care, 10*(1). doi:10.1186/s13613-020-00690-8
9. Shulman, S. T. (2020). Pediatric Coronavirus Disease-2019–Associated Multisystem Inflammatory Syndrome. *Journal of the Pediatric Infectious Diseases Society*. doi:10.1093/jpids/piaa062
10. Ducharme, J. (2020, May 12). What to Know About Kawasaki Disease and COVID-19. Retrieved June 07, 2020, from https://time.com/5832461/kawasaki-disease-covid-19/
11. HAN Archive - 00432. (2020, March 27). Retrieved June 07, 2020, from https://emergency.cdc.gov/han/2020/han00432.asp

PALFORZIA, THE FIRST APPROVED PEANUT ALLERGY TREATMENT FOR CHILDREN

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Every three minutes, a food allergy-related reaction results in an emergency room visit. Approximately, 32 million Americans have food allergies of which 5.6 million are children under the age of 18. Children with food allergies are 2 to 4 times more likely to have other conditions such as asthma or eczema when compared to children without food allergies. While there are many foods that have been reported to cause allergic reactions, peanuts are one of the eight major food allergens that are responsible for serious food related anaphylaxis[1]. The main treatment approach has been avoidance and rescue medications for anaphylaxis, but even with strict avoidance, accidental exposures can occur even with trace amounts[2]. The U.S. Food and Drug Administration has approved the first drug for treatment of peanut allergy, Palforzia, and when used in combination with peanut avoidance, it can reduce the risk of severe anaphylaxis in children with peanut allergy[3].

Palforzia is an oral immunotherapy used to reduce allergic reactions including anaphylaxis that may occur due to peanut exposure. It is approved for use in patients with confirmed diagnosis of peanut allergy, but it is not indicated for the emergency treatment of allergic reactions including anaphylaxis. Palforzia can be initiated in patients 4 to 17 years of age, and it may be continued in individuals 4 years and older. Palforzia comes in a powder dosage form made from peanuts and packaged in capsules that can be pulled apart and mixed with semisolid food like applesauce, yogurt, or pudding. Treatment with Palforzia is administered in three phases: initial dose escalation, up-dosing, and maintenance; the overall goal for this treatment is to facilitate desensitization by exposing the patient to increasing doses of peanut protein[2,4]. The initial dose escalation is given on a single day under the supervision of a health care provider who can manage severe allergic reactions if it occurs. The up-dosing phase consists of 11 increasing dose levels that are given over several months which is also administered under the supervision of healthcare providers. Although there is a risk of anaphylaxis at any time, the highest risks of anaphylaxis are during and after the initial dose escalation and the first dose of each up-dosing. If the patient tolerates the first dose of the increased dose level, the patient may continue that dose level at home. After completion of all up-dosing levels, the maintenance dose can be initiated which should be continued daily to maintain desensitization. Patients who may experience allergic reactions due to the medication may need to discontinue or modify the dosing regimen[4].

Palforzia was investigated in Study 1 (NCT02635776) which was a phase 3, randomized, double blind, placebo-controlled study of efficacy and safety in patients 4 through 55 years of age with a peanut allergy in the U.S, Canada, and Europe. The primary analysis population consisted of 496 subjects between the ages of 4 to 17 years in the intent-to-treat (ITT) population who received at least 1 dose of treatment. After subjects received 0.5mg to 0.6mg on day 1 of initial dose escalation and 3mg on day 2 to determine tolerability, they initiated up-dosing with 3mg and increased the dose to eventually reach 300mg for 24-40 weeks. Subsequentially, maintenance therapy was initiated with 300mg for 24-28 weeks until the end of the study after which a double-blind, placebo-controlled food challenge (DBPCFC) was

completed to assess the subjects' ability to tolerate protein with no more than mild allergic symptoms. The primary efficacy endpoint measured was the percentage of subjects that tolerated a single dose of 600mg of peanut protein in the DBPCFC with no more than mild allergic symptoms after 6 months of maintenance treatments. This primary efficacy endpoint was considered met if the lower end of the 95% confidence interval (CI) for the difference in the response rates between placebo and treatment groups was greater than 15%. Secondary endpoints considered were the comparisons of response rates after 300mg and 1000mg peanut protein and the severity of symptoms at any challenge dose of peanut protein during the DBPCFC. The secondary endpoints were evaluated for statistical significance (two-sided p <0.05) only if the primary endpoint and prior tests were statistically significant and in favor of Palforzia. The response rates at the exit DBPCFC for ITT population are shown in Table 1, and the maximum severity of symptoms at any challenge is show in Table 2. The population that completed the study consisted of all the subjects 4 through 17 years of age in the ITT population who stayed on the treatment and had an evaluable exit DBPCFC. In the completer population, the subjects who tolerated single highest doses of 300mg, 600mg, 1000mg with no more than mild symptoms were 96.3%, 84.5%, and 63.2%, respectively compared with 8.6%, 4.3%, and 2.6% for the placebo group[4]. In this phase 3 trial, children and adolescents who were highly allergic to peanuts were able to ingest higher doses of peanut protein without dose limiting symptoms and also experienced lower symptom severity during the peanut exposure at the exit food challenge than placebo[5].

Table 1. Response Rates at the Exit DBPCFC in Study 1 (ITT population)

Peanut challenge dose, single dose	300 mg [1]	600 mg [2]	1000 mg [1]
PALFORZIA (N = 372)	76.6%	67.2%	50.3%
Placebo (N = 124)	8.1%	4.0%	2.4%
Treatment difference (95% CI)	68.5% (58.6%, 78.5%)	63.2% (53.0%, 73.3%)	47.8% (38.0%, 57.7%)
P-value	< 0.0001	< 0.0001	< 0.0001

Table 2. Maximum Severity of Symptoms at any Challenge Dose During the Exit DBPCFC (IIT Population)

Symptom Severity	**PALFORZIA N = 372**	**Placebo N = 124**
None	37.6%	2.4%
Mild	32.0%	28.2%
Moderate	25.3%	58.9%
Severe [1]	5.1%	10.5%

The safety of Palforzia was evaluated in two phase 3, double-blind, placebo-controlled trials (Study 1 and Study 2) in 709 subjects allergic to peanuts. In both of these trials, the most common adverse reactions in subjects treated with Palforzia were gastrointestinal, respiratory, and skin symptoms (incidence ≥5% and at least 5% greater than the placebo group) commonly associated with allergic reactions as shown in Table 3. A total of 155 (21.9%) Palforzia-treated subjects and 19 (6.5%) placebo-treated subjects discontinued for any reason in both the studies.

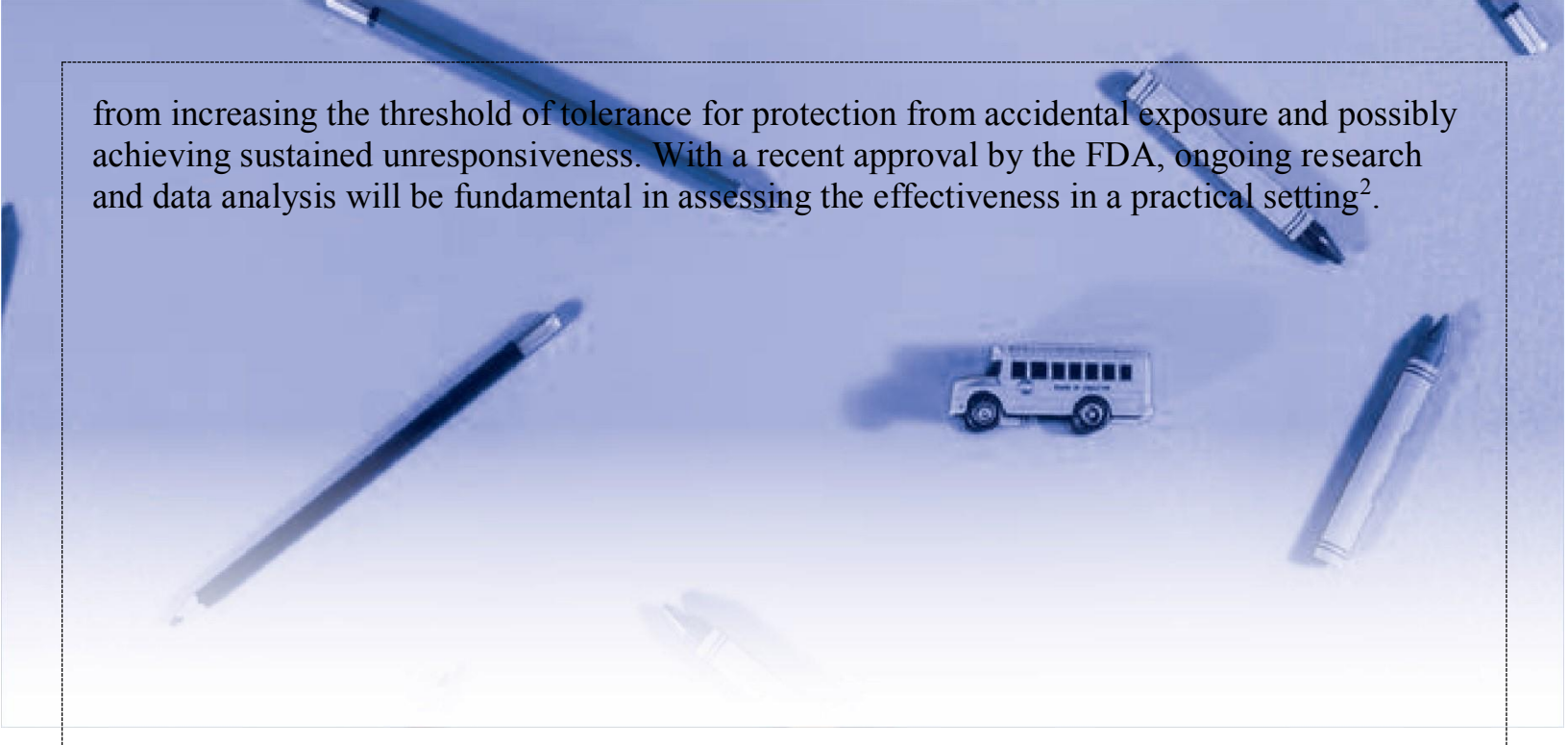
Discontinuation due to adverse reactions in the Palforzia-treated subjects was 9.2% and 1.7% in the placebo-treated subjects during the initial dose escalation and up-dosing phase in both studies. During the maintenance dosing in Study 1, there was 1% discontinuation due to adverse reactions in the Palforzia treated group and 0% in the placebo treated subjects. Gastrointestinal reactions were the most common reason for discontinuation (6.5% Palforzia, 1.0% placebo), followed by respiratory disorders (2.3% Palforzia, 1.0% placebo). The timing of symptoms after exposure to Palforzia in a clinical setting was also evaluated which revealed a median time onset of 4 minutes for 502 subjects (70.8%) and resolution time of the last symptom was 37 minutes. To minimize the risk of anaphylaxis with Palforzia, the FDA is requiring a Risk Evaluation and Mitigation Strategy (REMS) to assure safe use, and Palforzia is only available through specially certified healthcare providers, health care settings, and pharmacies who are enrolled in the REMS program[3,4].

Table 3. Treatment Emergent Adverse Reactions in ≥ 5% of Palforzia Treated Subjects and ≥ 5% Percentage Points Greater Than Placebo Treated Subjects in any Dosing Phase (Aged 4 through 17 Years)

System Organ Class / Preferred Term [2]	Study 1 & Study 2 IDE PALFORZIA (N = 709)	Study 1 & Study 2 IDE Placebo (N = 292)	Study 1 & Study 2 Up-Dosing PALFORZIA (N = 693)	Study 1 & Study 2 Up-Dosing Placebo (N = 289)	Study 1 [1] 300 mg PALFORZIA (N = 310)	Study 1 [1] 300 mg Placebo (N = 118)
Gastrointestinal disorders						
Abdominal pain [3]	185 (26.1%)	24 (8.2%)	465 (67.1%)	100 (34.6%)	90 (29.0%)	20 (16.9%)
Vomiting	22 (3.1%)	2 (0.7%)	253 (36.5%)	47 (16.3%)	50 (16.1%)	14 (11.9%)
Nausea	60 (8.5%)	2 (0.7%)	224 (32.3%)	41 (14.2%)	45 (14.5%)	8 (6.8%)
Oral pruritus [4]	62 (8.7%)	9 (3.1%)	216 (31.2%)	30 (10.4%)	51 (16.5%)	7 (5.9%)
Oral paresthesia	13 (1.8%)	7 (2.4%)	94 (13.6%)	11 (3.8%)	23 (7.4%)	2 (1.7%)
Respiratory, thoracic, and mediastinal disorders						
Throat irritation	66 (9.3%)	15 (5.1%)	279 (40.3%)	49 (17.0%)	43 (13.9%)	11 (9.3%)
Cough	18 (2.5%)	1 (0.3%)	221 (31.9%)	68 (23.5%)	61 (19.7%)	22 (18.6%)
Rhinorrhea	9 (1.3%)	4 (1.4%)	145 (20.9%)	50 (17.3%)	46 (14.8%)	9 (7.6%)
Sneezing	24 (3.4%)	8 (2.7%)	140 (20.2%)	31 (10.7%)	33 (10.6%)	5 (4.2%)
Throat tightness	18 (2.5%)	3 (1.0%)	98 (14.1%)	8 (2.8%)	20 (6.5%)	0 (0.0%)
Wheezing	4 (0.6%)	0 (0.0%)	85 (12.3%)	21 (7.3%)	19 (6.1%)	10 (8.5%)
Dyspnea	2 (0.3%)	1 (0.3%)	53 (7.6%)	5 (1.7%)	17 (5.5%)	1 (0.8%)
Skin and subcutaneous tissue disorders						
Pruritus	56 (7.9%)	16 (5.5%)	225 (32.5%)	59 (20.4%)	45 (14.5%)	14 (11.9%)
Urticaria	28 (3.9%)	10 (3.4%)	197 (28.4%)	54 (18.7%)	63 (20.3%)	17 (14.4%)
Immune system disorders						
Anaphylactic reaction [5]	5 (0.7%)	1 (0.3%)	63 (9.1%)	10 (3.5%)	27 (8.7%)	2 (1.7%)
Ear and labyrinth disorders						
Ear pruritus	5 (0.7%)	1 (0.3%)	41 (5.9%)	2 (0.7%)	7 (2.3%)	0 (0.0%)

Although clinical trials have shown data to suggest efficacy, reviewing risks vs. benefits of the treatment are imperative. While Palforzia can increase the threshold of reaction, there is an increased risk of anaphylaxis which can be life threatening. In a meta-analysis published by Chu et al. that included 12 randomized, controlled peanut oral immunotherapy trials (OIT), there was high-certainty evidence that peanut OIT increased the risk of anaphylaxis, frequency of anaphylaxis, and use of epinephrine during build up and maintenance dosing. Optimizing dosing regimens and selecting appropriate candidates (those with low IgE levels, those with milder reaction histories, and adherent to dosing guidance) may help minimize risks. Palforzia appears to be a promising treatment option for patients with peanut allergies who would benefit

from increasing the threshold of tolerance for protection from accidental exposure and possibly achieving sustained unresponsiveness. With a recent approval by the FDA, ongoing research and data analysis will be fundamental in assessing the effectiveness in a practical setting[2].



References

1. Food Allergy Research & Education. Food Allergy Facts and Statistics for the U.S. [PDF file]. Retrieved May 2020, from https://www.foodallergy.org/resources/facts-and-statistics
2. Patrawala, M., Shih, J., Lee, G. et al. Peanut Oral Immunotherapy: a Current Perspective. *Current Allergy Asthma Reports* 20, 14 (2020). https://doi-org.proxy-remote.galib.uga.edu/10.1007/s11882-020-00908-6
3. U.S. Food and Drug Administration. FDA Approves First Drug for Treatment of Peanut Allergy for Children. (2020, January 31). Retrieved June 06, 2020, from https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treatment-peanut-allergy-children
4. Palforzia [package insert]. Brisbane, CA: Aimmune Therapeutics Inc; 2020.
5. PALISADE Group of Clinical Investigators, Vickery BP, Vereda A, et al. AR101 Oral Immunotherapy for Peanut Allergy. *N Engl J Med*. 2018;379(21):1991-2001. doi:10.1056/NEJMoa1812856

IMPACT OF ELECTRONIC CIGARETTE OR VAPING PRODUCT USE-ASSOCIATED LUNG INJURY (EVALI)

BY: ANTOINETTE MORKEH, PHARM.D. CANDIDATE 2022

"Vaping" is the process of inhaling an aerosol that is created by heating a liquid or wax containing various substances, such as nicotine, cannabinoids, flavoring, and additives such as glycerol and propylene glycol. Several devices are available to generate this aerosol including battery-operated electronic cigarettes (e-cigarettes), vape pens, or vape mods[1]. These devices contain e-liquid cartridges or "pods" that come in a variety of flavors. The flavorings mask the chemical smell, and children and adolescents are more inclined to vape. Also, each pod of e-cigarette contains as much nicotine as a whole pack of cigarettes, so vaping a single pod can result in nicotine addiction and toxicity in children[2]. Nicotine toxicity is typically experienced as dizziness, lightheadedness, nausea, vomiting, and seizures[2]. In addition to nicotine addiction, vaping also causes performance problems in school and sports like decreased attentiveness and health risks such as increased breathing, heart rate, and blood pressure[2]. These dangers are important to consider.

E-cigarettes were initially introduced as a smoking cessation aid; however, the latest research from the National Youth Tobacco Survey (NYTS) shows that high school students who vape are more likely to smoke tobacco cigarettes. They are also more likely to use marijuana, alcohol, cocaine, and other drugs. Vaping products are currently not regulated by the FDA so there is no control on what they contain[2]. Some of the chemicals used to make the flavors in the pods or cartridges are approved by the FDA for food; however, they are dangerous when inhaled into the lungs[2]. "As of January 2020, FDA issued an enforcement policy on unauthorized flavored cartridge-based e-cigarette products, including fruit and mint flavors, that appeal to kids"[3]. Research has revealed that some of the chemicals can trigger the inflammatory system in the lungs, leading to lung disease and respiratory problems. This presentation is often referred to as Vaping Associated Pulmonary Illness (VAPI) or Electronic Cigarette or Vaping Product Use–Associated Lung Injury (EVALI)[1,2]. EVALI is an acute or subacute respiratory illness that can be severe and life-threatening[1]. Symptoms of EVALI include shortness of breath, coughing, chest pain, stomach pain, diarrhea, nausea, vomiting, fever, and extreme tiredness.

EVALI was initially recognized in the summer of 2019. More than 2,800 cases of EVALI have been reported to the CDC since February 18, 2020 and, among those, there have been 68 deaths. Reported patients who acquired EVALI range from 13 to 85 years of age. Approximately 66% of patients have been male, and 80% have been under 35 years old. Approximately 22% of patients have underlying asthma. While the pathogenesis is unknown, EVALI seems to be a form of acute lung injury with acute fibrinous pneumonitis, diffuse alveolar damage, or organizing pneumonia, accompanied by bronchiolitis. Individual reports of VAPI have been characterized by acute eosinophilic pneumonia, diffuse alveolar hemorrhage, lipoid pneumonia, and respiratory-bronchiolitis interstitial lung disease[1,4]. No evidence of an infectious etiology or bacterial contamination has been identified[1].

The key risk factor for EVALI is use of an e-cigarette or similar product[1]. Upon examination of products used by affected patients and analysis of bronchoalveolar lavage fluid

(BAL) samples, tetrahydrocannabinol (THC) and/or vitamin E acetate have been found as major causative agents. Other additives might be involved including nicotine, cannabinoid (CBD) oils, and substances such as coconut oil and limonene[1]. In a study of 51 patients with EVALI, 75% to 85% of patients with EVALI report use of THC containing products, 94% report use of vitamin E acetate containing products, and 13% to 58% of patients report use of nicotine containing products[1].

Formal diagnostic criteria for EVALI have not been determined, and the heterogeneous presentations suggest that EVALI comprises several different forms of lung injury[1]. EVALI is a diagnosis of exclusion requiring attention to exclude possible lung infection and other causes of progressive respiratory insufficiency. Exclusion of lung infection is based on negative influenza PCR or rapid test, and viral respiratory panel can also be utilized as clinical diagnosis criterion. Urine antigen tests for *Legionella* and *Streptococcus pneumoniae*, blood cultures, sputum culture (if producing sputum), bronchoalveolar lavage (if performed), and testing for HIV-related opportunistic infections are also used to exclude other infections. A variety of respiratory diseases are in the differential diagnoses of EVALI, but community-acquired pneumonia (CAP) is the most common. Because of this, all patients undergo evaluation of CAP[1].

Although the optimal treatment of EVALI is unknown, the most important step is to ensure that community-acquired pneumonia (CAP) is treated correctly with appropriate empiric antibiotics such ass amoxicillin or penicillin[5]. if a penicillin allergy is present a macrolide or cephalosporin can be used[5]. Furthermore, systemic glucocorticoids have been used in many patients with EVALI, but the efficacy has not been studied. The decision regarding initiation of glucocorticoid therapy is challenging and requires individualized assessment[1].

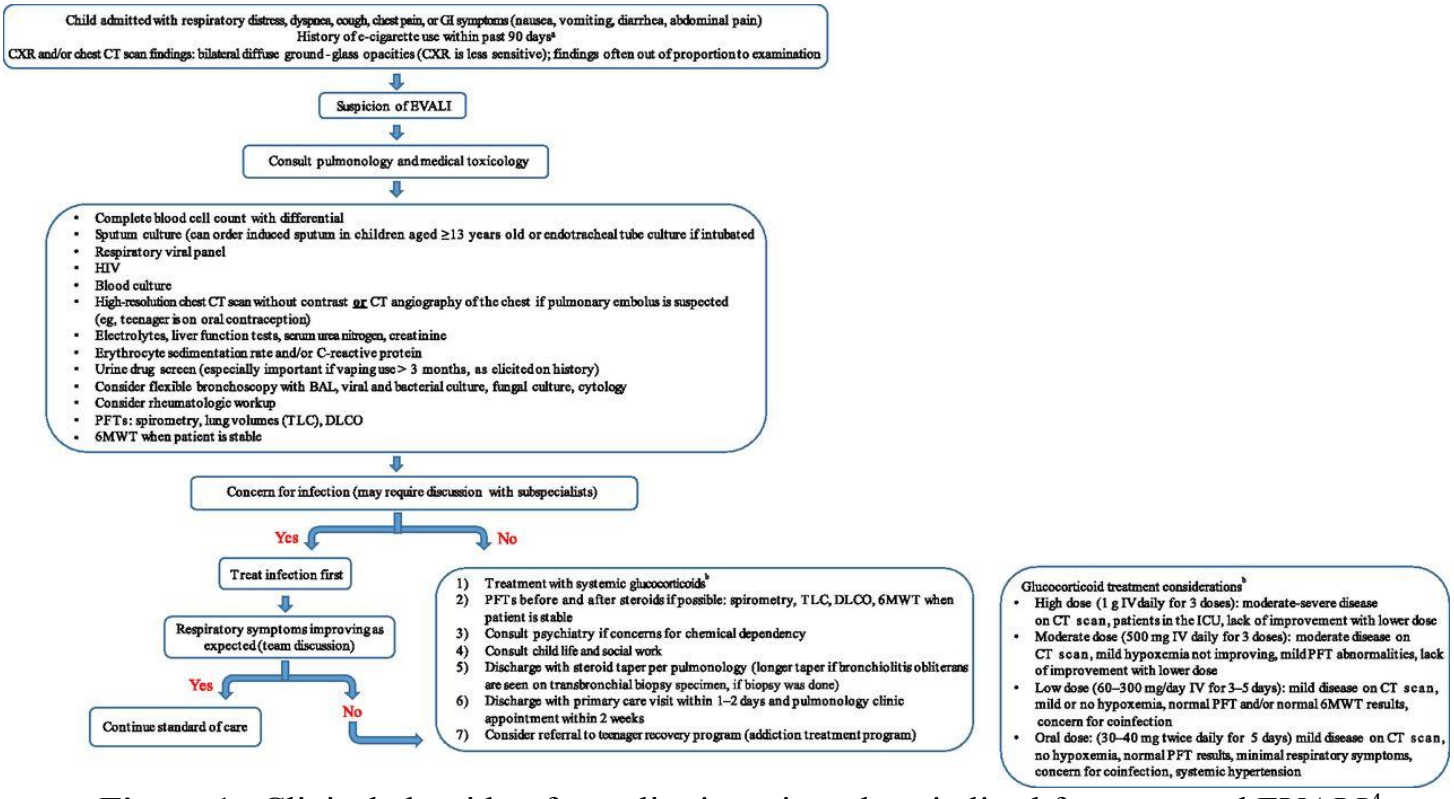


Figure 1. Clinical algorithm for pediatric patients hospitalized for suspected EVALI[4].

An EVALI committee composed of members from pediatric respiratory medicine, medical toxicology, pediatric emergency medicine, pediatric critical care, pediatric hospital medicine, and adult pulmonology and critical care put together a clinical algotithm to standardize the inpatient management of EVALI. The algorithm includes CDC-based diagnostic criteria, recommended consultations, laboratory workup and imaging, and recommended treatment and follow-up[6].

As the vaping epidemic continues to grow, the more teens are being affected[7]. As a result, a universal prevention-focused strategy could be the most effective approach starting early in middle school before teens begin vaping. The U.S. Preventive Services Task Force (USPSTF) recommends that pediatricians provide education or counseling to prevent school-aged children and adolescents from starting to use traditional tobacco products. While this approach is useful, the reduction in smoking initiation is very small. Moreover, e-cigarette use among teenagers is widely prevalent and strongly associated with the leading preventable cause of disease and death in the United States[7]. Focusing on screening via electronic questionnaires and providing education on the harmful effects of e-cigarettes could help prevent initiation. Additional research on the best mechanism to provide teens with an effective message encouraging avoidance of these products is necessary to slow the e-cigarette epidemic and prevent teens from the harmful effects of nicotine and tobacco[7].

References

1. Hollingsworth, Helen. “E-Cigarette or Vaping Product Use Associated Lung Injury (EVALI).” UpToDate, 26 May 2020, www.uptodate.com/contents/e-cigarette-or-vaping-product-use-associated-lung-injury-evali.
2. “Vaping: Boston Children's Hospital.” Boston Childrens Hospital, www.childrenshospital.org/conditions-and-treatments/conditions/v/vaping.
3. Products, Center for Tobacco. “Vaporizers, E-Cigarettes, and Other ENDS.” U.S. Food and Drug Administration, FDA, www.fda.gov/tobacco-products/products-ingredients-components/vaporizers-e-cigarettes-and-other-electronic-nicotine-delivery-systems-ends.
4. “Vaping Associated Pulmonary Illness” Am J Respir Crit Care Med Vol. 200, P13-P14, 2019 ATS Patient Education Series © 2019 American Thoracic Society
5. Stuckey-Schrock K, Hayes BL, George CM. Community-acquired pneumonia in children. Am Fam Physician. 2012;86(7):661-667. https://pubmed.ncbi.nlm.nih.gov/23062094/?dopt=Abstract
6. Rao, Devika R., et al. “Clinical Features of E-Cigarette, or Vaping, Product Use–Associated Lung Injury in Teenagers.” American Academy of Pediatrics, American Academy of Pediatrics, 1 May 2020, pediatrics.aappublications.org/content/early/2020/05/08/peds.2019-4104.
7. Lindsay, Capozzi. “Pediatricians' Answer to the Vaping Epidemic? Prevention.” Pediatricians' Answer to the Vaping Epidemic? Prevention., Children's Hospital of Philladelphia , 25 Feb. 2020, policylab.chop.edu/blog/pediatricians%E2%80%99-answer-vaping-epidemic-prevention.

Our Mission

The Student Society of Pediatric Advocates is a student organization affiliated with the University of Georgia College of Pharmacy. We are a student group associated with the Pediatric Pharmacy Advocacy Group. The Mission of the SSPA is to bring awareness to the proper use of medication therapy in pediatric populations through various service and education-based initiatives. Service activities center around lending our medication-based knowledge to pediatric patients and their parents in our community. Educational activities are directed toward student members in an effort to safely and effectively extend pharmacy practice to pediatric populations by building relationships with mentors and professionals in the health care community, as well as supplementing didactic coursework with lectures by specialists and our peers. Overall, SSPA advocates for the safety and happiness of young patients while learning and having fun along the way. The purpose of our newsletter is to educate pharmacy students about pediatric pharmacy and advocate for pediatric patients within the University of Georgia College of Pharmacy.

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