Commentary

Impasses and nuances of vaccination for COVID-19 in children aged 5-11 years

ABSTRACT

In relation to COVID-19, pediatric patients are usually asymptomatic or with mild manifestations of lesser severity. On the other hand, the literature demonstrates the reduced existence of cases that progressed to serious complications. In view of this, the release of a vaccine for this age group is extremely important for children's health and for reducing the spread of the virus. After the immunization of children against SARS-CoV-2 was implemented in some countries, the panorama regarding this subject has changed completely, being saturated with opinions and divergences related to the topic. Thus, we present current positions of health authorities, parents from different societies worldwide, as well as the adverse effects and challenges related to vaccines against COVID-19 aimed at this age group.

Keywords: COVID-19, SARS-CoV-2, vaccine, children, pandemic, coronavirus.

1. INTRODUCTION (ARIAL, BOLD, 11 FONT, LEFT ALIGNED, CAPS)

According to data from the World Health Organization (WHO), more than 440 million cases of COVID-19 have been reported worldwide, of which 5,978,096 died as of March 3, 2022 [1]. The prevalence and lethality of symptomatic cases in children is between 1 to 5% of cases [2]. Hence, with the advancement of vaccination in adult/elderly groups, more severe cases naturally tend to be concentrated in the pediatric age group. A North American study points out that a third of children who tested positive for COVID-19 were hospitalized, and 80% developed Pediatric Multisystem Inflammatory Syndrome (PIMS) [3].

Withal, important cases of vaccination hesitancy are being reported around the world. This stance is one of the biggest threats to global health today. The prevalence of acceptance of vaccination in developed countries such as the USA, France and Italy is less than 60%, and in countries such as Russia, the Middle East and African countries the values are worryingly lower [4]. This hesitation becomes more important when it comes to vaccinating children and adolescents [5-8].

According to the WHO, effective strategies to contain the pandemic, such as vaccination, are essential to reduce severe outcomes such as hospitalization in ward beds, ICU and death in the pediatric age group [9]. However, despite advances and recommendations on pediatric vaccination from health agencies around the world [10], there is still concern about vaccination in this age group, especially regarding side effects, efficacy and safety [11]. Therefore, the aim is to map the most prevalent side effects of vaccination against COVID-19 in children aged 5-11 years; the opinion of parents/guardians on this topic

and the guidelines of five health agencies, chosen for the convenience of the authors, from Europe, the United States, Brazil, Russia and China.

2. RESULTS AND DISCUSSION

When evaluating the side effects of vaccination in the pediatric age group (5 to 11 years), the most common symptoms were local pain (48.7%), headache (20.4%), followed by fatigue (27.7%), myalgia (11.4%) and local erythema (11.4%) (Table 1). These findings agree with studies conducted in China [12], Poland, France, Finland [13] and the United States [14] in which local erythema, pain and edema were more prevalent, with a higher incidence after the second dose [13, 14].

Regarding severe symptoms, myocarditis occurred in 0.16% of our sample (Table 1), with decreased ejection fraction and increased troponin levels being the most observed alterations, without post-discharge sequelae. These data agree with the literature, a North American cross-sectional study with children affected by myocarditis showed that most cases are mild and self-limiting [15]. Furthermore, reports of multisystem inflammatory response syndrome have rarely occurred after the second dose [16].

When evaluating the position of parents, it is interesting to note that most are in favor of vaccinating themselves and vaccinating their children in general. However, this view becomes quite heterogeneous when analyzing local realities throughout the world. In Brazil [5] and in the United States [8], respectively, 91% and 46% of parents are willing to vaccinate their children, while almost half of the Japanese population evaluated by Yoda and Katsuyama [7] and 38% of Australian parents would not vaccinate their children [6].

The most prevalent arguments in favor of vaccination are: (i) protection of family members and children; and (ii) community protection. On the other hand, the main arguments of parents who would not vaccinate their children are: (i) how fast the vaccines were approved, which makes them feel insecure / believe they are being treated as guinea pigs; (ii) fear of side effects (Table 1).

Finally, when evaluating the positioning of five health agencies on five continents (Table 1), there is unanimity in recommending vaccination due to the efficacy, safety and benefits of vaccination that outweigh the risks. In the West there are restrictions on ages 5-11 years, while Russia is already vaccinating children from the age of three. The first vaccines approved in the evaluated countries were Comirnaty for the European Union, Pfizer-BioNTech for the USA and Brazil, Sputinik for Russia and Coronavac/Sinovac for China.

Table 1. Main findings

Author (Year)	Country Vaccine Sex (M:F) Age (Mean)	Local Pain	Headcache	Local edema	myalgia	local erythema	diarrhea	arthralgia	Fatigue	vomiting	fever	Cough	nausea	myocarditis	Others (N)	Total
Dione et al (2021)	US BNT162B2 da Pfizer BioNTech 14:1 15 years	0	6	0	8	0	0	0	0	0	10	0	0	13	Increased troponin levels (1) Ejection fraction decrease (1) Arrhythmia (1)	15
Poussaint et al (2021)	US BNT162B2 da Pfizer BioNTech 1:0 12 years	0	1	0	0	0	0	0	0	1	1	0	0	1	encephalopathy (1) visual changes (1)	1
Han et al (2021)	China CoronaVac 235:201 8.75 years	25	2	3	0	2	2	0	0	2	17	8	2	0	Itching (2)	436
	US	43	24	10	10	14	6	4	34	2	9	0	0	0	-	Phase I

Walter et al (2022)	BNT162B2 da Pfizer BioNTech <u>Phase I</u> 24:24 7,9 years															48
	US, Poland, Spain and Finland BNT162B2 da Pfizer BioNTech Phase II 799:719 8.2 years	915	379	164	155	211	88	73	527	26	79	0	0	0	-	1518
Total	-	983 (48.7%)	412 (20.4%)	177 (8.7%)	227 (11.2%)	227 (11.2%)	96 (4.7%)	77 (3.8%)	561 (27.7%)	31 (1.5%)	116 (5.7%)	800 (0.3%)	2 (0.01%)	14 (0.16%)	-	2018

Health regulatory agency	**Country**	**Decision protocol number**	**Summary of the positioning of the agency on the vaccination of children and adolescents**
Food and Drug Administration (FDA)	US	153447	An Immune responses of children aged 5 to 11 years were comparable to those of subjects aged 16 to 25 years; -The safety of the vaccine was studied in approximately 3,100 children aged 5 to 11 years who received the vaccine and no serious side effects were detected; The vaccine was 90.7% effective in preventing COVID-19 in children aged 5 to 11 years;
European Medicines Agency (EMA)	Europe	EMA/702084/2021	The benefits of vaccination outweigh the risks; Recommend vaccination for children between 5 and 11 years of age;
National Health Surveillance Agency (Anvisa)	Brazil	SEI/ANVISA - 1712695	Vaccination provides protection against deaths, hospitalizations and severe forms of clinical presentation of COVID-19 in children; The quality, safety and efficacy data are satisfactory;

National Health Commission of People´s Republic of China	China	ND	Aprovaram o uso em crianças (abaixo dos três anos) devido aos riscos serem menores que os benefícios, haver eficácia na proteção contra formas graves e raros efeitos colaterais graves;
Russian Ministry of Health	Russia	ND	Aprovaram o uso em crianças/adolescentes entre 12-17 anos devido aos riscos serem menores que os benefícios, haver eficácia na proteção contra formas graves e raros efeitos colaterais graves;

Author (Year)	**Country** **Sex (M:F)** **Age (Mean)**	**Position of parents on vaccination of children and adolescents against COVID-19**		
		Positions in favor of vaccination - N (%)	**Position against vaccination – N (%)**	**No opinion on the matter – N (%)**
Bagateli et al (2021)	Brazil 426: 75 30 years or more	455 (91%) of parents believe vaccination is appropriate for themselves and their children	20 (4%) of parents refuse to vaccinate their children and get vaccinated	26 (4.6%)
Evans et al (2021)	Autralia 181: 903 39.2 years	520 (48%) of parents believe vaccination to protect their families and protect their children	151 (14%) of parents refuse to vaccinate their children due to the rapid approval of immunizers and feel like "guinea pigs"	413 (38%) prefer to wait and observe before making a decision
Yoda, Katsuya and Ma (2021)	Japan 468:632 40.2 years	471 (42,9%) of parents believe vaccination. This group is older and has a higher level of education.	158 (14.4%) due to concern about possible side effects	471 (42.7%) due to concern about possible side effects
Szilagyi et al (2021)	US 1582: 2177 18-50 years or more	1729 (46%) believe in medical recommendations, in the benefits of vaccination for the community and in the effectiveness	1578 (42%) believe that vaccines do not have enough time to prove their safety and can have long-term adverse effects on their children's health	452 (12%)

Legends: M – male; F – female; US – United States of America.

3. FINAL CONSIDERATIONS

The literature demonstrates a low incidence of side effects from vaccination in the pediatric age group (5 to 11 years) and, when present, they are mild/local. The recommendations of the main health agencies in the world are in favor of vaccination. However, such intervention in the pediatric age group still divides the opinions of the population/parents, mainly due to concerns about safety and efficacy.

In this context, there is a clear necessity of working with public opinion through a collective effort of Governments, health agencies and the third sector to demonstrate in a broad, reliable and accessible way to the community, especially parents/guardians, about the benefits of vaccination as an initiative of collective, safe and effective protection in the fight against the pandemic. Further studies are still needed for children under the age of five.

REFERENCES

1.WHOa. Who Coronavirus 2019 Dashboard, 2022. Available in: https://covid19.who.int/ [Acess in: 03 March, 2022].

2. Andrade et al. Lethality by COVID-19 in children: an integrative review. Residência Pediátrica. 2021; 11(1): 1-9.

3. She J, Liu L, Liu W. Providing children with COVID-19 vaccinations is challenging due to lack of data and wide-ranging parental acceptance. Acta Paediatrica. 2022; 111(1): 35-44. doi: 10.1111/apa.16137.

4. Wu J, Li Q, Tarimo CS et al. COVID-19 Vaccine Hesitancy Among Chinese Population: A Large-Scale National Study. Front Immunology. 2021; (12): sp. 10.3389/fimmu.2021.781161.

5. Bagateli LE et al. COVID-19 vaccine hesitancy among parents of children and adolescents living in Brazil. Vaccines, 2021; 9(10): 1115. doi: 10.3390/vaccines9101115.

6. Evans S et al. 'Poison' or 'protection'? A mixed methods exploration of Australian parents' COVID-19 vaccination intentions. J. Psychosom. Res, 2021; 150(110626): 110626. doi: 10.1016/j.jpsychores.2021.110626.

7. Yoda T, Katsuyama H. Parents' hesitation about getting their children vaccinated against COVID-19 in Japan. Hum. Vaccines Immunother, 2021;1–6. doi: 10.1080/21645515.2021.1981087.

8. Szilagyi PG et al. Parents' intentions and perceptions about COVID-19 vaccination for their children: Results from a national survey. Pediatrics, 2021; 148(4): e2021052335. doi: 10.1542/peds.2021-052335.

9.WHOb. COVID-19 advice for the public: Getting vaccinated, 2022. Available in: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/advice. [Acess in: 03 March, 2022].

10. Brasil. Ministério da Saúde. *Aprovada ampliação de uso da CoronaVac para crianças e adolescentes de 6 a 17 anos,* 2022*.* Available at: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2022/aprovada-ampliacao-de-uso-da-vacina-coronavac-para-criancas-de-6-a-17-anos (Accessed: February 16, 2022).

11. Lv M et al*.* Safety, immunogenicity, and efficacy of COVID-19 vaccines in children and adolescents: A systematic review. Vaccines, 2021; 9(10): 1102. doi: 10.3390/vaccines9101102.

12. Han B et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy children and adolescents: a double-blind, randomised, controlled, phase 1/2 clinical trial. Lancet Infect. Dis. 2021; 21(12): 1645–1653. doi: 10.1016/S1473-3099(21)00319-4.

13. Walter EB, Talaat KR, Sabharwal C, et al. Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. N Engl J Med. 2022; 386(1): 35–46. doi: 10.1056/NEJMoa2116298.

14. Dionne A et al*.* Association of myocarditis with BNT162b2 messenger RNA COVID-19 vaccine in a case series of children. JAMA cardiol, 2021; 6(12): 1446–1450. doi: 10.1001/jamacardio.2021.3471.15. Das BB et al. Myocarditis and pericarditis following mRNA COVID-19 vaccination: What do we know so far?, Children. 2021; 8(7): 607. doi: 10.3390/children8070607.

15. Das BB et al. Myocarditis and pericarditis following mRNA COVID-19 vaccination: What do we know so far?, Children. 2021; 8(7): 607. doi: 10.3390/children8070607.

16. Poussaint TY et al*.* Multisystem inflammatory-like syndrome in a child following COVID-19 mRNA vaccination. Vaccines, 2021; 10(1): 43. doi: 10.3390/vaccines10010043.