Commentary

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

ABSTRACT

Background: 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. Therefore, the release of a vaccine for this age group is extremely important for children's health and for reducing the spread of the virus. Furthermore, the immunization of children against SARS-CoV-2 was implemented in some countries and, as a result,the panorama regarding this subject has changed completely, being saturated with opinions and divergences related to the topic. In view of this, the present article aims to clarify the nuances of SARS-Cov-2 immunization in children between the ages of 5-11 years old.
Methodology: for this study, we have conducted a commentary on the literature regarding vaccination against COVID-19 on the 5-11 years pediatric age group, using the MeSh terms "COVID-19", "vaccination", "children", and "pandemic", in the following databases: "Google Scholar", "PubMed" and "BVS".
Results: Overall, the research has shown that the most common side effects in the pediatric age group, when present, were local pain (48,7%), headache (20,4%), fatigue (27,7%), myalgia (11,4%), and local erythema (11,4%), whilst severe symptoms, such as myocarditis, occurred with a low incidence (0,16%).
Conclusion: due to the absence or, if present, mild /local side effects on children, the recommendations of the main health agencies are in favor of the immunization of this age group, although, further work on the social opinion is needed in order to increase public acceptance concerning the importance and safety of vaccination against COVID-19 in children between the ages of 5-11.

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

1. INTRODUCTION

The pandemic caused by the new severe acute respiratory syndrome coronavirus 2 has generated different challenges related to the vaccination against its own disease COVID-19. 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 of COVID-19 in children is between 1 to 5% of cases [2]. As a result, it may be observed that pediatric lethality is still a matter that should be discussed. Patients from these ages are also an important group when referring to deaths caused by the COVID-19 pandemic, representing a threat not only to adults over 60 years old with risk factors as previous research has shown. (3)

Hence, with the advancement of vaccination in adult/elderly groups, more severe cases naturally tend to be concentrated in the pediatric age group. Prevention in this age range is extremely important considering that studies have shown that asymptomatic pediatric patients may have an equivalent or higher viral load when compared to symptomatic patients from the same age group or adults. (4) On the other hand, 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) [5], demonstrating the importance of vaccinating against SARS-CoV-2 in the age group being studied in this paper.

Withal, important cases of vaccination hesitancy are being reported around the world. Several groups have shown hesitance regarding this topic, becoming an obstacle to prevent major outcomes relevant to the COVID-19 pandemic. 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%, exhibiting lower values in places such as Russia, the Middle East and African countries [6]. Several studies have shown that this hesitation becomes more important when it comes to vaccinating children and adolescents [7-10].

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 [11]. The importance of strategy formulation would allow health organizations to have a different approach towards the actual point at issue. Therefore, despite advances and recommendations on pediatric vaccination from health agencies around the world [12], there is still a concern about vaccination in this age group, especially regarding side effects, efficacy and safety [13].

Providing this information would thereby improve the investigation of COVID-19 in this age group, aiding health agencies around the world with strategy formulation against vaccine hesitation and side effects presented by this group. At the same time, safety and efficacy would be discussed, allowing us to see a more precise overview of the existing concern of those responsible for making decisions relevant to this study. Therefore, the aim of this work 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. MATERIAL AND METHODS

The current study is a commentary on the literature regarding COVID-19 vaccination on the pediatric age group of 5 -11 years old. For this purpose, the analysis was conducted in the following databases: "Google Scholar", "PubMed", and "BVS", using the MeSh terms "COVID-19", "vaccination", "children", and "pandemic". The inclusion criteria used on this analysis were full text articles available in English or Portuguese published in the last 5 years. After a close review of the present literature, 18 articles were selected based on the criteria met and the relevance for this study.

3. RESULTS AND DISCUSSION

The selected articles for this paper were 6 original articles, 1 case report, 1 case series, and 5 official documents. 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 [14], Poland, France, Finland [15] and the United States [16] in which local erythema, pain and edema were more prevalent, with a higher incidence after the second dose [15, 16].

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 [17]. Furthermore, reports of multisystem inflammatory response syndrome have rarely occurred after the second dose [18].

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 [7] and in the United States [10], respectively, 91% and 46% of parents are willing to vaccinate their children, while almost half of the Japanese population evaluated by Yoda and Katsuyama [9] and 38% of Australian parents would not vaccinate their children [8].

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. As of February 2022, all continents, except Africa, have at least one country that has approved immunization against COVID-19 for the 5-11 years old pediatric age group.[19,20, 21,22].

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)
ione et (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)
oussain t 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)
an 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)
	US BNT162B2 da Pfizer BioNTech	43	24	10	10	14	6	4	34	2	9	0	0	0	-

alter et (2022)	Phase I 24:24 7,9 years														
	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	-
tal	-	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%)	-

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	153447colaterais	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 detect 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 ommission of People´s Republic of China	China	ND	Pediatric use approved under 3 years old children due to the risks being lower than the benefits, demonstrating efficacy protecting against severe forms and rare effects.
Russian Ministry of Health	Russia	ND	Pediatric use approved in children and adolescents between 12-17 years old due to the risks being lower than the benefits, demonstrating efficacy protecting agair forms and rare serious effects.

Author (Year)	**Country** **Sex (M:F)**	**Position of parents on vaccination of children and adolescents against COVID-19**

	Age (Mean)			
		Positions in favor of vaccination - N (%)	**Position against vaccination – N (%)**	**No opinion on the matter – N (%)**
agateli et (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%)
ans 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 d
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 effe
zilagyi et (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%)

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

4. CONCLUSION

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.

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