An epidemic of coronavirus disease 2019 (COVID-19) has spread rapidly throughout China and the world since 2019. As of March 3rd 2020, China had reported a total of 80,304 cases of COVID-19, including 2,946 deaths. Outside China, there are now 10,566 cases in 72 countries and 166 deaths. Of the deaths reported so far, most of them have been elderly men [1–4]. Adults are more likely to be infected with novel coronavirus (SARS-CoV-2) than children; and symptoms are relatively milder in pediatric patients than in adult patients. The same conditions occurred during the SARS and MERS outbreaks. It is still not clear why children seem to be escaping the worst effects of the coronavirus infection [5–7].

Unlike adults, who can actively protect themselves, children are less likely to protect themselves by avoiding touching things or covering their faces when they cough or sneeze [8]. If children with underlying health conditions (such as leukemia, tumor or other immune deficiencies) are infected with COVID-19, the severity of conditions and difficulty of treatments may be unpredictable [9]. In addition, whether the virus will exist for a long time remains to be verified. If SARS-CoV-2 acts like many other viruses (that is, remains long-lived relative to the lifespan of humans), antiviral treatments will face a great challenge, especially in pediatric patients.

The treatment guidelines are very cautious about recommending antiviral drugs for children. Almost all guidelines highlight that there are no effective antiviral drugs for children at present. The Interim Guidance for Diagnosis and Treatment of COVID-19 infection (the Sixth version) issued by the National Health Commission of China is only available for adults in the field of antiviral treatments. The recommended antiviral drugs are interferon-α (IFN-α), lopinavir/ritonavir, ribavirin, chloroquine diphosphate and arbidol [2] which have been used in the treatment of COVID-19 in adults. Based on the available evidences, IFN-α nebulization can be used in children, and it has shown good safety profiles under most circumstances. However, children are particularly sensitive to the accumulation of chloroquine phosphate in the body, which could possibly induce severe retinopathy, ototoxicity and cardiotoxicity. On the other hand, it lacks data on the safety of using lopinavir/ritonavir and abidor for children under 2 years of age. In the absence of adequate evidence for efficacy and safety, experts have not reached an agreement on using ribavirin in the pediatric population. Guidelines for diagnosis and treatment of COVID-19 in children (Second Edition) recommend the use of IFN-α, lopinavir/ritonavir and ribavirin in children, without specifying age limitation [10]. The recommended dosage of ribavirin infusion varies in different medical literatures. Some suggest intravenous infusion of ribavirin administered at a dose of 10 mg/kg every time (maximum 500 mg every time), 2–3 times daily [10], whereas others recommend 10–15 mg/kg per day, divided into 2–3 times daily [11].

At present, the efficacy and safety, appropriate dosage, course of treatment and mechanism of action for children’s anti-coronavirus drugs need to be studied, and that special attention should be paid to the particular adverse reactions and drug interactions in children [10–13].

Based on the current epidemiological survey, the ages of the confirmed COVID-19 cases in children range from days to 17 years old. These children may have no clinical manifestations, such as fever, fatigue, dry cough, abdominal discomfort, nausea, vomiting, abdominal pain, diarrhea and other gastrointestinal symptoms, etc. A case of a 1.5-month-old infant diagnosed with COVID-19 experienced frequent vomiting [1, 2, 4, 14–18]. The clinical characteristics of COVID-19 in children are different from those in adults, and it is likely that differences also exist between children at different ages.
It is unknown whether the disease process, treatment response and exposure response relationship of children with COVID-19 are like those of adults. According to the guidelines for clinical trials of pediatric drugs, it is not suitable to perform extrapolation on drug efficacy from adults to children. And children are not little adults. So, comprehensive and systematic drug safety and efficacy clinical trials in pediatric population should be planned and conducted as early as possible once the clinical trial data of preliminary safety and potential benefits for adults have been acquired [19].

At present, more than 200 clinical trials for COVID-19 treatment have been carried out in medical institutions all over China. The drugs and the therapies include anti-AIDS drugs, influenza medications, glucocorticoid, traditional Chinese medicines/injections, stem cell transplantation, etc. However, drug clinical trials for COVID-19 children are very limited. As of February 28, 2020, one registered drug clinical trial of traditional Chinese medicine for the prevention of COVID-19 infection in children was found in the China Clinical Trial Registry Center; another clinical trial of darunavir and cobicistat for treatment of COVID-19 in children has been registered in ClinicalTrials.gov. The designs of the two clinical trials are not so scientific with unclear age range defined in the inclusion criteria.

Although the proportion of infected children in the pediatric population to the whole population is relatively low, children are still at high risk of infection and should not be neglected. We should take precautions beforehand to carry out the clinical trials of pediatric drugs for the treatment of COVID-19.

It should be emphasized that the ethical principles of pediatric clinical research must be followed before conducting pediatric clinical trials. Experimental drugs should be selected first from the drugs that have already been on the market and have been used in children. All clinical trials designed for pediatric population should follow the principle of "minimum sample size, and minimum pain" as much as possible [20, 21].

In conclusion, SARS-CoV-2 infected "COVID-19" is a new and pandemic disease. There are differences in clinical manifestations between children and adults. It is very necessary for the government, industries and institutes to prepare well in the early stage and to conduct clinical trials to evaluate the safety and efficacy of pediatric medications on the infected children.

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