Vaccine trials in children during a pandemic

Minors can be enrolled when adequate safety data are available in adults

The conduct of clinical trials in paediatric populations poses unique challenges because of the differences in physiology and cognition between children and adults. Balancing the vulnerability of children as participants in clinical trials and the urgent need to protect them with a vaccine are vital in the planning process.

Ethically, the inclusion of minors in the trial is acceptable only if the potential benefits are significant or the risks are low.

Although COVID-19 infection has low prevalence and mild severity in children, the pandemic's potential for causing serious complications of multisystem inflammatory syndrome and its impact on schooling provide a strong justification for vaccinating children. Adolescents also play an important role in the transmission of infection. Since the risks of the new vaccine are unknown, children are included in trials only after there is evidence of safety and efficacy in adults. But waiting until the completion of trials in adults would delay the health and psychosocial benefits to children and their families. Hence, it seems prudent to enroll minors in vaccine trials when adequate safety data are available in adults.

Younger children do not have the cognitive ability to understand the experimental nature of vaccine trials and their potential risks. Hence, they would not be included in vaccine trials until data are available from a vaccine trial in older children. The older, 12-18 years old children may be able to understand research but lack the legal capacity to consent. So, recruitment

guardians and assent from the minor who can provide it. If the parents or guardians are illiterate, not only the consent process, but also the assessment of safety following the vaccination would be difficult.

The conduct of clinical trials requires the consideration of dose, design, and endpoints. The vaccine dose would be similar to the dose which is safe and well-tolerated in adults. The necessity of a placebo-controlled design means that some children would get the pain of injection without the potential benefit of protection. The collection of blood for immunogenicity assessment would be an additional risk. The assessment of efficacy would be based on symptoms of infection and RT-PCR for SARS-CoV-2. Safety assessment would require recording of local or systemic reactogenicity events in the patient diary. Children's potent immune response to the vaccine may cause severe symptoms, including high fever. Parent's understanding, training and education would be critical in observing the children and recording the data to support endpoints.

Children and their families will be required to visit the clinical trial centre for screening and follow-ups during the pandemic. They would be at increased risk of exposure to SARS-CoV-2. Hence, the sponsor and the investigator should put in place an appropriate COVID-19 prevention strategy, e.g., proper use of PPE, appropriate social distancing and surgical masks.

Overall, a systematic approach would be essential in planning and conduct of clinical

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