COVID-19: should oral vaccination strategies be given more consideration?

Therapeutic Advances in Vaccines and Immunotherapy

2020, Vol. 8: 1–2

DOI: 10.1177/2515135520946503

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Keywords: coronavirus, pandemics, respiratory tract, vaccine

The novel coronavirus, SARS-CoV-2, has led to an unprecedented international health crisis. The implementation of a vaccine is essential to accelerate herd immunity, enabling lockdown measures to be relaxed and socioeconomic activity to safely resume whilst limiting the case fatality rate. A concerted global effort has led to over 150 vaccines currently under development. However, it is apparent that oral administration has been markedly under addressed as a potentially effective immunological strategy.

Research has now revealed a high expression of the SARS-CoV-2 receptor, ACE2, and the serine protease for virus spike protein priming, TMPRSS2, in absorptive enterocytes of the ileum and colon.[1] This highlights a non-canonical route of host invasion for SARS-CoV-2, and a potential site at which artificial immune induction through an oral vaccine could be protective.

Oral immunisation is a viable strategy that has been implemented successfully in preventing respiratory illness.[2] For example, the live oral enteric-coated adenovirus type 4 and type 7 vaccines, approved for use in US military personnel 17–50 years of age, have been shown to be safe and highly effective in reducing disease burden in numerous clinical trials.[3] These vaccines cause an asymptomatic infection of the gut and subsequently generate mucosal immunity to protect against future respiratory illness.[4] More recently, an orally administered influenza vaccine has progressed successfully through phase II clinical trials, highlighting the promising potential and ongoing active development of oral vaccines for respiratory disease.[5]

Several benefits may be attained through employing an oral approach. Evidence suggests that the mucosal route may allow more potent induction of humoral (antibody-mediated) and cellular immune responses, priming the body to respond effectively to respiratory challenges.[6] In addition, as documented with the oral polio and rotavirus vaccines, the possibility of faecal shedding of oral vaccines may accelerate herd immunity through oro-faecal transmission in close contacts, particularly in the developing world.[7,8]

Oral vaccines may also be manufactured more simply, highlighting the scalability of this approach.[2] The ease of oral inoculation also removes the requirement for trained healthcare professionals to be present to administer the vaccine, minimising cross-infection risk at healthcare centres, whilst potentially maximising uptake and compliance. This may significantly expand practical options for vaccine distribution, particularly in resource-limited settings that are worst affected, given that other preventive measures, such as social distancing, may be harder to implement.[9] In addition, thermally stable oral formulations in the past have been independent of a temperature-controlled supply chain, potentially further simplifying distribution logistics by eliminating a significant contributor of cost in vaccine distribution programmes.[10] It is possible that oral vaccines may be effective as a complementary approach, preferentially employed in resource-limited, population-dense settings.

Taken together, the development of a successful oral formulation may offer relative advantages concerning safety, efficacy, compliance, ease of manufacturing and administration. These factors are essential to consider when developing globally scalable immunisation strategies against SARS-CoV-2.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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