



Intranasal COVID-19 vaccine: a modern vaccination approach

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Dear Editor,

The emergence of severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) which was originally reported to WHO in December 2019 resulted in the coronavirus illness and it was subsequently declared a global coronavirus disease 2019 (COVID-19) pandemic in March 2020. Recurring disease outbreaks repeatedly overloaded the public health sector, infecting over 613 million people and killing more than 6.5 million as of September 2022^[1]. As new strains emerge and natural immunity wanes, the population, particularly immunocompromised individuals, stand an increased risk of severe sickness and death due to this disease. Various research advances paved the way for developing multiple COVID-19 vaccines which have been approved to treat and prevent COVID-19. Currently, available COVID-19 vaccines including mRNA vaccines, recombinant adenovirus vaccines, and recombinant protein vaccines that have received Emergency Use Authorization (EUA) and have been subsequently used to immunize millions of people are all administered through intramuscular injection^[2]. Intramuscular vaccines have been designed to induce antibody-mediated and cell-mediated immune responses and minimal to no detectable mucosal immunity at the site of infection. Since the nose and upper respiratory tract are the primary routes for inhalation pathogens like SARS-CoV-2 and are more susceptible to infection,^[3] the vaccine response generated after intramuscular immunization can leave the upper respiratory tract vulnerable to viral replication and dissemination because these vaccines are inefficient in stimulating immunoglobulin A secretion in mucosal cells^[2].

Alternatively, it has been found recently that the intranasal (IN) vaccines for COVID-19 have shown a promising ability to induce sterilizing mucosal immunity against mucosal pathogens apart from inducing an antibody-mediated immune response and a robust

cell-mediated immunity^[2]. A single dose of effective SARS-CoV-2 vaccine via IN route boosts mucosal immunoglobulin A and T-cell responses in both upper and lower respiratory tract, providing almost complete prevention against viral infection, multiplication, and reducing virus shedding via nasal mucosa that acts as a first-line barrier to the virus entrance before spreading into the lungs^[2]. This immediate protection at the site of infection by restricting the viral replication and clearance of SARS-CoV-2 infection reflects the potency of IN COVID-19 vaccines in the alleviation of seeding new cases of COVID-19 amidst the pandemic; hence, preventing even mild cases of illness and inhibiting the virus transmission to other people. In addition, these vaccines are minimally invasive, have a needle-free mode of administration, and are usually in the form of a nasal spray^[2]. Owing to the easy transportation and storage, these vaccines are also more convenient to use^[2]. However, an essential consideration for IN COVID-19 vaccine is its safety. An extremely rare risk of reversion of live attenuated virus into replicating state, regaining its ability to cause disease in the individual has been observed^[4]. With that, the effectiveness of the vaccine is determined by the immunization type chosen and the addition of essential adjuvants. Phase I, II, and III clinical trials were performed to assess the efficacy of IN COVID-19 immunization by two companies; CanSino Biologics, a Chinese pharmaceutical company, and Bharat Biotech International, a biotechnology company headquartered in India, which received approval in their respective countries for its use after gaining successful results^[5]. These companies have created 'viral vector' vaccines that use a harmless adenovirus to deliver the genetic material of the SARS-CoV-2 into host cells.

Given the severity of the situation where the healthcare systems are challenged globally due to increased COVID-19-related hospitalizations, it is critical to continue developing effective and reliable COVID-19 vaccines in present times. In the context of respiratory pathogens like SARS-CoV-2, IN vaccines' pros conceivably outweigh their cons, along with offering both localized protection at the site of infection and activating systemic responses as compared with intramuscular vaccines eliciting only systemic responses. Large-scale clinical studies and trials should be conducted to gather further evidence to prove its effectiveness so that the availability of IN COVID-19 vaccines may be made feasible. This vaccine might also serve as an alternative to limited and inadequate vaccine supplies as well as a booster to intramuscular vaccines. Immunization with IN COVID-19 vaccines will hopefully help deal with the persistent COVID-19 pandemic and potential viral contagious diseases that might arise in the future.

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This manuscript has been peer reviewed.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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International Journal of Surgery (2023) 109: 43–44

Received 29 September 2022; Accepted 20 November 2022

Published online 27 January 2023

<http://dx.doi.org/10.1097/JS9.000000000000046>

Ethics approval

Not applicable.

Sources of funding

None.

Authors' contribution

All authors contributed equally.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

Research registration Unique Identifying number (UIN)

None.

Guarantor

Govinda Khatri.

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