The nasal Vaccine for Covid

Background

The sudden emergence of a highly transmissible and pathogenic coronavirus SARS-CoV-2 in December 2019 from China and its rapid global spread has posed an international health emergency.

The rapid development of an effective vaccine is imperative to control the spread of SARS-CoV-2. A number of concurrent efforts to find an effective therapeutic agent or vaccine for COVID-19 (coronavirus disease 2019) are being undertaken globally. Oral and nasal mucosal surfaces serve as the primary portal of entry for pathogens like coronaviruses in the human body.

As evidenced by studies on similar coronaviruses (SARS-CoV and MERS-CoV), mucosal vaccination can provide a safe and effective means for the induction of long-lasting systemic and mucosal immunity to confer protection against SARS-CoV-2. This article summarizes the approaches to an effective mucosal vaccine formulation which can be a rewarding approach to combat the unprecedented threat posed by this emerging global pandemic.

All COVID-19 vaccines now in use are injected into muscle, producing antibodies that circulate in the blood but aren't necessarily present in the nose and nasal passages, suggesting that vaccinated individuals could still become infected and transmit the virus.

Current vaccination status

Currently available COVID-19 vaccines are given by I/M route and are highly effective at reducing symptom severity, but they don't appear to prevent SARS-CoV-2 from gaining a toehold in the nose.

This lead to the observation that, the virus can stealthily replicate and then, expelled by coughing or sneezing, go on to infect others.

Hence the present vaccines, all administered as intramuscular injections, induce circulating antibodies in the blood *but not mucosal antibodies in the lining of the nose.*

Initial scientists' observations

1] According to Vincent Munster, PhD, chief of the Virus Ecology Section of the National Institute of Allergy and Infectious Diseases (NIAID) Rocky Mountain Laboratories, said in

an interview, “It’s actually very hard to protect the upper respiratory tract with these [injected] systemic vaccines,”

Both intranasal mucosal and systemic immunity are important, Munster noted. That’s because aerosol exposure deposits SARS-CoV-2 in both the upper and lower respiratory tract, so infection can originate in the lungs, Munster explained, citing a recent virus transmission study he co-authored.

Munster and co-authors found that the intramuscular Oxford/AstraZeneca vaccine, which isn’t authorized in the US, protected rhesus monkeys, exposed to SARS-CoV-2 against pneumonia but didn’t reduce viral shedding from their upper respiratory tract.

In the 469 cases identified in this past July’s COVID-19 outbreak in Provincetown, Massachusetts, diagnostic testing found that viral loads were similar in vaccinated and unvaccinated individuals’ noses.

Another recent study led by Munster suggested that an intranasal vaccine could effectively induce both types of immunity. He and his co-authors compared intranasal with intramuscular delivery of the Oxford/AstraZeneca vaccine.

They found that both the intranasal and injected vaccines produced high systemic antibody levels in hamsters, and the nasal spray even elicited higher levels than the injection. The scientists exposed the vaccinated and unvaccinated hamsters to SARS-CoV-2; both routes of administration protected the animals from serious disease compared with no vaccination.

2] As per Martin Moore, PhD, the CEO and cofounder of Meissa Vaccines in Redwood City, California, which has launched a phase 1 trial of its intranasal vaccine, “We think intranasal vaccines are important because they have the potential to block transmission,” unlike the available injected vaccines

There are other several scientists globally who had the same observation that studies suggest that individuals who receive injected COVID-19 vaccines may be protected against serious illness from SARS-CoV-2 but can still become infected and spread the virus.

3] Paul Spearman, MD, director of infectious diseases at Cincinnati Children’s Hospital Medical Centre, said in an interview. “The administration is incredibly simple. That doesn’t require years of training.” Plus, noted Spearman, who is principal investigator for a phase 1 trial of such a vaccine, intranasal delivery would likely be a welcome option for people who have needle phobia.

Development of the nasal vaccine

- A recent study led by a National Institute of Allergy and Infectious Diseases (NIAID) scientist found that administering the Oxford/AstraZeneca COVID-19 vaccine through the nose reduced viral shedding in animal models,(Hamsters and then Rhesus monkeys).
- University of Oxford researchers are now conducting an open-label clinical trial of the intranasal vaccine in healthy human volunteers.

Role of immunity against Covid by intranasal vaccine

The question about intranasal COVID-19 vaccines has been whether they could induce as strong a systemic immune response as vaccines injected intramuscularly.

History:

While the Oxford/AstraZeneca COVID-19 vaccine uses a novel chimp adenovirus–based vector, an investigational intranasal vaccine developed by CyanVac LLC, with offices in Athens, Georgia, and Los Gatos, California, uses a parainfluenza virus 5 (PIV5) vector, which is also known as canine parainfluenza virus.

It was noted that PIV5 has been used for more than 40 years as part of a canine distemper, or kennel cough, vaccine. Many veterinarians and dog owners have antibodies against PIV5, according to CyanVac. The humans likely were exposed when dogs sneezed after receiving an intranasal distemper vaccine and continued to shed the virus for a few days.(PIV5 has never been known to cause disease in people or, for that matter, dogs).

Synopsis of present study

Animals

The authors of the new study first compared the injected and the intranasal vaccines in hamsters. Both routes of administration produced high antibody levels, but the nasal spray outperformed the injection.

Previous studies in rhesus monkeys showed that the Oxford/AstraZeneca vaccine, which isn't authorized for use in the US, protected against pneumonia but did not reduce shedding from their upper respiratory tract and developed antibody levels similar to those seen in people who'd recovered from COVID-19.

The 4 vaccinated monkeys, along with 4 unvaccinated rhesus monkeys, were then exposed to SARS-CoV-2. The vaccinated monkeys had fewer viruses in their noses and lung tissue, and none of them developed symptoms of pneumonia, while 3 of the unvaccinated monkeys did.

Caveats in animal studies

Although the observed differences between the animals that received the intranasal vaccine and the ones that didn't were very encouraging, they weren't significant, the authors noted.

Too few animals were vaccinated to establish clear correlations, they wrote. The study has 4 groups: both high dose and low dose in one group aged 18 to 55 years and in another group aged 56 to 75 years. "We know that it's not easy now to do a trial in vaccine-naive individuals," Spearman noted. "We're still able to enroll those trials with some extra effort." Some individuals with needle phobia have expressed an interest in participating but changed their mind after learning that trial participants must have blood drawn, he said.

Healthy humans

The open-label trial aims to enroll at 3 sites a total of 80 healthy adults who have not yet received a COVID-19 vaccine.

Spearman's laboratory is also working on a universal coronavirus vaccine based on virus-like particles (VLPs), which bear virus antigens from multiple variants of concern on their surface but contain no infectious material.

In the future, it could mean combining the 2 vaccines, using the intranasal vaccine for primary immunization and then following it with a VLP vaccine boost.

"As a live virus, it should be immunogenic in the nose," Moore noted. "As an attenuated virus, it should be safe."

Already based on circulating antibodies, intranasal vaccine is always going to look inferior. However, high levels of antibodies in the blood don't always equate to good protection against a disease.

A phase 1 trial can't answer whether an intranasal vaccine adequately protects people. One has to take a chance and try this thing at a phase 2 level."

Too few animals were vaccinated to establish clear correlations, but the findings warrant further investigation of intranasal vaccine delivery, Munster and his co-authors concluded. University of Oxford researchers are now conducting an open-label trial of the Oxford/AstraZeneca intranasal vaccine in healthy human volunteers

There was an initial hindrance of using nasal vaccine in certain situations have been undergoing research to overcome the hindrances. These were:

- mRNA vaccines could not be used intranasally as, the nasal epithelium remains a major biological barrier to deliver antigens to nasal associated lymphoid tissue (NALT).
- The use of live attenuated vaccines, which are not suitable for certain groups of individuals.
- The poor stability, absorption and immunogenicity of antigens delivered by the mucosal route and the limited number of available technologies to overcome the setbacks associated with mucosal antigen delivery. Recent advances make feasible the development of efficacious mucosal vaccines with adequate safety profile.

Studies provided the first proof of evidence that cationic polymers can be used as safe and potent intranasal mRNA vaccine carriers to overcome the nasal epithelial barrier. The safe and versatile polymeric delivery system represents a promising vaccination platform for infectious diseases like Covid or HIV.

Contra-indications

- One concern with intranasal vaccines is that they could trigger respiratory illnesses, Spearman said, so the trial excludes people with lung disease, asthma, and other respiratory tract conditions.
- However, the CDC recommends against administering live attenuated virus vaccines to people who are severely immune-compromised or pregnant, the latter because of the theoretical risk to the fetus.

Summary

- Besides blocking transmission, intranasal vaccines' potential advantages over injected vaccines include ease of administration, perhaps even self-administration**.**
- According to scientists, as of date, because so little is understood about mucosal immunity in the respiratory tract, we don't really know how to evaluate [intranasal vaccines], other than do they protect people.
- It's unlikely that messenger RNA vaccines, such as Pfizer-BioNTech's and Moderna's COVID-19 vaccines, could be formulated as effective intranasal vaccines,

he said. “You can’t just take any old vaccine and put it in the nose and call it an intranasal vaccine.”(*However mRNA vaccines too have a future and can be used – discussed in Caveats above*)

- A respiratory immunologist with whom to collaborate on an intranasal COVID-19 vaccine.
- **Finally the above gist of research on nasal vaccine, as per Centre for Disease Control and Prevention (CDC) stated fully vaccinated people could remove their mask in most indoor settings**.