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Are Combination Vaccine Against Influenza and COVID-19 possible?

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Abstract

Respiratory viral infections have been a significant clinical burden on public health, particularly for elderly patients and those with underlying health conditions. The COVID-19 pandemic brought the importance of vaccinations against viral infections to the forefront of research and most recently the need for combination vaccines against respiratory viruses such as COVID-19 and influenza have been the subject of research. Whilst efficient, combination vaccines therapy does not come without its challenges. Examples such as vaccine hesitancy, especially during recent years has become a main challenge as articles and research have become easy for the population to access, accurate or not. Whilst combination factors are also useful, the range of serotypes and mutations make it costly and difficult to stay on top of. It is clear however, that with the correct resources and finance, a combination vaccine may become a standard in the future considering how fast the medical field of research is progressing. Moderna and several other biotechnological companies have already delved further into the development of COVID-19 and influenza vaccines, and only seem to be progressing.

What are combination vaccines?

Combination vaccines are a mixture of different individual vaccines that are then administered in vivo (within a living organism), the first of its kind being the diphtheria, tetanus, and pertussis vaccines (DTP)[18]. COVID vaccines work like most vaccines, exposing the immune system to antigens of COVID-19. In mRNA vaccines, the vaccine helps the body make the antigens found on COVID-19 which is then displayed on the cell surfaces in your body. This stimulates antibody secretion which can be later utilised for a faster immune response[10]. As a result, the next time the body contracts COVID-19, the immune response will be much quicker and efficient due to the body already having specific antibodies to the COVID-19 antigen.

There are three types of COVID vaccines: mRNA, protein subunit and viral vaccine. The flu vaccine works in a similar way, containing two major antigens: hemagglutinin (HA) and neuraminidase (NA). These vaccines are reformulated every year to be specific to the current strand of influenza circulating around due to the preserving antigen drift found in the influenza virus. Antigenic drift is an evolutionary process characterised by the accumulation of viral proteins that change the amino acid sequence, thus becoming unrecognisable to the hosts antibodies[4]. There are three main types of influenza vaccines worldwide: inactivated influenza vaccine (IIV), live attenuated influenza vaccine (LAIV), and recombinant HA vaccine[14].

A common use of combination vaccines is for diseases with several serotypes or variants, influenza being an example. The general aims for combination vaccines are to cut time and increase the efficacy of the vaccines. A study done in California from Andrejko et al, suggested that having both the COVID-19 and influenza was more effective than having either alone[1]. Whilst several studies show that the combination vaccine is useful, many members of the public remain wary about the side effects and long-term issues; this is known as vaccine hesitancy. A cross-sectional online survey of the population in England 31% of participants said they would not take the Influenza vaccine whilst 21.4% said they were unsure. For the COVID-19 vaccine, the figures were 23.7% and 37.3% respectively[2]. Campaigns, various community health

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workers and educational videos have been used in recent years to educate the population in order to reduce vaccine hesitancy[17]. From a group of chosen articles, the combination of influenza and COVID-19 vaccine had generally increased the uptake of the latter due to the familiarity of the flu jab, proving to be another effective strategy against vaccine hesitancy[19].

Current advances on combination vaccines of influenza and COVID-19

Combination vaccines against influenza and COVID-19 remain an area of active research. Moderna, a well-known biotechnology company, have already started clinical trials comparing the combination vaccine mRNA-1083 against a standard dose of the influenza vaccine alone[5]. Any adverse reactions from the combination vaccine were similar to reactions from the standalone COVID-19 vaccine group in the trial, such as a fever, injection sight pain, headache and fatigue[16]. Potential regulatory approval for the combination vaccine is expected in 2025[12]. The vaccine is an investigational messenger RNA vaccine which helps the body produce specific proteins that can aid your immune system when you catch a certain disease or to prevent it all together[11].

Effect on the wider picture

As most of the population is accustomed to taking influenza vaccines, using a combination vaccine against influenza and COVID-19 could increase the number of people who are vaccinated against debilitating and often life-threatening respiratory infections[19]. Large-scale vaccination programmes could also increase the general immunity of the population through herd immunity.

Recent research suggests that vaccine hesitancy during the COVID-19 pandemic was particularly high amongst members of the ethnic minority community. A study carried out in Greater Manchester suggested that those who were Black or Black British had lower vaccination uptake values amongst all minority ethnic groups which were collectively lower in comparison to white individuals. Similar trends can be seen with uptake of the influenza vaccine previously[6]. Low vaccine uptake was also observed in the most deprived communities in Greater Manchester, suggesting that socioeconomic status also plays a role in vaccine uptake rates. Socioeconomic factors show there was a decrease in vaccines administered in those with high income deprivation compared to those without. This may be because those with less income may have difficultly accessing vaccines sites. Factors such as language barriers may also interfere and reduce vaccine uptake alongside communities with racial segregation, making transport difficult and costly[20]. Taking these factors into account the success of combination vaccines may be limited so long as vaccine uptake remains low in many communities.

Future of the combination vaccines

There are some developments in combination vaccines against the four strains of influenza and COVID-19, but due to the nature of combination vaccines, they are multifaceted due to regulations, efficacy and safety[7]. With increasing knowledge in biotechnology, progress in combination vaccines is advancing quickly. Pfizer and BioNTech have also developed mRNA-based vaccines using BioNTech's mRNA platform technology; the hemagglutinin proteins of the four strands of influenza are used in the vaccine making it much more effective[8,15]. Novavax are also developing a combination vaccine against COVID-19 and influenza using the technology of nanoparticles. The antigens of recombinant spike proteins of COVID-19 and the recombinant hemagglutinin proteins from influenza are manipulated into nanoparticle complexes which can be recognised by the immune system for a faster response[9,13]. Icosavax, a subsidiary of AstraZeneca, have made some progress in combination vaccines however, against human metapneumovirus (hMPV) and respiratory syncytial virus (RSV). However, they are currently looking to develop other potential vaccines like those against COVID-19 and influenza[3].

Conclusion

Despite the several challenges faced particularly due to the recent COVID-19 pandemic, scientists and researchers have persevered leading to recent developments of combination vaccines to protect the general population.

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References:

1. Andrejko, K. L., Myers, J. F., Openshaw, J., Fukui, N., Li, S., Watt, J. P., Murray, E. L., Hoover, C., Lewnard, J. A., Jain, S., Pry, J. M., & Team, t. C. C.-C.-C. S. (2022). Receipt of COVID-19 and seasonal influenza vaccines in California (USA) during the 2021-2022 influenza season. *medRxiv*, 2022.2010.2021.22281343. https://doi.org/10.1101/2022.10.21.22281343
2. Antonopoulou, V., Goffe, L., Meyer, C. J., Grimani, A., Graham, F., Lecouturier, J., Tang, M. Y., Chadwick, P., & Sniehotta, F. F. (2022). A comparison of seasonal influenza and novel Covid-19 vaccine intentions: A cross-sectional survey of vaccine hesitant adults in England during the 2020 pandemic. *Hum Vaccin Immunother*, *18*(5), 2085461. https://doi.org/10.1080/21645515.2022.2085461
3. AstraZeneca. (2023). *AstraZeneca to acquire Icosavax, including potential first-in-class RSV and hMPV combination vaccine with positive Phase II data*. Retrieved 04/03/2024 from https://www.astrazeneca.com/media-centre/press-releases/2023/astrazeneca-to-acquire-icosavax-including-potential-first-in-class-rsv-and-hmpv-combination-vaccine-with-positive-phase-ii-data.html#:~:text=Icosavax's%20lead%20program%20is%20a,and%20SARS%2DCoV%2D2.
4. Boni, M. F. (2008). Vaccination and antigenic drift in influenza. *Vaccine*, *26*, C8-C14. https://doi.org/https://doi.org/10.1016/j.vaccine.2008.04.011
5. Clinicaltrials.gov. (2023). *A Study of mRNA-based Influenza and SARS-CoV-2 (COVID-19) Multi-component Vaccines in Healthy Adults*. Moderna. Retrieved 18/02/2024 from https://www.clinicaltrials.gov/study/NCT05827926?id=NCT05827926&rank=1
6. Coupland, C., Harcourt, S., Vinogradova, Y., Smith, G., Joseph, C., Pringle, M., & Hippisley-Cox, J. (2007). Inequalities in uptake of influenza vaccine by deprivation and risk group: Time trends analysis. *Vaccine*, *25*(42), 7363-7371. https://doi.org/https://doi.org/10.1016/j.vaccine.2007.08.032
7. Domnich, A., Orsi, A., Trombetta, C.-S., Guarona, G., Panatto, D., & Icardi, G. (2022). COVID-19 and Seasonal Influenza Vaccination: Cross-Protection, Co-Administration, Combination Vaccines, and Hesitancy. *Pharmaceuticals*, *15*(3), 322. https://www.mdpi.com/1424-8247/15/3/322
8. Harris, E. (2023). Combined COVID-19, Flu Vaccine Candidate Headed to Phase 3 Trials. *JAMA*, *330*(21), 2044-2044. https://doi.org/10.1001/jama.2023.22353
9. Massare, M. J., Patel, N., Zhou, B., Maciejewski, S., Flores, R., Guebre-Xabier, M., Tian, J.-H., Portnoff, A. D., Fries, L., Shinde, V., Ellingsworth, L., Glenn, G., & Smith, G. (2021). Combination Respiratory Vaccine Containing Recombinant SARS-CoV-2 Spike and Quadrivalent Seasonal Influenza Hemagglutinin Nanoparticles with Matrix-M Adjuvant. *bioRxiv*, 2021.2005.2005.442782. https://doi.org/10.1101/2021.05.05.442782
10. Mayo Clinic. (2021). *Different types of COVID-19 vaccines: How they work*. Mayo Clinic. Retrieved 26 Jan 2024 from https://www.mayoclinic.org/diseases-conditions/coronavirus/in-depth/different-types-of-covid-19-vaccines/art-20506465
11. Moderna Clinical Trials Inc. (2023). *Trial Details*. Retrieved 04/03/2024 from https://trials.modernatx.com/study/?id=mRNA-1083-P301
12. Moderna Inc. (2023). *Moderna Announces Positive Phase 1/2 Data from mRNA-1083, the Company's Combination Vaccine Against Influenza and COVID-19*. ACCESSWIRE News Room. Retrieved 04/03/2024 from https://www.accesswire.com/789816/moderna-announces-positive-phase-12-data-from-mrna-1083-the-companys-combination-vaccine-against-influenza-and-covid-19
13. Novavax. (2022). *COVID-Influenza combination (CIC) investigational vaccine*. Retrieved 04/03/2024 from https://www.novavax.com/science-technology/vaccine-pipeline/COVID-Influenza-combination-vaccine
14. Nuwarda, R. F., Alharbi, A. A., & Kayser, V. (2021). An Overview of Influenza Viruses and Vaccines. *Vaccines*, *9*(9), 1032. https://www.mdpi.com/2076-393X/9/9/1032
15. Pfizer. (2022). Pfizer and BioNTech Receive U.S. FDA Fast Track Designation for Single-Dose mRNA-Based Vaccine Candidate Against COVID-19 and Influenza. https://www.pfizer.com/news/announcements/pfizer-and-biontech-receive-us-fda-fast-track-designation-single-dose-mrna-based
16. Saeed, B. Q., Al-Shahrabi, R., Alhaj, S. S., Alkokhardi, Z. M., & Adrees, A. O. (2021). Side effects and perceptions following Sinopharm COVID-19 vaccination. *International Journal of Infectious Diseases*, *111*, 219-226. https://doi.org/https://doi.org/10.1016/j.ijid.2021.08.013

DOI: https://doi.org/10.57898/biosci.187

17. Singh, P., Dhalaria, P., Kashyap, S., Soni, G. K., Nandi, P., Ghosh, S., Mohapatra, M. K., Rastogi, A., & Prakash, D. (2022). Strategies to overcome vaccine hesitancy: a systematic review. *Systematic Reviews*, *11*(1), 78. https://doi.org/10.1186/s13643-022-01941-4
18. Skibinski, D. A., Baudner, B. C., Singh, M., & O'Hagan, D. T. (2011). Combination vaccines. *J Glob Infect Dis*, *3*(1), 63-72. https://doi.org/10.4103/0974-777x.77298
19. Tzenios, N., Tazanios, M. E., & Chahine, M. (2022). Combining Influenza and COVID-19 Booster Vaccination Strategy to Improve Vaccination Uptake Necessary for Managing the Health Pandemic: A Systematic Review and Meta-Analysis. *Vaccines (Basel)*, *11*(1). https://doi.org/10.3390/vaccines11010016
20. Watkinson, R. E., Williams, R., Gillibrand, S., Sanders, C., & Sutton, M. (2022). Ethnic inequalities in COVID-19 vaccine uptake and comparison to seasonal influenza vaccine uptake in Greater Manchester, UK: A cohort study. *PLoS Med*, *19*(3), e1003932. https://doi.org/10.1371/journal.pmed.1003932

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