Medical Xpress

World-first COVID vaccine booster randomized clinical trial in transplant patients proves third shot is very effective

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Scientists with the Ajmera Transplant Centre at UHN have conducted a first-in-the-world randomized placebo-controlled trial of third dose

COVID-19 booster vaccine for transplant patients that shows substantially improved protection.

"We knew from previous studies, that two doses were not enough to produce a good immune response against COVID-19 in transplant patients," says Dr. Deepali Kumar, Director of Transplant Infectious Diseases, UHN and joint-Senior Author of the study published today in the *New England Journal of Medicine*.

"Based on our study, a third dose of COVID vaccine is definitely the best way to increase protection in transplant recipients."

The study enrolled 120 transplant patients between May 25th and June 3rd. None of them had COVID previously and all of them had received two doses of the Moderna vaccine. Half of the participants received a third shot of the vaccine (at the 2-month mark after their second dose) and the other half received placebo.

The primary outcome was based on antibody level greater than 100 U/ml against the spike protein of the virus. In the placebo group—after three doses (where the third dose was placebo), the response rate was only 18% whereas in the Moderna three-dose group, the response rate was 55%.

"This is an important win for our patients because the results are quite conclusive," says Dr. Atul Humar, Medical Director of the Ajmera Transplant Centre, UHN and the joint-Senior Author of the clinical trial. "The third dose was safe and well tolerated and should lead to a change in practice of giving third doses to this vulnerable population."

Neutralizing antibodies and T-cell response

In addition to its primary outcome, this study also looked at the

effectiveness of neutralizing antibodies—antibodies that neutralize the virus—and in this case, 60% of the patients in the Moderna group developed neutralizing antibodies versus 25% in the placebo group.

The study also found a big difference in T-cell response between the two groups. T-cells are another arm of the immune system that functions to prevent severe disease, and there was a substantial improvement in the ability of the three-dose Moderna group to allow the patients to develop a robust T-cell response against the virus.

(L to R) Drs. Atul Humar and Deepali Kumar, joint-Senior Authors of the study. Credit: UHN

The randomized double-blind placebo-controlled study is considered the gold standard in medicine, for showing whether something truly works or not. This study showed a definitively positive response in both major arms of the immune system: the antibody arm and the T-cell arm.

Additionally, the third booster vaccine was very well tolerated with only mild side effects and did not cause acute organ rejections—an important finding, as there were concerns that repeated vaccinations could increase the incidence of organ rejection in transplant recipients.

Fast-tracking science amid a pandemic

Normally a study of this kind would take at least one year, but the team at the Ajmera Transplant Centre executed a rigorous and successful protocol in just a few months.

"We were able to do this because our team worked non-stop for months," says Dr. Humar. "And we are in a global emergency, lucky enough to have generous philanthropic donors and an existing vaccine trials infrastructure already set up."

The results have been shared with regulatory bodies and decision-makers including the United States Food and Drug Administration (FDA), The Canadian National Advisory Committee on Immunization (NACI), the American Society of Transplantation, and others. The research team hopes for an expedited approval to benefit as many transplant patients as possible.

Funding and next steps

Research into the effectiveness of COVID-19 vaccines in transplant recipients has recently received a boost in funding for a national study.

The Government of Canada, through its COVID-19 Immunity Task Force (CITF) and Vaccine Surveillance Reference Group (VSRG), is investing over $2.8 million so that Dr. Kumar's team can further study the effectiveness of COVID vaccines across multiple transplant centres in Canada.

"Our goal is to help coordinate the efforts of provincial and national organizations that are involved in public health and vaccination research and facilitate information sharing among public health agencies and patient partners," says Dr. Kumar.

More information: Victoria G. Hall et al, Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients, *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMc2111462

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