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EDITORIAL

Heterologous Prime-boost COVID-19 Vaccination

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There is a significant recent international interest in heterologous prime-boost COVID-19 vaccination. It may prove useful in avoiding the supply shocks or shortages that might otherwise reduce the speed of vaccine roll-out in any country including India. Additionally, several countries are now advising that individuals previously primed with this vaccine should now receive an alternative vaccine as their second dose, most commonly mRNA vaccines administered in a heterologous prime-boost schedule.

The proposed benefits of heterologous vaccination implementation are 100% seroconversion, greater efficacy and enhanced safety as well as tolerability then the homologous vaccination programme currently being operational worldwide. Further, it is also hypothesized that such heterologous vaccination may also prove very effective in combating emerging COVID variants including recent delta and delta plus variant.

In a recent such study, the heterologous rAd26 and rAd5 vector-based COVID-19 vaccine has been shown to possess a good safety profile and it induced strong humoral and cellular immune responses in participants. The said study recorded sero-conversion rate of 100%. Cell-mediated responses were detected in all participants at day 28, with median cell proliferation of 2.5% CD4+ and 1.3% CD8+ with the frozen formulation, and a median cell proliferation of 1.3% CD4+ and 1.1% CD8+ with the lyophilized formulation. Further, tolerability was better and adverse event following immunization rate was very less in the said study (1).

Further, in another recent study, safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV) has been compared in a single-blind, randomised, non-inferiority trial, suggesting the SARS-CoV-2 anti-spike IgG concentrations of both heterologous schedules were higher than that of a licensed vaccine schedule (ChAd/ChAd) with proven efficacy against COVID-19 disease and hospitalisation. Along with the higher immunogenicity of ChAd/BNT compared with ChAd/ChAd, these data support flexibility in the use of heterologous prime-boost vaccination using ChAd and BNT COVID-19 vaccines. Although mean concentration of SARS- CoV-2 anti-spike IgG in ChAd/BNT recipients was non-inferior to that in ChAd/ChAd recipients (2).

Similarly in another recent randomised, double-blind, placebo-controlled, phase 3 trial done at Russia, a heterologous recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V), showed a good safety profile and induced strong humoral and cellular immune responses in participants. The said heterologous vaccine showed 91.6% efficacy against COVID-19 and was well tolerated in a large cohort, which is very in comparison to any homologous vaccination in use in any country against COVID 19 virus and only 0.3% of the study population experienced serious ADRs (3).

Another study reported that sequential immunization

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with adenovirus vectored vaccine followed by inactivated/ recombinant subunit/mRNA vaccine administration specifically increased levels of neutralizing antibodies and promoted the modulation of antibody responses to predominantly neutralizing antibodies. Moreover, a heterologous prime-boost regimen with an adenovirus vector vaccine also improved Th1-biased T cell responses (4).

In an only study emerging from India, eighteen individuals, under the national program, inadvertently received Covishield as the first jab and Covaxin as the second. The study compared the safety and immunogenicity profile of them against that of individuals receiving either Covishield or Covaxin (n=40 in each group). The findings suggested that lower and similar adverse events following immunization in all groups. Immunogenicity profile against Alpha, Beta and Delta variants in heterologous group was superior; IgG antibody and neutralizing antibody response of the participants was also significantly higher compared to that in the homologous groups. The findings suggest that immunization with a combination of an adenovirus vector platform-based vaccine followed by an inactivated whole virus vaccine was not only safe but also elicited better immunogenicity (5).

Another study evaluating safety and efficacy of homologous vs heterologous vaccination against COVID 19 is under-process at AIIMS, New Delhi.in India.

Over all the results of the heterologous COVID vaccination appear to be superior in initial clinical trials both worldwide including India claiming it to be safe and more effective approach and even suggested to cover variants of concerns more effectively. However, two most important research questions still remain to be answered that how long the protection with heterologous COVID vaccination will remain and secondly which type of COVID vaccination combination will prove most effective. Thus, future, larger adequately powered clinical trials shall certainly be required to advocate such approach in the public domain. In India at present no such recommendation has yet followed in its favour and the said issue is at primitive research level only despite very encouraging results of the studies in its favour.

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