Post-vaccination antibodies and efficacy

A better understanding of the relation between vaccine-induced immunogenicity and protection against SARS-CoV-2 infection is critical

Clinical development of vaccines to counteract SARS-CoV-2 infection assumes that neutralizing antibodies (NAbs) directed at the spike protein will provide protection against the disease. Although IgM and IgG antibodies to SARS-CoV-2 are detectable within 1–2 weeks after the onset of symptoms in most infected individuals, the relationship between NAbs, disease severity and clinical outcomes is complex and not yet well understood.

COVID-19 vaccine development has progressed rapidly to clinical trials without prior evaluation of vaccines in exploratory animal studies. Phase I/II trials of all vaccines have reported detectable antibodies in participants. However, SARS-CoV-2 infected animal models were necessary in assessing the protective role of NAbs. Several vaccines - adenovirus vector, inactivated virion, mRNA - substantially reduced viral replication in the lower respiratory tract, and protected non-human primates infected with SARS-CoV-2. But, as the virus is novel, any surrogate endpoints – antibody titre in animal studies - would require confirmation in clinical trials to ensure that these antibodies adequately predict efficacy in human beings.

The type of vaccine platforms - live attenuated virus, recombinant viral- vectored vaccines, inactivated or killed virus, protein subunit vaccines, virus-like particles and nucleic acid-based (DNA or mRNA) vaccines - determine the relative immunogenic strength of vaccine-derived viral antigens. Pre-existing NAbs to Ad5 vector, reported to be prevalent in 35-95% of humans, could impair the immunogenicity of a vaccine. In the clinical trial of CanSino Ad5-nCoV vaccine, antibody levels were negatively associated with pre-existing anti-vector immunity, while low seroprevalence for ChAd vector resulted in strong immunogenicity with Oxford ChAdOx1nCov-19 vaccine in phase I/II trials.

Standardization of post-vaccination titres to NAbs in convalescent patients with COVID-19 could help in comparing the protective activity of vaccines. Post-vaccination antibody titres after 2 doses of the Oxford vaccine were similar to those detected in convalescent patients. In contrast, post-vaccination antibody titres after the second dose of mRNA vaccines were several folds higher than those observed in convalescent plasma. High antibody levels after the second dose of vaccine could explain higher phase III efficacy of mRNA vaccines >90% compared to the efficacy of Oxford 70%.

The longevity of antibody response to natural infection with SARS-Cov-2 is variable. Hence, there is a concern about the durability of post-vaccination immunogenicity response. A recent report of continuing detection of higher levels of NAbs several months after the mRNA vaccine compared to convalescing controls is encouraging.

NAbs are also linked to the safety of vaccines. Insufficient titres of NAbs might trigger vaccine-associated enhancement of respiratory disease or antibody-dependent enhancement (ADE) of disease. This syndrome results when vaccine-induced non-neutralizing or weakly NAbs bind to the newly infecting virus to promote enhanced virus uptake into host cells via Fcγ receptors.

Animal studies have suggested that apart from NAbs, additional immune functions may also be important in preventing infection. In the elderly, T cell-mediated immunity appears to be a more important factor in vaccine protection than NAbs.

Improved understanding of the relation between vaccine-induced immunogenicity and protection against SARS-CoV-2 infection and the protective role of cellular immunity is critical for the evaluation of clinical outcomes of vaccines.

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