

COMMENT

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Adverse effects of COVID-19 vaccines and measures to prevent them

Kenji Yamamoto*

Abstract

Recently, *The Lancet* published a study on the effectiveness of COVID-19 vaccines and the waning of immunity with time. The study showed that immune function among vaccinated individuals 8 months after the administration of two doses of COVID-19 vaccine was lower than that among the unvaccinated individuals. According to European Medicines Agency recommendations, frequent COVID-19 booster shots could adversely affect the immune response and may not be feasible. The decrease in immunity can be caused by several factors such as N1-methylpseudouridine, the spike protein, lipid nanoparticles, antibody-dependent enhancement, and the original antigenic stimulus. These clinical alterations may explain the association reported between COVID-19 vaccination and shingles. As a safety measure, further booster vaccinations should be discontinued. In addition, the date of vaccination should be recorded in the medical record of patients. Several practical measures to prevent a decrease in immunity have been reported. These include limiting the use of non-steroidal anti-inflammatory drugs, including acetaminophen to maintain deep body temperature, appropriate use of antibiotics, smoking cessation, stress control, and limiting the use of lipid emulsions, including propofol, which may cause perioperative immunosuppression. In conclusion, COVID-19 vaccination is a major risk factor for infections in critically ill patients.

Keywords: COVID-19, Risk factor, Critically ill patients, Vaccination, Vaccine-acquired immunodeficiency syndrome

Dear Editor,

The coronavirus disease (COVID-19) pandemic has led to the widespread use of genetic vaccines, including mRNA and viral vector vaccines. In addition, booster vaccines have been used, but their effectiveness against the highly mutated spike protein of Omicron strains is limited. Recently, *The Lancet* published a study on the effectiveness of COVID-19 vaccines and the waning of immunity with time [1]. The study showed that immune function among vaccinated individuals 8 months after the administration of two doses of COVID-19 vaccine was lower than that among unvaccinated individuals. These findings were more pronounced in older adults

and individuals with pre-existing conditions. According to the European Medicines Agency's recommendations, frequent COVID-19 booster shots could adversely affect the immune response and may not be feasible [2]. Several countries, including Israel, Chile, and Sweden, are offering the fourth dose to only older adults and other groups rather than to all individuals [3].

The decrease in immunity is caused by several factors. First, N1-methylpseudouridine is used as a substitute for uracil in the genetic code. The modified protein may induce the activation of regulatory T cells, resulting in decreased cellular immunity [4]. Thereby, the spike proteins do not immediately decay following the administration of mRNA vaccines. The spike proteins present on exosomes circulate throughout the body for more than 4 months [5]. In addition, in vivo studies have shown that lipid nanoparticles (LNPs) accumulate in the liver, spleen, adrenal glands, and ovaries [6], and

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that LNP-encapsulated mRNA is highly inflammatory [7]. Newly generated antibodies of the spike protein damage the cells and tissues that are primed to produce spike proteins [8], and vascular endothelial cells are damaged by spike proteins in the bloodstream [9]; this may damage the immune system organs such as the adrenal gland. Additionally, antibody-dependent enhancement may occur, wherein infection-enhancing antibodies attenuate the effect of neutralizing antibodies in preventing infection [10]. The original antigenic sin [11], that is, the residual immune memory of the Wuhan-type vaccine may prevent the vaccine from being sufficiently effective against variant strains. These mechanisms may also be involved in the exacerbation of COVID-19.

Some studies suggest a link between COVID-19 vaccines and reactivation of the virus that causes shingles [12, 13]. This condition is sometimes referred to as vaccine-acquired immunodeficiency syndrome [14]. Since December 2021, besides COVID-19, Department of Cardiovascular Surgery, Okamura Memorial Hospital, Shizuoka, Japan (hereinafter referred to as “the institute”) has encountered cases of infections that are difficult to control. For example, there were several cases of suspected infections due to inflammation after open-heart surgery, which could not be controlled even after several weeks of use of multiple antibiotics. The patients showed signs of being immunocompromised, and there were a few deaths. The risk of infection may increase. Various medical algorithms for evaluating postoperative prognosis may have to be revised in the future. The media have so far concealed the adverse events of vaccine administration, such as vaccine-induced immune thrombotic thrombocytopenia (VITT), owing to biased propaganda. The institute encounters many cases in which this cause is recognized. These situations have occurred in waves; however, they are yet to be resolved despite the measures implemented to routinely screen patients admitted for surgery for heparin-induced thrombocytopenia (HIT) antibodies. Four HIT antibody-positive cases have been confirmed at the institute since the start of vaccination; this frequency of HIT antibody-positive cases has rarely been observed before. Fatal cases due to VITT following the administration of COVID-19 vaccines have also been reported [15].

As a safety measure, further booster vaccinations should be discontinued. In addition, the date of vaccination and the time since the last vaccination should be recorded in the medical record of patients. Owing to the lack of awareness of this disease group among physicians and general public in Japan, a history of COVID-19 vaccination is often not documented, as it is in the case of influenza vaccination. The time elapsed since

the last COVID-19 vaccination may need to be considered when invasive procedures are required. Several practical measures that can be implemented to prevent a decrease in immunity have been reported [16]. These include limiting the use of non-steroidal anti-inflammatory drugs, including acetaminophen, to maintain deep body temperature, appropriate use of antibiotics, smoking cessation, stress control, and limiting the use of lipid emulsions, including propofol, which may cause perioperative immunosuppression [17].

To date, when comparing the advantages and disadvantages of mRNA vaccines, vaccination has been commonly recommended. As the COVID-19 pandemic becomes better controlled, vaccine sequelae are likely to become more apparent. It has been hypothesized that there will be an increase in cardiovascular diseases, especially acute coronary syndromes, caused by the spike proteins in genetic vaccines [18, 19]. Besides the risk of infections owing to lowered immune functions, there is a possible risk of unknown organ damage caused by the vaccine that has remained hidden without apparent clinical presentations, mainly in the circulatory system. Therefore, careful risk assessments prior to surgery and invasive medical procedures are essential. Randomized controlled trials are further needed to confirm these clinical observations.

In conclusion, COVID-19 vaccination is a major risk factor for infections in critically ill patients.

Abbreviations

COVID-19: Coronavirus disease 2019; HIT: Heparin-induced thrombocytopenia; LPN: Lipid nanoparticle; VITT: Vaccine-induced immune thrombotic thrombocytopenia.

Acknowledgements

The author would like to thank Editage (www.editage.com) for English language editing.

Author contributions

KY wrote the entire manuscript text and reviewed it. The author read and approved the final manuscript.

Funding

None.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The author declares that he has no competing interests.

Received: 20 March 2022 Accepted: 1 June 2022
Published online: 05 June 2022

References

- Nordström P, Ballin M, Nordström A. Risk of infection, hospitalisation, and death up to 9 months after a second dose of COVID-19 vaccine: a retrospective, total population cohort study in Sweden. *Lancet*. 2022;399:814–23. [https://doi.org/10.1016/S0140-6736\(22\)00089-7](https://doi.org/10.1016/S0140-6736(22)00089-7).
- European Centre for Disease Prevention and Control. Interim public health considerations for the provision of additional COVID-19 vaccine doses. <https://www.ecdc.europa.eu/en/publications-data/covid-19-public-health-considerations-additional-vaccine-doses>. Accessed 4 May 2022.
- Mallapaty S. Fourth dose of COVID vaccine offers only slight boost against Omicron infection. *Nature*. 2022. <https://doi.org/10.1038/D41586-022-00486-9>.
- Krienke C, Kolb L, Diken E, Streuber M, Kirchhoff S, Bukur T, et al. A noninflammatory mRNA vaccine for treatment of experimental autoimmune encephalomyelitis. *Science*. 2021;371:145–53. <https://doi.org/10.1126/science.aay3638>.
- Bansal S, Perincheri S, Fleming T, Poulson C, Tiffany B, Bremner RM, et al. Cutting edge: circulating exosomes with COVID spike protein are induced by BNT162b2 (Pfizer–BioNTech) vaccination prior to development of antibodies: a novel mechanism for immune activation by mRNA vaccines. *J Immunol*. 2021;207:2405–10. <https://doi.org/10.4049/jimmunol.2100637>.
- BNT162b2 Module 2.4. Nonclinical Overview. FDA–CBER–2021–4379–0000681 JW–v–HHS–prod–3–02418.pdf (judicialwatch.org) Access 6 May 2022.
- Ndeupen S, Qin Z, Jacobsen S, Bouteau A, Estanbouli H, Igyártó BZ. The mRNA–LNP platform's lipid nanoparticle component used in preclinical vaccine studies is highly inflammatory. *Science*. 2021;24:103479. <https://doi.org/10.1016/j.jsci.2021.103479>.
- Yamamoto K. Risk of heparinoid use in cosmetics and moisturizers in individuals vaccinated against severe acute respiratory syndrome coronavirus. *Thromb J*. 2021. <https://doi.org/10.1186/s12959-021-00320-8>.
- Lei Y, Zhang J, Schiavon CR, He M, Chen L, Shen H, et al. SARS-CoV-2 spike protein impairs endothelial function via downregulation of ACE 2. *Circ Res*. 2021;128:1323–6. <https://doi.org/10.1161/CIRCRESAHA.121.318902>.
- Liu Y, Soh WT, Kishikawa JI, Hirose M, Nakayama EE, Li S, et al. An infectivity-enhancing site on the SARS-CoV-2 spike protein targeted by antibodies. *Cell*. 2021;184:3452–66.e18. <https://doi.org/10.1016/j.cell.2021.05.032>.
- Cho A, Muecksch F, Schaefer-Babajew D, Wang Z, Finkin S, Gaebler C, et al. Anti-SARS-CoV-2 receptor-binding domain antibody evolution after mRNA vaccination. *Nature*. 2021;600:517–22. <https://doi.org/10.1038/s41586-021-04060-7>.
- Desai HD, Sharma K, Shah A, Patoliya J, Patil A, Hooshanginezhad Z, et al. Can SARS-CoV-2 vaccine increase the risk of reactivation of Varicella zoster. Systematic review. *J Cosmet Dermatol*. 2021;20:3350–61. <https://doi.org/10.1111/jocd.14521>.
- Barda N, Dagan N, Ben-Shlomo Y, Kepten E, Waxman J, Ohana R, et al. Safety of the BNT162b2 mRNA Covid-19 v in a nationwide setting. *N Engl J Med*. 2021;385:1078–90. https://doi.org/10.1056/NEJMOA2110475/SUPPL_FILE/NEJMOA2110475_DISCLOSURES.PDF.
- Seneff S, Nigh G, Kyriakopoulos AM, McCullough PA. Innate immune suppression by SARS-CoV-2 mRNA vaccinations: the role of G-quadruplexes, exosomes, and MicroRNAs. *Food Chem Toxicol*. 2022;164:113008. <https://doi.org/10.1016/j.fct.2022.113008>.
- Lee EJ, Cines DB, Gernsheimer T, Kessler C, Michel M, Tarantino MD, et al. Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination. *Am J Hematol*. 2021;96:534–7. <https://doi.org/10.1002/AJH.26132>.
- Yamamoto K. Five important preventive measures against the exacerbation of coronavirus disease. *Anaesthesiol Intensive Ther*. 2021;53:358–9. <https://doi.org/10.5114/ait.2021.108581>.
- Yamamoto K. Risk of propofol use for sedation in COVID-19 patient. *Anaesthesiol Intensive Ther*. 2020;52:354–5. <https://doi.org/10.5114/ait.2020.100477>.
- Gundry SR. Observational findings of PULS cardiac test findings for inflammatory markers in patients receiving mRNA vaccines. *Circulation*. 2021;144(suppl_1):A10712–A10712. https://doi.org/10.1161/circ.144.suppl_1.10712.
- Lai FTT, Li X, Peng K, Huang L, Ip P, Tong X, et al. Carditis After COVID-19 vaccination with a messenger RNA vaccine and an inactivated virus vaccine: a case-control study. *Ann Intern Med*. 2022;175:362–70. <https://doi.org/10.7326/M21-3700>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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