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BNT162b2 mRNA Vaccine Interference with Co-Administration of Tdap Vaccine

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Conflict of interest: None declared

Patient: Female, 29-year-old
Final Diagnosis: Delayed immune response
Symptoms: None
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases

Objective: Unusual or unexpected effect of treatment

Background: It is unknown if the efficacy of the coronavirus disease-19 (COVID-19) vaccine is affected by the co-administration of other vaccines. The Centers for Disease Control and Prevention (CDC) has shifted their recommendations recently, allowing for the co-administration of the currently available COVID-19 vaccines with other vaccines. This is based on the experience with non-COVID-19 vaccines, where the immunogenicity and adverse event profiles were generally similar when vaccines are administered simultaneously or alone.

Case Report: We present a case of a 29-year-old Asian woman who received the first dose of BNT162b2 mRNA vaccine and the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine at around the same time. BNT162b2 mRNA vaccine and Tdap vaccine were administered into the deltoid region of the left arm and right arm, respectively. We then monitored for immunogenicity. We observed a delay in the development of SARS-CoV-2 Spike (S1) protein antibodies at around 8 weeks after the second dose.

Conclusions: Unless warranted, it is important to adhere to current CDC recommendations with regards to the co-administration of vaccines. Although the administration of Tdap with COVID-19 vaccine in our case caused delay in immunogenicity, it did not negate the ability of the BNT162B2 mRNA vaccine to elicit an adequate immune response. The reason for delay in immune response with co-administration of COVID-19 vaccines with other vaccines is unknown and further studies are needed.

Keywords: COVID-19 Vaccine • Immunogenicity, Vaccine • Tetanus Toxoid

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Background

The CDC currently recommends that the currently available COVID-19 vaccine and other vaccines may now be administered without regard to timing [1]. This differs from prior recommendations that had recommended an interval of 14 days before or after the administration of any other vaccines, a recommendation that was likely based on previous experience of immune interference [2-5] with the co-administration of vaccines.

The BNT162b2 mRNA vaccine trial reported no data on the outcomes of immune response with vaccine co-administration or vaccine interaction with other drugs. We present a case of co-administration of BNT162b2 mRNA vaccine and the booster tetanus toxoid-reduced diphtheria toxoid-acellular pertussis (Tdap) vaccine in a health care worker and its outcomes on vaccine immunogenicity.

Case Report

Our patient was a 29-year-old Asian woman with a history of acne vulgaris for which she takes doxycycline 50 mg and spironolactone 50 mg twice daily as well as a topical application of a dapsone 5% gel once daily.

She received the first dose of BNT162B2 mRNA vaccine on December 2020 via an intramuscular injection into the left deltoid region. One day after receiving the COVID-19 vaccine, she sustained a mechanical fall which resulted in wounds that required tetanus prophylaxis. The Tdap vaccine was administered via an intramuscular injection into the right deltoid region. Three weeks later, she received a second dose of the BNT162B2 mRNA vaccine to complete the vaccination series.

During that time, the CDC had recommended that COVID-19 vaccines be administered alone, with a minimum interval of 14 days before or after administration of any other vaccines.

Due to a concern expressed by the patient with regards to vaccine co-administration and its resulting efficacy, serological testing was done to assess for immunity after COVID-19 and Tdap vaccination at the patient's request.

The patient was initially tested using the VITROS COVID-19 antibody assay (sensitivity 100%, specificity 100%), which was the first COVID-19 serology assay available at our institution. Serological testing using this assay was performed at day 42 after the completion of her COVID-19 vaccination series, and it was significant for negative IgM and negative IgG to the Spike (S1) protein of the SARS-CoV-2 virus. The Roche Elecsys Anti-SARS-CoV-2-S (Spike) IgG/IgM total antibody test (sensitivity 96.6%, specificity 100%) was subsequently made available at our institution. At the request of the patient, repeat serological testing was done using this assay at day 57 after the completion her COVID-19 vaccination series, and it was positive for antibodies to the Spike (S1) protein of the SARS-CoV-2 virus.

Additional serological testing during this time period with the Roche Elecsys Anti-SARS-CoV-2 nucleocapsid (N) antigen assay was negative. The immunoassay for diphtheria and tetanus antitoxoids revealed protective post-vaccination antibody levels.

Discussion

In the BNT162b2 mRNA vaccine trial, the development of immunogenicity was detected as early as 7 days after vaccine administration, with the highest titers of neutralizing antibodies detected between days 7-14 after the second dose [6]. Vaccine interference with tetanus toxoid containing vaccines has been well reported with other vaccines, with potentiation or suppression of immunogenicity of the co-administered vaccine [2-5,7,8]. Carrier-induced epitope-specific suppression, intra-product pharmaceutical interactions, viral interactions, and inter-product interferences due to systemic effects are some of the underlying mechanisms resulting in the alterations in immunogenicity [9,10].

In our reported case, our patient had received the co-administration of the Tdap and the BNT162B2 mRNA vaccines due to the need for tetanus prophylaxis. Post-vaccination antibody testing has shown an undetectable immune response at week 6, and the subsequent development of an immune response at approximately 8 weeks after the completion of her vaccination series for COVID-19. These serological findings, the positive antibody for S1 and negative for N, combined with the absence of any clinical symptoms suggesting COVID-19 infection during this time period, indicates that our patient had likely developed a detectable immune response to the BNT162B2 mRNA vaccine 8 weeks post-vaccination, and that seroconversion from an infection is unlikely.

Our findings are discordant with the aforementioned immunogenicity data from the COVID-19 vaccine clinical trials, suggesting the possibility of a delayed immune response in our case. Delayed antibody response to COVID-19 vaccination has been reported recently in a study by Schwarz et al, where this was observed in elderly patients, in which underlying diseases or medications could have impaired the vaccine-induced immune response [11].

There are currently no reported cases of vaccine interference pertaining to our patient's active medications, including oral doxycycline and topical dapsone. Topical dapsone has not been

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shown to result in immunosuppression, and doxycycline has been shown in a few in-vitro studies to inhibit activated B cell function, and in a study by Woo et al, to suppress the antibody response of mice to T-cell-dependent and T-cell-independent antigens [12,13]. There are no clinical studies published to date. We postulate, upon a review of all other factors pertaining to our case, that the co-administration of the Tdap vaccine could have contributed to a delayed immunogenicity to the COVID-19 vaccine as observed in this generally healthy young adult. The mechanism remains to be elucidated.

This is the first report of a delayed immune response to BNT162b2 mRNA vaccine when co-administered with Tdap in an otherwise healthy adult. This report also illustrates that despite a delayed immune response, there was eventually a detectable immune response, as measured by positive anti-spike antibody levels, when co-administered with Tdap. The post-vaccination protective level of tetanus anti-toxoid in our patient suggests that the immunogenicity of the Tdap vaccine was not affected by the co-administration.

The limitations of our study include the different serological assays that were used due to their availability at our institution. Both assays had received emergency use authorization by the FDA. It is also prudent to note that a negative serology result in our case could be a false-negative, and can occur if the quantity of the anti-SARS-CoV-2 antibodies that are detected and are not present in the specimen is below the detection limits of the assay.

Conclusions

Co-administration of BNT162b2 mRNA vaccine and Tdap may appear to delay the development of immunogenicity in the former. It is unknown if the efficacy of COVID-19 vaccine is affected with the co-administration, including with other vaccines, and it is important to adhere to current CDC recommendations. When deciding whether to co-administer another vaccine with COVID-19 vaccine, providers should consider the risks and benefits. More studies are needed to further validate the findings of our study and to elucidate the mechanism behind the interaction observed in the co-administration of these 2 vaccines.

Conflict of Interest

None declared.

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