International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 5 Sep-Oct 2021, pp: 106-110 www.ijprajournal.com ISSN: 2249-7781

Evaluation on the difference between first and second dose of Covid19 mRNA vaccine

Sanjay.R.Nair
[1]*Student, Amrita School of Biotechnology, Kollam, Kerala, India*

Date of Submission: 30-08-2021 Date of Acceptance: 08-09-2021

ABSTRACT: Covid-19 pandemic have afflicted millions of people worldwide owing to its high prevalence, long incubation time and strain variation. The desperate need for vaccines, lead to the development of messenger RNA (mRNA) vaccine that emerged as a rapid and versatile platform to resolve the crisis, among all other candidates. Most of the vaccines developed require at least two doses, but there are single dose vaccine as well. The interval between two doses depends on the type of vaccine which we take and the guidelines framed by the health department. This review discusses about the efficacy and need of having the varying dosages of Covid-19 mRNA vaccines.

KEYWORDS:miTT, RBD, GMT, HCW, seropositivity.

I. INTRODUCTION

With the rapid outbreak of the Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-COV-2) the demand for safe and effective therapeutics has become a global need as well as economic priority. By 16th September 2020, more than 30 million cases have been reported worldwide with 930,000 deaths owing to the prevalence of the current pandemic. The genome sequencing along with the protein structure analysis of novel corona virus strain lead to the development of inactivated and attenuated viral vaccines along with subunit vaccines for prophylaxis and treatment. It is important to note that suboptimal adherence to vaccination schedules and vaccine-handling logistics influence vaccine effectiveness [1]. There are many vaccines under development and each of them administered with different dosage regimen and among them the messenger RNA (mRNA) vaccines are the ones that elicit host cell immunity using lipid nanoparticle encapsulated form or optimised sequence of naked mRNA. Only a few mRNA vaccines were tested in early stage clinical trials focussing on a small group of recipients but now the situation changed from the year 2020 and mRNA vaccines became the top candidates to cure the pandemic as fast as possible. Being non-infectious and non-integrative agents they do not cause host genome mutation (insertional mutagenesis) and efficacy that include rapid uptake and function in cytoplasm.

The two doses of mRNA vaccine are: immune response dose and booster dose strengthen the immune system for future attacks. Currently three candidates were tested for human trials and are from Pfizer-BioNtech, Cure Vac and Moderna. In view of the data from performed trials, Pfizer-BioNtech vaccine (BNT162b2) found to be 95% and Moderna vaccine (mRNA-1273) to be 94.1% effective after two doses.

II. EFFECT OF FIRST DOSE (IMMUNE DOSE)

The 0.5 ml intramuscular injection, elicited a strong CD4 cytokine response involving type1 helper T-cells that induce the neutralisation effect. Intramuscular cytokine staining quantifies the antigen specific T-cell response against the spike protein (S-2P) [2]. This was estimated from the results seen on day 1, 29 and 43 in clinical trials of mRNA-1273. Also after observing 10 severe covid19 participants of BNT162b2 trial, who had undergone 30ug of first dose, 9 occurred in placebo list and 1 in BNT162b2 that evidenced its efficacy.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 5 Sep-Oct 2021, pp: 106-110 www.ijprajournal.com ISSN: 2249-7781

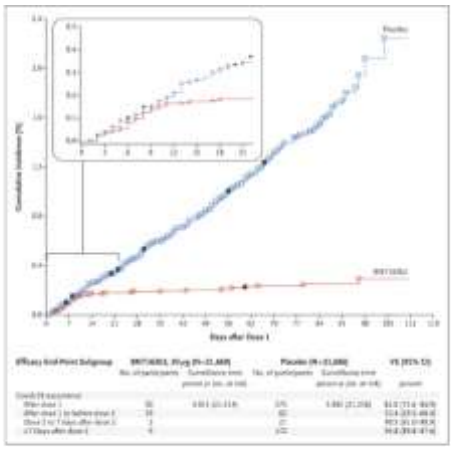

Figure 1. BNT162b2 Efficacy after first dose mITT population (cases of covid19 after first dose). Among them about 39 covid cases were listed in BNT162b2 group and 82 in placebo group with 52% efficacy soon as 12 days after the dose. [3]

In elderly (aged 65 and above) anaphylaxis after vaccination was milder or less reported. Immunogenicity assessments were performed for both placebo and vaccine administration for 7 and 21 days respectively, after dose 1. Symptom reduction and viral clearance play a major role in reducing disease transmission [4]. Effectiveness of about 52% was observed 12 days after administration. An analysis in Israel stated 51% reduction in positive PCR tests 14 days after first vaccination [5].

III. EFFECT OF SECOND DOSE (BOOSTER DOSE)

In view of the efficacy rate (90%) of first dose in reducing the early symptomatic disease and also the anaphylaxis resulting from it, the importance of having second dose was questioned initially. Results from SARS-CoV-2 serum neutralizing titres (day 28 sample marked highest titre value), RBD binding IgG concentrations analysis and GMC, virus neutralizing response to vaccine with 10ug to 30ug were boosted after receiving second dose. T-cell response got boosted along with spike specific IgG antibodies and markedly no boosted response were seen in individuals with a pre-existing immunity against SARS-CoV-2[6].

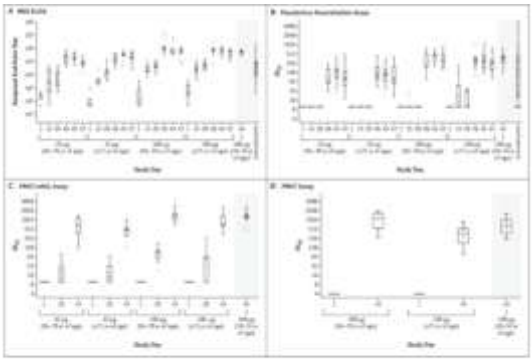

Figure 2. Antibody binding and neutralisation responses: **A)** IgG titres on receptor binding domain (RBD) ELISA. **B)** Pseudovirus neutralisation assay. **C)** Focus reduction neutralization test-mNeon Green assay (FRNT mNG ID50). **D)** plaque reduction neutralisation test (PRNT)[7]

After vaccination, the neutralising activity remained high through 4 weeks in all subgroups. The increased titre value reported from GMT data suggests the need of having second dose importantly for upper age groups (>76 years immune stimulation was similar to younger ones, after second dose administration) [8].

I. Distinct antibody neutralization effects on patients with different clinical profiles

Varied disease conditions and their treatment strategies likely affect SARS-CoV-2 vaccine efficacy. To be more specific, the immunosuppressive effects of those strategies

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 5 Sep-Oct 2021, pp: 106-110 www.ijprajournal.com ISSN: 2249-7781

render poor vaccine immunogenicity among patients. The immunosuppresants OCR (ocrelizumab), used for the treatment of multiple sclerosis reduced the humoral response induced by vaccination in patients compared to those of the OCR untreated ones [9]. This highlights the unfavourable impact of steroids and other monoclonal antibodies targeting (CD20 B cells) upon the altered immunogenicity of vaccine.

Covid19 case fatality rate was reported high among the patients with haematological malignancy. A novel finding from the study stated the use of ruxolitinib and other anti-CD20 antibodies, treated 2 months prior to vaccination, doesn't induced immunogenicity after vaccination and remained unprotected, blocking the dendritic cell activation and thereby reduces the CD8 T cell potentiation[10]. And for them the second dose of vaccine should not be delayed, since T cell immunisation is more important and the anti S1 IgG antibodies (90% efficacy) provide complete protection for about 6 months.

A study from Israel, tested autoimmune inflammatory rheumatic diseased (AIIRD) patients with similar immunosuppressive trend. The candidates had undergone therapies with drugs like rituximab, methotrexate as part of treatment protocol. Report stated low seropositivity rate for individuals who had undergone this therapy within 6 months prior to vaccination and high rate for those who treated 1 year prior to vaccination [11]. Vaccine immunogenicity was evaluated from the serum IgG neutralising antibody levels against S1/S2 glycoproteins tested for 2-6 weeks after second dose. A comparative immunogenic analysis was done with them using different drug combination. The use of methotrexate alone gave reduced seropositivity and lower S1/S2 IgG antibodies. Also anti-CD20 therapy using rituximab decreased the vaccine induced humoral response marking 43% seropositivity rate. Later the combination of MTX and rituximab shown 36% low rate. This concluded the role of immunosuppresants in reducing the vaccine efficacy over diseased patients.

Another report marked the high risk of covid19 in patients receiving hemodialysis where safety and immunogenicity was rare. These individuals resulted in low anti-RBD IgG levels than healthy control group after having first dose. One dose of vaccine is insufficient and failed to elicit humoral response in them. 94% of individuals developed full efficient spike IgG antibodies only 30 days after second dose. Serial PCR and prevaccination anti RBD IgG regular testing had sensitivity for Covid19 detection [12]. Also among the cohorts of kidney transplanted recipients, reduced seroposivity rate was detected (< 40%). This was reported in US and had shown inhibition of B-cell function in patients with the action of tacrolimus and mycophenolic acid. Here immunosuppression therapy was done to prevent graft rejection and ended in T-cell suppression which was expected [13]. Some strategies were designed suggesting to improve the immunogenicity and most prominent among them were a third booster dose vaccine and combination of different vaccine types to produce an integrated effect. But no data currently support these strategies since researches are still on-going.

II. Temporary Side Effects

The occurrence of side effects were reported high after the first dose in clinical trials. Composition of the lipid nanoparticle RNA sequence selected could play a vital role in side effect profile. Based on the results obtained from a study done among HCWs of USA, a detailed side effect profile of BNT162b2 was obtained, showing symptoms during the early phase of the post-vaccination period that includes fever, chills, diarrhoea, muscle pain, dizziness, decreased appetite, localized swelling at the injection site, itching, tingling, nasal stuffiness and high heart rate were reported[14].

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 5 Sep-Oct 2021, pp: 106-110 www.ijprajournal.com ISSN: 2249-7781

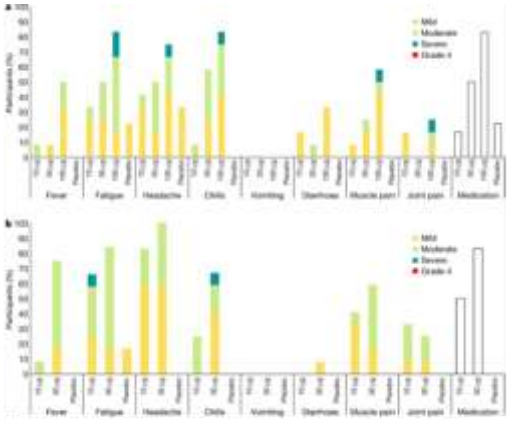

Figure 3. a) Systemic events and medications reported within 7 days after vaccination1 for all doses. **b)** Events reported within 7 days after vaccination 2 for 10 and 30 ug. Medication here refers to the proportion of participants who used antipyretic or pain relievers[15].

Serious adverse events were less reported for mRNA-1273 vaccine, moderate or temporary illness seen after first dose. These were dose dependent responses, fever was observed about 8.3% among individuals who received 10ug and 30ug of the vaccine (≥38.0 ℃). And the trend increased after having 100ug of dose (50%). Also after second dose, 8.3% of 10ug recipients and 75% of 30ug recipients occurred fever. But this resolved within 1 day and most local reactions peaked for 2 days and got resolved by 7th day.

Also an increased number of myocarditis cases were also reported after second dose of vaccine especially among the male adolescents [16].

IV. CONCLUSION

This article features the general evaluation done on the two doses of covid19 mRNA vaccine over the population. With the help of neutralisation assays such as FRNT-mNG, PRNT assay also receptor binding ELISA etc, marked neutralising responses for varying doses administered among different subgroups. Potentially immunogenic vaccine designs are more relevant and needful for adults (56 above), since immunosenescence occurs in old age and thereby reducing the immune development after vaccination. In reference from the previous works the use of spike protein S-2P as the target for production effective proved to be effective. The genetic sequence of SARS-CoV-2 determined in January 2020 led to the production of mRNA, expressing perfusion stabilized spike glycoprotein. Also the varying side effect profile (shown within few days) of individuals who had taken both the doses are elaborated as well.

REFERENCES

[1]. N. Dagan et al., “BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting,” N. Engl. J. Med., vol. 384, no. 15, pp. 1412–1423, Apr. 2021.

[2]. L. A. Jackson et al., “An mRNA Vaccine against SARS-CoV-2 — Preliminary Report,” N. Engl. J. Med., vol. 383, no. 20, pp. 1920–1931, Nov. 2020.

[3]. F. P. Polack et al., “Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine,” N. Engl. J. Med., vol. 383, no. 27, pp. 2603–2615, Dec. 2020.

[4]. L. Coppeta et al., “First Dose of the BNT162b2 mRNA COVID-19 Vaccine Reduces Symptom Duration and Viral Clearance in Healthcare Workers,” Vaccines, vol. 9, no. 6, Jun. 2021.\

[5]. G. Zacay et al., “BNT162b2 Vaccine Effectiveness in Preventing Asymptomatic Infection With SARS-CoV-2 Virus: A Nationwide Historical Cohort Study,” Open Forum Infect. Dis., vol. 8, no. 6, Jun. 2021.

[6]. D. Lozano-Ojalvo et al., “Differential effects of the second SARS-CoV-2 mRNA vaccine dose on T cell immunity in naive and COVID-19 recovered individuals,” Cell Rep., p. 109570, Aug. 2021.

[7]. E. J. Anderson et al., “Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults,” N. Engl. J. Med., vol. 383, no. 25, pp. 2427–2438, Dec. 2020.

[8]. C. A, N. C, S. F, G. P, F. C, and M. D, “Vaccination in the elderly: The challenge of immune changes with aging,” Semin. Immunol., vol. 40, pp. 83–94, Dec. 2018.

[9]. A. Gallo et al., "Preliminary evidence of blunted humoral response to SARS-CoV-2 mRNA vaccine in multiple sclerosis patients treated with ocrelizumab," Neurol. Sci., vol. 1, p. 1, 2021.
[10]. K. Maneikis et al., "Immunogenicity of the BNT162b2 COVID-19 mRNA vaccine and early clinical outcomes in patients with haematological malignancies in Lithuania: a national prospective cohort study," Lancet. Haematol., vol. 8, no. 8, p. e583, Aug. 2021.
[11]. V. Furer et al., "Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in adult patients with autoimmune inflammatory rheumatic diseases and in the general population: a multicentre study," Ann. Rheum. Dis., 2021.
[12]. R. Goupil et al., "Short-term antibody response after 1 dose of BNT162b2 vaccine in patients receiving hemodialysis," C. Can. Med. Assoc. J., vol. 193, no. 22, p. E793, May 2021.
[13]. B. Rozen-Zvi et al., "Antibody response to SARS-CoV-2 mRNA vaccine among kidney transplant recipients: a prospective cohort study," Clin. Microbiol. Infect., vol. 27, no. 8, p. 1173.e1, Aug. 2021.
[14]. R. A. K. Kadali, R. Janagama, S. Peruru, and S. V. Malayala, "Side effects of BNT162b2 mRNA COVID-19 vaccine: A randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers," Int. J. Infect. Dis., vol. 106, pp. 376–381, May 2021.
[15]. M. MJ et al., "Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults," Nature, vol. 586, no. 7830, pp. 589–593, Oct. 2020.
[16]. B. Singh et al., "COVID-19 mRNA Vaccine and Myocarditis," Eur. J. Case Reports Intern. Med., vol. 8, no. 6, Jun. 2021.