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Waning of Anti-Spike IgG Antibody Titer after COVID-19 Vaccination: Myth or Reality?

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Abstract

This observational prospective study was conducted on 25 patients who had received a full 3-dose COVID-19 vaccination scheme with a follow-up ranging from 12 to 19 months after the last injection. The aim of the study was focused on a single biological indicator the anti-spike IgG antibody titer. The age of the patients ranged from 51 to 85 years old. 15 out 25 patients (60%) presented a comorbidity. Our data showed a persistent positive anti-spike IgG antibodies titer ranging from 105 to 5680 BAU/mL (mean: 2661 BAU/mL) in all patients. In view of these results, systematic administration of a SARS-CoV-2 vaccine booster is questionable and should be individually tailored according to the patient medical condition and the anti-spike IgG antibody level.

Keywords

SARS-CoV-2, COVID-19 Vaccines, Anti-Spike IgG Antibodies

1. Introduction

After the outbreak of the COVID-19 pandemic, COVID-19 vaccines have been considered as frontline treatments for protecting from the disease and promising studies at the early stages claimed that they could offer a 95% protection rate against transmission [1]. More optimistic studies supported by health authorities postulated that they could eradicate the disease. Three years later, the history showed hopefully a dramatic decrease in the pandemic but the role of the vaccines on this evolution is questionable as the new variants escape from vaccines. We had already noticed this in a previous study with patients having received a full vaccination scheme [2], but the problem is even more crucial as we have already observed a vaccine escape on patients vaccinated with 4 or 5 doses. This led us to include the monitoring of the anti-spike IgG titer in our patients to

help them to make a decisional choice before a hypothetic booster shot.

2. Material and Methods

This prospective study was conducted on a cohort of 25 patients having a 3 doses vaccination scheme. This included 10 males and 15 females. The ages ranged from 51 to 85 years old (mean: 69 years). Among these patients, 4 had a heterologous vaccination scheme (2 AstraZeneca plus Corminaty: one case, 2 AstraZeneca plus Moderna: one case, 2 Moderna plus Corminaty: one case, 2 Corminaty plus Moderna: one case). The other 3 shot homologous vaccinated patients were distributed between 17 Comirnaty and 4 Moderna. 15 out 25 patients presented one or several comorbidities including 7 cardiopathies, 4 diabetes and 2 autoimmune diseases, one emphysema, one cancer. 6 out 25 patients (24%) experienced a COVID-19 infection after the third COVID-19 vaccine dose.

The time elapsed between the last vaccine injection and the blood test ranged from 12 to 19 months (mean: 15 months). The single biological indicator tested was the anti-spike IgG titer. Although the blood test is not reimbursed by the health assurance (costs between 30 and 50 euros), all patients agreed to have this blood test. The SARS-CoV-2 IgG (anti-spike antibody) titer was measured by chemiluminescence with the SARS-CoV-2 IgG Architect (Abbott) assay. The results were expressed in BAU (binding antibody unit) which is the standard reference by the world health organization. The referenced positive index for anti-spike IgG is >7.1 BAU/mL with the Abbott assay. For indicative purposes, one non-vaccinated 35-year-old COVID-19 infected patient was included with a 16 months convalescent time since the infection.

3. Results

All patients exhibited a positive anti-spike IgG antibody titer ranging from 105 to 5680 BAU/mL (mean: 2661 BAU/mL). The anti-spike IgG antibody titer was below 1500 BAU/mL in 11 patients (44%), between 1500 and 3000 BAU/mL in 5 patients (20%), between 3000 and 4500 BAU/mL in 2 patients (8%), and over 4500 BAU/mL in 7 patients (28%). In a subgroup of 13 patients over 70 years old, the anti-spike IgG titer ranged from 105 to 5680 BAU/mL (mean: 2706 BAU/mL). 3 of them had the highest anti-spike IgG level of the cohort. In the subgroup of 15 patients with comorbidities, the anti-spike IgG antibody titer ranged from 105 to 5680 BAU/mL (mean: 2553 BAU/mL). The single unvaccinated indicative patient had a 9 BAU/mL anti-spike IgG titer.

4. Discussion

The first way to assess the effectiveness of COVID-19 vaccines is to consider the clinical data in the medical literature. But unfortunately, most of these studies, even those published in prestigious journals [3] [4] [5] are no more relevant at the present time. The main reason is that most of these studies have an observation time of less than one year and thus are obsolete. Clinically, we can only

conclude from our clinical results that no vaccine can completely prevent virus transmission as a significant proportion of our vaccinated patients have experienced COVID-19 infections. Thus, eradication of the COVID-19 pandemic by any COVID-19 vaccine is illusory. Furthermore, the hypothesis of a waning of immunity after COVID-19 vaccination is contradictory with the timing of the infections as all of them occurred shortly after the last vaccine shot. Instead, it is likely that these failures result from a complete immune escape with new variants that can be linked to an antibody-dependent enhancement [6]. Another way to assess the immune response after these vaccines is the serologic survey of the population by the anti-spike IgG titer. This subject has also been abundantly studied in the medical literature. Most of these studies are dynamic with two observation time points and have converging results showing a waning IgG titer with time [7] [8]. These studies have theoretically more force than our static study but most of them have important limitations. The main one is that they have a short follow-up caused by the emergency of the COVID-19 outbreak. To provide rapid informations, many studies have been conducted on healthcare workers [9]-[16], but none of them reach our prolonged observation time over one year. Moreover, these selective populations are not exactly representative of the general population as healthcare workers are younger and extrapolation of these results to other populations is hazardous. On the opposite, a significant proportion of our cohort had comorbidities which give a wider scope than these studies. We were surprised to discover that the subgroup of elderly patients had a noticeable residual anti-spike IgG titer which is at odds with previous studies that claimed that they are less sensitive to COVID-19 vaccines [17] [18] and they should be targeted for a booster injection [19] [20]. After considering these questions, the other fundamental problem is to determine the protective threshold of IgG titer. Although some data are available on the subject, these results are confusing because of their variability. The main reason, as already evoked in a previous study [2] is the lack of standardization of laboratory automats and assays even with the introduction of the BAU units by the world health organization [21] [22]. The immune response level is also varying according to the type of vaccine [23] [24] [25]. But even by selecting the higher threshold (over 2000 BAU/mL) in our literature screening [23], the booster injection would be unnecessary in 14 out 25 of our patients (56%).

Finally, another pertinent parameter to determine the immune response in vaccinated patients is to compare their anti-spike IgG titer with the titer of a control group of non-vaccinated COVID-19 infected patients. Several studies report a higher seroconversion of COVID-19 vaccinated patients compared with naturally infected naïve patients [26] [27] [28]. This was suggested by our unique non-vaccinated case control in our study; this result is amazing as he had a ten-fold less anti-spike IgG titer than the lowest titer in the study group. Nevertheless, more favorable studies concluded that a natural infection confers a valuable protection against the disease because function is more important than quantity [29] [30] [31]. Moreover, some studies suggest that the serologic immune re-

sponse is lasting longer in naturally-infected patients than with COVID-19 vaccinated naïve patients [32]. For this reason, the booster injection for a COVID-19 infected or vaccinated population is questionable, except for immunocompromised patients. As already debated in our previous publication [2], the hypothesis to explain that natural infection is equivalent to COVID-19 vaccination is that it induces the strongest T-cell mediated immunity by comparison with COVID-19 vaccines, more particularly mRNA vaccines.

5. Conclusion

The results from our limited cohort study need to be confirmed on a larger scale before being extrapolated to the general population, but our noticeable long-term follow-up gives useful indications as we have observed that all COVID-19 vaccinated patients maintained a persistent anti-spike IgG titer that is not influenced by the age or the preexisting pathologic condition. For these reasons, complementary long-term scientific studies are strongly needed to assess the durability of the immune response and to correlate the anti-spike IgG titer with the level of protection [33]. At the present time, this problem has not been solved [34], but can only be achieved by an active pharmacologic survey.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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