



COVID-19 Preoperative Blood Tests : What Do They Tell Us About COVID-19 Vaccines ?

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Abstract

This observational real-world study was conducted on 14 patients who needed a minor office surgery or procedure and who were eligible for a COVID-19 booster according to the French Health Agency. The aim of the study was focused on biological markers which might have an incidence after surgery. The platelet count, D-dimer level, and anti-spike IgG antibodies levels, were the numeric parameters studied. The study showed no perturbation in the platelet count. Conversely, we observed an abnormal elevation of D-dimer levels in 4 patients (28 %). The most remarkable data was the constant residual positive level anti-spike IgG antibodies observed in all patients after 6 months ranging from 44 to 5680 BAU/mL. For these reasons, further studies on a bigger cohort would be useful to clarify the possible incidence of COVID-19 vaccines on D-dimer levels and a monitoring of the immune response should be proposed to all patients eligible for a SARS-CoV-2 vaccine booster in order to evaluate the benefit-risk ratio of this injection.

- Received Date: 04 Jan 2023
- Accepted Date: 09 Jan 2023
- Publication Date: 11 Jan 2023

Keywords

SARS-CoV-2, COVID-19 vaccines, platelet count, D-dimer, anti-spike IgG

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Introduction

Since the outbreak of COVID-19 and introduction of vaccines in the treatment of the pandemic, we have observed only a limited incidence in our surgical practice, except the risk of cross contamination. However, the recent emergence of coagulation alterations with COVID-19 vaccines, mainly thrombotic thrombocytopenia, led us to reconsider the problem [1]. For this reason, we decided to include a platelet count and D-dimer titer which are the most easily available laboratory tests to detect this pathology [2]. Another recurrent concern now expressed by many patients at our office is vaccine hesitancy because everyone is aware of a friend, neighbour, or family member who has contracted COVID-19 despite the fact that they have been fully vaccinated. For this reason, we have proposed to our patients a control of their immunological condition.

Material and methods

The study was conducted on a cohort of 14 patients having a full COVID-19 vaccination regimen (2 or 3 doses). This included 7 female and 7 male. The ages ranged from 64 to 89 years old (mean: 80 years). Two patients received a 2 shots course (first dose of AstraZeneca and Janssen and second dose of Moderna) and the remaining 12 patients a 3 shots course. Among the 12 patients with a 3 shots course,

two had an heterologous vaccination scheme (Comirnaty plus Moderna). The other 3 shots vaccinated patients were distributed between 5 Comirnaty and 5 Moderna.

Only patients eligible for a booster shot according to of the French Health Agency were included [3]. Main inclusive criteria for the booster shot are: age over 60 years old, patients with comorbidities, immuno-compromised patients [3]. Eleven patients were treated with an anticoagulant medication (one with aspirin (Kardegic 75 ®), one with fluidione (Previscan ®), 9 with novel oral anticoagulants (2 with Rivaroxaban (Xarelto ®) and 7 with Apixaban (Eliquis ®)). The surgical procedure involved one cosmetic medical procedure, 7 dermatologic surgery procedures and 6 oral surgery procedures (tooth extraction). The postoperative course was normal except for one elderly patient treated with an anticoagulant medication who experienced marked bruising after two stages of dermatologic surgery. The investigations of biologic markers were conducted by the same laboratory and included platelet count (by impedance), D-dimer titer (D-Dimer HD500, ACL TOP werfen) and SARS-CoV-2 IgG (anti-spike antibody) titer by chimiluminescence (SARS-CoV-2 IgG ARCHITECT, Abbott). The results of the antibody titer were expressed in binding antibody unit (BAU) allowing inter laboratory comparison. All patients agreed to

Citation: Dupoirieux L. COVID-19 Preoperative Blood Tests: What Do They Tell Us About COVID-19 Vaccines?. Med Clin Sci. 2023; 5(2):3-5.

complete these blood tests despite the fact that the antibody titer is not financially supported by the French health assurance. The antibody dosage was performed by the same laboratory. The time elapsed between last vaccine injection and the blood test ranged from 6 to 14 months (mean 9.4 months). The reference positive index for anti-spike IgG is > 7.1 BAU/mL.

Results

Three out of 14 patients reported having been infected with COVID-19 although they had a complete vaccination course. No minor adverse effect was reported by the patients but one patient (vaccinated with the Janssen vaccine initially) had experienced a more severe condition. She reported an unexplained massive weight loss (15 kilogrammes) after the second vaccine shot. The platelet count was normal in all patients ranging from 149 to 392 G/L (mean: 240 G/L). The D-dimer level ranged from 269 to 7500 μ g/L (mean: 1156 μ g/L). The concentration lower than 500 μ g/L measured by immune-turbidimetric dosage is excluding thrombotic disease but this threshold must be adjusted with age. Over 50 years-old, 100 μ g/L for each decade must be added for a valuable reference. After this adjustment, we found 4 out of 14 patients with abnormally high D-dimer values but one elderly patient had been recently infected with COVID-19.

The most noticeable rise with the D-dimer level was observed with the 2 shots course vaccinated patients (respectively 1452 μ g/L and 7500 μ g/L). All patients exhibited a positive anti-spike IgG antibody titer ranging from 44 to 5680 BAU/mL (mean: 2055 BAU/mL).

Discussion

The clinical history of the patients gave us the first relevant information. 21 % of vaccinated patients experienced a COVID-19 infection and it cannot be disputed that none of the COVID-19 vaccines can provide an absolute protection against COVID-19 infection [4]. Moreover, the failure rate in most of these clinical studies is probably underestimated as many COVID-19 infections are asymptomatic. This is more particularly evident for the new Omicron variant that displays a much more important immune escape rate [5,6]. Thus the most important evidence-based argument for these COVID-19 vaccines remains the prevention of severe clinical forms of the disease [7]. The difficulty of assessing the benefit-risk ratio of COVID-19 vaccines was already pointed out in 2021 by Hodgson [8] but it is still more pressing in 2022 as the incidence of severe form has sharply decreased [9]. Regarding the biology, the results of this small cohort study gives important results. The main parameter (platelet count) that can interfere with surgery was normal and corroborates the data obtained from the world medical literature showing that thrombocytosis thrombocytopenia remains an exceptional adverse effect with COVID-19 vaccine (8353 reports in the openvaers data base on 23 th december 2022) (available at <https://openvaers.com/covid-data>). The interpretation of D-dimer abnormally high titer in a small percentage (28.5 %) of our patients is more controversial. The first reason is that this biological marker is not specific and is modified in various pathologic conditions [10]. Secondly, there is also a variability of the cut-off value requiring an adjustment with age [11]. But the main obstacle is that there is no clear data on this subject in the medical literature for comparison with our results. Thus, the query with the MeSH words (« COVID-19 vaccine clinical trial » and « D-dimer test ») showed no results. For this reason, it would be useful to conduct a prospective longitudinal study monitoring pre and

postoperative levels of D-dimer after vaccination to detect a possible significant statistical difference. Such a study has already been conducted on the international normalized ratio (INR) coagulation biomarker in COVID-19 vaccinated patients following an anticoagulant treatment giving reassuring results [12]. Despite this lack of sufficient data on the incidence of COVID-19 vaccine on D-dimer, the prescription of this easily available and affordable biomarker for a preoperative check-up is useful as it has a predictive value for an adverse outcome [13].

Our most noticeable result was the regular findings of residual anti-spike antibodies whatever the age or comorbidities of the patients. These findings were surprising as most of the studies on the immunogenicity of SARS-CoV-2 vaccines show a declining humoral immunity with time [14-18]. Although our single time point study does not allow conclusions on the durability of the immune response, it deserves consideration as we have a noticeable longer follow-up than most randomized vaccine trials that are limited to a 6 months follow-up [19]. Furthermore, our results raise several disturbing questions. The first one is: is it ethically acceptable to administer a booster jab without controlling the previous immune response of the vaccinated patients ? We found only little information in the literature concerning the threshold of protective antibodies, widely varying from 141 BAU to 700 BAU/mL according to the sensitivity of the laboratory equipment [20- 22]. Even by applying the highest benchmark, the booster shot would be unnecessary in 7 (50%) of our patients eligible for this injection. The other question is: are the anti-spike antibodies a reliable immunity against COVID-19 infection? The former question may be considered provocative as it is scientifically proven that there is a correlation between the level of antibodies and COVID-19 severity [23], but it deserves attention as we have already observed COVID-19 infections in several patients vaccinated with four doses of vaccines who are supposed to have high levels of antibodies. The most evident explanation is that immunity against COVID-19 infection is complex and multifactorial and involves cellular immunity (more particularly B cell response) that is difficult to quantify. Thus, laboratory indicators cannot supply real-world clinical observations to assess the effectiveness of COVID-19 vaccines [24].

In conclusion, this modest but easily reproducible scientific study raises several ethical and scientific questions. First of all, the most reassuring data is that we did not observe modifications in platelet count and surgery can be performed safely in most vaccinated patients. Nevertheless, we observed a rise in D-dimer level in a small proportion of patients, however it is not possible to input this biological alteration to the vaccines because of the lack of specificity of this laboratory marker. Only a proven chronologic link of this rise in D-dimer level with the vaccine schedule can settle the discussion. The most noticeable result concerns the long-term positive residual level of anti-spike antibodies all of our patients whatever their age and their medical history. Thus, monitoring of anti-spike IgG antibody titer can be useful to adjust the indication of a COVID-19 vaccine booster injection more specially with new variants [24]. Finally, a thorough pharmacovigilance of all COVID-19 vaccinated patients will be critical in the future.

Conflict of interest

The author received no source of financial support for this study and has no conflict of interest with any COVID-19 vaccine providers.

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