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Case Report: Preliminary Study on Expression of Oxidative Distress in Vaccinated Patients with Anti Sars Cov-2 Vaccine Bnt162b

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ABSTRACT

Background: *The study aims to investigate oxidative distress in patients vaccinated for Sars COV-2 by comparing them to patients infected with the virus.*

Case Presentation: *The tests carried out on a small population of the female gender showed that the vaccine essentially does not create any oxidative distress unlike Sars COV-2 which instead generates an oxidative storm which, as per literature data, precedes the well-known cytokine storm. We assume that this is due to the different response induced by the vaccine which selectively stimulates lymphocytes without therefore stimulating the activity of macrophages which is instead activated by COVID-19.*

Conclusion: *This study aims to be the starting point for a larger population study that correlates oxidative mechanisms with the vaccine-induced immune response.*

Keywords

Oxydative distress, Sars COV-2, Vaccinated patients.

Introduction

Oxidative stress is a physiological adaptive mechanism that most of living organisms enable as a reaction to a number of physical/chemical/biological stressors, like viruses, in order to survive. Oxidative stress is managed by the redox system, a ubiquitous biochemical system, partially shared with gut microbiota, which exploits the transfer of electrons ("redox reactions") by antioxidants to oxidants to realize signalling, defense and detoxifying responses [1]. An optimal successful response is properly indicated as "oxidative eu-stress" while "oxidative di-stress" depicts the consequences of an abnormal response, ultimately responsible, together other factors, of early aging and common chronic diseases (e.g., atherosclerosis, diabetes, colitis, dementia, cancer and so on), among which there is probably just COVID 19 [1,2]. On this background, we want study a different reaction of the body about vaccine and infection.

It is well established that the SARS-CoV-2 infection starts normally by the invasion of lungs, that for many reasons are particularly prone to oxidative di-stress, even in physiological conditions. Indeed, lungs manage around 12,500 liter/day of oxygen and 1 to 2% of such oxygen generates, in the mitochondria, reactive oxygen species (ROS), like superoxide anion, hydroxyl radical and hydrogen peroxide; such production may further increase in case of mitochondrial dysfunction or fluctuations of oxygen bioavailability (e.g., hypoxia, ischemic-reperfusive damage, and so on [1,3]. Moreover, neutrophils as well as resident lung macrophages show highly oxidant enzymatic activities as a part of the redox sensing system; for instance, their membrane host the NADPH oxidase (often categorized as NOX/DUOX), that, after proper stimulation (e.g., bacterial infection) converts respiratory molecular oxygen to superoxide anion or hydrogen peroxide, as essential step of phagocytosis, in order to kill the pathogen ("oxidative eu-stress")

[1,4]. In case of host/pathogen unbalance, the excess of hydrogen peroxide can cause the oxidation of chloride ions to hypochlorous acid, a powerful oxidant (active against all amin groups), in a reaction catalyzed by myeloperoxidase; this enzyme normally is stored in cytoplasmic membrane-bound azurophilic granules but, after proper stimulation, it is secreted out to the extracellular space by degranulation or exocytosis and becomes active [5,6]. Moreover myeloperoxidase, together with extracellular webs of chromatin and microbicidal proteins, can be a component of Neutrophil Extracellular Traps (NETs), that neutrophils release to contain infections; a dysfunction of this system can lead to tissue damage [7,8]. Such unwanted reactions ("oxidative di-stress") can be amplified by endothelial cells which endothelial nitric oxide synthase (eNOS) generates the nitrogen-centered free radical nitric oxide (NO) from arginine thus contributing to the pathogen killing and endothelial function; however, uncoupling of eNOS as well as an excess of superoxide anion cause the switch of nitric oxide to peroxynitrite, a powerful vasoconstrictor, that can worsen hypoxia and further stimulate macrophages, as it happen in SARS- CoV-2 infection [1,9].

Case Presentation

In this experimental study we recruited a total of 11 patients, females, aged between 39 and 61 years, health personnel of the ASL Napoli 2 Nord, of which 6 females belonging to the vaccination study group, 3 females belonging to the post infection control group. sars-cov2 and 2 females not belonging to the previous categories. The d-ROMs test and the PAT test at time 0 before the vaccine first dose, at time 1-10 days from the vaccine, at time 2 after 20 days from vaccine and at time 3 10 days after the second dose. In the second group the d-ROMs test and the PAT test were analyzed at time 1 immediately after the sars-cov2 infection and at time 2 after 30 days from the negative swab. In the third group, control, only the baseline of the d was analyzed. -ROMS test and PAT. Each analysis was carried out after capillary sampling of 10 microliters of blood and collected in special micro peaks and subsequently subjected to centrifugation before the analysis. The FRAS 5 instrument is a POCT (Point of Care Testing) Photometer dedicated to in Vitro diagnostics in order to perform the analysis of free radicals (d-ROMs test) and antioxidant potential (PAT) on blood. d-ROMs fast test - ANALYSIS (FRAS - Rev 1.00). Once centrifugation is complete, take microlitres of d-ROMs test reagent R3 (with the White pipette) and deposit it in the small cuvette containing the liquid reagent R2 of the d-ROMs test. Take 10 microlitres of plasma (with the White pipette) from the micro pipette with the pipette and a new tip and insert it into the small cuvette containing the liquid reagent R2 of the d-ROMs test. Carefully insert the tip onto the pipette. Mix by inversion for at least 15 seconds. Put into the cuvette with the green cap. Mix by inversion for at least 10 seconds. Avoid the formation of foam. Insert the cuvette into the reading compartment making sure that the knurled sides are oriented as indicated on the label. Make sure the cuvette is fully seated in the reading compartment. Wait for the result. PAT test - ANALYSIS (FRAS - Rev 1.00) Take the cuvette containing the PAT reagent R1 and add 40 microliters of reagent R2 using the special green pipette. Close the cuvette with its cap and mix by inversion for 10 seconds. Insert the cuvette into the reading compartment making sure that the knurled sides are oriented as indicated on the label. Make sure that the cuvette is fully seated in the reading compartment. Wait for the result. Take 10 microlitres of plasma from the micro-tip with the white pipette and place the plasma in the cuvette containing the PAT test liquid R1 + R2 just removed from the reading compartment. Carefully insert the tip onto the pipette. Transfer the plasma to the cuvette. Mix by inversion for 10 seconds. Insert the cuvette into the reading compartment making sure that the knurled sides are oriented as indicated on the label. Make sure that the cuvette is fully seated in the reading compartment. Wait for the result.

Patient Anamnesis table

Patient N°	Age	Sex	Desease history
1	39	female	Not any significative pathology
2	45	female	Liken sclerosing for 25 years Former smoker from age 20 to 42
3	48	female	Gastric bypass surgery Smoking addict 20 / day from the age of 13
4	47	female	Hypertension Reactive arthritis
5	61	female	Type 2 diabetes mellitus Menopause
6	44	female	Menopause

Vaccinated BNT162b Patients table

Patients	Basale D-ROMS	Basale PAT	D-romsII (10days I dose)	PatII (10 days I dose)	D-roms III (20 Days I dose)	PATIII (20 days I dose)	D-RoMS IV (10 days II dose)	PAT IV (10 days II dose)
1	335	2636	316	2636	268	2607	316	2791
2	363	3071	530	1499	400	3060	282	1791
3	182	3589	348	3009	340	3000	348	3066
4	318	2997	427	2896	478	2980	318	2887
5	381	2807	263	5344	260	2900	267	1446
6	310	2900	336	4668	270	2966	438	2163

Positive Control Covid Patients

Covid Patients	Age	Sex	Desease history	D-RoMS I (initial)	PAT I (initial)	D-Roms II (final)	PAT II (final)
1	27 anni	Female	Not any significative pathology	376	3642	278	2686
2	52 anni	Female	Menopause	419	3889	430	2943
3	22 anni	Female	Not any significative pathology	304	2426	312	2307

Discussion and Conclusions

The tables must be read on the basis of the values of the D-Roms and correlated to the values of the PAT, normal values of the D-ROMS are estimated between 250-300 Carr. U; while normal PAT values are estimated between 2200 and 2800 Cor. U; therefore, high values of D-ROMS suggest an alteration of the redox balance due to high inflammatory levels caused by a lymphocyte, macrophage and / or Mast-cell response in association with altered PAT values above the threshold value of 2800.

We can observe that in all COVID-19 patients an increase in D-ROMS and PAT was detected at the time of expression of the pathogen, testifying to the inflammatory process (oxidative-storm), while in remission on average a reduction is observed (especially in patient 1) of the D-ROMS, with reduced PAT values in all the subjects under examination. This indicates how the pathogen creates an inflammatory phenomenon (oxidative storm) that starts from the activation of macrophages [7] in an inflammatory increasing. In vaccinated patients, on the other hand, D-ROMS conditions are observed at baseline which on average remain constant at 10 days from the vaccine and which tend to decrease at 20 days from the first dose and remain within threshold values at ten days from the second dose. Therefore, it can be argued that compared to COVID-19 patients [5-13], patients vaccinated with I and II dose Pfizer would appear not to develop oxidative disterss during vaccination. This could be justified by the different type of immune stimulation that occurs between the pathogen and the m-RNA vaccine, since the latter creates a type of response set mainly on T lymphocytes [11].

In conclusion, could the decrease in oxidative stress in vaccinated subjects unlike Covid-19 patients depend on the lack of involvement of pulmonary macrophages? Or another reason may lie in the direct involvement of the lymphocytic response, bypassing the innate response. Therefore, it would be interesting to carry out a study on a greater number of subjects to document the different response of ROS in vaccinated and covid-19 positive, comparing the lymphocyte subpopulations in the subjects involved in a larger study, thus trying to understand the possible link between the immune cells directly involved and the different redox reactions generated (vaccinated - sick).

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