


COVID-19 Vaccines in Inherited Retinal Degenerations (IRD), Fears, Ideas and Real Interactions

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Purpose: In the COVID-19 pandemic era, vaccines are one of the most efficient weapons, as well established by WHO, that humans have, in all their variants (mRNA, AAV or others). Unfortunately, in western nations skepticism within different groups has been generated by the fast approval processes, driven by the urgent need to confront the rapid increase of hospitalized patients and number of deaths by regulation authorities as FDA and EMA. Moreover, several scientific and non-scientific perplexity, also amplified by the media, created hard no-vax strategies, that lead many patients to refuse vaccine administration. Also in this selected population higher rate of COVID-19 infections and severe diseases are registered and consequently there was an increase of death number. Furthermore, to avoid vaccine shots, people frequently ask exemption querying ophthalmological and systemic diseases, in this situation most patients affected with orphan ophthalmological conditions as inherited retinal degenerations have profound fears and doubt. The goal of our study was to ascertain if these fears are based on real facts and if there are interactions or severe visual impairment after each shot of vaccinations.

Methods: Five hundred randomly selected patients affected by IRD at each patient was asked anonymously, number of vaccine administrations and eventually reported side effects.

Results: Of 500 selected patients 61 (12,2%) did not underwent to Covid-19 vaccination, reasons were various (fear, laziness, caregiver unavailability etc.). Remaining 439 patients (87,8%) had first shot of vaccine. Only 30% of patients complained side effects of vaccine, none of them was serious.

Conclusion: The number of patients is wide enough to draw some considerations: In IRD vaccination is safe, in all doses ocular side effects were reported only in one third of subjects and this is not different from the percentage shown by normal people, COVID-19 effects may be more dangerous than vaccine.

Keywords: COVID-19, Retinitis pigmentosa, vaccination, inherited retinal degenerations

Introduction

In the COVID-19 pandemic era vaccines are the most efficient weapon, as well established by WHO,^{3,4} in all their variants (mRNA, AAV or others).^{1,2} Moreover, several scientific and non-scientific perplexity, mostly amplified by the media, created hard no-vax strategies, that lead many patients to refuse vaccine administration and therapy, or to suggest non-sense drugs (ie paracetamol or hydroxychloroquine). This selected population today presents higher rate of COVID-19 infections and severe diseases and consequently increase of death number.

In Italy, to avoid vaccination, people frequently use systemic or ophthalmological diseases as exemption, in this environment patients affected with orphan ophthalmological conditions as inherited retinal degenerations have profound fears and doubt whether to vaccinate themselves or not. Comorbidity in this scenario (immune-deficit, vascular damage etc.) have been used as strategies to avoid vaccine administration, and very often rare ophthalmological conditions as Inherited Retinal Degenerations (IRD) as defined by Pagon⁴ are invoked as exemption.⁵⁻⁸

In these cases, the number of patients is so small that is not sure take a right decision either in one direction of the other, as results of this defensive strategy many doctors frequently opt for a non-vaccine administration also in patients

that intend undergo to vaccine administration. This results in high contagion risk and more viral spread and circulation with high mutation rate. Moreover, despite several studies on ocular complications of COVID-19 vaccines on normal population, no data are reported in literature in IRD patients on the real impact of feared complications as vision loss or progression of retinal damage, so it is very difficult to understand which is better behavior for these patients.

The goal of our study was to ascertain if these fears are based on real facts, and if there are interactions or severe visual impairment after each dose of vaccinations.

Methods

Retinal Diseases Center in our hospital have more than one thousand patient file report with Inherited Retinal Degenerations, we have proposed them a short questionnaire if they were Vaccinated for COVID-19. From our file of 1234 patients affected by IRD were randomly selected 500 telephone numbers using the RNG random Generator Application for MacOS (dev. Alex Rutkowski RUS). Telephone interview was always realized outside a time window of three weeks after the vaccination.

In our choice this value, considering that IRD are disease with prevalence of 1/10,000 to 1/15,000 (depending on region), it is very high, we calculate those 500 patients analyzed in the study correspond to a normal population sample of 5,000,000 to 7,500,000 subjects. And considering of total estimated total amount of IRD sick people in Italy of 4000 to 6000 persons in my opinion must be considered a relevant sample.

For each patient informed consent was drawn before starting the questionnaire, according to our ethical committee procedures, after that were asked, number and date of vaccine administrations and eventually reported side effects systemic and ocular, with special focus on severe vision loss even transitory.

Anonymous data were analyzed by Microsoft Excel for frequency distribution and general statistics in a double-blind way. If there were no telephonic answers, we passed to following selected patient and randomly included a new one. If the selected patient was not vaccinated they were included in the study but no questionnaire was collected. According to our protocol we performed phone interview between September and December 2021 every interview was based on a few points as follows: first of all was required if the IRD patient was vaccinated, if the answer was positive questionnaire was filled out, in which was registered the time of each vaccine shot, and eventually raised side effects.

Were recorded 439 filled questionnaires, by telephone and for each question was recorded the answer in relationship to the number of vaccine doses, side effects eventually registered, time elapsed from the last dose. All patients are usually referred yearly in our Center For Rare Disease, they usually perform clinical evaluation (Visit, OCT, VF, ERG), the choice of telephonic interview was done because in a very short time in Italy were performed a wide number of vaccinations, moreover many patients came far away from our center and evaluate them from ophthalmological point of view might not be necessary in relationship to the aim of the study to evaluate if those fears of patients may correspond to a real visual function loss.

Our data were drawn according to Helsinki declaration on Human rights in clinical research and was approved from our Ethical Committee, our study complies with internationally accepted standards for research practice and reporting, this research is in line with COPE guidelines.

Results

Of 500 selected patients 61 (12,2%) did not underwent Covid-19 vaccination, reasons were various (fear, laziness, caregiver unavailability etc.). At the end of questionnaire collection mean age of the study group was 56.31 (SD±14,7) years; selected people's gender was 271 female and 229 males.

Of these 439 patients 87,8% had first shot of vaccine, only with mRNA preparations due to Italian regulations that allow only this type of vaccine for disabled or fragile people, side effects were reported in [Table 1](#) but none of them was dangerous or life threatening for the patient.

Of them 381 (86,8%) had second shot after one month (3–4 Weeks), and 356 (81,1%) the booster dose between October and December 2021 representing a good performance for Italian population giving them a good protection against COVID-19 infection.

Table 1 Frequency Distribution of Systemic and Ocular Disturbances in IRD

Side Effects	First Dose	Second Dose	Booster
Site injection pain	297	275	261
Overnight fever	366	319	307
Eye redness/swelling	29 (6.6%)	32 (8.4%)	35 (9.8%)
Ocular discomfort	86 (19.6%)	88 (23.1%)	83 (23.3%)
Blurred Vision	5 (1.2%)	3 (0.8%)	6 (1.7%)
Transitory Floaters	12 (2.7%)	9 (2.4%)	9 (2.5%)
No ocular effects	307 (69.9%)	249 (65.3%)	223 (62.7%)
Total	439	381	356

Note: In grey background are highlighted systemic side effects.

In our IRD patient files COVID-19 infections (PCR positive test) were reported in 261 (21,5%) patients during the Italy vaccination period (December 2020–December 2021) this data is within the range of COVID-19 general infection rate in Italy.

Discussion

Starting from an analysis of the literature on eye complications of COVID-19 vaccines, it is evident that nevertheless trillions of vaccine administrations ocular side effects generally are very rare, less than one hundred severe ophthalmological side effects are described in normal population in the last three years either in registration trials or in literature.^{8–12} Main ocular complication are inflammatory manifestations both in anterior or posterior segment, and ocular thrombosis or ischemic manifestations,^{13–17} occurred in strict time relation, one to three days, with vaccine shot release.^{23–32} But no reports are present on the occurrence of side effects in patients affected by rare ophthalmological disease. This group of the population is small but is still numerically influent and psychologically weakened by the fear that something might worsen or simply interact with degenerative process, damaging the retina and reducing retinal performance, especially in low luminance situations. In these conditions the patients might think that their autonomy and life expectance of good quality of vision would be shortened or reduced. We may consider that very frequently these patients already present in association with their disease behavioral and psychologic alterations like anxiety, depression or humor alterations.^{18,19}

As well described previously in literature usually inherited retinal diseases impact not only on the visual system, but patients frequently present night/day cycle disturbances, insomnia and there are several others psychological interactions. IRD patients frequently present overexpressed moods like fear for vision loss, anxiety and aggressive status as previously evaluated in our papers on Retinitis pigmentosa and Usher disease.^{20,21} This causes unconscious less predisposition to have complete vaccination, they escape from doctors and ophthalmologists. Inexplicable feeling despite authority approval lasts more than two years and that mRNA vaccines that were given since late 2020 in more than a trillion doses.^{22–28} Moreover ischemic manifestations rarely described and occurred on eyes and retina, are exasperated often by the social media and the lack of precise data on IRD patients threaten as a heavy hammer above the head more weak patients and their living mood, and also in the relatives there is the perception of an incoming fearing event after the vaccination.

Our retrospective study does not include a complete clinical examination of IRD patients because these patients are widely distributed in the country and even most of them are part of fragile patients' vaccination number time and/or COVID-19 disease infection was different by region even we included all doses that were done in a period starting from December 2020 until December 2021.

Conclusions

Obviously main limit of this brief report is that analyze a spot situation on a selected population in a country (Italy) in which COVID-19 vaccination cover more than 70% of population (>12years) where people is well prepared at it,

moreover, this report is based on a telephonic questionnaire on few and easy answer and does not is a complete clinical interview of patients neither there is any correlation to their clinical situation. Particularly we do not have systematic ophthalmological evaluation of investigated patients. Despite this, the number of patients it is enough wide to draw some “take home messages” as follows:

1. In IRD vaccination is safe,
2. In all doses ocular side effects were reported only in one third of subjects and this is not different from the percentage shown by normal people,
3. COVID-19 effects may be dangerous than vaccine.

Main limitations of the study are due to the impossibility to have a real ophthalmological examination to precisely evaluate an eventual progression of the degenerative process, so the study remains subjective related to the perception of vision performances from the patient itself.

Data Sheets Availability

Our data are available in digital conservatory of AUSL Latina p.za P.L. Nervi snc 04100 Latina.

Ethic Statement

Our data were drawn according to Helsinki declaration on Human rights in clinical research and was approved from University “Sapienza” Department “Sense Organs” Ethical Committee (CD 4.12 of 6th.May,2021). This study research complies with international standards for research practice and reporting and is in line with COPE guidelines.

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Author Contributions

Enzo Maria Vingolo Authorship, writing, conceptualization, final draft analysis. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The author reports no conflicts of interest in this work.

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