SARS-CoV-2 vaccines tolerability: A perspective by people with multiple sclerosis

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The SARS-CoV-2 pandemic has represented a global emergency with shocking health and socio-economic effects. One of the most impactful actions to contrast the pandemic has been the massive vaccination campaign implemented by health authorities worldwide. The large-scale application of recently approved vaccines, still lacking a robust real-life experience, has generated questions about their safety. The fear of unknown adverse effects of SARS-CoV-2 vaccines has been particularly evident in people suffering from chronic autoimmune diseases, including multiple sclerosis (MS), motivated by the risk of aberrant immune-mediated responses triggered by the vaccination.[1] Case-reports on the occurrence of MS relapses after SARS-CoV-2 vaccination have been published.[2,3] At the same time, however, several monocentric and multicentre studies conducted in Europe and in other countries where the vaccination campaign started early, have produced reassuring results regarding the safety of SARS-CoV-2 vaccines in MS.[4–6]

In this scenario, the work conducted by Frahm and colleagues,[7] published in this issue of *The Lancet Regional Health - Europe*, helps to shed light on SARS-CoV-2 vaccines tolerability, focusing on vaccination reactions directly reported by people with MS. The authors used data obtained from a cohort of 6142 people with MS from Germany and the United Kingdom (UK) who took at least one dose of SARS-CoV-2 vaccine. The most frequently used vaccines were *BNT162b2 (Pfizer-BioNTech)* in the German cohort and *ChAdOx1 nCoV-19 (AZD1222; AstraZeneca)* in the UK cohort. The German MS Society and the UK MS Registry acquired health data through serial interviews after the first and second dose of vaccine, and approximately three months later, using a patient reported online questionnaire. The information collected covered both immediate vaccination reactions and MS clinical changes, these latter only in the German cohort.

A key finding of this study is that people with MS reported at least one vaccination reaction with a frequency up to 65.4%. The most frequently reported adverse event was pain at the site of vaccine inoculation, followed by fatigue and headache. The lack of a control population of non-MS subjects does not allow to effectively compare SARS-CoV-2 vaccines tolerability in MS with respect to the general population. However, when comparing the obtained results with data from literature,[8] it could be derived that people with MS did not experience an higher frequency of vaccination reactions. Interestingly, the authors found that vaccination reactions were reported more frequently by women than men with MS, a finding that confirms that sex and gender may impact vaccine outcomes, as already demonstrated for other vaccinations.[9]

One of the most interesting findings of the study deals with the clinical changes reported by people with MS after SARS-CoV-2 vaccines in the German cohort. A relevant percentage of subjects (around one out of ten) said they noticed worsening of their pre-existing MS symptoms. Specifically, in most cases, people with MS noticed a worsening in fatigue, walking difficulties, and pain. Also in this case, despite the interpretative limits due to the lack of a control group, the obtained information is useful when discussing the issue of tolerability with people with MS undergoing vaccination. It is worth noting that the presence of moderate/severe disability was independently associated with MS deterioration after vaccination in the described cohort. Approximately one out of five people with MS from the German cohort had progressive MS, a clinical phenotype typically characterized by higher levels of disability and a steady worsening of symptoms including walking difficulties and fatigue.[10]

The approach used by Frahm and co-workers, based on data collection through online questionnaires, provides a precious point of view on SARS-CoV-2 vaccines tolerability, from the perspective of people living with MS. At the same time, however, the exclusive use of patient reported outcomes might limit the interpretation of some results. This becomes particularly relevant when addressing the occurrence of disease relapses. In this study, the authors describe a patient-reported relapse rate of 7.7% in the German cohort. However,

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the lack of a physician-based diagnosis, of magnetic resonance imaging data, together with the study design and the absence of clear information on the time interval between vaccines administration and relapse onset, does not allow to draw conclusions about a causal relationship between the reported relapses and vaccination in the described population.

All such observations suggest the need of well-designed large cohort studies that could allow to go beyond the current methodological heterogeneity of studies on vaccines safety in MS Despite the potential limitations, the study by Frahm and colleagues[7] has the merit to provide us with an informative patient-reported perspective on SARS-CoV-2 vaccines tolerability, collected from a large group of European subjects undergoing both mRNA and viral vector-based vaccines. The obtained results add another useful piece to the complex puzzle of vaccinations in MS.

Contributors

MDF: conceptualization of commentary, revision of drafts and review of the literature.
LG: first draft and review of literature.

Declaration of interests

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