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EDITORIAL

Emerging COVID-19 vaccines: A rheumatology perspective

The coronavirus disease 2019 (COVID-19) pandemic gripped the world unexpectedly and little was known about the virus or its effects on various cohorts of patients. In the first wave, rheumatology patients on immunosuppressive agents were asked to shield or self-isolate because they were deemed highly clinically vulnerable. As evidence emerged, it became apparent that most of our patients were not adversely affected with their disease management and so it gradually returned to normal.[1] Nevertheless, in light of the second wave much uncertainty remains. In this regard, the COVID-19 vaccine is eagerly anticipated to be one of the solutions to the pandemic. Emergence of several potential vaccines has been the topic of discussion in recent weeks. In this Editorial we explore the emerging vaccines and the perception, anxieties, and concerns around them from a rheumatology perspective.

COVID-19 vaccines are being developed by various pharmaceutical companies but there are three that seem to be the most promising. Pfizer/BioNTechs COVID-19 vaccine is an RNA vaccine, which is reported to be 95% effective against COVID-19 and is currently in phase 3 of its trials with over 43 000 participants; 41% of global and 45% of US participants are between 56 and 85 years, and 42% of the overall study population have a diverse ethnic background including Asian, Black, Hispanic, and Native American. Most participants have received a second dose as part of a two-dose regimen, but the details of this regimen have not been released.[2] Moderna, has also developed an RNA-based vaccine, which is up to 94.5% effective when given over two doses on days 1 and 29.[3] The clinical trial cohort includes over 30 000 participants including 7000 over 65 years of age and 5000 participants under 65 years of age with high-risk chronic diseases. AstraZeneca has produced a slightly different COVID-19 vaccine consisting of a viral vector, which is 90% effective when using one of its vaccination regimens consisting of giving a half dose initially then a full dose 1 month later. The trial population is slightly smaller than the others with over 23 000 participants and it is being conducted in the UK, Brazil and South Africa. The cohort consists of participants who are healthy and have medically stable chronic diseases.[4] At the time of writing this editorial (November 2020), the results of the phase 3 trials of these three vaccines are yet to be published and peer-reviewed, therefore available data so far are limited to press-releases.

Efficacy and safety of these emerging vaccines in the rheumatology population are unknown. It is unclear in the trials which chronic disease patient groups were included or if they were on immunosuppressive therapy. Published phase 1/2 trial data included healthy patients between the ages of 18 and 55 years, patient demographics for phase 3 trials have not been released. However, as none of these vaccines are live attenuated it is assumed that they are safe to be taken by patients on immunosuppressive treatment. The main resistance we envisage with some of the rheumatology patients in taking the vaccine is likely to be their perception rather than scientific reasoning. The RNA vaccine is the first of its kind and understandably we are all apprehensive, as little is known about the long-term side effects of this novel vaccine. So far, none of the three pharmaceutical companies has reported any serious short-term adverse effects. The most common side effects have been fatigue and headache, similar to the influenza vaccine.[2,3]

The relationship between vaccination uptake and perception is complex. The measles, mumps, and rubella (MMR) controversy in 1998 demonstrates how MMR vaccine uptake fell in subsequent years and the efforts of health authorities to rebuild public trust. Knowledge is power, and educating parents on the correct information was key after the MMR controversy. Milward describes certain features that affect public perception of health messages, which include the relevance of information to everyday life, its relation to other perceived risks, and the extent to which the source of information is trusted.[5] Information sourced from informal sources on the internet, social media, and print media will have a potential negative impact. Rheumatology patients are eager to have more information regarding the COVID-19 vaccine so that they can make an informed decision about their long-term disease management. Reflecting on times when vaccines have been introduced or publicized, we can appreciate how the distribution of data regarding their safety and use is imperative to enable rational patient decisions. There are other factors that influence patients' health decisions on a personal level, which include cultural norms, and religious, educational, and philosophical views, which can all influence attitudes to vaccinations.[6] Many patients also rely on the advice and opinion of their healthcare professional and so disseminating accurate information is vital.

The concept of vaccination is based on herd immunity where most people in a population have immunity against an infection either directly by previous infection or indirectly via a vaccine to reduce the risk of transmission to those who lack immunity.[7] The proportion of people that need to be vaccinated to achieve herd immunity depends on the infection, for example for measles it is 95%, for polio it is 80%.[8] Nevertheless, it is usually most of the population that needs to be vaccinated to protect those who cannot be

vaccinated. The level to achieve herd immunity against COVID-19 is unknown, but until it is achieved patients must strictly adhere to the advice from the Government to protect themselves and the community. Indeed, one of our main concerns is that rheumatology patients may become complacent after taking the vaccine. Although the full efficacy of the vaccine will only be determined with mass vaccination, it does not necessarily confer complete immunity. It is imperative that we stress to our rheumatology patients that they should continue to take protective measures.

Lockdown, social distancing, and increased hand washing have gone some way in reducing the incidence of the virus below a reproduction rate of 1, but this will not be enough to eliminate the virus. History has demonstrated recurrent epidemic cycles with other contagious infections such as measles, mumps, and smallpox in the pre-vaccine period.[9] It is unknown whether the COVID-19 immunization program will achieve disease elimination or eradication. Elimination is the absence of sustained endemic community transmission in a geographical area and eradication is the reduction of cases to zero globally. Another factor contributing to eradication vs elimination is how long a patient will retain immunogenicity to COVID-19 after the vaccine. There have been a handful of patients globally who seem to have been re-infected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) after recovering from their first infection and having a negative swab. Gouseff et al highlight 11 patients who had a second episode of COVID-19.[10] The patients are of a variety of ages and some have no co-morbidities, one patient was on rituximab as chemotherapy but there does not seem to be any consistent clinical characteristics. Zhang et al describe two patients who had reduced IgG anti-SARS-CoV-2 antibody before the second re-infection and subsequent increase in titers in the second re-infection, and one patient had reactivity of IgM anti-SARS-CoV-2 antibody [11] . This demonstrates that patients who did not mount a strong response from the first infection are perhaps at increased risk of a second SARS-CoV-2 infection. However, as all the proposed COVID-19 vaccines are two dose regimens the second dose will hopefully cover those patients who did not produce a strong immune response with the first dose.

A concern among clinicians is whether immunosuppressed patients will mount a sufficient immune response to the vaccine. The current vaccines being produced use "next-generation platforms",[12] there are no RNA vaccines currently licensed and the only viral vector vaccine approved is the vesicular stomatitis virus (VSV) -based Ebola vaccine. In the VSV-Ebola vaccine trial a smaller proportion of human immunodeficiency virus (HIV)-positive patients developed an antibody response compared with HIV-negative patients.[13] However, there are few data from practical use because the vaccine was used for "compassionate use", so only a small number of patients who were considered to be high risk were given the vaccine in sub-Saharan Africa. In terms of adverse effects, the main side effects were flu-like symptoms in the first 4 days following vaccination, which is like live virus vaccines. The influenza vaccine is an annual inactivated vaccine recommended to certain groups of vulnerable people including those who are immunocompromised. In the rheumatology population it seems the vaccine mounts a good immune response and reduces the risk of respiratory morbidity and mortality.[14] Apart from live vaccines, all other vaccines are currently safe to use in the rheumatology population and it seems that they mount a sufficient response to provide immunity. This creates an optimistic outlook for the new COVID-19 vaccine and its anticipated therapeutic effect.

The need for revaccination is yet to be determined. The genome of the current SARS-CoV-2 virus strongly resembles its predecessor SARS-CoV, with novel glycosylation sites secondary to antigenic divergence. Therefore, although a vaccine now may confer protection against the current SARS-CoV-2 strain, it begs the question if the vaccine will be effective against evolving genomics in the coming years. There is yet the possibility that because of antigenic drift, further modifications in the vaccine maybe necessary to protect against novel coronaviruses.[15]

The COVID-19 vaccine brings hope to what has seemed quite a bleak and uncertain year. Vaccines provide a long-term solution to the pandemic; however, before we recommend these vaccines to our rheumatology patients, we must have adequate information about their efficacy and safety in the immunosuppressed population. Patients are both eager and anxious to receive the COVID-19 vaccine. Therefore, as healthcare professionals we need to be armed with the correct information before counseling our patients.

KEYWORDS

coronavirus disease 2019, rheumatology, safety, vaccine

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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