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REVIEW ARTICLE

SARS-CoV-2 vaccination and practical points in psoriasis patients: A narrative review

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Abstract

SARS-CoV2 vaccines were approved without long-term monitoring due to emergent situations. This has raised some issues about timing and protocol of receiving vaccines in specific situations including patients with chronic inflammatory disorders such as psoriasis. Here, we present different aspects of SARS-CoV-2 infection and vaccination in psoriasis patients and aim to provide solutions to overcome the potential challenges. In brief, the benefits of vaccination outweigh the potential risk; vaccine-triggered de novo or flares of psoriasis is uncommon. As such, all psoriasis patients, especially those receiving systemic treatments including anti tumor necrosis factor agents, are strongly recommended to get SARS-CoV-2 vaccines. It is recommended that new immunosuppressive/immunomodulatory therapies be initiated at least 1 week after the second SARS-CoV-2 vaccine dose, if possible. In addition, in severe and active forms of psoriasis, it is better to delay vaccination until stabilization of the disease.

KEYWORDS
biologic therapies, COVID-19 vaccine, immunosuppressive therapies, psoriasis

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) has led to a great rate of morbidity and mortality since its emergence. COVID-19 vaccination has proven to be highly safe and effective in clinical trials and real world, however, some unique challenges have risen especially in individuals with underlying diseases who are at as higher risk of complications.[1] Vaccination against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been followed by several local and systemic cutaneous adverse events. Among them, local injection site reactions, urticarial eruptions and maculopapular rash have occurred with the highest frequency, most of which have been self-limited.[2–7] New-onset and exacerbation of some dermatological disorders, including lichen planus and psoriasis, have been reported following COVID-19 vaccination.[8]

Psoriasis is a common chronic inflammatory dermatosis which can affect the skin, nails, and the axial and peripheral joints.[9,10] Psoriasis patients on immunosuppressive medications are at increased risks of infectious complication potentially including more severe forms of SARS-CoV-2 infection.[11,12] Vaccination, along with social distancing and utilization of masks, can be an excellent strategy to decreased the risk of acquisition and complications associated with COVID-19 in

psoriasis patients, particularly those on immunomodulatory/immunosuppressive therapy.[13,14] Immunosuppressive medications, however, are likely to affect the vaccine response and interfere with antibody production.[15] Therefore, planned timing of vaccination, as much as possible may be crucial in some patients. Furthermore, studies suggest that individuals with inflammatory conditions such as psoriasis may have vaccine hesitancy due to concerns for disease exacerbation following vaccination.[8,16]

Here, we present different aspects of SARS-CoV-2 infection and vaccination in psoriasis patients and aim to provide solutions to overcome the potential challenges.

1.1 | The impact of psoriasis and psoriasis treatments on COVID-19 infection

Psoriasis, per se, is not a state of immunosuppression, but it causes a milieu of systemic inflammation in the body.[17] Tissue angiotensin converting enzyme (ACE) activity, which is the main component for SARS-CoV-2 spike protein binding, is higher in psoriasis patients, which, in theory, could lead to more severe COVID-19 infections.[18] Moreover, immunosuppressant agents used for psoriasis precipitate the host to get an infection.[19] Agents such as interleukin (IL)-17 inhibitors, which are the cornerstone of psoriasis treatment, can impair the mucosal immunity, thereby increase the risk of lower respiratory tract infections.[20] Anti-tumor necrosis factor (anti-TNF) agents as well as conventional immunosuppressive agents such as methotrexate and cyclosporine which are sometimes utilized for psoriasis management would also increase the risk of pulmonary infections, including SARS-Cov-2 ones.[21–23] On the other hand, retinoids such as acitretin, due to their anti-inflammatory characteristics, may even have antiviral effects.[24] These problems had led the dermatologist to cease or reduce the dosage of certain medications in psoriasis patients.[25]

1.2 | The impact of SARS-CoV-2 infection and medications used for its management on the course of psoriasis

Considering the hyper-inflammatory state and cytokine release along with ACE over-activity occurring in the settings of SARS-CoV-2 infection, psoriasis can be induced or exacerbated by COVID-19.[26,27] Moreover, hydroxychloroquine (HCQ), which was widely utilized in the early days of COVID-19 pandemic, can be trigger psoriasis onset in predisposed individuals or its exacerbation.[28] The pathophysiologic mechanism might be blockade of epidermal transglutaminase activity by HCQ, which results in epidermal barrier break and subsequently psoriasis induction or flare-up. The increased production of IL-17 by HCQ can lead to keratinocyte overgrowth.[29,30] Azithromycin, which was also commonly used in the beginning of the COVID-19 outbreak, may potentially improve psoriatic lesions by its immunomodulatory effect on keratinocytes and epidermal Langerhans cells.[31]

1.3 | Vaccination challenges in patients with psoriasis

Since some individuals with psoriasis are potentially at increased risk of severe COVID-19 due to immunosuppressant agent usage, vaccination against COVID-19 seems to be necessary for this population.[32] However, there are several challenges for vaccinating these patients.

In general, several factors, such as genetic, stress, trauma, drugs and infections, are involved in the introduction or exacerbation of skin disorders, including psoriasis.[33] Reviewing the literature reveals, several cases of de novo psoriasis or disease flare up following SARS-CoV-2 infection.[34–36] Vaccination has also been reported as a triggering factor for the evolution or exacerbation of psoriasis. The vaccine-induced psoriasis is so prevalent that the term "psoriasis vaccinalis" has been suggested for vaccine-induced new-onset psoriasis.[37] New-onset psoriasis or flare-up has been reported following several vaccines, including yellow fever, tetanus-diphteria, BCG, pneumococcal polysaccharide, and influenza vaccines.[38–44] A variety of clinical presentation of psoriasis have been reported in association with the latter vaccines such as plaque, guttate, erythrodermic, and pustular psoriasis.[41,45,46] Accordingly, as the number of SARS-CoV-2 vaccinated psoriasis patients increases, the prevalence of vaccine-induced consequences increases proportionately.[47] Up to the present time, various forms of psoriasis flares, including Similarly, erythrodermic, guttate, plaque, and acute generalized pustular psoriasis have been reported following COVID-19 vaccines.[32,48–53] A case of nail limited psoriasis was also observed.[52] These complications have been observed irrespective of the vaccine platform and reported with various vaccine types such as Oxford-AstraZeneca, BNT162b2, Pfizer-BioNTech, and ChAdOx1 nCoV-19 Corona virus vaccines.[32,51,54,55] Most cases have occurred within 1 month of the vaccine and following the second vaccine dose.[8]

The underlying mechanism could be the immunologic reaction to vaccine adjuvants and immune system dysregulation due to viral component, which may lead to epidermal changes and induction or exacerbation of certain cutaneous disorders such as psoriasis.[38,56] It is believed that induction of neutralizing antibodies and T-cell responses by vaccines can lead to increased TNF-α and interferon (IFN)-γ production.[57] In addition, plasmacytoid and dermal myeloid dendritic cells might be activated with vaccination. All of these conditions can be a trigger for psoriasis cascade.[57,58] Moreover, vaccines might induce IL-6 production, which is the trigger for T helper (Th) 17 cells to produce IL-22, which itself stimulates keratinocyte proliferation, lead to epidermal changes, and consequently psoriasis induction or exacerbation.[56,59] However, it is believed that mRNA vaccines, due to their modifying effect on toll-like receptors, can potentially decrease the risk of exacerbation in autoimmune diseases like psoriasis.[60] Nonetheless, this hypothesis should be proved since several psoriasis flares have been reported following receiving SARS-CoV-2 mRNA vaccines.[32,61] It is also important to know that psoriasis patients on Apremilast, which is a phosphodiesterase (PDE)-4 inhibitor, have not experienced disease flare-up after any of COVID-19 vaccines.[62]

1.4 | The impact of psoriasis treatment regimens on vaccine immune response

Psoriasis is treated with several regimens which have various impacts on vaccine-induced immune response.[63] However, literature review reveals conflicting results about the interaction between vaccines and therapeutics used in psoriasis and other autoimmune disorders.[64] It has been demonstrated that psoriasis patients on systemic treatment, such as secukinumab and other biologics, are protected against vaccine-induced exacerbation, while those who are receiving merely topical treatment are more likely to develop flare-ups following vaccination.[65]

1.5 | The decision to vaccinate psoriasis patients

Despite the small risk of new-onset or flares following vaccination, psoriasis patients are strongly encouraged to receive SARS-CoV-2 vaccines, because vaccine-induced psoriasis, is rare, short-lived, has a favorable prognosis and responds well to standard treatments.[66,67] Moreover, psoriasis patients are at increased risk of severe SARS-CoV-2 infection due to the inflammatory nature of this dermatological disorder and also the immunosuppressive medications they use.[27] Therefore, authorities recommend COVID-19 vaccination in all psoriasis patients without confirmed history of allergy to vaccine or any of its components, particularly individuals on any kind of immunosuppressive treatment.[68] However, it should be kept in mind not to administer attenuated live vaccines in those individual on immunomodulatory/immunosuppressive therapy.[69] In these conditions, non-live vaccines should be considered. Fortunately, none of the currently used SARS-CoV-2 vaccine platforms are live vaccines. Therefore, all psoriasis patients without a history of vaccine allergy or any contraindications, should receive SARS-CoV-2 vaccines as soon as possible.[70]

1.6 | Vaccine response in psoriasis patients on immunosuppressive therapy

The immunosuppressed states, such as those induced by medications, can affect the ability of an individual to mount an effective and long-standing humoral, cellular and innate immunity to vaccines.[71]

It seems that vaccination is well-tolerated in patients with autoimmune disorders like psoriasis, even though the vaccine-induced immunity might be diminished in those individuals on immunosuppressive agents, namely methotrexate or CD20-targeted agents.[72,73] However, real world data suggest that even this sub-optimal reduced response can be effective enough to prevent severe forms of SARS-CoV-2 infection.

The most prevalent therapeutics used for psoriasis management include methotrexate, and biologics which target the cytokines such as TNF and ILs.[74]

Methotrexate, which is an antimetabolite agent and used in several autoimmune dermatoses including psoriasis, had been showed to impair antibody responses to certain vaccines such as influenza and pneumococcal vaccines.[75,76] Studies on serologic response to COVID-19 vaccines showed lower seroconversion rates in vaccinated psoriasis patients who were on methotrexate, compared with healthy individuals. Patients on methotrexate achieve the lowest antibody response after vaccination.[75] It appears that methotrexate dampens the humoral immune response, however, the cellular immune response may be relatively intact. Thus, despite the diminished antibody levels, a relatively favorable vaccine response is expected.[77]

Biologic agents are other therapeutic regimens approved and commonly utilized for psoriasis patients. This class include anti-TNF-α, and anti-ILs including etanercept, infliximab, and secukinumab.[78] The impact of biologic agents on vaccine immunogenicity are more controversial; some studies acknowledge that targeted biologics, especially anti TNF agents, do not impair antibody response to vaccines and psoriasis patients receiving these agents show normal immunogenicity against SARS-CoV-2 vaccination.[79] For example, secukinumab, which is an IL-17A inhibitor, was shown to have no negative effect on vaccine-induced immunity.[80]

Despite all the aforementioned challenges in individuals on immunosuppressant agents, the degree of seroconversion alone does not represent vaccine immunogenicity, since vaccine-induced cellular immunity seems to have a more important role, compared with humoral immunity for achieving protection against respiratory viruses such as influenza and SARS-CoV-2.[81,82] It has been demonstrated that despite the decreased vaccine-induced humoral immune responses in patients receiving B-call depleting agents, T-cell responses are still intact and the mere cellular responses following vaccination may suffice for protection against SARS-CoV-2.[83] Moreover, supposed that COVID-19 vaccines responses are diminished in psoriasis patients on immunosuppressive agents, it is still unclear whether this leads to increased rate of breakthrough SARS-CoV-2 infections.[84] In addition, vaccine immunogenicity in those patients undergoing immunomodulatory agents varies for different SARS-CoV-2 variants. This highlights the need to receive vaccine booster doses.[85]

1.7 | Timing of vaccination in psoriasis patients who are on immune modulators/ immune suppressants

Due to the potential for reduced vaccine immune response in patients receiving immunosuppressive therapy, vaccination status should be assessed prior to initiating these therapeutic regimens.[86]

Guidelines recommend patients on immunosuppressive therapy to receive live vaccines either 2–4 weeks before starting therapy or 1–3 months after stopping or ending therapy. In contrast, non-live vaccines are allowed concomitantly to immunosuppressive therapy.[14] However, different guidelines have various opinions. In general, SARS-CoV-2 vaccination should be ideally completed at least 2 weeks prior to starting immunosuppressive agents. As COVID-19 vaccines doses are administered at least 4 weeks apart, the decision to hold

psoriasis treatment until vaccination completion can have adverse effects on the course of psoriasis, leading to recurrences.[87] Therefore, the risk–benefit should be weighed.

Psoriasis patients are allowed to continue certain immunosuppressive medications, such as biologics during COVID-19 vaccination. These agents are considered safe and noninterfering with vaccine-induced responses and their dosage does not need to be modified before vaccination. Hence, they can safely be administered concomitant with inactive vaccines, unless used along with methotrexate.[88]

Conversely, some authorities recommend psoriasis patients to discontinue treatment with methotrexate during vaccination, due to the diminished antibody response, while some believe it should be stopped 2 weeks before and 2–4 weeks after vaccination.[89] However, due to the risk of exacerbation, some authorities recommend that this agent should be suspended only for 1 week after each vaccine dose.[90] Cyclosporine, a calcineurin inhibitor, despite having similar modifying effect on vaccine response, does not need to be stopped around vaccination time, since it has a relatively short half-life.[91] Mycophenolate mofetil (MMF), it has been shown that temporary holding MMF for at least 1 week helps immune response to COVID vaccination.[92] Azathioprine has a more favorable profile than MMF and cyclosporine in affecting humoral vaccine response, therefore, its continuation seems to be harmless concomitantly with vaccination.[93,94] Apremilast, which is a selective PDE-4 inhibitor and is widely used for psoriasis, seems to have little adverse effect on vaccine-induced immune response due to its immunomodulatory properties. Therefore, it can probably be used before, during and after the vaccination program.[95]

The issue may be somewhat different for timing of treatment with monoclonal antibodies such as rituximab which have seldom been used to treat psoriasis, compared to other dermatoses.[96–99] It is advised to give space between the last rituximab infusion and vaccination, in order for the immune system to reconstitute B cells and achieve higher seroconversion. If patients are not at risk of organ damage or disease relapse, it is better to delay rituximab administration until completion of COVID-19 vaccination.[99] Some guidelines even recommend to postpone vaccination to at least 6 months after the last rituximab infusion.[100] Nonetheless, every patient should be decided individually based on the risk–benefit ratio.

In brief, for achieving the optimal vaccine response, it is recommended that new immunosuppressive/immunomodulatory therapies be initiated at least 1 week after the second SARS-CoV-2 vaccine dose, if possible. In addition, in severe and active forms of psoriasis, it is better to delay vaccination until stabilization of the disease.

Another important point of view is the fact that although vaccine-induced immune responses are attenuated in psoriasis patients receiving immunosuppressive agents, repeating vaccine doses can further increase T-cell responses following vaccination. Therefore, booster doses seems to be beneficial in these patients.[73] However, booster doses might not be given priority in patients under treatment with anti TNF agents due to reaching to an acceptable level of post-vaccine immunity compared to those receiving other immunosuppressant agents.[101]

2 | CONCLUSION

Vaccine-triggered de novo or flares of psoriasis is uncommon and the benefits of vaccinations significantly outweighs the risks, psoriasis patients are strongly recommended to get SARS-CoV-2 vaccines. The majority of post-vaccination psoriasis flare have reported to be relatively mild in severity and responsive to topical treatments. Thus, psoriasis patients can be reassured about the slight risk of psoriasis flare up with COVID vaccination. Some medications, such as anti-TNFs, IL-17 inhibits and apremilast may potentially have protective effect against COVID vaccine-induced flares.

CONFLICT OF INTERESTS

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

All authors contributed to the preparation of data and finalization of this article.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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