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REVIEW ARTICLE

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# COVID-19 vaccines: What dermatologists should know?

Azin Ayatollahi | Hamed Hosseini | Rojin Firooz | Alireza Firooz

Center for Research & Training in Skin Diseases & Leprosy, Tehran University of Medical Sciences, Tehran, Iran

**Correspondence**
Alireza Firooz, MD 415 Taleghani Ave., Center for Research & Training in Skin Diseases & Leprosy, Tehran University of Medical Sciences, Tehran, Iran.
Email: firozali@sina.tums.ac.ir

## Abstract

As COVID-19 vaccination has started worldwide to control this pandemic, dermatologists may face various challenges with these new vaccines. In this manuscript, we review different types of available COVID-19 vaccines and their various production platforms. Vaccination considerations in patients with skin diseases, especially those using immunomodulatory drugs will be presented. Finally, adverse cutaneous reactions of COVID-19 vaccines will be reviewed.

**KEYWORDS**
COVID-19, dermatologist, immunomodulatory drugs, vaccine

## 1 | INTRODUCTION

SARS-CoV-2 is a novel coronavirus causing COVID-19 infection with high infectivity and severe morbidity and mortality. The COVID-19 pandemic urged the world of medicine to conduct multifaceted research leading, among other things, to development of novel vaccine platforms (i.e., mRNA, DNA, non-replicating viral vectors, and so on.).[1]

Since the onset of the pandemic in early 2020, dermatologists have observed that various cutaneous manifestations such as diffuse erythematous eruptions, widespread urticaria, and chickenpox-like vesicles are related to COVID-19.[2]

Now, with the COVID-19 vaccination effort being ramped up around the world, dermatologists also need to become aware of its considerations in patients with skin diseases, as well as possible vaccine-related cutaneous reactions.[3]

This narrative review was performed by searching PubMed up to June 10, 2021, for the COVID-19 vaccine and dermatology practice-related manuscripts.

## 2 | COVID-19 VACCINES

Various approaches to the development of a viral vaccine exist killed whole or split virus vaccines, subunits or single proteins, live-attenuated vaccines, vectored or chimeric virus approaches, naked DNA, and so on.[4]

A year into the pandemic, the global efforts to develop and distribute an effective vaccine have produced several favorable options. Based on the WHO report, until May 15, 2021, there were 100 vaccines in clinical development and 164 vaccines in pre-clinical development. In different countries, eight vaccines have been licensed for emergency use.[5]

The following are the examples of available COVID-19 vaccines:[1]

- Viral vector DNA vaccines: Sputnik V (Russia), Oxford-AstraZeneca (Sweden), Johnson & Johnson (USA).
- mRNA vaccines: Pfizer (BNT162b2, USA), MODERNA (mRNA-1273, USA).
- Whole virus vaccines (inactivated and attenuated vaccines): SINOVAC (China), SINOPHARM (China), BHARAT Covaxin (India).
- Protein subunit recombinant vaccines: NOVAVAX (USA), SOBERANA (Cuba).

## 3 | COVID-19 VACCINATION IN DERMATOLOGICAL DISEASES

The published studies of COVID-19 vaccines have revealed excessive reactogenicity, with fever, headache, and fatigue being more common than in other vaccines. This higher than usual observed side effects may relate to the characteristic inflammatory nature of these vaccines.

Older generation vaccines with lower reactogenicity are still deemed to be triggering flares of dermatological diseases like psoriasis. These observations hint that COVID-19 vaccines might cause flares in patients with dermatological diseases.

These vaccines have been shown to reinforce the cellular immune system and produce a predominantly Th1 type response with high

  

levels of TNFa, IFNg, and IL2. Therefore, theoretically, they may have a role in the flare of dermatological diseases such as psoriasis, lichen planus, vitiligo, and other diseases that have a proven Th1 role in their pathogenesis.[6]

## 4 | ATOPIC DERMATITIS AND OTHER SKIN ALLERGIC DISEASES

There are rare reports of severe allergic reactions to different particles of vaccines in those with a history of allergies. However, it is recommended that all atopic dermatitis (AD) patients and others with allergic skin diseases follow the routine vaccination program. The risk/benefit of vaccination is considered promising for the overall AD population.

Currently, there is no evidence to suggest that AD is an independent risk factor for acquiring SARS-CoV-2, or of having a more severe course of COVID-19. Based on European Task Force for Atopic Dermatitis (ETFAD) recommendation, Atopic dermatitis is not a contraindication to vaccination.

Systemic drugs used to treat AD, except for dupilumab, may attenuate the vaccination response. It is preferable to pausing or lowering the dosage of immunosuppressant agents, typically from the vaccination day until 1 week after for Janus kinase (JAK)-inhibitors and cyclosporine, or until 2 weeks after for methotrexate and azathioprine, to possibly improve chances of appropriate vaccination response.[7]

In selected cases, the use of anti-allergic medication before vaccination, such as antihistamines and oral glucocorticoids, may be helpful. These patients should be observed for 30 min after the vaccine injection. The only contraindication is related to patients with documented severe allergic reactions to ingredients of the vaccine.[8]

## 5 | PSORIASIS

According to National Psoriasis Foundation there is not any contraindication for COVID vaccination in psoriasis patients. The effect of psoriasis treatment on the efficacy of COVID-19 vaccines is not known completely. Based on currently available evidence, it is recommended that patients continue their therapies during the vaccination period.[9]

An observational study of 941 patients (713 psoriasis patients and 228 other patients with bullous disorders, atopic dermatitis, and hidradenitis suppurativa) in Greece, who used immunosuppressive medication, revealed that patients with psoriasis were 32% more willing to receive the vaccine compared with others. Among patients with psoriasis, individuals with concomitant psoriasis arteritis were nearly 20% more likely to undergo COVID-19 vaccination.

Factors such as comorbidities with diabetes, malignancies, and COPD, receiving the biological treatment, younger age, female gender, and higher education are related to the degree of willingness showed by an individual in receiving vaccines.[10]

Pacific et al. recently reported the safety and efficacy of Pfizer and Astra-Zeneca-Oxford vaccines in 3 psoriasis patients treated by apremilast. There was no flare of psoriasis, and the patients had enough SARS-COV2 S1 receptor binding domain antibodies.[11]

Assessing the possible benefits and risks of vaccination suggests that vaccinating all psoriatic patients who are on immunosuppressant drugs, although it may not be as effective as in healthy subjects, still provides some degree of protection against COVID-19. In the face of this pandemic, having some degree of immunity is better than having none. EADV task force on quality of life and patient-oriented outcome recently advised psoriatic patients to receive COVID-19 vaccine and those who had COVID-19 infection to continue following health measures to protect themselves and others.[12]

## 6 | PEMPHIGUS

The ideal timing of vaccination for patients treated by Rituximab, due to the immunosuppressive effect of this drug, is unknown. However, it is recommended that individuals who have not initiated rituximab therapy get vaccinated at least 4 weeks before rituximab infusion. Those who are actively receiving rituximab often receive the influenza vaccine, 12 to 20 weeks after completion of a treatment cycle, so that the patients have at least 4 weeks before their next cycle (assuming a six-month treatment cycle).[13]

## 7 | VACCINATION AND IMMUNOSUPPRESSIVE AGENTS

Three principal vaccine platforms have been used to develop already approved vaccines that are considered safe for patients on immunosuppressive agents: inactivated vaccines, protein subunit vaccines, and virus-like particle vaccines.

At the present time, there is a lack of data of COVID-19 vaccines. Despite this limited knowledge, it appears that COVID19 vaccines would be safe and effective. Some suggest checking the antibody titers after vaccination and using the additional vaccinations, if needed, to boost the level of protective antibodies. Gresham et al. is a comprehensive review that is currently available.[1]

Australian Medical Dermatology Group recommended vaccination against COVID-19 based on the available standard protocols for all patients on immunomodulatory drugs and/or biologic agents. No specific additional risk in this group of patients has so far been identified. Presently, there is inadequate data to recommend one COVID-19 vaccine or vaccine type over another.

If initiation of an immunosuppressive agent is planned, patients should be vaccinated beforehand. Current effective immunomodulatory therapy should not be stopped before vaccination. In patients who are on a biologic agent and have not been vaccinated, it is suggested that vaccination should be administered at least 1 week apart from the biologic dosing and at a different anatomical location.[14]

**TABLE 1** Skin adverse reactions following injection of COVID-19 vaccines

| First author, reference number | Vaccine type | Adverse reaction | Number of patients with reaction | Onset of reaction after vaccine (d = day, h = hour) | Outcome |
|---|---|---|---|---|---|
| McMahon,[17] | Moderna | Local injection site reaction | 143/267 first dose (fd)<br>71/102 second dose (sd) | 0-1d | All reactions were mild and recovered by antihistamines and topical corticosteroids |
| | Pfizer | | 8/34 first dose<br>10/40 second dose | | |
| | Moderna | Delayed large local reaction | 175/267 f.d<br>31/102 s.d | 1-3d | |
| | Pfizer | | 5/34 f.d<br>7/40 s.d | | |
| | Moderna | Urticaria | 13/267 f.d<br>5/102 s.d | 0-2d | |
| | Pfizer | | 9/34 f.d<br>7/40 s.d | | |
| | Moderna | Morbilliform | 11/267 f.d<br>7/102 s.d | — | |
| | Pfizer | | 6/34 f.d<br>3/40 s.d | | |
| | Moderna | Erythromelalgia | 5/267 f.d<br>6/102 s.d | — | |
| | Pfizer | | 1/34 f.d<br>2/40 s.d | | |
| | Moderna | Vesicular | 4/267 f.d<br>1/102 s.d | — | |
| | Pfizer | | 3/34 f.d<br>2/40 s.d | | |
| | Moderna | Pernio/chilblains | 3/267 f.d<br>0 | — | |
| | Pfizer | | 3/34 f.d<br>2/40 s.d | | |
| | Moderna | Zoster | 5/267 f.d<br>0 | — | |
| | Pfizer | | 1/34 f.d<br>4/40 s.d | | |
| | Moderna | Angioedema | 5/267 f.d<br>0 | — | |
| | Pfizer | | 0<br>1/40 s.d | | |
| | Moderna | Pityriasis rosea | 1/267 f.d<br>0 | — | |
| | Pfizer | | 2/34 f.d<br>1/40 s.d | | |
| | Moderna | Erythema multiforme | 3/267 f.d<br>0 | — | |
| | Pfizer | | 0<br>0 | | |
| | Moderna | Filler reaction | 3/267 f.d<br>5/102 s.d | — | |
| | Pfizer | | 0<br>1/40 s.d | | |
| | Moderna | Vasculitis | 2/267 f.d<br>0 | — | |

(Continues)

**TABLE 1** (Continued)

| First author, reference number | Vaccine type | Adverse reaction | Number of patients with reaction | Onset of reaction after vaccine (d = day, h = hour) | Outcome |
|---|---|---|---|---|---|
| | Pfizer | | 1/34 f.d<br>0 | | |
| | Moderna | Contact dermatitis | 3/267 f.d<br>1/102 s.d | – | |
| | Pfizer | | 0<br>2/40 s.d | | |
| | Moderna | Petechiae | 1/267 f.d<br>2/102 s.d | – | |
| | Pfizer | | 1/34 f.d<br>0 | | |
| Corbeddu,[18] | Pfizer | Itchy erythemato-oedematous plaque at injection site | 1/11 f.d | 1d | Mild and very mild |
| | | Erythema & swelling of left foot dorsum | 1/11 s.d | 2d | |
| | | Erythema and itch of face | 1/11f.d | 8d | |
| | | Diffuse erythematous rash | 1/11 s.d | 3d | |
| | | Itchy erythemato-oedematous plaque at injection site | 1/11 f.d | 1 h | |
| | | Erythema of both legs | 1/11 f.d | 1 h | |
| | | Urticaria at injection site | 1/11 f.d | 1 h | |
| | | Diffuse erythematous rash of trunk | 1/11 s.d | 5 h | |
| | | Erythema and swelling of left chest | 1/11 f.d | 7d | |
| | | Diffuse erythematous rash of trunk | 1/11 s.d | 2d | |
| | | Urticarial rash, flare-up of atopic dermatitis | 1/11f.d | 2d | |
| Pileri,[19] | Pfizer | Chilblain lesions | 1, f.d | – | Not worsening by second dose |
| Temiz,[20] | CoronaVac (inactivated virus) | Acral chilblain like lesions | 2, f.d | 7d | Complete improvement after 3 weeks |
| Piccolo,[21] | Pfizer | Chilblain like lesion | 1, s.d | 1d | The lesions were extremely painful, the outcome not mentioned |
| Davido,[22] | Pfizer | Chilblain like lesion | 1, f.d | 4d | 4 weeks after vaccination she remained totally asymptomatic, except for one remaining chilblain-like lesion until 150 days |
| Nawimana,[23] | Pfizer | Flare of preexisting erythema multiforme | 1, f.d & s.d | 12 h (fd), 24 h (sd) | Topical corticosteroid treatment |
| Busto Leis,[24] | Pfizer | Pityriasis rosea | 2, s.d | 1, 7d | Mild, self limited |
| Akdas,[25] | CoronaVac | Pityriasis rosea | 1, f.d | 4d | Mild, self limited |
| Carballido Vazquez,[26] | Pfizer | Pityriasis rosea | 1, f.d & s.d | – | Improvement after 2 weeks. |

**TABLE 1** (Continued)

| First author, reference number | Vaccine type | Adverse reaction | Number of patients with reaction | Onset of reaction after vaccine (d = day, h = hour) | Outcome |
|---|---|---|---|---|---|
| Cyrenne,[27] | Pfizer | Pityriasis rosea | 1/2, f.d<br>1/2;, s.d | 2, 21d | Improvement after 2-3 weeks |
| Cohen,[28] | Pfizer | Leukocytoclastic vasculitis flare | 1, f.d & s.d | 2d | Topical corticosteroids |
| Kharkar,[29] | COVAXIN (inactivated vaccine) | Cutaneous small vessel vasculitis | 1, f.d | 4d | Rest, leg elevation, antihistamine |
| Hiltun,[30] | Pfizer | Lichen planus flare | 1, s.d | 2d | Topical corticosteroids |
| Ackerman,[31] | Pfizer | Persistent maculopapular rash | 1, f.d | 3 h | The rash persisted over a month with a gradual improvement over the days with dermocorticoid treatment |
| Bostan,[32] | CoronaVac | Herpes zoster | 1, f.d | 5d | oral valacyclovir thrice a day for 1 week |
| Lee,[33] | Pfizer | Herpes zoster | 3/20, f.d<br>3/20, s.d | 4-38d | oral valacyclovir |
| | Moderna | | 12/20, f.d<br>2/20, s.d | | |
| Arora,[34] | COVAXIN | Herpes zoster | 1, not mentioned | 4d | valacyclovir three times a day for 7 days |
| Tessas,[35] | Pfizer | Herpes zoster | 1, .fd | — | oral valacyclovir |
| Nanova,[36] | Pfizer | Recurrent varicella | 1, f.d | 7d | — |
| Fernandez Nieto,[37] | Pfizer | Delayed injection site reaction | 49/103, f.d<br>54/103, s.d | Less than 8 hours to more than 3 days | — |
| Gyldenløve,[38] | Pfizer | Recurrent injection-site reactions | 1, f.d (incorrect s.c administration) & s.d | 12d (fd), few hours (sd) | The rash disappeared without treatment |
| Tammaro,[39] | Pfizer | Local reaction on the site of injection | 2/3,s.d<br>1/3 not mentioned | 1d (2/3)<br>7d (1/3) | topical corticosteroid cream |
| Mintoff,[3] | Pfizer | Fixed drug eruption | 1,f.d&s.d | 15d(fd), 14d (sd) | Self-limited |
| Mazzantenta,[40] | Pfizer | Purpuric lesions on eyelids | 1/3 f.d<br>2/3 s.d | 10-21d | Self-limited |
| Afacan,[41] | CoronaVac | Radiation recall dermatitis | 1, f.d | 5d | — |
| Soyfer,[42] | Pfizer | Radiation recall dermatitis | 2, s.d | 5-6d | resolved within a few days |
| Dash,[43] | Not mentioned | Steven-Johnson syndrome | 1, f.d | 3d | oral cyclosporine 300 mg, improved completely after 7 days |
| Onsun,[44] | CoronaVac | Generalized pustular psoriasis flare | 1, f.d | 4d | Intravenous infliximab afforded a complete response |

Literature shows that in patients on nonbiologic immunotherapy most of the available vaccines are safe for administration. Specifically, there is convincing evidence on the safety of nonviral vaccines in dermatologic patients being treated with standard dermatologic doses of immunosuppressives.

Studies reported few vaccine-related adverse reactions in patients receiving biological therapies, although no causal relationship was established between the reported reactions and vaccination.

Despite the potential effect of systemic immune-targeting therapies on reducing the vaccine efficacy in these patients, additional vaccination and/or temporary drug withdrawal are recommended for providing the patients with sufficient protection.[1]

Studies report that systemic corticosteroids cause dose-dependent variable effects on immunity. Many dermatology patients do not receive more than 20 mg/day of prednisone. Since this corticosteroid dose seems to have very little to no effect on patient's

immune response, vaccination, regardless of its type, is also recommended for these patients.[1]

## 8 | COVID-19 VACCINES ANAPHYLAXIS AND SKIN REACTIONS

Vaccination-related risk of anaphylaxis is known to be rare, with approximately 1.31 events per million doses administered.[15] Active ingredients of a vaccine or its excipients are the potential culprits causing allergic and anaphylactic reactions to vaccines.[16]

The cutaneous adverse reactions after COVID-19 vaccines are uncommon. Since the first approved and widely used vaccines are the mRNA vaccines (Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273)), most side-effects reported after vaccination are from this type.

The American Academy of Dermatology's cutaneous vaccine reactions registry has registered 414 patients with a median age of 44 (90% female) with one or more cutaneous reactions. The Moderna vaccine is responsible for 83% of these reactions.

21% reported reactions after the first dose only, 63% reported a reaction after the second dose only, and 16% reported reactions to both doses.

The skin adverse reactions to different COVID-19 vaccines are summarized in table 1.

## 9 | INFLAMMATORY REACTIONS TO DERMAL FILLERS AFTER COVID-19 VACCINATION

Some cases of temporary swelling at the site of previous filler injection were reported after mRNA vaccine injection. These reactions can be immunologically triggered. Because these reactions are rare and temporary, the American Society for Dermatologic Surgery recommended that patients already treated with dermal fillers could receive vaccines of any kind without worry and that those who have injected vaccines should not be disallowed from receiving dermal fillers.[45]

In conclusion, dermatologists should be aware of the different types of COVID-19 vaccines and keep in mind their effects on skin diseases and their cutaneous side effects.

### CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

### DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

### ORCID

*Alireza Firooz* https://orcid.org/0000-0001-7274-4840

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