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SHORT PAPER

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Recommendations for treatment of nail psoriasis during the COVID-19 pandemic

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Abstract

The novel coronavirus disease 2019 (COVID-19) pandemic has resulted in a paradigm shift in disease management. Since immunosuppression may cause increased susceptibility to COVID-19, there is uncertainty as to whether systemically treated nail psoriasis patients are at increased infection risk. While specific data on nail psoriasis treatments and COVID-19 is lacking, we present clinical trial data on rates of upper respiratory infections, nasopharyngitis, viral infection, pneumonia and overall infections. Some systemic medications and biologics are associated with increased in infections risk compared to placebo in clinical trials. However, this data should be regarded cautiously since clinical trials on nail psoriasis, particularly controlled studies, are lacking. Our recommendations may be helpful in guiding physicians managing nail psoriasis patients during the COVID-19 pandemic.

KEYWORDS

biologics, COVID-19, immunosuppression, nail disorders, nail psoriasis, psoriasis, SARS-CoV-2

The rapid dissemination of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19), caused a global pandemic. As immunosuppression is a COVID-19-related mortality risk factor,[1] it is hypothesized that systemically treated psoriasis patients may be more susceptible to COVID-19. Prior efforts focused on cutaneous psoriasis therapy during the pandemic, with no guidelines for nail psoriasis (NP) treatment. Therefore, in this communication, we review the literature and recommend safe and effective NP therapies during the COVID-19 pandemic.

Randomized controlled trials (RCT) reporting on adverse events with NP treatment are scarce. Table 1 lists infection rates in clinical trials involving NP patients.

Tumor necrosis factor-alpha (TNF-α) inhibitors theoretically impair immunity against viral infections,[2] with a black box warning of increased infection susceptibility. Amplified TNF-α levels are implicated in cytokine release syndrome (CRS), the main cause of COVID-19 mortality.[3] Thus, TNF-α blockers may be beneficial for COVID-19-related CRS treatment. There was no increased susceptibility to respiratory infections with TNF-α inhibitors in NP clinical trials.

The interleukin (IL)-17 inhibitors interfere with mucosal immunity against *Candida* infections.[4] As SARS-CoV-2 infects through ocular, airway and oral mucosae, impaired mucosal integrity may increase SARS-CoV-2 susceptibility.[5] In RCTs, secukinumab-treated NP patients had increased nasopharyngitis and overall infections rates were 9.7% and 17%, respectively, compared to placebo. For ixekizumab, compared to placebo, overall infections increased by 7%, while upper respiratory infection (URIs) increased by 4.1%.

Ustekinumab, an IL-12/23 inhibitor, showed 36.1% and 39.5% increases in nasopharyngitis and overall infection rates compared to placebo. Although IL-12 protects against viral infections,[6] patients with inherited IL-12 signaling defects are not severely impacted by viral respiratory infections.[7]

For the Janus kinase (JAK) 1/3 inhibitor tofacitinib, viral infections increased by 13.1%, while URIs increased by 2.3%. Nonetheless, nasopharyngitis and overall infections were comparable to placebo. JAK inhibitors have short half-lives and can be discontinued in the setting of acute infection.[8]

Abbreviations: COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome; IL, interleukin; NP, nail psoriasis; RCT, randomized controlled trial; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TNF-α, tumor necrosis factor-alpha.

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TABLE 1 Rate of infections with immunosuppressive and biologic therapies for NP

Class/drug	Number of patients	Mean age (years)	Upper respiratory infection (drug/control; N [%])	Nasopharyngitis (drug/control; N [%])	Viral infection (drug/control; N [%])	Pneumonia (drug/control; N [%])	Infections, overall (drug/control; N [%])
TNF-α							
Adalimumab[10-14]	347	Unknown	5 (1.4)	None reported	None reported	1 (0.3)	11 (3.2)
Etanercept[11,13]	31	49.6	None reported	None reported	None reported	None reported	None reported
Infliximab[11,13,15]	74	46.6	None reported	None reported	None reported	None reported	None reported
IL-17							
Secukinumab[16,17]	594	44.1	29 (4.9)/8 (6.1)	148 (24.9)/20 (15.2)	0 (0)/4 (3.0)	None reported	281 (47.3)/40 (30.3)
Ixekizumab[18]	115	46.5	9 (7.8)/1 (3.7)	13 (11.3)/5 (19)	None reported	None reported	38 (33.0)/7 (26)
IL-12/23							
Ustekinumab[11,19,20]	187	Unknown	None reported	85 (45.5)/3 (9.4)	None reported	None reported	109 (58.3)/6 (18.8)
Janus kinase 1/3							
Tofacitinib[21,22]	1532	Unknown	80 (5.2)/11 (2.9)	133 (8.7)/34 (8.8)	20 (13.1)/0 (0)	None reported	207 (13.2)/47 (12.2)
Conventional treatments							
Acitretin[23,24]	66	Unknown	None reported	None reported	None reported	None reported	None reported
Methotrexate[25,26]	180	43	12 (6.7)	45 (25)	9 (5)	None reported	105 (58.3)
Cyclosporine[14,26]	56	Unknown	1 (1.8)	None reported	None reported	None reported	2 (3.6)
Apremilast[27,28]	1184	45.6	178 (15.0)/27 (6.5)	163 (13.8)/29 (6.9)	None reported	None reported	343 (29)/56 (13.4)

Note: All superscript numbers in the "Class/drug column" are references provided in Data S1. [10,14]Psoriatic arthritis study involving cutaneous and NP patients. [11-13,15,16,19,23,24]NP study. [17,18,20-22,25-28]Cutaneous psoriasis study involving NP patients.
Abbreviations: IL, interleukin; NP, nail psoriasis; TNF-α, tumor necrosis factor-alpha.

There are no controlled studies on conventional systemic treatments for NP. Cyclosporine showed minimal incidence of URI and overall infections and there were no infections reported with acitretin use. Notably, cyclosporine has anti-coronavirus activity *in vitro*[9]; there are no data on COVID-19 patients. Retinoids inhibit viral replication (human herpesvirus eight, human immunodeficiency one, herpes-simplex one, measles, mumps, polyoma, hepatitis B and hepatitis C viruses) *in vitro*. Methotrexate is associated with a 25% and 58.3% incidence of nasopharyngitis and overall infections, respectively. Therefore, methotrexate should be tapered to the lowest effective dose in patients without COVID-19 during the pandemic; in infected patients, the medication should be discontinued. In cutaneous psoriasis and NP patients treated with apremilast, URIs, nasopharyngitis and overall infections were 8.5%, 6.9% and 15.6% compared to placebo.

There are inherent limitations in extrapolating NP infection rates to COVID-19-related infection susceptibility. NP studies are generally small and controlled studies on NP patients exclusively are virtually non-existent. Studies on cutaneous psoriasis that include NP patients did not report on NP-specific adverse events. Minor infections may be underreported in clinical studies.

There are several other considerations for treatment of NP patients during the pandemic. The mean age of study patients was approximately 45 years; therefore, these recommendations may not be applicable to older individuals, who on average have higher COVID-19-associated mortality.[1] For confirmed COVID-19 infections, conventional systemic and biologics should be discontinued. Biologics generally have longer half-lives than JAK inhibitors, making them less practical in cases of acute infection. When restarting some biologics, there may be decreased efficacy and development of antibodies to the medication.[6] Further studies are needed on NP patients with COVID-19 for definitive guidelines; in the interim, our literature review may guide physicians in making informed treatment decisions for NP patients during the pandemic.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

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