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COVID-19 PANDEMİSİNDE DERMATOLOJİK TEDAVİLER

Sevda ÖNDER[1]

Giriş

Koronavirüs hastalığı (COVID-19), SARS-CoV-2 virüsünün neden olduğu oldukça bulaşıcı, hayatı tehdit edebilen bir hastalıktır. Dünya Sağlık Örgütü tarafından Mart 2020 tarihinde COVID-19 salgını pandemi olarak ilan edildi. Hastalık tüm dünyayı etkiledi, milyonlarca insanın enfekte olmasına ve yüzbinlerce insanın ölümüne neden oldu. Bu ölümlerin çoğu yaşlı, immünyetmezliği olan veya kronik hastalığı olanlarda görüldü (1).

Günümüzde dermatologlar günlük pratiklerinde bir çok farklı kronik dermatozu olan hasta takip etmekte ve bu hastaların bir çoğuna sistemik tedaviler kullanmaktadırlar. Pandemi döneminde dermatologlar sistemik tedavi alan hastalarının SARS-CoV-2 enfeksiyonu riskini en aza indirmek ve dolayısıyla enfeksiyona bağlı oluşabilecek morbidite ve mortaliteyi azaltmak için yeni yaklaşımlar geliştirmeye çalıştılar. Bu nedenle bir çok dermatoloji topluluğu pandemi döneminde dermatolojik hastalıklara ve tedavilere yaklaşımı değerlendiren önerilerde bulundular. Burada COVID-19 pandemisi döneminde dermatoloji pratiğinde sık kullanılan dermatolojik tedavilere yaklaşımı güncel literatür bilgisi ışığında gözden geçirmeyi amaçladık.

COVID-19 Pandemisinde Dermatolojik Tedaviler

Günümüzde bir çok inflamatuvar, immün-mekanizma aracılı veya otoimmün dermatolojik hastalıklarda farklı konvansiyonel tedaviler, biyolojik tedaviler, küçük molekül inhibitör tedavileri dahil olmak üzere çeşitli immünmodulatör tedaviler kullanılmaktadır (2).

Çoğu konvansiyonel immünmodülatör tedavi artmış enfeksiyon riski ile ilişkilidir. Bu risk genellikle doz bağımlı olmakla beraber kullanılan ajana, doza ve altta yatan tedavi edilen hastalığa bağlı olarak değişmektedir. Son zamanlarda çeşitli dermatolojik hastalıkların patogenezinde etkili olan tek molekül veya proteinleri hedefleyen yeni tedavilerin kullanılması immünmodulasyonu daha da selektif hale getirmektedir. Genel olarak bazı biyolojikler ve küçük molekül inhibitörleri ile klinik çalışmalarda üst solunum yolu enfeksiyonlarında artmış hafif risk gösterilmiştir. Ancak bu enfeksiyonlar genellikle hafif ve kendiliğinden iyileşen enfeksiyonlardır ve ciddi enfeksiyon oranları çok düşüktür (3). Ancak pandemi döneminde dermatologlar iki soru ile karşı karşıya kalmıştır. Birincisi bu tedaviler hastaların

[1] Dr Öğr. Üyesi Sevda ÖNDER, Ordu Üniversitesi Tıp Fakültesi, Deri ve Zührevi Hastalıkları AD. drsevdaonder@gmail.com

KAYNAKLAR

1. Yang Y, Peng F, Wang R, et al. The deadly coronaviruses: The 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China.J Autoimmun. 2020;109:102434.
2. Ricardo JW, Lipner SR. Considerations for safety in the use of systemic medications for psoriasis and atopic dermatitis during the COVID-19 pandemic. Dermatol Ther. 2020;33:e13687.
3. Wang C, Rademaker M, Baker C, et al. COVID-19 and the use of immunomodulatory and biologic agents for severe cutaneous disease: An Australian/New Zealand consensus statement. Australas J Dermatol. 2020 61:210-216.
4. Yim RM, Singh I, Armstrong AW. Updates on treatment guidelines for psoriasis, atopic dermatitis (eczema), hidradenitis suppurativa, and acne/rosacea during the COVID-19 pandemic. Dermatol Online J. 2020 15;26:13030
5. Aljebab F, Choonara I, Conroy S. Systematic Review of the Toxicity of Long-Course Oral Corticosteroids in Children. PLoS One. 2017 ;26;12:e0170259.
6. Ni YN, Chen G, Sun J, et al. The effect of corticosteroids on mortality of patients with influenza pneumonia: a systematic review and meta-analysis. Crit Care. 2019:23:99.
7. Jung C, Inder WJ. Management of adrenal insufficiency during the stress of medical illness and surgery. Med. J. Aust 2008;188: 409–13.
8. McLean-Tooke A, Aldridge C, Waugh S et al. Methotrexate, rheumatoid arthritis and infection risk- what is the evidence. Rheumatology 2009; 48: 867–871.
9. Ibrahim A, Ahmed M, Conway R et al. Risk of infection with methotrexate therapy in inflammatory diseases: A systemic review and meta-analysis. J Clin Med. 2018;8; pii: E15.
10. Lopez-Olivo MA, Siddhanamatha HR, Shea B et al. Methotrexate for treating rheumatoid arthritis. Cochrane Database Syst. Rev. 2014: CD000957.
11. Berth-Jones J, Exton LS, Ladoyanni E et al. British Association of Dermatologists guidelines for the safe and effective prescribing of oral ciclosporin in dermatology 2018. Br. J. Dermatol. 2018; 180: 1312-38.
12. Krupp P, Monka C. Side-effect profile of cyclosporine A in patients treated for psoriasis. Br. J. Dermatol. 1990; 122: 47–56.
13. De Wilde A, Raj VS, Oudshoorn D et al. MERS-coronavirus replication induces severe in vitro cytopathology and is strongly inhibited by cyclosporine A or interferon-alpha treatment. J. Gen. Virol. 2013; 94: 1749–1760.
14. Dávila-Seijo P, Dauden E, Descalzo MA, et al. BIOBADADERM Study Group. Infections in Moderate to Severe Psoriasis Patients Treated with Biological Drugs Compared to Classic Systemic Drugs: Findings from the BIOBADADERM Registry. J Invest Dermatol. 2017;137(2):313-321.
15. Goujon C, Viguier M, Staumont-Sallé D, et al. Methotrexate Versus Cyclosporine in Adults with Moderate-to-Severe Atopic Dermatitis: A Phase III Randomized Noninferiority Trial. J Allergy Clin Immunol Pract. 2018;6:562-569.e3.
16. American Academy of Dermatology Association. Managing your practice through the COVID-19 outbreak. https://www.aad.org/member/practice/managing/coronavirus adresinden 29/12/2020 tarihinde girilmiştir.
17. International Psoriasis Council. Statement on the coronavirus (COVID-19) outbreak. https://www.psoriasiscouncil.org/blog/State adresinden 29/12/ 2020 tarihinde girilmiştir.
18. Bernatsky S, Hudson M, Suissa S. Anti-rheumatic drug use and risk of serious infections in rheumatoid arthritis. Rheumatology. 2007;46:1157-60.
19. Anstey AV, Wakelin S, Reynolds NJ. Guidelines for the prescribing azathioprine in dermatology. Br. J. Dermatol. 2004; 151: 1123–32.
20. Caufield M, Tom WL. Oral azathioprine for recalcitrant pediatric atopic dermatitis: clinical response and thiopurine monitoring. J Am Acad Dermatol. 2013;68:29-35.
21. Berth-Jones J, Takwale A, Tan E, et al. Azathioprine in severe adult atopic dermatitis: a double-blind, placebo-controlled, crossover trial. Br J Dermatol. 2002 ;147:324-330.
22. Schneeweiss MC, Perez-Chada L, Merola JF. Comparative safety of systemic immuno-modulatory medications in adults with atopic dermatitis. J Am Acad Dermatol. 2019;S0190-9622(19):30877-1.
23. Ritter ML, Pirofski L. Mycophenolate Mofetil: effects on cellular immune subsets, infectious complications, and anti-microbial activity. Transpl. Infect. Dis. 2009; 11: 290–297.
24. Pilkington T, Brogden RN. Acitretin : A Review of its Pharmacology and Therapeutic Use. Drugs. 1992;43:597-627.
25. Dommasch ED, Kim SC, Lee MP, et al. Risk of Serious Infection in Patients Receiving Systemic Medications for the Treatment of Psoriasis. JAMADermatol.2019:155:1142–1152.
26. Caselli E, Galvan M, Santoni F, et al. Retinoic acid analogues inhibit human herpesvirus 8 replication. Antivir Ther. 2008;13:199-209.
27. American Academy of Dermatology. Taking isotretinoin during the coronavirus pandemic. https://www.aad.org/public/diseases/acne/derm-treat/isotretinoin/coronavirus-pandemic adresinden 29/12/2020 tarihinde girilmiştir.
28. Crowley J, Thaci D, Joly P, et al. Long-term safety and tolerability of apremilast in patients with psoriasis: pooled safety analysis for ≥156 weeks from 2 phase 3, randomized, controlled trials (ESTEEM 1 and 2). J Am Acad Dermatol. 2017;77:310-317 e1.
29. Warren RB, Smith CH, Yiu ZZN, et al. Differential drug survival of biologic therapies for the treatment of psoriasis: a prospective observational cohort study from the British Association of Dermatologists Biologic Interventions Register (BADBIR). J Invest Dermatol. 2015;135:2632-2640.
30. National Psoriasis Foundation.NPF Forms COVID-19

Task Force 2020.https://www.psoriasis.org/advance/coronavirus 29/12/2020 tarihinde girilmiştir.
31. European Academy of Dermatology and Venerology. Management of Psoriasis Patients Under Systemic Treatments 2020. https://www.eadv.org/cmsadmin/showfile/7_PSORIASISSPIN%20TF%20Recommandations_Covid-Corner.pdf 29/12/2020 tarihinde girilmiştir.
32. Lebwohl M, Rivera-Oyola R, Murrell DF. Should biologics for psoriasis be interrupted in the era of COVID-19? J Am Acad Dermatol. 2020 ;82:1217-1218.
33. Yiu ZZN, Ashcroft DM, Evans I, et al. Infliximab is associated with an increased risk of serious infection in patients with psoriasis in the U.K. and Republic of Ireland: results from the British Association of Dermatologists Biologic Interventions Register (BADBIR). Br J Dermatol. 2019;180:329-337.
34. Yiu ZZN, Smith CH, Ashcroft DM, et al. Risk of serious infection in patients with psoriasis receiving biologic therapies: a prospective cohort study from the British Association of Dermatologists Biologic Interventions Register (BADBIR). J Invest Dermatol. 2018;138:534-541.
35. Kalb RE, Fiorentino DF, Lebwohl MG, et al. Risk of Serious Infection With Biologic and Systemic Treatment of Psoriasis: Results From the Psoriasis Longitudinal Assessment and Registry (PSOLAR). JAMA Dermatol. 2015;151:961-969
36. Burlando M, Carmisciano L, Cozzani E, et al. A survey of psoriasis patients on biologics during COVID-19: a single centre experience. J Dermatolog Treat. 2020 ;25:1.
37. Carugno A, Gambini DM, Raponi F, et al. COVID-19 and biologics for psoriasis: A high-epidemic area experience-Bergamo, Lombardy, Italy. J Am Acad Dermatol. 2020 ;83:292-294.
38. Conti A, Lasagni C, Bigi L, et al. Evolution of COVID-19 infection in four psoriatic patients treated with biological drugs.J Eur Acad Dermatol Venereol. 2020;34:e360-e361.
39. Damiani G, Pacifico A, Bragazzi NL, et al. Biologics increase the risk of SARS-CoV-2 infection and hospitalization, but not ICU admission and death: Real-life data from a large cohort during red-zone declaration. Dermatol Ther. 2020;33:e13475-e13481
40. Gisondi P, Facheris P, Dapavo P, et al. The impact of the COVID-19 pandemic on patients with chronic plaque psoriasis being treated with biological therapy: the Northern Italy experience. Br J Dermatol. 2020 ;183:373-374.
41. Monteleone G, Sarzi-Puttini PC, Ardizzone SJTLR. Preventing COVID-19-induced pneumonia with anticytokine therapy. Lancet. 2020;2:E255-E256.
42. Deodhar A, Mease PJ, McInnes IB, et al. Long-term safety of secukinumab in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis: integrated pooled clinical trial and post-marketing surveillance data. Arthritis Res Ther. 2019; 21:111.
43. Saunte DM, Mrowietz U, Puig L, Zachariae C. Candida infections in patients with psoriasis and psoriatic arthritis treated with interleukin- 17 inhibitors and their practical management. Br J Dermatol. 2017; 177:47-62.
44. Gordon KB, Papp KA, Langley RG, et al. Long-term safety experience of ustekinumab in patients with moderate to severe psoriasis (part II of II): results from analyses of infections and malignancy from pooled phase II and III clinical trials. J AmAcadDermatol. 2012;66:742-751.
45. Megna M, Napolitano M, Patruno C, et al. Biologics for psoriasis in COVID-19 era: What do we know? Dermatol Ther. 2020;33(4):e13467. doi: 10.1111/dth.13467
46. Eichenfield LF, Bieber T, Beck LA, et al. Infections in dupilumab clinical trials in atopic dermatitis: a comprehensive pooled analysis. Am J Clin Dermatol. 2019;20:443-456.
47. *Busse WW, Morgan WJ, Gergen PJ, et al.* Randomized trial of omalizumab (anti-IgE) for asthma in inner-city children. N Engl J Med. 2011; *364:* 1005-1015.
48. *Teach SJ, Gill MA, Togias A, et al.* Preseasonal treatment with either omalizumab or an inhaled corticosteroid boost to prevent fall asthma exacerbations. J Allergy Clin Immunol. 2015; *136:* 1476-1485.
49. Klimek L, Pfaar O, Worm M, et al. Use of biologicals in allergic and type-2 inflammatory diseases during the current COVID-19 pandemic: Position paper of Ärzteverband Deutscher Allergologen (AeDA)[A], Deutsche Gesellschaft für Allergologie und Klinische Immunologie (DGAKI)[B], Gesellschaft für Pädiatrische Allergologie und Umweltmedizin (GPA)[C], Österreichische Gesellschaft für Allergologie und Immunologie (ÖGAI) [D], Luxemburgische Gesellschaft für Allergologie und Immunologie (LGAI)[E], Österreichische Gesellschaft für Pneumologie (ÖGP)[F] in co-operation with the German, Austrian, and Swiss ARIA groups[G], and the European Academy of Allergy and Clinical Immunology (EAACI) [H]. *Allergol Select*. 2020;4:53-68.
50. Welsch K, Holstein J, Laurence A, Ghoreschi K. Targeting JAK/STAT signalling in inflammatory skin diseases with small molecule inhibitors. Eur J Immunol. 2017;47:1096-1107.
51. Peterson D, Damsky W, King B. The use of Janus kinase inhibitors in the time of SARS-CoV-2. J Am Acad Dermatol. 2020;82:e223-e226.
52. Mease P, Hall S, FitzGerald O, et al. Tofacitinib or adalimumab versus placebo for psoriatic arthritis. N Engl J Med. 2017;377:1537- 1550.
53. Papp KA, Menter MA, Abe M, et al. Tofacitinib, an oral Janus kinase inhibitor, for the treatment of chronic plaque psoriasis: results from two randomized, placebo-controlled, phase III trials. Br J Dermatol. 2015;173:949-961.
54. Schmidt E. Rituximab as first-line treatment of pemphigus. Lancet. 2017;389:1956-1958.
55. Joly P, Maho-Vaillant M, Prost-Squarcioni C, et al. First-line rituximab combined with short term prednisone versus prednisone alone for the treatment of pemphigus (Ritux 3): a prospective, multicentre, parallel-group, open-label randomised trial. Lancet. 2017;389:2031- 2040.
56. Atkinson JR, Bergmann CC. Protective humoral im-

munity in the central nervous system requires peripheral CD19-dependent germinal center formation following coronavirus encephalomyelitis. J Virol. 2017;91:e01352.
57. Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host–virus interaction, and proposed neurotropic mechanisms. ACS Chem Nerosci. 2020;11:995-998.
58. Kasperkiewicz M, Schmidt E, Fairley J, et al. Expert recommendations for the management of autoimmune bullous diseases during the COVID-19 pandemic. J Eur Acad Dermatol Venereol. 2020;34:e302- e303.
59. Elmas ÖF, Demirbaş A, Türsen Ü, et al. Pemphigus and COVID-19: Critical overview of management with a focus on treatment choice. Dermatol Ther. 2020 : 3:e14265.