CEO Clinical and Experimental Otorhinolaryngology Vol. 15, No. 2: 125-126, May 2022
https://doi.org/10.21053/ceo.2022.00612
pISSN 1976-8710 eISSN 2005-0720

Editorial

Application of Biologics in Treating Chronic Rhinosinusitis With Nasal Polyps in Asian Populations

Dae Woo Kim · Seung Koo Yang

Department of Otorhinolaryngology-Head and Neck Surgery, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul National University College of Medicine, Seoul, Korea

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a relatively common inflammatory disorder, diagnosed when nasal obstruction or rhinorrhea lasts for more than 12 weeks and signs of inflammation are identified via nasal endoscopy or computed tomography [1]. The pathophysiology of CRSwNP has been studied and elucidated over the past two decades via *in vitro* experiments and analyses of cytokines in nasal tissues from patients. The role of type 2 inflammation was brought to light, as the severity of type 2 inflammation is related to comorbid lower respiratory tract diseases, such as asthma, and the severe form of chronic rhinosinusitis accompanied by nasal polyps [2].

New therapeutic strategies, such as biologics or reboot surgery, were introduced as a response to treat the recalcitrant nature of severe type 2 CRSwNP, which often shows a poor response to traditional treatment. The prevalence of type 2 inflammation in CRSwNP and severe type 2 inflammation related to severe infiltration of eosinophils and neutrophils with staphylococcal enterotoxin-specific immunoglobulin E in Asian population is below 50% and 4.4%–11.2%, respectively [3], much lower than in Western populations [4]. In addition, a study proposed that the response of type 2 CRSwNP to surgery is very much different from that of non-type 2 CRSwNP [5], and as a result, the role of biologics in treating CRSwNP in Asian populations seemed to be limited.

However, the use of dupilumab and omalizumab, which were recently approved for the treatment of CRSwNP in South Korea, has led to some interesting findings. Postoperative steroid-dependent anosmia, independent of disease severity, is one of many symptoms in type 2 CRSwNP patients and is an unresolved problem even in Asian populations with a relatively low prevalence of type 2 CRSwNP. Olfactory dysfunction greatly diminishes patients' quality of life and is not well controlled with surgical treatment [6]. In such patients, the postoperative use of a systemic corticosteroid in a repetitive manner may result in a variety of adverse drug reactions, prompting a need to switch to biologics. Interestingly, patients with olfactory dysfunction usually have low disease burden, as the extent of the nasal polyp or disease entity is often limited to the olfactory cleft. As a result, such patients respond well to biologics, as the first couple of doses can dramatically slow down nasal polyp formation and improve olfaction.

Monoclonal antibodies are usually eliminated by proteolytic catabolism, because their size exceeds the glomerular filtration cut-off threshold, and their distribution is limited to vascular and interstitial spaces due to their large size and hydrophilicity [7]. Considering that monoclonal antibodies are eliminated partly via target-mediated clearance, the number of target molecules in patients with a low disease burden is presumably small, which also means that extending the dosing interval can result in the maintenance of a certain degree of therapeutic effects. A randomized, double-blind phase 3 trial of dupilumab demonstrated that there was no statistically significant difference in efficacy between a group of patients treated with dupilumab every 2 weeks for 52 weeks and another group of patients treated with dupilumab every 2 weeks for 24 weeks and every 4 weeks for the remaining 28 weeks [8]. This result suggests the possibility of extending dosing intervals in CRSwNP patients after lowering the disease

• Received May 4, 2022
Accepted May 9, 2022

• Corresponding author: **Dae Woo Kim**
Department of Otorhinolaryngology-Head and Neck Surgery, Seoul Metropolitan Government Seoul National University Boramae Medical Center, 20 Boramae-ro 5-gil, Dongjak-gu, Seoul 07061, Korea
Tel: +82-2-870-2446, Fax: +82-2-831-2826
E-mail: kicubi73@gmail.com

burden to a certain degree. In fact, there have been attempts at adjusting dosing intervals for conditions other than CRSwNP [9].

In summary, establishing a dosing strategy based on patients' disease burden can certainly result in an individualized approach in treating CRSwNP with biologics, which would provide substantial benefits for Asians with CRSwNP, who tend to show low disease burden and mild to moderate type 2 inflammation, and would contribute to securing the cost-effectiveness of biologics for CRSwNP treatment.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Dae Woo Kim https://orcid.org/0000-0001-5166-3072
Seung Koo Yang https://orcid.org/0000-0003-3519-7395

AUTHOR CONTRIBUTIONS

Conceptualization: DWK. Data curation: DWK. Formal analysis: DWK. Methodology: DWK. Project administration: DWK. Writing–original draft: DWK. Writing–review & editing: SKY.

REFERENCES

1. Stevens WW, Schleimer RP, Kern RC. Chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol Pract. 2016 Jul-Aug;4(4): 565-72.
2. Bachert C, Akdis CA. Phenotypes and emerging endotypes of chronic rhinosinusitis. J Allergy Clin Immunol Pract. 2016 Jul-Aug;4(4): 621-8.
3. Yao Y, Zeng M, Liu Z. Revisiting Asian chronic rhinosinusitis in the era of type 2 biologics. Clin Exp Allergy. 2022 Feb;52(2):231-43.
4. Zhang Y, Gevaert E, Lou H, Wang X, Zhang L, Bachert C, et al. Chronic rhinosinusitis in Asia. J Allergy Clin Immunol. 2017 Nov;140(5): 1230-9.
5. Kim SY, Park JH, Rhee CS, Chung JH, Kim JW. Does eosinophilic inflammation affect the outcome of endoscopic sinus surgery in chronic rhinosinusitis in Koreans? Am J Rhinol Allergy. 2013 Nov-Dec;27(6):e166-9.
6. Calus L, Van Bruaene N, Bosteels C, Dejonckheere S, Van Zele T, Holtappels G, et al. Twelve-year follow-up study after endoscopic sinus surgery in patients with chronic rhinosinusitis with nasal polyposis. Clin Transl Allergy. 2019 Jun;9:30.
7. Kamath AV. Translational pharmacokinetics and pharmacodynamics of monoclonal antibodies. Drug Discov Today Technol. 2016 Sep-Dec;21-22:75-83.
8. Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, Lee SE, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. Lancet. 2019 Nov;394(10209):1638-50.
9. Lee Y, Kim ME, Nahm DH. Real clinical practice data of monthly dupilumab therapy in adult patients with moderate-to-severe atopic dermatitis: clinical efficacy and predictive markers for a favorable clinical response. Allergy Asthma Immunol Res. 2021 Sep;13(5): 733-45.