Will Biological Therapy become a Game Changer in Chronic Rhinosinusitis

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Chronic rhinosinusitis (CRS) poses a significant burden on the global health. The incidence of CRS is 5-12 % in the western world. The understanding about chronic rhinosinusitis has changed considerably over the years. The currently available treatment options like antibiotics, corticosteroids and surgery provide relief in most of the patients. However, a subset of patients come with recalcitrant disease. Recurrent chronic rhinosinusitis with nasal polyposis (CRSwNP) present a depressing situation to the treating clinician.

Though much remains unknown about the exact biochemical pathways for polyp formation, it is clear that T-helper 2 (Th2) inflammation and its associated cytokines, interleukin-4 (IL-4), IL-5 and IL-13, play a significant role.[1]

Biologics are monoclonal antibodies developed through recombinant technology. They act by targeting a specific protein considered important in the pathogenesis of a disease.[2] Three biological options approved by the FDA for the treatment of nasal polyps' target type 2 inflammation via different approaches. Omalizumab is a monoclonal antibody to immunoglobulin E (IgE); dupilumab works against the alpha subunit receptor for interleukin-4 (IL-4), consequently causing blockade of IL-4 and IL-13; and mepolizumab is an anti-interleukin-5 monoclonal antibody.

Omalizumab was initially approved by the FDA for the treatment of chronic idiopathic urticaria and moderate to severe asthma. Its use for nasal polyps was theorized based on the high nasal tissue expression of IgE in this condition. Two randomized phase 3 trials (POLYP 1 and POLYP 2) were conducted for use in nasal polyps and concluded in 2020.[3] Dupilumab was first approved for noncontrolled moderate to severe atopic dermatitis. Two randomized phase 3 trials on use in nasal polyps (LIBERTY NP SINUS 24 and LIBERTY NP SINUS 52) were concluded in 2019.[4] Mepolizumab was first approved for severe eosinophilic asthma and is also approved for patients with eosinophilic granulomatosis with polyangiitis (EGPA). A randomized phase 3 trial (SYNAPSE 52) for nasal polyps was concluded in 2021.[5]

Based on EPOS 2020[6] and the EPOS/EUFOREA update on biologics 2023[7] the EUFOREA expert panels recommend biologics in CRSwNP patients that are uncontrolled despite appropriate medical treatment and appropriate sinus surgery and who fulfil 3 of 5 criteria (presence of Type 2 inflammation, regular need for systemic corticosteroids (SCS)/contra-indications to SCS, significant impact on QOL, loss of smell and comorbid asthma)

Despite strong evidence for the efficacy of dupilumab in treating polyps, factors such as cost and uncertain efficacy over surgery have limited its use to patients who have failed the use of topical nasal steroids and initial surgical management. There are arguments against the widespread use of biologicals.[8] First, biologics have

not been found superior to endoscopic surgery in the recent studies. Surgery gives a better reduction in the disease load than biologicals. Second, initial studies have shown better safety profile but allergic reactions and other side-effects have been reported. Long term safety data is still pending. Third, cost is a concern in our part of the world considering the long duration of treatment that is needed.

Further elaboration is needed on the underlying fact that biological therapy is beneficial to a subset of patients with recalcitrant disease. Judicious use of this treatment will reap benefits. Cost reduction and ensuring treatment compliance will make it a useful option in the management of recalcitrant and recurrent CRSwNP.

END NOTE

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