Efficacy of plasma kallikrein inhibitors in the long-term prophylaxis of hereditary angioedema in patients treated at the Otorhinolaryngology Department of Šibenik-Knin County General Hospital

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Hereditary angioedema (HAE) is a rare genetic disorder characterized by the swelling of the extremities, genitals, and abdomen, as well as a potentially life-threatening swelling of the upper airways. Depending on the mutated gene and the concentration and activity of the C1 inhibitor, several types of the disease are distinguished, all sharing a similar clinical presentation and treatment approach. To prevent angioedema (AE) attacks, patients with high disease activity (swelling of the upper airways or abdomen three or more times per month) require long-term prophylaxis (LTP), while patients with mild disease activity only require treatment with specific therapies (C1 inhibitor concentrates, bradykinin inhibitors) during acute attacks. Until June 2024, only attenuated androgens were available for LTP in Croatia, which in women caused side effects such as permanent voice changes, virilization, and others. Since then, modern drugs for LTP, plasma kallikrein inhibitors (PKI), have also become available. We examined the efficacy of PKI in patients with a previously confirmed diagnosis of HAE type 1 (low concentration and function of C1 inhibitor, SERPING1 gene mutation) treated at the ENT Department of Šibenik-Knin County General Hospital (GH). We analyzed the disease activity in eight patients with HAE who had already been receiving LTP with attenuated androgens for at least four months (according to the Croatian Health Insurance Fund criteria for the use of high-cost medicines) and identified four female patients with high disease activity (all had confirmed upper airway swelling) who met the criteria for switching to LTP with PKI. Three patients received lanadelumab, a monoclonal antibody for subcutaneous administration once monthly during the first four months and, after the reevaluation of efficacy, once monthly. One patient had been receiving therapy for the past 14 months, and the other two for five months. During that time, they experienced no breakthrough AE attacks. The fourth patient had been taking berotralstat tablets once daily for the past four months and experienced two breakthrough attacks, which was considered to meet the criteria for the continuation of therapy. Apart from mild redness at the injection site and mild nausea during the first 10 days of treatment in the patient on oral therapy, no serious side effects have been observed.

Key words: angioedema, lanadelumab, berotralstat