Azelastine HCl Common and Emerging Uses

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Azelastine HCl, Common Uses

Azelastine is commercially available as both a nasal spray and ophthalmic drop for management of seasonal allergic rhinitis and conjunctivitis in adults and pediatric patients.1,2 Combination azelastine and fluticasone nasal sprays are also available and approved in adult and pediatric patients.3 Azelastine is a phthalazinone derivative with antihistamine H1 receptor antagonist activity.3 Histamine 1 (H1) receptors are present throughout the body. In the lungs they meditate bronchoconstrictive effects and increase vascular permeability, they are also present on various immune cells including T cells, B cells, monocytes, and lymphocytes where activation of these receptors can induce pro-inflammatory effects.4

Though azelastine is commercially available as a solo agent and in combination with fluticasone, it has also been studied in combination with other active pharmaceutical ingredients (APIs) to improve management of allergic rhinitis. One study evaluated combination azelastine and mometasone in an animal model with induced allergic rhinitis. The study found that azelastine and mometasone combination had a synergistic effect on allergic inflammation as compared to the azelastine and mometasone alone groups.5 Later studies evaluated the potential of this combination in humans. One study in pediatric patients evaluated combination azelastine 0.1% at two sprays twice daily with mometasone 50mcg nasal spray once in the morning compared with the same dose of azelastine alone. Symptoms of allergic rhinitis after two weeks of treatment were lower for the combined therapy group as opposed to the group treated with azelastine alone.6 Studies evaluating fluticasone/azelastine combinations compared to mometasone/azelastine combinations are not currently available, however, studies of fluticasone vs mometasone have noted a trend towards greater improvement in

allergy symptoms with mometasone as compared to fluticasone, though, the difference did not reach the level of statistical significance.7 Another steroid that has been studied in conjunction with azelastine is budesonide. One randomized, double-blind, placebo-controlled cross-over study of patients suffering from seasonal rhinitis evaluated budesonide 32mcg, azelastine 137mcg in combination applied nasally noted significant improvement in allergic ocular symptoms as compared to the placebo.8 Though head to head data is limited and mixed, some studies suggest budesonide once daily is significantly better at controlling symptoms of allergic rhinitis, such as nasal blockage, than fluticasone, which is the only steroid currently available in a combination product with azelastine.9 A second meta-analysis aimed at determining the difference in safety or efficacy among nasal corticosteroids for allergic rhinitis concluded that mometasone and triamcinolone have the greatest benefit-to-risk ratio followed by budesonide then fluticasone propionate.10 Patients struggling to find relief with existing azelastine/fluticasone combination products could potentially benefit from the use of an alternative steroid in combination with azelastine.

In addition to steroid combinations, azelastine has also been studied in combination with steroids and vasoconstrictors in triple agent combinations. One study of azelastine in combination with triamcinolone and oxymetazoline in 97 patients found the combination product was rated by patients to be superior for sinus pressure relief.11

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Azelastine has a long history of use for allergic conditions, however, new evidence is emerging that it may have some antiviral activity as well. Though the mechanism of action of azelastine's antiviral effect has yet to be fully elucidated, some sources posit that the mechanism is related to phospholipidosis (modulation of lipid processing pathways) demonstrated by azelastine at low concentrations.12 Modulation of lipid processing pathways is critical for viral replication, and inhibition of phospholipid production has been shown to inhibit viral replication including replication of coronaviruses.13 In vitro data evaluating the impact of SARS-CoV-2 infection on human cells found that exposure to diluted azelastine HCl nasal spray containing just 0.02% azelastine inhibited viral propagation.12 Follow up studies have evaluated the impact of azelastine HCl in vivo. One study in 90 SARS-CoV-2 positive patients evaluated placebo vs 0.02% azelastine HCl vs 0.1% azelastine nasal spray applied one puff per nostril three times daily testing viral load each day by quantitative PCR. By day 8, 18.52% of the azelastine 0.1% group and 21.43% of the azelastine 0.02% group presented with negative PCR results as compared to 0% of the placebo group with all groups reporting comparable numbers of adverse events.14

This research has recently been expanded to other viruses as well. One in vitro study evaluated azelastine HCl activity against other respiratory viruses including respiratory syncytial virus A (RSV A) and H1N1 influenza virus. The human tissue models showed that azelastine protected tissue integrity and function and was able to reduce viral load and inhibit viral replication of both viruses.15

Azelastine HCl has robust data to support its use alone and in various combination products for management of seasonal allergies. Emerging data suggests potential expanded utility in patients with viral illness as well, though, more data in human models is still needed. If you have further questions on current and emerging data on azelastine HCl or would like to review existing formulas, head to www.fagronacademy.us to get started!

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