A randomized trial of icatibant in ACE-inhibitor-induced angioedema.

Angioedema induced by treatment with angiotensin-converting-enzyme (ACE) inhibitors accounts for one third of angioedema cases in the emergency room; it is usually manifested in the upper airway and the head and neck region. There is no approved treatment for this potentially life-threatening condition. In this multicenter, double-blind, double-dummy, randomized phase 2 study, we assigned patients who had ACE-inhibitor-induced angioedema of the upper aerodigestive tract to treatment with 30 mg of subcutaneous icatibant, a selective bradykinin B2 receptor antagonist, or to the current off-label standard therapy consisting of intravenous prednisolone (500 mg) plus clemastine (2 mg). The primary efficacy end point was the median time to complete resolution of edema. All 27 patients in the per-protocol population had complete resolution of edema. The median time to complete resolution was 8.0 hours (interquartile range, 3.0 to 16.0) with icatibant as compared with 27.1 hours (interquartile range, 20.3 to 48.0) with standard therapy (P=0.002). Three patients receiving standard therapy required rescue intervention with icatibant and prednisolone; 1 patient required tracheotomy. Significantly more patients in the icatibant group than in the standard-therapy group had complete resolution of edema within 4 hours after treatment (5 of 13
vs. 0 of 14, P=0.02). The median time to the onset of symptom relief (according to a composite investigator-assessed symptom score) was significantly shorter with icatibant than with standard therapy (2.0 hours vs. 11.7 hours, P=0.03). The results were similar when patient-assessed symptom scores were used. Among patients with ACE-inhibitor-induced angioedema, the time to complete resolution of edema was significantly shorter with icatibant than with combination therapy with a glucocorticoid and an antihistamine. (Funded by Shire and the Federal Ministry of Education and Research of Germany; ClinicalTrials.gov number, NCT01154361.).