in the treatment group compared with the control group in 1 trial but not the other (1 trial, n=40; MD 6.3; 95% CI, 1.5–11; and 1 trial, n=29; MD –1.6; 95% CI, –9.4 to 6.2). A significant improvement was noted in serum ferritin level in the treatment groups of both trials (MD 51 µg/L; 95% CI, 34–69; and MD 17 µg/L; 95% CI, 7.5–27).[2]

A 2001 RCT (n=557) compared the efficacy of iron supplementation once daily with 3 times daily in anemic children (ages 6–24 months; hemoglobin values 7–9.9 g/dL).[3] Patients were randomized to ferrous sulfate drops 40 mg once daily or 40 mg divided in 3 equal doses daily for 2 months.

Mean hemoglobin levels significantly increased from baseline to final visit for both groups (8.8 to 10.2 g/dL and 8.7 to 10 g/dL, respectively, *P*<.001) as did mean ferritin levels (35 to 101 µg/L and 40 to 107 µg/L, respectively, *P*<.001). The percentage of patients advancing from an anemic to a nonanemic state was similar for both the once daily and 3 times daily groups (61% and 56%, respectively, *P*=.51).[3]

Thomas W. Allen, DO, MPH
Douglas Ivins, MD
Kristina Petsas, MD
Jason Chung, MD
University of Oklahoma School of Community Medicine
Tulsa, OK

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Are angiotensin receptor blockers (ARBs) safe to use in patients with a history of angiotensin-converting enzyme inhibitor (ACEI)–induced angioedema?

Evidence-Based Answer

The use of an ARB is not contraindicated in patients with a history of ACEI-induced angioedema. A cautious trial of ARBs by these patients appears to be safe (SOR: **B**, RCTs).

A 2008 RCT of patients intolerant to ACEIs randomized 5,926 patients to telmisartan 80 mg/d (n=2,954) or placebo (n=2,972) to assess the primary outcome of cardiovascular (CV) death, myocardial infarction (MI), stroke, or hospitalization for congestive heart failure (CHF); it also measured angioedema recurrence.[1] The mean follow-up duration was 56 months.

Of the 75 patients with angioedema as the reason for initial intolerance (1.3% of the study population), there was 1 recurrence in the placebo group and none in the ARB group. There were 2 new cases of angioedema in the ARB group (0.07%) and 2 new cases in the placebo group (0.07%).[1]

A 2003 RCT of patients intolerant to ACEIs randomized 2,028 patients to candesartan 32 mg/d (n=1,013) or placebo (n=1,015) to assess the primary outcome of CV death or hospitalization for CHF; it also measured angioedema recurrence.[2] The mean follow-up was 33.7 months.

Of the 83 patients with angioedema as the reason for initial intolerance (4.1% of the study population), there were 3 recurrences in the candesartan group, with 1 patient discontinued from treatment, and none in the placebo group. There were no new cases of angioedema in either group.[2]

In a 2011 retrospective cohort study of 111 patients with a history of ACEI-induced angioedema, 59 were switched to an ARB, 31 to a calcium channel blocker (CCB), 11 to a beta-blocker (BB), and 7 to another antihypertensive agent.[3] Patients were followed for a minimum of 12 months after ACEI discontinuation.

Of the 59 patients who were switched to an ARB, 31 (53%) had a recurrence of angioedema. However, 16 of the 31 (52%) patients prescribed CCBs and 5 of the 11 (45%) patients prescribed BBs also had a recurrence, suggesting that the episodes may have been independent of the antihypertensive agent. No statistical analysis was performed on the data.[3]

Amanda Wojtusik, PharmD, BCPS
Providence Medical Group
Portland, OR

Soo Jung Lee, MD
Heritage Valley Health System
Beaver Falls, PA

Stephen A. Wilson, MD, MPH, FAAFP
UPMC St. Margaret
Pittsburgh, PA

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