Characterising Endovascular Profiles in ACE Inhibitor-Induced Angioedema in a South African Cohort

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BACKGROUND AND AIMS

Angiotensin-converting enzyme inhibitor-induced angioedema (AE-ACEI) is more frequent in Black African populations.[1,2] Although bradykinin (BK) is central to current models, incomplete response to B2 receptor antagonism[3] suggests additional inflammatory and endothelial activation mechanisms during acute attacks.
The authors' aim was to characterise inflammatory and endothelial markers in AE-ACEI cases by measuring plasma and serum profiles during acute episodes and recovery, compared with ACEI-tolerant controls.[4]

MATERIALS AND METHODS

Over 4 years, 54 patients with AE-ACEI were sampled during acute episodes (AE) and at follow-up (FU; 3–6 months post-AE), alongside 91 ACEI-tolerant matched controls (MC; median [interquartile range]: 10.4 [7.9] years on ACEI). Plasma BK, secreted phospholipase 2 (sPLA2), and vascular endothelial growth factor (VEGF) were quantified by ELISA. Serum tryptase and total IgE were measured using UniCAP fluoroimmunoassay. C-reactive protein (CRP), D-dimer, and fibrinogen were processed at the local National Reference Laboratory. A total of 92 inflammation-related proteins were profiled using proximity extension assay (Olink®, Thermo Fisher Scientific, Waltham, Massachusetts, USA). Wilcoxon testing with correction for multiple comparisons was applied.

RESULTS

Plasma BK levels were significantly higher in AE-ACEI cases, at both AE and FU, compared to MC. During AE, VEGF and sPLA2 levels were increased relative to FU and MC for VEGF only. Total IgE (measured only AE) was higher in AE-ACEI cases compared to MC. Acute CRP, D-dimer, and fibrinogen levels were elevated

relative to FU and MC. Proteomic analysis demonstrated a distinct acute endovascular signature. Pairwise comparison between AE and FU revealed increased EN-RAGE and OSM in AE samples, accompanied by vascular permeability and repair mediators (VEGFA, HGF), and endothelial–immune interaction markers (TNFSF14/LIGHT, CD40, TGF-α). Importantly, FU samples did not differ from MC after multiple-testing correction, indicating resolution of the acute proteomic signature.

CONCLUSION

AE-ACEI is characterised by a transient, attack-specific endovascular inflammatory programme involving RAGE-axis activation, endothelial permeability mediators, and immune–endothelial crosstalk, rather than isolated BK excess. The absence of proteomic differences at FU supports a reversible, event-locked vascular inflammatory process. Further work is required to understand distinct endotypes and compare with other acute angioedemas.

References

1. Brown NJ et al. Black Americans have an increased rate of angiotensin converting enzyme inhibitor-associated angioedema. Clin Pharmacol Ther. 1996;60(1):8-13.
2. Burkhart DG et al. Angiotensin converting enzyme inhibitor-associated angioedema: higher risk in blacks than whites. Pharmacoepidemiol Drug Saf. 1996;5(3):149-54.
3. Jeon J et al. Effect of icatibant on angiotensin-converting enzyme inhibitor-induced angioedema: a meta-analysis of randomized controlled trials. J Clin Pharm Ther. 2019;44(5):685-92.
4. Pedretti S et al. Characterising endovascular profiles in ACE inhibitor–induced angioedema in a South African cohort. Abstract 100370. EAACI Congress, 12-15 June, 2026.