Dokumenttyp: journal article

Autor(en) des Beitrags:
Bas, M; Kirchhartz, N; Hochfeld, J; Tüllmann, C; Kumpf, S; Suvorava, T; Oppermann, M; Hafner, D; Bier, H; Hoffmann, TK; Balz, V; Kojda, G

Titel des Beitrags:
Potential role of vasomotor effects of fibrinogen in bradykinin-induced angioedema.

Abstract:
BACKGROUND: Although bradykinin is known to play a major role in the pathophysiology of hereditary and angiotensin-converting enzyme inhibitor (ACEi)-induced angioedema, other factors acting as triggers or enhancers are likely important as well. OBJECTIVE: We hypothesized that fibrinogen might contribute to ACEi-induced angioedema (eg, through direct actions on vascular tone). METHODS: Plasma levels of fibrinogen were determined in 59 patients with acute angioedema. Vascular activity of human and bovine fibrinogen and its effects on bradykinin-induced vasodilation and phosphorylation of vasodilator-stimulated phosphoprotein were investigated in small (0.8-1.4 mm in diameter) porcine coronary artery and human internal thoracic artery (ITA) segments. RESULTS: In patients with ACEi-induced angioedema, fibrinogen levels (481 +/- 22 mg/dL, n = 39) were significantly higher than in patients with idiopathic angioedema (302 +/- 15 mg/dL, P< .001). Fibrinogen (1-15 mumol/L) induced a concentration-dependent vasodilation in preconstricted small porcine coronary arteries (n = 13), reaching a maximum vasodilator effect of 70% +/- 4.7%. Likewise, fibrinogen induced a 52.1% +/- 9.1% (n = 7) vasodilation in ITA rings. Fibrinogen vasorelaxations were completely inhibited by abciximab and diminished by endothelial denudation and
treatment with the nitric oxide synthase inhibitor L-nitroargininemethylester and glibenclamide (P< .01). Importantly, fibrinogen increased the vasodilator potency of bradykinin by 10-fold (P< .0001) and increased bradykinin-induced vasodilator-stimulated phosphoprotein phosphorylation (P< .01).

CONCLUSION: The increase of plasma fibrinogen levels, its vasodilator activity in human ITAs, and the potentiation of bradykinin-induced vasodilation suggest that fibrinogen might contribute to the pathophysiology of ACEi-induced angioedema. Thus acute-phase proteins, such as fibrinogen, might be viewed as risk factors for bradykinin-induced angioedema.