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Introduction and aims: Hyperbradykininemia was reported in case of angioedema and dry cough as an adverse effect of angiotensin-converting-enzyme (ACE) inhibitors. There is a possibility that the choking sensation, shortness of breath, or smothering sensation in anxiety neurosis could be induced by bradykinin (BK). We sought to examine plasma-BK concentration of Generalized Anxiety Disorder (GAD) and postulated a new concept of anxiety disorders.

Methods: We identified 11 GAD patients. All subjects had signed written informed consent. We measured inflammatory markers (WBC, ESR, CRP), C1-inhibitor activity and circulating BK (normal values : < 10.0 pg/ml). Anxiety was measured using the Hamilton Anxiety Rating Scale (HAM-A).

Results: No abnormalities were found in WBC, ESR, CRP and C1-inhibitor activity. There were substantial rises in BK in GAD with a mean plasma-BK concentration of 100.1 pg/ml (SD=44.6). There was a significant correlation between HAM-A and plasma-BK concentration in the 11 GAD patients, expressed by the regression: $BK=5.10(HAM-A)-51.5$, $r=0.62$, $p<0.05$.

Conclusions: 11 GAD patients did not have any focal infection but presented hyperbradykininemia and free-floating anxiety. The symptoms of free-floating anxiety could be explained by the nature of BK which acts to produce pain, vasodilation, increased vascular permeability, and synthesis of prostaglandins. Therefore, GAD may be termed a diffuse nociceptive state, or an incomplete inflammatory state uncoupling from other inflammatory markers.