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PLASMA BRADYKININ LEVEL IS RELATED TO ANGIOTENSIN-CONVERTING ENZYME INHIBITION AND GENE POLYMORPHISM IN HYPERTENSIVE PATIENTS

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Background: Bradykinin is a vasodilator which may be involved in the pathophysiology of hypertension. Angiotensin converting enzyme (ACE) mediates its degradation. As ACE activity is affected by an insertion/deletion polymorphism of the gene and by ACE inhibitors, we investigated if plasma bradykinin level is related to these factors.
Methods: 34 patients with essential hypertension (19 men, 15 women; mean age 55, range 35-76) were studied with informed consent. Venous blood (3 ml) was drawn from a forearm vein into pre-chilled polypropylene tubes containing protease inhibitors. These samples were promptly centrifuged and the plasma stored at -40°C. Plasma bradykinin was measured by radioimmunoassay. DNA was extracted from the buffy coat and amplified by polymerase chain reaction (PCR) using specific primers. The insertion and deletion alleles were identified as separate bands after electrophoresis of PCR products.
Results: Mean plasma bradykinin level was 48.1 $\pm$ 4.9 pmol/l in these patients. Plasma bradykinin level correlated with ACE genotype ($r = 0.36$, $p = 0.046$) and use of an ACE inhibitor ($r = 0.42$, $p = 0.02$), but was not related to age or gender. In multiple regression analysis, 19% of the variance was accounted for by ACE genotype and ACE inhibition ($R = 0.44$, $p = 0.036$).
Conclusions: Our results suggest that the insertional genotype and ACE inhibitor usage are associated with higher plasma bradykinin level in hypertensive patients. Further studies are needed to clarify the role of bradykinin in cardiovascular diseases in man.

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PLASMA LEVEL OF ADRENOMEDULLIN IS ELEVATED IN SYSTEMIC LUPUS ERYTHEMATOSIS

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Adrenomedullin (AM) is a peptide hormone first isolated from phaeochromocytoma and the adrenal medulla. It is synthesised in the vascular endothelium and circulates in plasma. Cytokines including TNF-α and IL-1β stimulate its secretion. Plasma AM is markedly increased in endotoxic shock, whilst transgenic mice overexpressing AM are resistant to endotoxic shock, suggesting that AM interacts with the immune system. We therefore investigate its role in a systemic autoimmune disease.

47 patients with systemic lupus erythematosis (SLE) (mean age 38 yrs, range 24-61 yrs; 46 females, 1 male) and 23 normal healthy subjects were studied. The immunoreactivity of human AM in the plasma was measured using a specific radioimmunoassay (lower limit of detection 2 pg/tube, coefficient of variation 7%).

The mean plasma AM level in normal subjects was 8.1 $\pm$ 1.0 pmol/l and 26.0 $\pm$ 3.5 pmol/l patients with SLE ($p<0.0001$). The increase in plasma AM level was not explained by known factors including hypertension, heart failure, renal failure, respiratory diseases, liver disease, diabetes and pregnancy. Moreover, plasma AM level in SLE patients correlated with DNA titre ($r = 0.39$, $p = 0.008$) and SLE disease activity index ($r = 0.35$, $p = 0.04$). Immunosuppressive drugs (prednisolone, azathioprine and cyclophosphamide) tended to normalise AM levels in patients with active disease.

In conclusion, the plasma level of AM is elevated in patients with SLE and correlates with disease activity. AM may have a role in the pathophysiology of SLE.