

Regulatory peptides in clinical diagnosis

ELVAR THEODORSSON

Regulatory peptides are biologically active peptides present in specific endocrine cells widespread e.g. in the gastrointestinal tract or in neurones of both the central and peripheral nervous systems, frequently in co-existence with monoamines. Regulatory peptides present in nervous tissues are called neuropeptides.

Regulatory peptides appear in peptide families united by a common sequence of amino acids and similar biological activities. Furthermore, peptides are synthesised as large precursor molecules which are cleaved to smaller biologically active forms by specific enzymes or modified by addition of chemical groups. The immunological methods used to monitor peptide concentrations are usually specific for a small sequence of the peptide, a sequence which may be present in other family members. This means that when we mention the concentration or the biological activities of a regulatory peptide we frequently mean the overall impact of the peptide family in question, including precursor forms and metabolites.

The first regulatory peptide characterised was secretin described by Bayliss and Starling in 1902. The past two decades have seen an explosive increase in the number of regulatory peptides characterised. Their number is now well above 50. Regulatory peptides are believed to be involved in the regulation of a very large number of biological processes including nerve transmission in the central and in the peripheral nervous systems, control of the heart and the blood circulation, regulation of gastrointestinal functions, growth and many others. In nerve cells neuropeptides are synthesised in the cell body and it takes days or weeks for them to be transported to the site of release in the axon or dendrites of the neurone. This probably means that neuropeptides mainly serve a function of fine-tuning the function of neurones closely interacting with the monoamines contained in the neurones.

Regulatory peptides in endocrine tumours

Since regulatory peptides are involved in a multitude of biological functions it would be logical for their functions to be deranged in a number of diseases. Measuring their concentrations in biological fluids could therefore

potentially be of diagnostic importance. However, measuring regulatory peptides has hereto only been found clinically useful in few but important clinical conditions. These are mostly neoplastic conditions, mainly endocrine tumours originating in cells of the gastrointestinal tract including carcinoid tumours, endocrine pancreatic tumours, multiple endocrine neoplasias, pheochromocytoma and neuroblastoma. Recent increase in the knowledge of the biopathological characteristics of the endocrine tumours has brought new treatment modalities some of which are based on treatment effects on peptidergic systems. Survival time is prolonged and there is an increased need for reliable tumour markers monitoring an increasing number of patients.

The sensitivity and specificity of the diagnosis of peptide producing endocrine tumours can be considerably improved if timed samples are taken in relation to symptoms, or stimulation tests are applied e.g. by meal or injection of pentagastrin.

Regulatory peptides in non- endocrine disease states

Recent evidence indicates, however, that measurement of regulatory peptides can be of clinical importance in other and more common clinical conditions. Our own studies have shown that children with acute lymphoblastic leukaemia of B-precursor differentiation present with high concentrations of neuropeptide Y (NPY) in plasma correlating closely with the expression of CALLA (CD10) on leukaemic blasts. High concentrations of NPY in the plasma of these children correlated with a favourable prognosis in leukaemia. In children with leukaemia and lymphoma of B-cell precursor differentiation, plasma concentrations of NY followed the clinical course with decreased concentrations at remission and increase at relapse.

Atrium natriuretic peptide (ANP) is a peptide secreted from the atrial myocytes as a result of atrial distension. Acting as a paracrine agent and as a hormone ANP increases sodium and water excretion by the kidneys, thus acting as an endogenous diuretic. Mounting evidence indicates that elevated plasma concentrations of ANP constitute a very

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