

Regulatory peptides in renal failure: effects and possible pathophysiological role

Regulatory peptides are present in most of the tissues of the body where they are stored in and released from widespread specific endocrine cells and neurons. Regulatory peptides are believed to participate in the regulation of several body functions including digestion, respiration, kidney functions, mental functions, cardiovascular functions and response to injury. The kidneys play an important role in the metabolism and excretion of several regulatory peptides (1-3), and many regulatory peptides regulate or modulate kidney functions, either directly by acting on the glomerulus and tubular systems (4, 5) or indirectly by acting on the cardiovascular system, renin-angiotensin-aldosterone system, the antidiuretic hormone or the adrenergic or cholinergic nervous systems. Kidney dysfunction, therefore, results in derangement (usually elevations) of peptide concentrations in plasma. Furthermore, renal failure and hemodialysis are frequently accompanied by symptoms from several organ systems, some of which may be partly due to elevated concentrations of regulatory peptides in the circulation. Of particular interest in this context are the cardiovascular, renal, gastrointestinal and inflammatory effects of regulatory peptides known to be present in elevated concentrations in renal failure.

Chronic renal failure is frequently associated with hypertension, and hypotensive episodes may develop during hemodialysis. Vasoactive regulatory peptides are likely to play a role in the pathogenesis of these cardiovascular symptoms. Several regulatory peptides have powerful effects on the motility and secretory mechanisms of the gastrointestinal tract. Elevated plasma concentrations of these peptides may contribute to the anorexia, nausea and diarrhea associated with renal failure. Itching, a distressing symptom of renal failure, is frequently associated with secondary hyperparathyroidism, which, however, cannot be the sole pathogenetic mechanism of this symptom. Interestingly, several regulatory peptides which are present

in elevated plasma concentrations in renal failure have been shown to participate in inflammatory reactions in the skin, and cause itching upon local injection in the skin.

The purpose of the present brief presentation is to bring together information about regulatory peptides in renal failure, with emphasis on the renal, cardiovascular and gastrointestinal systems and on symptoms which may be due to derangement of the peptidergic transmitters. The well known important role of the renin-angiotensin-aldosterone system in this respect will only be briefly mentioned whereas emphasis will be on the more recently discovered peptides atrium natriuretic peptide (ANP), calcitonin gene-related peptide (CGRP), endothelin, neurokinin B (NPY), vasoactive intestinal polypeptide (VIP) and the tachykinins (TK). ANP because of its established role in sodium and volume regulation under conditions of chronic fluid overload and NPY, VIP, tachykinins, CGRP and endothelin because of their unequivocal presence in perivascular nerve structures. Several of these latter regulatory peptides are believed to participate in the non-adrenergic, non-cholinergic nervous control of the cardiovascular nervous system, in control of secretory mechanisms and smooth muscle functions as well as in inflammatory reactions. Furthermore, since drugs which decrease the plasma concentrations of regulatory peptides have become available recently for use in humans, the potential benefit of these drugs in selected patients with renal failure will be discussed.

Renal metabolism of regulatory peptides

Metabolism and excretion of regulatory peptides in the kidneys accounts for a major fraction of their total metabolic clearance rate in mammals (6, 7). Inactivation of regulatory peptides in the kidney is accomplished by at least three different mechanisms; a) endocytosis by the proximal tubular cells by a

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