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Urodilatin, the renal natriuretic peptide: preclinical and clinical review

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Pre-Clinical background

Natriuretic peptides were identified as regulatory diuretic-natriuretic substances responsible for salt and water homeostasis and as hormones lowering blood pressure. Urodilatin is a natriuretic peptide type A which is synthesized in the kidney and generated from the prohormone ANP-1-126. While the circulating ANP-99-126 is synthesized in the heart atrium and processed during exocytosis Urodilatin (ANP-95-126) is differentially processed in the kidney and detected only in urine.

Physiologically, Urodilatin acts in a paracrine fashion. After release from distal tubular kidney cells into the tubular lumen, Urodilatin binds to luminal NPR-A-receptors in the collecting duct resulting in a cGMP-dependent signal transduction. cGMP generation is followed by an interaction with the amiloride-sensitive sodium channel which induces diuresis and natriuresis. In this way, Urodilatin regulates fluid balance and sodium homeostasis. Moreover, Urodilatin excretion and natriuresis are in turn dependent on different physiological states, such as directly on sodium homeostasis.

Animal models were used to further investigate Urodilatin's clinical potential. Urodilatin given intravenously in acute renal failure-models induced strong diuretic and natriuretic effects while in congestive heart failure beneficial hemodynamic effects were demonstrated. Urodilatin was also shown to relax bronchi in animal models with drug-induced bronchoconstriction. These renal, pulmo-

nary, and cardiovascular effects indicated that Urodilatin is a putative drug for several related diseases.

Clinical background

Urodilatin was then used in the treatment and prophylaxis of acute renal failure following major surgery and heart transplantation. A first pilot study in patients with acutely decompensated heart failure demonstrated beneficial hemodynamic effects of Urodilatin and treatment of asthmatic patients showed beneficial effects of Urodilatin on pulmonary function such as an increase in forced expiratory volume.

Conclusion

Urodilatin is a natriuretic peptide synthesized in the kidney. Based on its pharmacological profile Urodilatin is a promising drug-candidate for different clinical indications.