Farmacologia Cardiovascolare dei Donatori di Ossido d'Azoto (NO): Prospettive Terapeutiche

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NITRIC OXIDE AND RENAL DAMAGE

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Nitric Oxide (NO), a gaseous free radical derived from *L*-arginine, is a potent modulator of vascular tone and platelet functions. A number of recent studies, both in the experimental model of renal mass reduction (RMR) in rats and in uremic patients, have raised the hypotesis that abnormalities of NO synthetic pathway could have a key role in mediating the complex hemodynamic and hemostatic disorders associated to the progression of renal disease. Thus, kidneys from rats with RMR produce less NO than normal rats and NO generation negatively correlates with markers of renal damage. The abnormality is due to a strong defect of inducible NO synthase (iNOS) content in the kidney. Recent in vitro and in vivo data have raised the possibility that excessive renal synthesis of the potent vasoconstrictor and promitogenic peptide endothelin-1 (ET-1) is a major determinant for progressive iNOS loss in the kidney of RMR rats.In contrast, uremia is associated with excessive systemic NO release, both in experimental model and in human beings. In the systemic circulation of uremic rats, as well as uremic patients, NO is formed in excessive amounts. Possible cause of the increased NO levels is higher release from systemic vessels due to the augmented expression of both iNOS and endothelial NOS. A putative cause for excessive NO production in uremia can be guanidinosuccinate, an uremic toxin that accumulates in the circulation of uremic patients and upregolates NO synthesis from cultured endothelial cells. Upregolation of systemic NO synthesis might be a defense mechanism against hypertension of uremia. On the other hand, more NO available to circulating cells may sustain the bleeding tendency, a well-known complication of uremia.