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Early diagnosis and preventive treatments for the progression of renal fibrosis[1]

Press release from the French National Academy of Medicine

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Chronic kidney disease (CKD) affects more than 10% of the world's population. Its continuous expansion results from several causes, including aging, diabetes and high blood pressure to which can be added genetic and autoimmune diseases (1). Whatever its origin, the progression of CKD follows identical mechanisms leading to end-stage renal failure which requires substitution treatment by dialysis or kidney transplantation consuming up to 2.5% of the Health Insurance budget (1).

One of the main mechanisms of deterioration of renal function is the extension of renal fibrosis, which results from a chronic inflammatory process leading to an accumulation of extracellular matrix and the irreversible loss of functional nephrons. The cell responsible for fibrosis is the myofibroblast, which produces pro-fibrosis molecules. The chronic, persistent inflammation of kidney tissue attracts polymorphonuclear cells and macrophages that evolve from a pro-inflammatory to a pro-fibrotic phenotype (2).

Early diagnosis of chronic kidney disease, and ideally of renal fibrosis, is essential, as the drugs currently available can slow its progression and delay the switch to replacement therapy:

- Angiotensin II (Ang II) inhibitors, the direct action of Ang II on fibrogenesis having been shown (3);

- Inhibitors of sodium-glucose cotransport in the proximal tubule (SGLT2 inhibitors), initially used in diabetes, which reduce morbidity and mortality by 20 to 30 % in CKD patients (4);

[1] Press release from the Academy's Rapid Communication Platform.

- Glucagon-like peptide 1 receptor (GLP1R) agonists reducing proteinuria, slowing the loss of renal function (5) without severe side effects;

- Endothelin receptor inhibitors and, even more so, mixed endothelin and Ang II receptor inhibitors, such as sparsentan, whose efficacy would be linked to the dual blockade that they induce (6);

- Finally, more recently, non-steroidal mineralocorticoid receptor blockers, notably finerenone (not available in France) (7), initially recommended for the treatment of CKD associated with type 2 diabetes, which reduce the risk of progression of renal failure by slowing the extension of fibrosis.

Clinical experience leads to combining some of these drugs, the diversity of their mechanisms of action allowing a personalized approach. New molecules, whose effects are being tested in therapeutic trials, target other molecules involved in fibrogenesis, such as TGF-β or other signaling pathways; reduction of Ang II production by inhibiting hepatic angiotensinogen synthesis; inhibition of tyrosine kinase receptors involved in the development of fibrosis; selective antagonism of macrophage recruitment.

Faced with the public health burden of CKD, the National Academy of Medicine underlines the importance of:

- Detecting patients with diabetes, hypertension, dyslipidemia or with a history of cardiovascular disease, and therefore at risk of renal failure as early as possible, by using routine urinary and plasma biomarkers (albuminuria and plasma creatinine), but also by developing non-invasive renal investigations (8);

- Instituting a treatment for at-risk patients to avoid or limit their progression towards end-stage renal failure.

- Combining therapeutic trials with the use of cohort studies (9);

- Strengthening research on the mechanisms of fibrosis development, with a view to adapting treatment to the specific features of renal fibrosis in each patient, and reinforcing the efficacy of current drugs (tissue targeting) (10, 11).

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