NEW THERAPEUTIC STRATEGIES UNDER DEVELOPMENT TO HALT THE PROGRESSION OF RENAL FAILURE

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OBJECTIVES

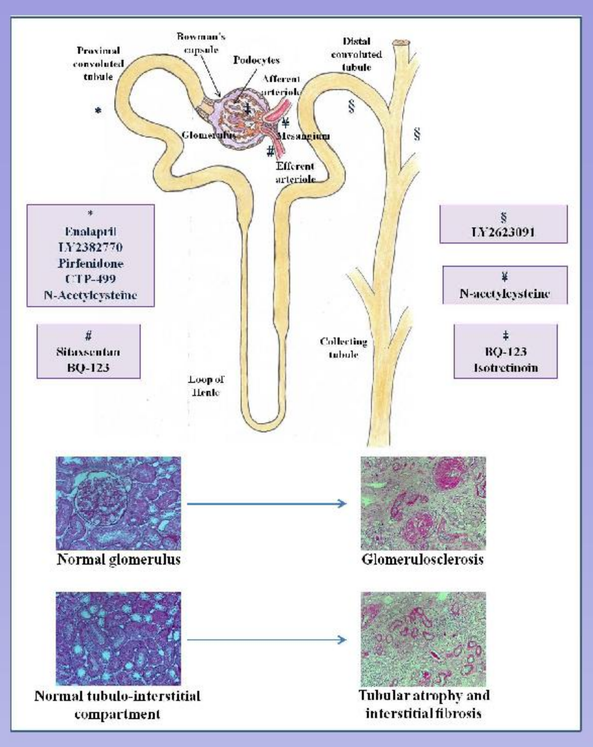
Chronic kidney disease (CKD) is a global concern since its incidence is constantly increasing. Accordingly, prevention of CKD onset and progression is mandatory. Since pharmacological agents already used in clinical practice are not yet able to halt the progression of renal damage, new therapeutic strategies are currently explored. We carried out a systematic review on phase 1/2 clinical trials, already concluded or ongoing, which aim at evaluating the safety and efficacy of novel therapeutic approaches to CKD[1].

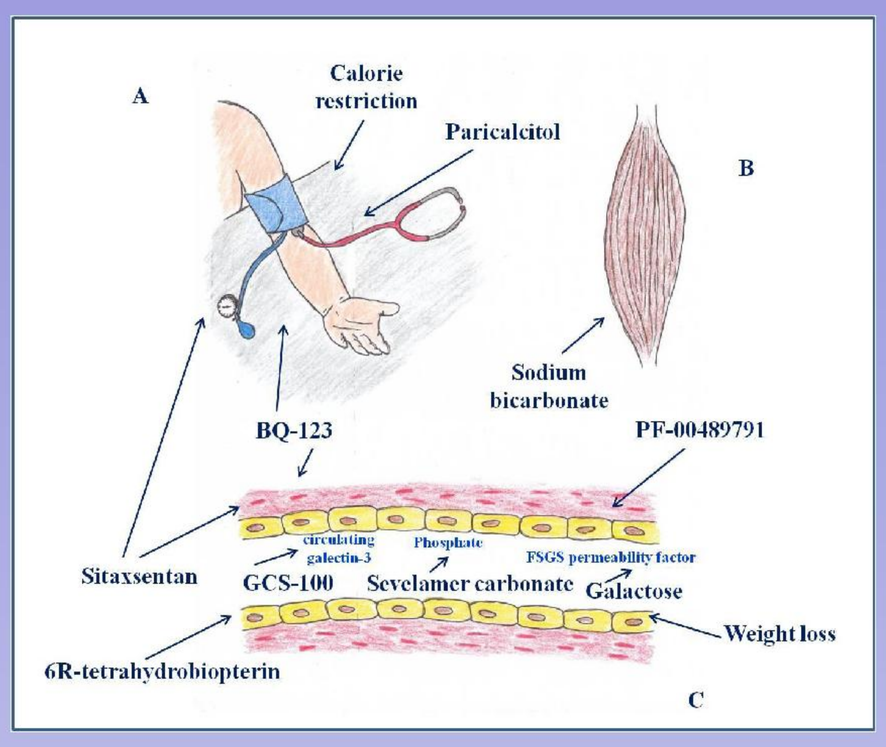
METHODS

We performed the research through November 2013. Data were retrieved from scientific literature and from the ClinicalTrials.gov registry. We used the "advanced search" section of the ClinicalTrials.gov website and filled in the "search terms" field with the expression "chronic kidney disease"; then we selected "adult" and "senior" among the age groups, "phase 1" and "phase 2" as type of studies of interest, and all fields regarding funder type, namely "NIH", "Other U.S. Federal Agency", "Industry", and "All others (Individual, University, Organization, ...)". By doing so, we obtained 238 records and among them, two expert nephrologists manually selected 44 clinical trials which specifically explored the drugs used to arrest the progression of renal disease. Then, we searched for the existence of publications related to the inserted clinical trials on Pubmed to get more information.

RESULTS

Several drugs are currently under investigation due to their supposed anti-proteinuric action, such as selective endothelin-A receptor antagonists or vitamin D analogues. Other drugs are being studied in CKD because of their anti-fibrotic, anti-inflammatory and anti-oxidative properties (e.g. LY2382770, pirfenidone and CTP-499) or due to the hypothetical ability to repair damaged podocytes (e.g. isotretinoin and BQ-123). A fascinating therapeutic approach involves the use of progenitor/stem cells. In most cases, studies have not yet been completed; some trials have been concluded but results are not available so far.





CONCLUSIONS

Numerous clinical trials are evaluating new strategies to halt the progression of CKD. Many of them aim primarily at identifying pharmacological agents able to reduce proteinuria, a significant factor of progression of renal damage. Other drugs under investigation are thought to exert anti-fibrotic, anti-inflammatory and anti-oxidative effects that could interfere with tubulo-interstitial fibrosis. A further field of research is the use of stem cells that should repair renal tissue after an injury. We are still far from application of stem cells in clinical practice but remarkable progresses have been achieved in the understanding of their biology and behaviour as well as in the procedures required to mobilize and activate endogenous stem-cells in damaged kidneys or to introduce exogenous stem cells for tissue repair. If these studies report positive results, nephrologists will be provided with the opportunity to slow down CKD progression, a constantly increasing serious health issue worldwide which is associated with high morbidity and mortality.

REFERENCES:

1. Cernaro V et al. Expert Opin Investig Drugs. 2014;23(5):693-709.

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H) Clinical Nephrology, CKD. H5) Pathophysiology and clinical studies in CKD 1-5.
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