Perspective
Volume 6:4, 2022

Journal of Formulation Science & Bioavailability

ISSN: 2577-0543 Open Access

A More Tubulocentric Perspective on Diabetic Kidney Disease

David Sane*

Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

Introduction

Diabetic nephropathy is the most typical cause of ESRD in the Western world. Early-stage diabetes causes changes to the kidney's structure and function, and these changes have an ongoing effect on future renal function as well as the onset and development of overt diabetic nephropathy. In-depth research on these early structural and functional changes, including kidney hypertrophy and glomerular hyperfiltration, has been done in diabetes animal models. Both are thought to be the initial causes of kidney function loss due to glomerulosclerosis.

A fraction of diabetic individuals are found to have kidney hypertrophy in the clinical setting, and this finding is linked to the progression of diabetic nephropathy later on. Similar to early hyperfiltration, early hyperfiltration has been seen in a minority of diabetic patients in the early stages. These patients appear to be more prone to later develop overt diabetic nephropathy, which affects about one-third of diabetic patients. These and other related early pathophysiological alterations in the diabetic kidney, as well as their underlying processes, are the main topics of this review.

Description

Hypertrophy

Kidney development has been noticed relatively early in streptozotocin-induced experimental diabetes. For the first four days of the first phase, there is hyperplasia, which is followed by a change to hypertrophy, which is mostly mediated by transforming growth factor-β1. The transition from hyperplasia to hypertrophy appears to be dependent on protein kinase C β1, and the initial hyperplasia may require stimulation of the renin-angiotensin system (PKC β 1). After streptozotocin diabetes is induced, PKC β 1 is expressed in the proximal tubule and can trigger transforming growth factor- β.

Angiotensin-converting enzyme inhibition prevents the diabetes-induced activation of PKCb in the kidney, which may link the positive effects of angiotensin inhibition to tubular reabsorption and renal growth in the diabetic kidney. Increased mTOR activity seems to be made possible in the diabetic kidney by reduced AMPK phosphorylation, and decreasing AMPK phosphorylation reduces kidney development without changing hyperglycemia.

It has been suggested that diabetic kidney disease results in the loss of kidney cells due to apoptosis, a mode of cell death that is mediated by the activation of the caspases and causes the cleavage of protein substrates and DNA fragmentation. In cell culture experiments, glucose-induced apoptotic signals caused kidney podocytes, epithelial cells, and tubular cells to undergo apoptosis.

***Address for Correspondence:** David Sane, Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden; E-mail: david.sane@yahoo.com*

Date of Submission: 29 June, 2022, Manuscript No. FSB-22-80140; **Editor Assigned:** 30 June, 2022, PreQC No. P-80140; **Reviewed:** 12 July, 2022, QC No. Q-80140; **Revised:** 18 July, 2022, Manuscript No. R-80140; **Published:** 25 July, 2022, DOI: 10.37421/2577-0543.2022.6.133

Several other non-kidney cells have also been shown to undergo in vitro apoptosis when exposed to hyperglycemia. The dysregulation of the Fas/Fas ligand (FasL) system and of mitogen-activated protein (MAP) kinase (p38 MAPK) intracellular signalling have been suggested to favour apoptotic cell loss in diabetes in addition to hyperglycemia.

Hyperfiltration

Early hyperfiltration has been seen in rat models of experimental diabetes utilising streptozotocin, a model of type 1 diabetes mellitus (T1DM) caused by pancreatic beta-cell damage. If an animal is hyperglycemic, hyperfiltration can also happen even in the presence of insulin, but insulin-intensive blood sugar management consistently delays the development of glomerular hyperfiltration.

Based on the material that is currently available, it is not possible to draw any definitive conclusions about the precise contribution of changes in known hormonal vasoconstrictors or vasodilators as the cause of renal vasodilation. Our own lab is one of many that have looked into the function of the tubuloglomerular feedback (TGF) system in early diabetes. Whether the glomerular hyperfiltration, which is predominantly caused by renal vasodilation, is mediated by factors external to the kidney or whether it is secondary to some internal kidney mechanism is a crucial topic that has to be answered.

The inactivation of the TGF system and a significant increase in tubular reabsorption close to the MD, which leads to secondary vasodilation and an increase in SNGFR, are implied if luminal Na and Cl are lowered below normal. In diabetic rats, micropuncture investigations have shown an increase in absolute and fractional proximal tubular reabsorption, as well as a decrease in the concentration of MD NaCl and an increase in SNGFR.

Hyperreabsorption

An explanation of the mechanisms behind the primary increase in proximal reabsorption is necessary to comprehend the pathophysiology of the early diabetic kidney. On the basis of the literature that is currently accessible, three factors seem to be involved in the rise in proximal reabsorption.

The first is proximal tubular hyperplasia and hypertrophy, the second is increased proximal reabsorption brought on by amplified Na-glucose cotransport, which is mediated by SGLT2 and SGLT1, and the third is an exaggerated and adverse reabsorption effect of NaCl intake on the proximal tubule in the diabetic kidney. Hypertrophy was covered in the part before, and now we'll go into more detail about the other 2 variables.

Beginning with significant urinary protein excretion and hyperfiltration, DN is initially thought to be a progressive disease that eventually results in renal failure. The classic model of DN categorises it into two phases, incipient and overt, and lists five progressive stages: normoalbuminuria (30 mg/g creatinine); microalbuminuria (30-299 mg/g); macroalbuminuria (>300 mg/g) or proteinuria (>0.5 g/g); (4) estimated glomerular filtration rate (eGFR) 30 ml/min, regardless of albuminuria or proteinuria Microalbuminuria and an increase in GFR, both of which are thought to be markers of glomerular damage, are the main characteristics of the earliest and most obvious stage 2. However, numerous exceptions to this have been discovered in studies involving patients with Type 1 and Type 2 DM [1-5].

Growing evidence suggests that the traditional understanding of DN, which holds that increasing albuminuria and proteinuria precede ESRD, is not always accurate. The "non-albuminuric phenotype" is now the predominant mode of DN presentation, according to recent clinical studies. Although renin-angiotensin system (RAS) inhibitors have been demonstrated to play a significant role in lowering urinary albumin excretion, not everyone responds

favourably, and their impact may still be influenced more by slight drops in blood pressure and GFR. Therefore, in addition to glomerular hemodynamics and the filtration barrier, could there be another aspect of nephron function that contributes to the pathophysiology of DN?

Conclusion

We have looked into the data supporting the renal tubule's role in DKD. Although closely related to glomerular damage, diabetic tubulopathy is a real condition that may have a different pathophysiology. In both the early and late stages of DKD, various metabolic and non-metabolic factors compromise tubular function and probably contribute to some specific histological tubular changes. The identification and clinical assessment of new functional or structural tubular biomarkers will help to address the shortcomings of microalbuminuria as an early and predictive biomarker of DKD.

References

1. Lee, Philip J., R. Neil Dalton, Vanita Shah and Peter C. Hindmarsh, et al. "Glomerular and tubular function in glycogen storage disease." *Pediatr Nephrol* 9 (1995): 705-710.
2. Duarte, Cristobal G. and Harry G. Preuss. "Assessment of renal function—glomerular and tubular." *Clin Lab Med* 13 (1993): 33-52.
3. Asagba, SO. and FO Obi. "Effects of oral cadmium exposure on renal glomerular and tubular functions in the rat." (2004).
4. Fux, Christoph A., Anna Christen, Susanne Zgraggen and Markus G. Mohaupt, et al. "Effect of tenofovir on renal glomerular and tubular function." *Aids* 21 (2007): 1483-1485.
5. Thomson, Scott C., Timo Rieg, Cynthia Miracle and Hadi Mansoury, et al. "Acute and chronic effects of SGLT2 blockade on glomerular and tubular function in the early diabetic rat." *Am J Physiol Regul Integr Comp Physiol* 302 (2012): R75-R83.

How to cite this article: Sane, David. "A More Tubulocentric Perspective on Diabetic Kidney Disease." J Formul Sci Bioavailab 6 (2022): 133.