Urinary Claudin-1 Level As a Marker of Podocyte Injury in Patients With Proteinuria

Thesis

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List of Abbreviations

Abb.	Meaning
ASDN	Aldosterone sensitive distal nephron
CD	Collecting duct
CD2AP	CD2 adaptor protein
COIP	Co-immunoprecepitation
ECL	Extracellular loop
FHHNC	Familial hypomagnesemia with hypercalcuria and nephrocalcinosis
FPs	Foot processes
FSGS	Focal Segmental glomerulosclerosis
GBM	Glomerular basement membrane
HEK	Human embryonic kidney
IMCD	Inner medullary collecting duct
JAM	Junctional Adhesion Molecules
LLC-PK	Lilly laboratories cell - porcrine kidney
MAGI-1	Membrane associated granulate kinase inverted-1
MAGUK	Membrane associated granulate kinase homologues
MCD	Minimal change disease
MCNS	Minimal change nephrotic syndrome
MDCK	Madin-Darby canine kidney
MUPP1	Multi PDZ domain protein 1
PAN	Puromycin aminonucleoside
PEC	Parietal epithelial cells
PT	Proximal tubule
SD	Slit diaphragm
TAL	Thick ascending limb

List of Abbreviations

Abb.	Meaning
tAL	Thin ascending limb
TALH	Thick ascending limb of Henle
tDL	Thin descending limb
TG	Transgenic
ZO-1	Zonula occludens-1
PGC	PPAR Gamma Co-activator

Abstract

Background: The biology of claudins is a rapidly evolving field, and many intriguing questions remain unanswered. Although it had been assumed that the reason there are ≥24 isoforms of claudin is that each one has distinct permeability properties. The nephron displays a wide spectrum of claudins, whose distribution varies in each tubular segment. In diabetic nephropathy and glomerulonephritis the gene expression of claudin-1, is markedly upregulated in the podocyte, accompanied by a tighter filtration slit diaphragm (cell-cell junction made by the glomerular podocytes) and the appearance of TJ-like structures between the foot processes causing further podocytes injury and proteinuria.

Aim of the work: to assess urinary claudin -1 level as a marker of podocyte injury in patients with proteinuria.

Patients and Methods: it is a case control study which was conducted upon 90 subjects who were divided into three groups: group I included 30 patients with type II DM, group II included 30 patients with glomerulonephritis and group III had 30 healthy subjects as controls. Urinary claudin-1 level was measured by Enzyme linked Immunosorbent Assay (ELISA)

Results: In this study, we found that urinary claudin-1 level was significantly higher in diabetics group and GN group than in control group. In comparison between GN group and diabetic group, we found that urinary claudin-1 level was higher in GN group than in diabetics group but with no statistically significant difference between the two groups.

Conclusion: urinary claudin-1 level was significantly higher in diabetics and GN group and has positive correlation with uACR. So it can be used as marker of podocytes injury and proteinuria.

Keywords: Thin descending limb, Transgenic, Zonula occludens-1, PPAR Gamma Co-activator

INTRODUCTION

Claudins were first purified and identified by Mikio Furuse in the tight junction laboratory of the late Shoichiro Tsukita. Their name was derived from the Latin word "claudere," which means to close, because it was anticipated that these proteins might constitute the tight junctional barrier. It soon became apparent that the claudins are part of a large multigene family of 24 members of claudins ***(Angelow et al., 2008).***

Claudins are tight-junction membrane proteins that function as both pores and barriers in the paracellular pathway in epithelial cells. In the kidney, claudins determine the permeability and selectivity of different nephron segments along the renal tubules ***(Alan, 2014).***

The nephron displays a wide spectrum of claudins, whose distribution varies in each tubular segment; pore claudins are associated with leakier tubule segments, whereas barrier claudins are expressed in tighter distal segments ***(Molina et al., 2014)***.

Each claudin gene exhibits a unique nephron segment pattern of expression, and each nephron segment expresses multiple claudins.It is believed that the particular combination of claudins determines the unique paracellular permeability properties of each nephron segment.