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Effects of Salt Intake upon Glomerular Blood Pressure, Albuminuria and Aging Kidneys

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Summary

Hypertension and diabetes are major causes of end-stage renal disease. Intraglomerular hypertension and subsequent increase in albuminuria, presumably, play a pathophysiologically important role in such renal disorders. However, detailed and quantitative analysis have remained elusive. Furthermore, salt intake is one of determinants of blood pressure. Since measurement of intraglomerular pressure is technically quite difficult, total amount of albumin filtered through glomeruli was measured as its surrogate marker. Changes in filtered albumin were also investigated in response to salt loading, induction of diabetes and in a model of aging kidneys.

Two lines of genetically modified mice were mated and megalin knockdown mice were generated, in which albumin reabsorption was potently suppressed at the proximal tubules. Salt intake was altered or diabetes was induced in those mice. Salt loading did not alter urinary albumin excretion, but glomerular albumin filtration was increased by 3-fold. Moreover, diabetic mice exhibited 2-fold larger amount of glomerular albumin filtration compared to control mice. Salt restriction in megalin knockdown mice, as a model of aging kidneys with impaired albumin reabsorption activity at proximal tubules, resulted in salt loosing phenotypes.

Through these findings, it was suggested that intraglomerular pressure is elevated by salt loading and hyperglycemia. The present study in basic science provides a rationale for the current guidelines recommending to aim reduction of systemic blood pressure and intraglomerular pressure among patients with hypertension or diabetes. Furthermore, malfunctioning of proximal tubules seems to be a possible cause of salt loosing syndrome in the elderly.