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Fabry disease mouse is resistant to high-salt diet-induced hypertension probably via dysfunctional aquaporin 2

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Objectives: Fabry disease is a rare X-linked lysosomal storage disorder resulting from an error in glycosphingolipid metabolism caused by the *GLA* gene mutation. It has been previously reported that the expression of aquaporin 2 (AQP2) in mice with Fabry disease is decreased in the kidney but the significance of this finding was not well characterized. This study examined whether a high salt intake could affect transport of sodium and water and induce hypertension in Fabry disease mice.

Methods: Fabry disease model mice (B6;129-Gla^{tm1}Kul/J) and wild-type (WT) mice received 8% or normal NaCl salt diet for 2 weeks.

Results: A high-salt diet for 2 weeks generated higher blood pressure in WT mice but not in Fabry disease mice. Fabry disease mice fed a high-salt diet showed significantly higher free water clearance and electrolyte-free water clearance than WT mice fed a high-salt diet without difference in fractional excretion of sodium between them. In Fabry disease mice fed a high-salt diet, renal expressions of Na^+/H^+ exchanger isoform 3, Na^+-K^+-$2Cl^-$ cotransporter, and epithelial Na^+ channel were not different from those of WT mice fed a high-salt diet. A high salt intake significantly increased the expression of renal medullary AQP2 in WT mice while there was only a modest increase in the abundance of renal AQP2 in kidneys of Fabry disease mice with a high salt intake despite the increase in vasopressin V2 receptor.

Conclusions: These findings suggest that the impaired response of renal AQP2 in kidneys of Fabry disease to a salt load could be one of mechanisms by which Fabry disease could have resistance to the development of hypertension.