

## Decreased Aquaporin Expression in Kidney Contributes to Urinary Concentrating Defect in Hypothyroid Rats

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Hypothyroidism is associated with impaired urinary concentrating ability in humans and animals. The purpose of this study was to examine the effect of hypothyroidism on maximal urinary concentration and renal aquaporin (AQP) expression. Twenty one male Sprague-Dawley rats were divided into three groups: control (C), hypothyroid (HT), and hypothyroid-L thyroxine (HT+T). Hypothyroidism was induced by feeding aminotriazole for 4 weeks (0.5 g/kg food), and confirmed by free T4 level measurement. HT+T rats were subsequently treated with daily intraperitoneal administration of L-thyroxine (100 mg/kg BW) for 7 days after 4 weeks of aminotriazole. Rats received drinking water ad libitum. Body weight (BW), water intake (WI), urine output (UO), serum osmolality (SOsm), and urine osmolality (UOsm) were measured at baseline, and after 24 and 36 hours dehydration (DH), after which the rats were sacrificed, and the kidney AQP 1, 2, 3 levels were measured. Both HT and HT+T groups had significantly lower increase in BW throughout the study than C group. At baseline, WI and UO were not different between groups. UOsm was significantly lower in HT group than in either C or HT+T groups, with even more profound differences after

24- and 36-hours DH. UOsm increase after 24 and 36-hour DH was not different between groups. BW loss with 36-hour DH was significantly higher in HT group than in either C or HT+T. SOsm was not different between groups at either time point.

	C	HT	HT+T
△BW throughout study (%)	27±2 <sup>†</sup>	-4±4	5±1
Baseline UO (mL/day)	14±3	17±5	14±2
Baseline SOsm	304±6	321±19	317±11
Baseline UOsm	2,193±434 <sup>†</sup>	1,221±82	1,682±140*
BW loss 36-h DH (%)	8±1 <sup>†</sup>	10±1	8±1 <sup>†</sup>
UO 24-36 h DH (mL)	1.3±0.3*	1.9±0.2	1.0±0.5 <sup>†</sup>
UOsm 24-h DH	3,085±624 <sup>†</sup>	1,830±216	2,627±162*
UOsm 36-h DH	4,755±565 <sup>†</sup>	3,150±150	4,403±197 <sup>†</sup>

UOsm and SOsm in mOsm/kgH<sub>2</sub>O

\*p<0.05 vs HT, <sup>†</sup>p<0.01 vs HT, <sup>‡</sup>p<0.001 vs HT and HT+T

Western blot analysis revealed significantly lower abundance of inner medullary AQP2 (p=0.05) and AQP3 (p<0.01) in HT group versus C and HT+T groups, while AQP1 abundance was not different

The results suggest that decreased kidney AQP2 and AQP3 expression contributes to the urinary concentrating defect in the hypothyroid state

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