

Analysis on the process of maturation in the urine-concentrating mechanism in early-neonatal rat kidneys

Yoshiaki Kondo, Kazuie Inuma, Chiyoko N. Inoue, Tetsuji Morimoto, Wen Liu, Masashi Imai

Department of Pediatrics, Tohoku University School of Medicine

Department of Pharmacology, Jichi Medical College

Summary

To answer to why the urine-concentrating ability is immature and diluting ability is mature in the neonate, we investigated the function and the expression of the ion transporters in the inner medullary tubules of early-neonatal rat kidneys. The renal tubules including the ascending thin limb (ATL), descending thin limb (DTL) and collecting duct (IMCD) were microdissected from fetal, neonatal and adult rat kidneys, and microperfused in vitro and transepithelial voltages (V_t), ionic diffusional potentials (V_d) of NaCl, diffusional water permeabilities, hydraulic conductivities, and urea permeabilities were measured.

On one day before birth, the V_t s of the ATLs were zero. On the day of birth, the average V_t s were 13.2 ± 1.6 mV ($n=11$, lumen positive). The lumen-positive V_t decreased gradually and became zero on day 5. On the day of birth, V_t was inhibited by 10^{-4} M ouabain in the bath from 7.5 ± 1.7 to 4.1 ± 1.8 mV ($n=6$, $p<0.01$). V_t was also inhibited by 10^{-4} M bumetanide or 1mM Ba^{++} added to the luminal solution. To characterize the V_d , the effects of 5-nitro-2-(3-phenylpropylamino)-benzoate (NPPB) were examined. The V_d s evoked by 100 mM NaCl gradient across the ATL were genative at birth and were reversed on day 5. On day 0, NPPB did not decrease the V_d s induced by 100mM NaCl gradient across the ATLs. The magnitude of the effect of NPPB on the V_d s were greater depending on days after birth. On day 0, mRNAs for both rBSC-1 and ClC-K1 were detected in the ATL, while the message for rBSC-1 was not present in the adult ATL. Immunofluorescent studies using the polyclonal antibodies to both transporters revealed that the ATLs on day0 express only rBSC-1 in the luminal membrane, while the adult ATLs only express that ClC-K1 in both cell membranes.

The LDLs were impermeable to water at birth, and became permeable thereafter. The IMCDs were almost impermeable to water and urea in the absence of vasopressin at birth. The sensitivity to vasopressin of water and urea permeability became obvious after day 14.

These results indicate that neonatal inner medulla forms qualitatively different organization of the tubular function, which may lead to the low ability to concentrating urine in early-neonatal period.