STRONG CHILDREN'S RESEARCH CENTER

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ABSTRACT

Title: Maternal acidosis down-regulates beta-intercalated cell differentiation in progeny

Background: In the kidney cortical collecting duct (CCD), adjustments of acid-base balance are mediated by two types of intercalated cells (IC's): α and β. α-IC's secrete protons via a basolateral AE1 exchanger and an apical B-1-V-ATPase (B1), while β-IC's secrete bicarbonate (HCO_3^-) via an apical pendrin exchanger and basolateral B1. In the current study, we sought to confirm and extend a study in rats suggesting that modulation of acid-base status during pregnancy influences α- and β-IC differentiation.

Objective: To determine whether maternal acid/base status influences intercalated cell differentiation in progeny.

Design/Methods: A pregnant rabbit's typical alkaline ash diet was modified by acid-loading with ammonium chloride during the fourth and final week of gestation. Kidneys were harvested from rabbits in the corresponding litter at 1 week (3 kits) and 3 weeks (2 kits). Tissues were then paraffin-embedded, sectioned onto slides at 4-6μm thickness, and IC subtypes were identified by immunofluorescence staining for AE1, pendrin, and B1. Two serial slides for each rabbit were stained: one labelling pendrin only and one double-labelling B1 and AE1. The number of α- and β-IC's was determined by cell counting using B1 cells as a total IC number, AE1 cells as the α-IC number, and pendrin cells as the β-IC number. These cell counts were then compared to those of a normal adult rabbit.

Results: Pendrin staining revealed fewer β-IC's in 1 week-old kits compared with an adult normal rabbit with 4.3±0.2 β-IC's/100 μm in the CCD in 1 week-old kits versus 7.4 in the adult and 6.3±0.05 in the 3 week-old kits. The AE1/B1 staining revealed similar differences. There were 6.3±0.2 total IC's/100 μm at 1 week kits versus 7.8 in the adult and 9.1±0.1 in 3 week-old kits. Although neonatal collecting ducts contained α-IC's in numbers comparable to the adult and 3 week-old kits, with 2.8±0.1 α-IC's/100 μm at 1 week, 3.1±0.2 at 3 weeks, and 2.4 in the adult, β-IC's were lower in neonates compared with adults and 3 week-old kits with 3.5±0.1 β-IC's/100 μm at 1 week versus 5.4 in the adult and 6.0±0.3 in the 3 week-old kits. As a result, the proportion of β-IC's is lower in kits from an acidotic doe compared with a normal adult. The ratios of α:β cells were 44:56 at 1 week , 34:66 at 3 weeks, and 31:69 in the adult. These data suggest that IC differentiation is incomplete in the neonate.

Conclusions: Previous data has shown that the number of α- and β-IC's per tubule length is comparable between neonate and adult rabbits. The decreased β-IC's in offspring from acid-loaded pregnant rabbits is likely due to down-regulation of β-IC differentiation, not an increase in α-IC differentiation. Thus, maternal acidosis may delay β-IC differentiation in progeny.