

CESAREAN VERSUS VAGINAL BIRTH BLUNTS BILE ACID-FGF19 SIGNALING IN NEONATAL PIGS

Caitlin E Vonderohe¹, Gregory Gurthrie², Barbara Stoll³, Valeria Melendez-Hebib³, Doug Burrin⁴

¹ Baylor College of Medicine, Department of Pediatrics, Nutrition

² Baylor College of Medicine , Pediatrics, Nutrition

³ Baylor College of Medicine , Pediatrics , Nutrition

⁴ Baylor College of Medicine, USDA, Pediatrics , Nutrition

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Background: Birth by scheduled cesarean section has been shown to affect the development of the small intestine, brain, and microbiome. However, the impact of cesarean versus vaginal birth on the development of bile acid and fibroblast growth factor-19 (FGF19) signaling is unknown. FGF19 is produced in the distal ileum when bile acids interact with the nuclear farnesoid X receptor, then circulates to the liver where it down-regulates the expression of the rate-limiting enzyme in bile acid synthesis. Thus, FGF19 functions as a negative feedback on bile acid production and homeostasis. The objective of this study was to determine the effect of birth modality (cesarean vs. vaginal) on bile acid pool distribution, expression of genes in the bile acid-FXR-FGF19 pathway and plasma levels of FGF19 at birth and on day 3 of life in neonatal piglets.

Materials/Methods: Two sows underwent a cesarean section on gestation day 114 (term=115 day) and two additional sows were allowed to give natural birth vaginally at term. Half of the piglets were euthanized at birth for tissue and blood collection, and the remaining pigs were nutritionally supported on total parenteral nutrition (TPN) then fed a bolus meal of formula on day 3 of life, at which time tissue and blood were collected. Ex-vivo tissue explants were used to test ileal and jejunal responsiveness to bile acid stimulation.

Results: Piglets born vaginally had a markedly (30x) higher plasma FGF19 at birth than pigs born via cesarean section, however FGF19 gene expression in the distal ileum was similar in both groups. FGF19 expression was higher in skeletal muscle of vaginally born piglets at birth. On day 3 of life, after a bolus feeding, plasma FGF19 levels in vaginally pigs were similar to those born via cesarean section, but ileal FGF19 expression was greater in vaginally -born pigs. Ileal explants from cesarean and vaginally-derived pigs showed similar responsiveness to bile acid stimulation

Conclusions: Birth modality may have a profound effect on the development of the bile-acid-FGF19 pathway. Marked differences in plasma FGF19 at birth, despite similar ileal expression, suggests humoral or endocrine factors acutely affected FGF19 secretion. Future work is focused on characterizing how changes in the endocrine factors in the perinatal period influence the bile acid-FGF19 signaling axis.

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