LRH-1 agonist has anti-inflammatory properties and could be potential for are involved in the pathogenesis of parenteral nutrition associated cholestasis

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Background & Hypothesis

Parenteral Nutrition Associated Cholestasis (PNAC)

Parenteral nutrition (PN) is life saving therapy of infants with intestinal failure. But long-term parenteral nutrition carries the risk of complications and potentially fatal complications. Parenteral nutrition associated cholestasis (PNAC) also called intestinal failure associated liver disease (IFALD) is mainly histologically characterized by intrahepatic cholestasis but can progress to fibrosis and cirrhosis with continued exposure to parenteral nutrition. PNAC occurs in 40-70% of infants with intestinal failure. A component of the bile acids (BAs) accumulation is that BA binds to its target during inflammation

Methods

- HepG2 cells were treated with full GHSR1 agonist (GHSR1 agonist) and full GHSR1 antagonist (GHSR1 antagonist) and treated for 14 days with or without treatment. Impaired and cholesterol secretion was measured by using LC-MS.
- Mouse BMDC cells, Raw cell and THP1 were treated with DMSO or DLPC (LRH-1 agonist) followed by LPS next morning.
- For CoCl2 study, HepG2 cells or mouse liver extract was used.

Conclusions

- This study supports that if LXR agonist (LXR1 agonist) is inhibited, DLPC is expressed to protect HUH7 cells from LPS effect
- DLPC suppresses IL1β production in THP1
- LRH1 agonist protects HU71 cells from LPS effect
- DLPC stimulates STAT6 phosphorylation and its target during inflammation