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Prenatal Administration of Heparin-Binding EGF-Like Growth Factor (HB-EGF) In An Experimental Model Of Necrotizing Enterocolitis Decreased Neuroinflammation In The Neonatal Brain

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INTRODUCTION AND OBJECTIVES: Necrotizing enterocolitis (NEC) is the leading gastrointestinal cause of death in premature infants. Postnatal enterally administered Heparin-Binding EGF-like Growth Factor (HB-EGF) decreases the incidence and severity of intestinal injury in a neonatal rat model of NEC. In this study, we hypothesized that NEC-induced inflammation would increase the expression of cytokines in the autonomic control regions of the nucleus tractus solitarii (NTS) and that prenatal administration of HB-EGF would decreased the incidence of NEC and associated neuroinflammation.

METHODS: HB-EGF 800 µg/kg/dose, was delivered by means of tail vein injection or intraperitoneally 2 hours prior to delivery of the rat pups. Rat pups were delivered prematurely by C-section and subjected to NEC protocol. Pups were sacrificed upon signs of NEC and intestines were harvested and graded. Cytokine expression in the pup brain (IL-1β, IL-6, TNFα) was assessed.

RESULTS: Compared to untreated pups, the prenatal administration of HB-EGF to pregnant female rats significantly decreases the incidence and severity of NEC in rat pups with best results seen when HB-EGF is administered in an intraperitoneal fashion 2 hours before C-section. (62.9% vs 30%*, p =0.02) IL-6 was not significantly different in the untreated pups versus pups that received HB-EGF prenatally (p= 0.75) but IL-1β and TNFα were significantly reduced by tail injections at 2 hours prior to birth (p =0.0018 IL-1β and p=0.00005 TNFα).

CONCLUSIONS: Prenatal HB-EGF administration decreases the incidence and severity of experimental NEC and reduces the inflammatory markers. This suggests a novel prophylactic strategy that could have beneficial neurodevelopmental effects in NEC patients.

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