Epidermal Growth Factor (EGF) as reliable marker in necrotizing enterocolitis in preterm neonates

(Running title: Epidermal Growth Factor in necrotizing enterocolitis)

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Necrotizing enterocolitis (NEC) is the most common surgical gastrointestinal emergency in premature neonates.\textsuperscript{1,2)} The prevalence of NEC is 7\% in infants born between 500 and 1500 g in the United States and Canada, with a mortality rate nearing 42\% \textsuperscript{3}, and the overall mortality rate of NEC is 20 \textendash 40 \%.\textsuperscript{4)} Clinical signs of NEC can vary in severity, ranging from nonspecific symptoms such as apnea and temperature instability, to abdominal distension, bloody stools, pneumatosis intestinalis and shock.\textsuperscript{2) } Medical treatments of NEC consist of administration of broad spectrum antibiotics, volume loading and bowel rest. However, many patients of NEC require surgery to remove necrotic bowel, so develop short bowel syndrome with prolonged medical expenses and chronic gastrointestinal difficulties. Further, surgical NEC is a significant predictor of neurodevelopmental morbidity in preterm infants.\textsuperscript{5) } The exact pathogenesis of NEC remains poorly understood, the cause of NEC is likely multifactorial and treatment strategies are mainly supportive.

A layer of epithelium lining the intestine provides the first line of defense against bacteria, viruses, and toxins, as barrier function. Epidermal growth factor (EGF) is essential to epithelial cell proliferation. It also decreases expression of inflammatory mediators and reduces epithelial apoptosis.\textsuperscript{3) } Many studies about the effect of EGF in NEC have been performed. Recent studies show that administration of exogenous EGF reduces mucosal histological damage in animal models.\textsuperscript{6) } Also, EGF treatment of NEC has been shown to normalize expression of occluding and claudin.\textsuperscript{7) } All the studies mentioned above conducted in animals, few studies for humans.

In this issue of the Korean Journal of Pediatrics, Heba et al.\textsuperscript{8) } presented the relation between serum levels of EGF and NEC in an interesting issue in neonatology. In this prospective study,
EGF level was significantly lower in the sera of NEC group as compared to both sepsis and control group. And there was a significant negative association between both EGF and gestational age as predictors of the development of NEC. He et al.\textsuperscript{9} reported that mothers with premature infants have 50\textasciitilde80\% more EGF in their breast milk than those with full-term infants. These results mean that the NEC correlates with low EGF levels in lower gestational age. Also, high EGF level in breast milk of mothers with premature infants was evidence that breast milk is protective of NEC.\textsuperscript{3, 10} Noteworthy, Heba et al. presented the cutoff value of EGF using the ROC curves. This value could be the basic data as a biomarker of NEC.

Early diagnosis and treatment is very important in NEC. EGF could be a reliable biomarker of NEC in preterm infants. Additional research is needed to be considered to using EGF as early diagnostic tool of NEC.
References


