Research Letter

The Relationship between Glucagon-Like Peptide 2 and Feeding Intolerance in Preterm Infants

Summary

Glucagon-like peptide 2 (GLP-2) is a hormone produced primarily in the distal intestine, stimulated by enteral nutrients, and playing diverse roles in the intestinal adaptation and growth. We aimed to investigate whether GLP-2 may play a role in the development of feeding intolerance which is a common problem in preterm newborns resulting from the intestinal immaturity. The study included 20 term and 28 preterm neonates. Of preterm babies, 13 showed feeding intolerance fulfilling at least one of the following criteria: abdominal distension, increased gastric residual volume and presence of bile in the gastric aspirate. The plasma GLP-2 levels measured prior to enteral feeding (fasting level) and at 60 min after the beginning of the feeding (post-pradial level) were correlated with of clinical parameters. There was no statistical difference between GLP-2 levels of overall preterm babies and those of term newborns. However, preterm neonates with feeding intolerance showed significantly lower levels of GLP-2 and increased duration to achieve full enteral feeding and hospitalization. It is suggested that GLP-2 plays a significant role in the regulation of feeding in newborns and that preterm babies with low levels of GLP-2 carry a risk for development of feeding intolerance. It may, therefore, be of relevance to investigate the therapeutic and prophylactic effects of GLP-2 administration in the preterm babies.

GLP-2 is an intestinal peptide exhibiting trophic and reparative effects on the gut mucosa. This prospective study indicates that preterm infants with feeding intolerance have lower levels of GLP-2 in the blood samples and this decrease is associated with nutritional problems and retarded neonatal growth, predisposed to developing feeding intolerance due to immaturity of the intestinal mucosa. The decreased level of GLP-2 in these patients may have resulted from inadequate response to enteral stimulus that in itself a consequence of the immaturity of the gut. Immaturity of the expression of GLP-2 specific receptors and therefore inadequate growth effects of GLP-2 may contribute to the increased vulnerability of the gut (or deficiency of dipeptidyl peptidase-IV enzyme playing a role in the secretion of GLP-2) [1]. In addition, there may be a linear relation between intestinal tissue mass and GLP-2 levels. Likewise, smaller preterms were more likely to have feeding intolerance in our study. Of the significant factors that are associated with feeding intolerance including low levels of GLP-2, only low birth weight appeared to be an independent factor. Petersen *et al.* [2] suggested that the prenatal increase in circulating GLP-2 in the pig plays a limited role for the intestinal growth because plasma GLP-2 concentration increases gradually during late gestation, peaks at 1–2 day after birth and is temporarily increased in enterally nourished term newborn piglets. However, in preterm newborn pigs, this elevation of GLP-2 level is delayed compared with pigs delivered at term. This may explain why the babies with earlier gestational age carry risk of development of feeding intolerance. In our study, the infants with feeding intolerance had longer hospitalization resulting in a delay with respect to achieving full feeds. We think that longer hospitalization may result from feeding difficulties due to enteral feeding. In addition, these were small babies usually needing longer hospitalization. Therefore, we think that the longer administration of total parenteral nutrition (TPN) in preterm infants may cause decreased level of GLP-2, and increase the incidence of feeding intolerance in our study. In conclusion, we hypothesize that GLP-2 plays a pivotal role in the development of feeding intolerance in preterm babies. Lower levels of plasma GLP-2 are associated with retarded neonatal growth and nutritional problems. GLP-2 may be of potential therapeutic benefit in neonatal intestinal dysfunction. Further studies are required for careful assessment in the properly controlled clinical trials.

Esra Arun Ozer[a], Jens Juul Holst[b], Nuray Duman[c], Abdullah Kumral[c], *and* Hasan Ozkan[c]

[a]*Izmir Tepecik Training and Research, Hospital, Clinic of Neonatology, Izmir, Turkey,* [b]*Department of Medical Physiology, University of Copenhagen, the*

Downloaded from https://academic.oup.com/tropej/article/55/4/276/1672535 by Dokuz Eylul University Library (DEU) user on 02 September 2021

© The Author [2008]. Published by Oxford University Press. All rights reserved. For Permissions, please email: journals.permissions@oxfordjournals.org

Panum Institute, Copenhagen, Denmark and [c]*Dokuz Eylul University, School of Medicine, Department of Neonatology, Izmir, Turkey*

doi:10.1093/tropej/fmn033
Advance Access Published on 22 May 2008

References

1. Drucker DJ. Glucagon-like peptide 2. J Clin Endocrinol Metab 2001;86:1759–64.
2. Petersen YM, Hartmann B, Holst JJ, *et al*. Introduction of enteral food increases plasma GLP-2 and decreases GLP-2 receptor mRNA abundance during pig development. J Nutr 2003;133:1781–6.

Correspondence: Prof. Dr Hasan Ozkan, Dokuz Eylul University School of Medicine, Department of Neonatology, Inciralti 35340 Izmir, Turkey. Tel.: + 90 232 4123643; Fax: + 90 232 2590541.
E-mail <hasan.ozkan@deu.edu.tr>

Downloaded from https://academic.oup.com/tropej/article/55/4/276/1672535 by Dokuz Eylul University Library (DEU) user on 02 September 2021