Acta Pædiatrica ISSN 0803–5253

CORRESPONDENCE

Discrepancy of milk ghrelin level

Suleyman Aydin (saydin1@hotmail.com)

Firat University, School of Medicine, Firat medical Center, Department of Biochemistry and Clinical Biochemistry, 23119 Elazig, Turkey

Correspondence
Dr. Suleyman AYDİN, Firat University, School of Medicine, Firat medical Center, Department of Biochemistry and Clinical Biochemistry, 23119 Elazig, Turkey.
Tel.: (90) 533-493-4643 | Fax: (90) 424-2388660 |
Email: saydin1@hotmail.com

Received
8 October 2006; accepted 30 October 2006.

DOI:10.1111/j.1651-2227.2007.00134.x

Sir,

I have read the recently published article by Dr. Kierson's group with considerable interest (1). I have seen that they present a novel observation of the presence of ghrelin (GAH; Ref. 2) peptide in the breast tissue (1), and confirm that milk contains GAH (3). There are however, some points in the article, which requires well addressing. Here, I wish to expand upon the interpretation of the milk ghrelin levels.

First, even though several assays [Phoenix Pharmaceuticals (cat. no. RK-031-30) and Linco Research (cat. no. GHRT-89HK)] are available to measure human serum GAH, there are no commercial milk ghrelin assay kit present yet. If someone uses those kits for different purpose they are supposed to validate them with a basic clinical chemistry methods such as linearity and so (3). In that study, I have not seen such a validation assay. Contrary to our results (3), they reported that breast milk GAH level were higher than plasma levels (1). Here, I assumed that Linco Research kits might not be as much specific as for milk ghrelin levels as in the plasma ghrelin levels. Thus, discrepancy was observed in between us.

Second, the high level of GAH identified in their study (1) differ considerably from the levels reported by our group (3). Again, Dr. Kierson's group and our group used different ghrelin detection kits. So, the comparability of results among assays is not known yet. Groschl et al. (4) have been previously tested serum ghrelin assays comparability [Phoenix Pharmaceuticals (cat. no. RK-031-30) and Linco Research (cat. no. GHRT-89HK)]. They found that Linco assay was 10-fold higher than that of the Phoenix assay. We used Phoenix Pharmaceuticals (cat. no. RK-031-30) kit in our ghrelin milk detection. Therefore, It is likely that the milk ghrelin level in our groups (3) was considerably lower than that obtained by Kierson et al. (1). This means that comparison of the two manufacturers ghrelin results is not a good way.

Finally, Dr. Kierson's group, and our group measured only total milk ghrelin level. Whereas, Linco recently introduced an additional system for analysing the so-called 'active' aGAH (cat. no. GHRA-88HK). Active ghrelin (aGAH) is essential for binding to the growth hormone secretagogue receptor 1a (GHSR-1a) (5). So, additional studies are needed to determine the physiologically active ghrelin in milk and their potential long-term impact on bone and appetite regulation beside total milk ghrelin level.

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Reply to ghrelin in human breast milk

Jennifer A Kierson[1,2], Darlise M DiMatteo[3], Robert G Locke (rlocke@christianacare.org)[1,2,3], Amy B Mackley[1], Michael L Spear[1,2,3]

1. Department of Pediatrics, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, USA
2. Division of Neonatology, Christiana Care Health Services, Newark, Delaware, USA
3. Alfred I. duPont Hospital for Children, Wilmington, Delaware, USA

Correspondence
Robert G. Locke, D.O., Division of Neonatology,
Christiana Care Health Services,
4755 Ogletown-Stanton Road, Newark, DE 19718,
USA.
Tel.: (302) 733-2410 | Fax: (302) 733- 2602 |
Email: rlocke@christianacare.org

Received
26 October 2006; accepted 30 October 2006.

DOI:10.1111/j.1651-2227.2007.00137.x

To the Editor:

We appreciate Dr. Aydin's thoughtful comments. The purpose of our study was to determine if ghrelin is present in human breast milk and breast tissue. Through our extensive previous work with Linco's human leptin kit and breast milk samples, we determined that there is no interference of the RIA with skimmed milk, which has very little fat, and only minimal interference introduced by the fats and proteins in whole milk. Since the principles for the ghrelin and leptin assays are the same, it is reasonable to assume that the interference pattern is similar.

We utilized Linco's total ghrelin kit for our experiments because of our extensive experience with kits from that company. We used the CCK RIA from Phoenix Pharmaceuticals because it was the only source available at the time. We are not aware of evidence in the literature supporting the use of one kit over another.

Prior to the initiation of our study, we did not know which form of ghrelin would be present in human breast milk. Since this stage of our investigation was not intended to determine the physiological effects of different forms of ghrelin in breast milk, we chose to use a kit that would maximize detection of all epitopes.

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Epidemiological study of constipation and other gastrointestinal symptoms in 8000 children (Acta Paediatr 2006; 95: 573–580)

Gokhan Baysoy (baysoy_g@ibu.edu.tr)

Department of Pediatrics, Abant Izzet Baysal University Medical School, Bolu, Turkey

Correspondence
Gokhan Baysoy, Abant Izzet Baysal University,
Department of Pediatrics,
AIBU Izzet Baysal Medical School, Golkoy Bolu
14280, Turkey.
Tel: 00903742534656 } Fax: 00903742534615 }
Email: baysoy_g@ibu.edu.tr

Received
1 Aug 2006; accepted 21 Aug 2006.

DOI:10.1111/j.1651-2227.2007.00083.x

Sir,

I read the article by Ludvigsson, JF for the ABIS study group with interest (1). This large population-based cohort study demonstrates an interesting relationship between anorexia and paracetamol use between 1 and 2.5 years. Anorexia might be a result of abdominal pain; however, authors have clearly suggested that paracetamol use was not linked to abdominal pain. Anorexia as well as abdominal pain is more common in constipated children (2). Roma E et al. demonstrated that anorexia was 27.5% in constipated children and 5.2% in control subjects. We also investigated the prevalence and associated factors in constipation in Bolu in 3453 primary school children (age 6–14 years) (a city located in the western Black Sea region of Turkey) and found that 12.7% of 820 constipated children had poor appetite (whereas remaining had good or moderate appetite according to mothers) compared to 7.3% in non-constipated children according to the mother's self report ($p < 0.01$, OR = 1.8 95% CI 1.4–2.3) (3). So it might be interesting to examine the correlation of anorexia to paracetamol use while controlling for the constipation in the present study.

Actually the missing link between anorexia and paracetamol use might be the infection. Most common signs of infection are fever and decreased food consumption (4). Anorexia as well as fever is a defense mechanism of the host. Fever during infections might have been treated with antipyretics mainly paracetamol in toddlers. So it is crucial to reveal the infection rate in the study population. In conclusion, paracetamol use might not be directly related to anorexia in toddlers. It might be a surrogate for infection in this case.

Respectfully,

Gokhan Baysoy
Abant Izzet Baysal University Medical School
Department of Pediatrics, Bolu-Turkey

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The importance of considering children's- and adults'-cognitive functions when discussing living conditions and psychosomatic complaints*

Elisabeth Fernell (elisabeth.fernell@karolinska.se)[1], Ulla Ek[2]

1. Department of Neuropaediatrics, Astrid Lindgren Children's Hospital, Stockholm, Sweden
2. Department of Psychology, Stockholm University, Stockholm, Sweden

Correspondence
Elisabeth Fernell, Department of Neuropaediatrics,
Astrid Lindgren
Children's Hospital,
SE-176 76 Stockholm, Sweden.
Tel.: +46 (8) 517 770 71 | Fax: +46 (8) 517 776 08 |
E-mail: elisabeth.fernell@karolinska.se

Received
6 September 2006; accepted 21 September 2006.

DOI:10.1111/j.1651-2227.2007.00119.x

Sir,

As pointed out in the paper by Östberg et al. (1), psychosomatic complaints have increased in children during recent decades, in parallel with major structural changes in the Swedish society, such as higher unemployment rates amongst the youth and young adults, growing housing segregation and inequalities in income for households with children.

In addition to this, in our modern Western society, increasing calls are being made for elaborate cognitive/executive functioning – such as planning, organizing and flexibility – at school, at work and during leisure time. Research on these issues is still in short supply (2).

The study by Östberg et al. (1) demonstrated that economic stress (defined as having no cash margin), but not

*Comments on the paper by Östberg, Alfvén and Hjern in Acta Paediatrica 2006; 95:929-934. Living conditions and psychosomatic complaints in Swedish schoolchildren.

social class, was a significant determinant of psychosomatic symptoms in Swedish schoolchildren. However, before inferring a causal relationship between these two factors, additional aspects, such as the influence of cognitive dysfunctions should, in our opinion, be considered and discussed. Unemployment, poor money management and trouble organizing and running a household are classical symptoms in adults with ADHD (3). Therefore, different cognitive disabilities, belonging to the category of 'high prevalence/low severity dysfunctions' (4) ought to be considered in research dealing with psychosomatic symptoms and psychiatric disorders.

From our experience of working with children with developmental disorders, we would like to stress that psychosomatic complaints in children have to be studied from a broader perspective. In particular, it is necessary to reflect upon the complex interplay between a variety of cognitive factors and the demands being made and the expectations held.

It has repeatedly been reported that children with cognitive dysfunctions exhibit more stress owing to excessive demands at school and regarding homework. In a recent study by Holmberg and Hjern (5), recurrent abdominal pain, sleeping problems and tiredness were associated with ADHD. The authors concluded that treatment strategies for children with ADHD need to include an effective evaluation of and treatment for recurrent abdominal pain, tiredness and sleeping disturbances and that an evaluation should be made to consider whether ADHD is an issue for children with recurrent health complaints.

Thus, to conclude this correspondence, the possibility of underlying cognitive vulnerability has to be taken into account when overt manifestations – such as economic problems in adults and psychosomatic complaints in children are the presenting symptoms. In our opinion, this is decisive when it comes to the optimal provision of intervention and support. If the influence of cognitive dysfunctions on psychiatric ill health is overlooked, appropriate intervention will fail and measures and resources may be directed exclusively to the overt expressions, instead of highlighting the main issue. We have to consider that many children are at both biological and environmental risk, a combination being referred to as 'double jeopardy' (6).

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