Hyper-γ-Glutamyltransferase Is Commonly Present in Non–Breast-Fed Infants with Biliary Atresia Successfully Treated with Portoenterostomy

To the Editor:

We read with great interest the letter entitled “High γ-Glutamyltransferase (GGT) Activity in Human Breast Milk Confounds Interpretation of High Serum GGT Activity in a Nursing Infant with Liver Disease” by Colagiovanni et al. (1). The authors suggested that the persistence of a high GGT activity in the circulation of a single infant with surgically treated biliary atresia (BA) may reflect, at least in part, ingestion and absorption of GGT from breast milk.

We think that the hypothesis of a close correlation between GGT concentrations in breast milk and in infant’s serum should be interpreted with caution. Although milk proteins can be absorbed by mucosal cells of the gut in the early neonatal period by pinocytosis, this absorption decreases greatly beyond the neonatal period, owing to maturation of the intestinal cells (2). Furthermore, it should be noted that most children with surgically treated BA, apart from the kind of diet, have persistently high serum concentrations of GGT, a sensitive marker of cholestasis (3,4). Only 11% of patients successfully treated with portoenterostomy show GGT concentrations within reference values (3).

We report the behavior of GGT serum concentrations in infants with BA successfully treated with portoenterostomy. Eleven infants (5 boys) with BA, surgically treated with Kasai portoenterostomy at a median age of 68 days (range, 37–111 days), were enrolled in this study. GGT serum activity was measured as reported elsewhere (5). None of these patients required liver transplantation during the observation.

After portoenterostomy and during the following months of observation, none of the studied patients was breast-fed; all received a medium-chain triglyceride (MCT)-based formula of bovine origin. MCT-based formula is recommended in cholestatic infants because these patients show malabsorption of fatty acids, and MCTs are absorbed directly by intestinal mucosa, without requiring emulsification by bile acids (6). GGT is absent in milk formulas as a consequence of the usual pasteurization process (7). No GGT activity was detectable in a sample of the MCT formula used with our patients, and none of an age- and sex-matched control group of 10 noncholestatic infants fed with an MCT-based formula for malabsorption had hyperGGT.

Serum GGT concentrations were abnormal in all studied patients, both at the time of diagnosis of BA and during the first 3 months after portoenterostomy. At diagnosis, median serum concentrations of GGT and total bilirubin were 730 U/L (range, 238–1254 U/L) and 35.8 mg/L (range, 7.1–103 mg/L), respectively; 3 months after portoenterostomy, GGT and total bilirubin were 507 U/L (range, 92–2027 U/L) and 10 mg/L (range, 2–12 mg/L), respectively.

Normalization of GGT occurred in 8 children after a median period of 12 months (range, 3–52 months) after portoenterostomy, probably as a consequence of improved biliary flow. The remaining patients showed hyperGGT for the entire period of observation. Diet did not differ between the patients whose GGT normalized and those whose GGT did not. All studied patients were treated after portoenterostomy with ursodeoxycholic acid (20 mg·kg⁻¹·day⁻¹), which commonly lowers serum GGT concentrations in cholestatic patients.

On the basis of these data, we postulate that a sizable proportion of children with BA who undergo Kasai show hyperGGT, even when not breast-fed. In this context, it seems very likely that, in the single patient described by Colagiovanni et al. (1), high concentrations of GGT were related to cholestasis rather than to GGT content in the breast milk. On the other hand, if serum concentrations of GGT were related to the GGT concentrations in breast milk, all breast-fed infants should have increased serum GGT concentrations, even in the absence of cholestasis, but this phenomenon is not documented.

References


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Historical Background of the Invention of EIA and ELISA

To the Editor:

Colleagues have brought to my attention the article “Enzyme Immuno-
To the Editor: 

Professor Avrameas is indeed correct, and I acknowledge the fact that the cited references should have been mentioned in my historical note (1). Avrameas’ pioneering work on the use of enzymes rather than radio-active labels was cited twice in that historical note [as references 5 and 6 in (1)]. These cited papers, together with the work of many other pioneers, such as Nakane and Pierce in Los Angeles and Wide and Forath in Uppsala, were presented in the historical note as “building blocks” in the research sequence that led to the development and validation of non-radioactive immunochromatographic techniques. The application of the enzyme-labeled techniques of Avrameas and colleagues focused on immunocytochemistry and immunochemistry.

The historical note focused on the 2 other groups (in Stockholm and Oss) because the intended audience was clinical chemists, not histologists or cytologists. The groups in Stockholm and Oss vigorously expanded on their first findings of ELISA and EIA and applied them to a wide variety of analytes in clinical chemistry/laboratory medicine in the years after their publications in 1971.

The correlation coefficient was 0.96 for both RIAs and 0.81 between the SBD-RIA and the CL assay; in the latter case, the coefficient decreased to 0.28 for the lowest values of the curve [aldosterone <277.43 pmol/L (100 pg/mL)]. Passing–Bablok regression analysis of values obtained by both RIAs yielded a good slope [slope, 0.94; 95% confidence interval (CI), 0.88–0.99; intercept, 70.82 pmol/L (95% CI, 50.49–89.39 pmol/L); Fig. 1A]. The slope obtained for the comparison of the SBD-RIA and CL methods was less satisfactory [slope, 0.65 (95% CI, 0.61–0.68); intercept, −44.09 pmol/L (95% CI, −56.12 to −30.71 pmol/L; Fig. 1B), and was even poorer when aldosterone values

References
2. Avrameas S, Guilbert B. A method for quantitative determination of cellular immunoglobulins (3), although this method was not a classic (in the strictest sense), quantitative solid-phase immunoassay.

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Plasma Aldosterone Assays: Comparison between Chemiluminescence-Based and RIA Methods

To the Editor:

Measurement of plasma aldosterone is increasingly required in clinical practice because primary aldosteronism (PA) is the most frequent secondary cause of hypertension (1–4). Chemiluminescence-based (CL) assays are attractive alternatives to traditional RIAs for hormones such as aldosterone.

We compared aldosterone results obtained with a new CL method (Nichols Advantage) and an RIA [Sorin Biomedical Diagnostics (SBD)] in blood samples from 236 hypertensive patients. Blood samples were collected and immediately stored in separate aliquots at −20 °C until analysis. For 104 of the samples from these patients, we also compared the SBD-RIA results with results from a second RIA method [Maia Adaltis (MA)]. We then used the CL assay and SBD-RIA to analyze samples obtained from 27 patients before and after inhibition testing (saline loading or fludrocortisone acetate) to confirm the diagnosis of PA. In all 27 patients, the inhibition test was performed because of a previous finding of an increased aldosterone-to-renin ratio (ARR).

Aldosterone was assayed in 2 aliquots from the same sample of each patient, and mean values were used for statistical analyses.

For the CL aldosterone assay, the mean within- and between-assay CVs were 2.6% and 4.7%, respectively, for samples between 213 and 1956 pmol/L. For the SBD-RIA method, within- and between-assay CVs were 3.8% and 3.6%, respectively, at a mean value of 371 pmol/L. For the MA-RIA method, within- and between-assay CVs were 3.5% and 4.1%, respectively, at a mean value of 845 pmol/L.

The correlation coefficient was 0.96 for both RIAs and 0.81 between the SBD-RIA and the CL assay; in the latter case, the coefficient decreased to 0.28 for the lowest values of the curve [aldosterone <277.43 pmol/L (100 pg/mL)]. Passing–Bablok regression analysis of values obtained by both RIAs yielded a good slope [slope, 0.94; 95% confidence interval (CI), 0.88–0.99; intercept, 70.82 pmol/L (95% CI, 50.49–89.39 pmol/L); Fig. 1A]. The slope obtained for the comparison of the SBD-RIA and CL methods was less satisfactory [slope, 0.65 (95% CI, 0.61–0.68); intercept, −44.09 pmol/L (95% CI, −56.12 to −30.71 pmol/L; Fig. 1B), and was even poorer when aldosterone values

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The author of the article cited above responds:

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The assertion made in that article, that EIA/ELISA was first introduced, independently and simultaneously, by 2 scientific research groups, is correct but incomplete. In fact, a 3rd group, our team at the Pasteur Institute, also developed and published in 1971 an enzyme-immunological method, this one for the measurement of serum IgG, with the aid of immunoadsorbents and enzyme-labeled antigens (2).

Incidentally, we also published in 1971 an immunoenzymatic method for the measurement of cellular immunoglobulins (3), although this method was not a classic (in the strictest sense), quantitative solid-phase immunoassay.

References

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