To the Editor:

We conducted two studies of serum antibodies against oxidized LDL (IgoxLDL) in mothers and infants during the past 2 years. We used an ELISA (oLAb; Eli-Tec Laborreagenzien GmbH) based on the use of Cu\(^{2+}\)-oxidized LDL particles bound to the surface of microtiter plate wells and an anti-human IgG-peroxidase conjugate. In the first study of mothers and their infants at birth and again at the age of 3 months (1), we found that the values were not homogeneous in the sera of 3-month-old infants: some infants had markedly increased IgoxLDL, whereas others had values below those in newborns. The mean value was 815 ± 469 units/L compared with 337 ± 214 units/L in newborns. At that time, we were unable to explain these findings.

One year later, we repeated the study and obtained similar results. All mothers were familiar with the aim of the study and gave informed consent. Of the fourteen 3-month-old infants in the study, 8 had low serum IgoxLDL, but 6 subjects had extremely high values. In this study, we were unable to explain these findings.

Table 1. Serum IgoxLDL in mothers and in their children at birth and 3 months later.

<table>
<thead>
<tr>
<th>Group</th>
<th>IgoxLDL, (^a) units/L</th>
<th>At birth</th>
<th>3 months later</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mothers</td>
<td>Newborns</td>
<td>Mothers</td>
</tr>
<tr>
<td>Breast-fed (n = 6)</td>
<td>803 ± 375</td>
<td>657 ± 316</td>
<td>721 ± 297</td>
</tr>
<tr>
<td>Formula-fed (n = 8)</td>
<td>1418 ± 1271</td>
<td>739 ± 605</td>
<td>1025 ± 818</td>
</tr>
<tr>
<td>Total (n = 14)</td>
<td>1059 ± 874</td>
<td>691 ± 435</td>
<td>848 ± 562</td>
</tr>
</tbody>
</table>

\(^a\)Values expressed as mean ± SD.

Surprisingly, the infants with extremely high IgoxLDL had not been breast-fed during the first 3 months of life, whereas the others had been (Table 1). The difference between the values in breast-fed and formula-fed infants was statistically significant (\(P < 0.001\), Wilcoxon unpaired test).

The Spearman rank correlation between IgoxLDL concentrations in the sera of mothers and their newborns was statistically significant (\(r = 0.79; P < 0.001\)); on the other hand, no significant correlation was found between values for 3-month-old infants and their mothers. The early correlation reflects transplacental transport of class G IgoxLDL, whereas the infants were later able to produce their own antibodies. The production rate was individual and could be influenced by nutrition type. We also compared the number of DNA breaks in peripheral lymphocytes from 3-month-old infants by single-cell gel electrophoresis (comet assay). This method in combination with endonuclease III (endoIII) treatment of cells is able to detect oxidized pyrimidines (2). When compared with breast-fed infants, formula-fed infants had a higher number of DNA strand breaks (0.39 ± 0.06 vs. 0.14 ± 0.02 DNA strand breaks/\(10^9\) Da) and endoIII-sensitive sites representing predominantly oxidized pyrimidines (0.24 ± 0.10 vs. 0.07 ± 0.04 endoIII sites/\(10^9\) Da; \(P = 0.027\) and 0.007, respectively, Mann–Whitney). Because the nutrition of infants contributes for their future health (3), our preliminary data may be important.

There are several possible ways to interpret our findings. One possibility is that milk formulas contain higher concentrations of IgGoxLDL than breast milk; this explanation can be omitted because our method was sensitive only to IgGoxLDL. Another explanation for these results is that milk formula diminishes oxidative stress more than breast milk and consequently leads to increased free IgGoxLDL in the circulation of infants because these antibodies are unable to bind to oxidized LDL (4).

A completely different explanation is that formula feeding might cause some kind of gastrointestinal inflammatory reaction followed by early production of IgGoxLDL in these children. This may be likely if the milk formula is of nonhuman, e.g., bovine, origin, but we are also aware of the hypothesis that self-non-self recognition develops after the third month of life. On the other hand, our results show a significant increase of oxidative DNA damage in formula-fed infants compared with breast-fed infants. This increase may be a consequence of a higher oxidative load in formula-fed children, resulting from metabolic processes, or a consequence of higher antioxidative protection in breast-fed infants. The higher number of oxidized LDL particles, which are cytotoxic and able to induce apoptosis (5), may explain the enhanced oxidative DNA damage.

On the basis of our preliminary findings, we are not able to answer these questions properly, but we are convinced that additional studies should be initiated to get clearer recommendations regarding optimal nutrition for children during the first months of life.

References


Alexandra Steinerová 1
František Stožický 2
Jaroslav Racek 3 *
Franz Tatzber 4
Tomáš Zima 5
Rudolf Štětina 6

1 Medica Centrum
301 22 Plzen, Czech Republic
2 Department of Pediatrics and
3 Institute of Clinical Biochemistry and Laboratory Diagnostics
Charles University Hospital
304 60 Plzen, Czech Republic
4 University Clinic for Nuclear Medicine
A-1090 Vienna, Austria
5 Institute of Clinical Biochemistry
1st Faculty of Medicine
Charles University
120 00 Prague, Czech Republic
6 Purkyne Military Medical Academy
Department of Toxicology
500 01 Hradec Kralove, Czech Republic

*Author for correspondence. Fax 420-19-7104234; e-mail racek@fnplzen.cz.