BREAST MILK COMPONENTS AND POTENTIAL INFLUENCE ON GROWTH

Maria Grunewald, Hans Demmelmair, Berthold Koletzko

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AGENDA

Breast Milk
Macronutrients in breast milk
  Carbohydrates
  Protein
  Lipids
Hormones
  Adiponectin
  Insulin
BREAST MILK

- exclusive breastfeeding widely recommended
  - optimal nutrition for health, growth and development
- a highly complex mixture of nutrients dissolved or emulsified in water
- human milk composition is influenced by:
  - genetic factors
  - term or preterm delivery
  - maternal nutrition
  - stage of lactation
  - time of day
  - foremilk or hindmilk
  - milk volume
BREASTFEEDING OR FORMULA FEEDING?

- First nutrition: choice between breast milk or formula

- Koletzko et al. 2005
  - Breastfeeding is protective against later obesity
  - “Growth acceleration hypothesis”: early and rapid growth within first 2 years → programs metabolic profile → obesity risk
  - Breastfeeding decreases the odds ratio for obesity at school age about 20%
CASE: BABY M.D.

- healthy born male
  - birth weight: 4.5 kg
  - birth height: 54 cm
  - birth head circumference: 38 cm
    → 97th percentile

- 41st week of pregnancy, Cesarean section

- Parents: normal weight
- Mother: no gestational diabetes
CASE: BABY M.D.
CASE: BABY M.D.

Weight-for-age BOYS
Birth to 2 years (percentiles)

exclusive bf + complementary foods
DID HIS MOTHER’S BREAST MILK LEAD TO THE EXCESSIVE WEIGHT GAIN DURING THE FIRST MONTHS OF BABY M.D.?

WHICH COMPONENTS IN MILK DO PLAY A ROLE IN REGULATING GROWTH, DEVELOPMENT AND RISK OF OBESITY?
MACRONUTRIENTS IN BREAST MILK

Carbohydrates
Protein
Lipids
BREAST MILK
COMPOSITION OF 100 ML MILK

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Handbook of milk composition (adapted from Michaelsen et al. 1991)
*Mitoulas et al. 2002, Shehadeh et al. 2006
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CARBOHYDRATES

- most constant macronutrient in milk
- mainly lactose, very low levels of glucose, galactose

![Diagram of lactose, lactase, glucose, galactose, and liver]

- human milk oligosaccharides (HMOs)
  - 3-32 sugars, very heterogenic
  - prebiotic → promote growth for probiotic bacteria in child’s gut
    (Dai et al., 2000)
NITROGENOUS COMPOUNDS

- protein (whey and casein fraction)
- NPN fraction (~20-25%), like urea, creatine, amino acids, carnitine
- Early High Protein hypothesis: (Koletzko et al. 2005)

Milk of preterm mothers has higher protein content:

Milk protein concentrations, comparing mothers who delivered preterm and term, by gestational age at delivery and weeks postpartum (Ballard et al., 2013)

Protein

Insulin, IGF-I

Early growth (first 2 years) Adipogenic activity (adipocyte differentiation)
CARNITINE

- function: transports long chain FA across mitochondrial membrane for FA oxidation
- content in breast milk: highest values after 2 weeks postpartum (98.2 µmol/l), than decrease (4 months: 62.3 µmol/l)
- important for newborns because of limited endogenous carnitine synthesis (low gamma butyrobetaine hydroxilase)

<table>
<thead>
<tr>
<th>µmol/l</th>
<th>Range (1-10m pp) (Mitchell et al., 1991)</th>
<th>M.D. Foremilk</th>
<th>M.D. Hindmilk</th>
</tr>
</thead>
<tbody>
<tr>
<td>total</td>
<td>28.01 – 72.18</td>
<td>49.3</td>
<td>31.5</td>
</tr>
<tr>
<td>free</td>
<td>22.68 – 56.25</td>
<td>39.2</td>
<td>22.3</td>
</tr>
</tbody>
</table>
LIPIDS AND FATTY ACID COMPOSITION

- 98% of the milk fat as TAG
- crucial for the newborn: up to 55% of the calories are supplied as fat
- most variable milk component:
  - hindmilk: significant higher fat content (Mitoulas et al. 2002)
  - lower content in night/morning than in afternoon/evening milk
- perinatal LC-PUFA status may influence neurological development, immune system

<table>
<thead>
<tr>
<th>fatty acid (%)</th>
<th>12 m postpartum (mean ± SEM, adapted from Mitoulas et al. 2003)</th>
<th>M.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>C10:0</td>
<td>1.14 ± 0.026</td>
<td>1.39</td>
</tr>
<tr>
<td>C12:0</td>
<td>6.53 ± 0.169</td>
<td>7.89</td>
</tr>
<tr>
<td>C14:0</td>
<td>9.27 ± 0.220</td>
<td>8.96</td>
</tr>
<tr>
<td>C16:0</td>
<td>24.15 ± 0.222</td>
<td>21.77</td>
</tr>
<tr>
<td>C16:1n-7</td>
<td>2.32 ± 0.073</td>
<td>1.47</td>
</tr>
<tr>
<td>C18:0</td>
<td>8.43 ± 0.267</td>
<td>7.51</td>
</tr>
<tr>
<td>C18:1n-7</td>
<td>1.45 ± 0.043</td>
<td>1.47</td>
</tr>
<tr>
<td>C18:1n-9</td>
<td>30.21 ± 0.261</td>
<td>31.77</td>
</tr>
<tr>
<td>C18:2n-6</td>
<td>9.28 ± 0.345</td>
<td>13.15</td>
</tr>
<tr>
<td>C18:3n-3</td>
<td>0.79 ± 0.031</td>
<td>0.93</td>
</tr>
<tr>
<td>C20:0</td>
<td>0.66 ± 0.014</td>
<td>0.21</td>
</tr>
<tr>
<td>C20:4n-6 (AA)</td>
<td>0.34 ± 0.006</td>
<td>0.44</td>
</tr>
<tr>
<td>C22:6n-3 (DHA)</td>
<td>0.18 ± 0.005</td>
<td>0.20</td>
</tr>
</tbody>
</table>
PHOSPHOLIPIDS

- Sphingomyelin, Phosphatidylcholine
  - Membrane constituent
  - Regulation of cell growth, differentiation, apoptosis
  - Neonatal gut maturation

<table>
<thead>
<tr>
<th>µmol/l</th>
<th>PC</th>
<th>PC M.D.</th>
<th>SM</th>
<th>SM M.D.</th>
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<tr>
<td>foremilk</td>
<td>115.7 ± 5.5</td>
<td>65.7</td>
<td>163.4 ± 11.3</td>
<td>63.3</td>
</tr>
<tr>
<td>hindmilk</td>
<td>179.5 ± 10.0</td>
<td>133.4</td>
<td>206.4 ± 9.4</td>
<td>147.0</td>
</tr>
</tbody>
</table>

(mean ± SEM, Data adapted from Zeisel et al. 1986)
HORMONES IN BREAST MILK

Adiponectin
Insulin
**ADIPONECTIN**

- reduced serum levels in **obese** adults (although produced by adipose tissue)

- functions:
  - regulates lipid and glucose metabolism
  - improves insulin sensitivity
  - increases fatty acid oxidation
  - anti-inflammatory

- Mouse: adiponectin receptor 1 in small intestine $\rightarrow$ absorption of breast milk adiponectin into blood (Zhou et al. 2005)
ADIPONECTIN

- breast milk adiponectin: range between 0.8-110 ng/ml (Ozarda et al. 2012)
- higher concentration than other milk adipokines
- average after one year: 25.7 ± 1.4 ng/ml (Bronsky et al. 2011)
- M.D.: adiponectin content 35 ng/ml
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- Woo et al. 2009:
  - breast milk adiponectin is associated with lower infant weight-for-age and WA Z-score during the first six months of life

- Weyermann et al. 2007:
  - high levels of breast milk adiponectin were associated with higher risk for overweight at 2 years of age

→ different results
INSULIN

- key hormone in blood glucose homeostasis

- orally administered breast milk insulin promotes gut maturation (Shehadeh et al. 2003)

- breast milk insulin is increased in obese and overweight mothers (pre-pregnancy BMI) (Ahuja et al. 2011; Ley et al. 2012)

- Insulin mean ± SEM: 15.64 mU/l ± 1.03 (Whitmore et al 2012)

- M.D.: 16.65 mU/l
INSULIN

- Fields et al. 2012
  breast milk insulin is negatively associated with infant weight and lean mass (not fat mass)

- Plageman et al. 2002
  increased concentration of breast milk glucose and breast milk insulin of diabetic mother predict obesity in adulthood

→ different results
CONCLUSION

- for many milk components the influence on growth and development is still not surely known
- sometimes the studies lead to contrary results
- M.D. was growing very fast – just because high protein?
  - influence of higher adiponectin?
  - influence of lower saturated FA, polar lipids?

→ single case does not say enough about the potential influence growth
→ more information is needed
PREVENTCD STUDY

- European research project to prevent coeliac disease, started January 2007
- more than 1000 children in 10 study centers from 7 countries
- Intervention study: influence of dietary history in prevention of CD

- 600 breast milk samples from 5 countries from M1-3 and M4
- 250 matching serum samples

- available growth data up to 6 years of age

- analysis of milk components
ACKNOWLEDGEMENTS
REFERENCES


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