MATERNAL GESTATIONAL DIABETES MELLITUS AND PLACENTAL LIPIDS

Olaf Uhl
Gestational diabetes mellitus (GDM) is the most common form of diabetes in pregnancies.

Maternal glucose status is linked to higher risk for perinatal mortality [1] and offspring macrosomia [2].

Despite of glycemic control in T2DM mothers, infants are still at higher risk for macrosomia [3] and various deviations in the lipid status were observed.

Macrosomia and dyslipidemia might be induced by other factors than glucose \( \rightarrow \) Lipids?

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METABOLISM OF PREGNANT WOMEN

- First trimester → adipose tissue accumulation
  - ↑ Lipoprotein lipase activity (LPL)

- Last trimester → enhanced lipolysis
  - ↓ FA synthesis of AT
  - ↓ LPL activity
  - ↑ Lipolytic activity of AT

Results of IR? [1]

Increasing metabolites:
- TCA intermediates
- β-hydroxybutyrate
- Phospholipids
- Threonine

Decreasing metabolites:
- BCAA
- Free carnitine, acyl-carn
- Lyso-Phospholipids

[1] Sivan, Diabetes, 1999
PREOBE – STUDY DESIGN

Aim
• To better understand the intrauterine effects of GDM and obesity, separately

Study design
• Pregnant women were recruited at the University of Granada
• 3 Groups (Median BMI):
  • 31 Healthy controls (22.5 kg/m2)
  • 29 Obese (31.6 kg/m2)
  • 32 GDM (23.3 kg/m2)
• GDM were treated with nutrition counselling, antidiabetics or insulin

<table>
<thead>
<tr>
<th></th>
<th>CTR</th>
<th>GDM</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (IQR)</td>
<td>n</td>
<td>M (IQR)</td>
</tr>
<tr>
<td>Maternal age [y]</td>
<td>31 (6)</td>
<td>31</td>
<td>32 (5)</td>
</tr>
<tr>
<td>Prepregnancy BMI [kg/m²]</td>
<td>22.5 (2.5)</td>
<td>31</td>
<td>23.3 (2.7)</td>
</tr>
<tr>
<td>Weight gain (week 34) [kg]</td>
<td>13.3 (3.5)</td>
<td>31</td>
<td>11 (6.6)</td>
</tr>
<tr>
<td>Placenta weight [g]</td>
<td>480 (100)</td>
<td>29</td>
<td>500 (175)</td>
</tr>
</tbody>
</table>
PREOBE - METHODS

- Immediately after delivery, placentas were frozen at -80°C
- Frozen placentas were divided into small pieces
- Placenta samples were defrosted and washed with saline solution to remove blood
- Lipids were extracted with chloroform/methanol
- Phospholipids were analysed by liquid chromatography coupled to triple quadrupole mass spectrometry [1]

BAYON, LIPIDS, 1993
PREOBE - RESULTS

- Unique PL pattern: highest LC-PUFA concentration of all kinds of tissues
- DHA was counted to 67.3% in PE
- AA was counted 66.7% in PC
- Highest species: PC(16:0/16:0), PC(16:0/20:4), PC(16:0/18:2), PC(16:0/18:1)
- PC sn-1: 75% palmitic acid (16:0)
- PS sn-1: 100% oleic acid (18:0)

### Phospholipid classes

- PC 72%
- PE 21%
- PS 7%
- LPC <1%

### PREOBE - RESULTS

<table>
<thead>
<tr>
<th>Species</th>
<th>Comp. [%]</th>
<th>Species</th>
<th>Comp. [%]</th>
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</thead>
<tbody>
<tr>
<td>LPC(16:0)</td>
<td>0.32</td>
<td>PE(16:0/18:1)</td>
<td>1.03</td>
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<tr>
<td>PC(16:0/14:0)</td>
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<td>PE(16:0/18:2)</td>
<td>0.88</td>
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<tr>
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<td>PE(16:0/22:6)</td>
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<tr>
<td>PC(16:0/18:2)</td>
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<td>PE(18:0/18:1)</td>
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<tr>
<td>PC(16:0/20:3)</td>
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<td>1.28</td>
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<td>PS(18:0/22:6)</td>
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</tbody>
</table>
GPL PATTERN OF GDM AND OBESE IN COMPARISON TO CONTROLS

* Mann-Whitney-U test, Significance was accepted at p < 0.05

DHA TRANSFER

Maternal Circulation

13C-labeled FA before caesarean section [1]

Newborn: ↑ AA, ↑ DHA [3]

Preferred transfer of DHA through the placenta

DHA TRANSFER IN GDM PREGNANCIES

Maternal Circulation

Membrane

Receptor

LDL

HDL

VLDL

NEFA

FABP/FATP

LPL

PL/TAG

NEFA

Umbilical vein

Liver

Fetal Circulation

Membrane

GDM: ↓ DHA (maternal/fetal)
No difference in (maternal/placental) [3]

GDM No differences reported [4]

GDM ↑ DHA in PC, PE [1]

GDM ↑ DHA just in artery plasma [2]

DGLA TRANSFER IN GDM PREGNANCIES

Maternal Circulation

<table>
<thead>
<tr>
<th>LDL</th>
<th>HDL</th>
<th>VLDL</th>
<th>NEFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptor</td>
<td>EL</td>
<td>FABP/FATP</td>
<td></td>
</tr>
<tr>
<td>Membrane</td>
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</table>

GDM/Obese: ↓ DGLA [1]

Fetal Circulation

<table>
<thead>
<tr>
<th>NEFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPL</td>
</tr>
<tr>
<td>Membrane</td>
</tr>
</tbody>
</table>

GDM: ↓ DGLA in venous cord plasma [2]

Umbilical vein

Birth weight: ↑ LPC(20:3) ↑ FA(20:3n-9) [5]

Precursor of prostaglandin E1, a vasorelaxant and anticoagulant mediator. Increase in DGLA from pre-term to term placentas → labor induction [6]

Pre-pregnancy BMI ↑ DGLA [4]

Pre-pregnancy BMI ↑ DGLA [4]

References:
PLACENTAL STRUCTURE

• Complex structure with different cells with different function

• GDM leads to histological changes in the syncytiotrophoblast [1]

• Lipid Droplets [2]:
  • Intracellular structures
  • Surrounded by phospholipids and proteins
  • Contain triacylglycerols and cholesterol ester
  • Role in placenta?


→Poster I-4
Antonio Gázquez

„Placental Lipid Droplet Composition is Associated with Maternal Clinical Parameters and Cord Blood Metabolites“
PREOBE - RESULTS

AA: ↑ cell and tissue growth [1]

PE(AA) ~ birth weight [2]

Plasma TAG(AA) ~ body weight [3]

[1] Sellmayer, Lipids, 1999
SUMMARY

Results

• Elevated levels of AA and DHA in GDM placentas
• Lower levels of DGLA in GDM
• Comparable disarrangement of GPL species pattern between obese and GDM
• PC(AA) → Fetal supply
• PE(AA) → Placental development

Limitations

• Dietary bias of GDM patients
• Complex structure of placental tissue
• No correction for multiple testing
THANKS FOR YOUR ATTENTION