Metformin in PCOS pregnancies
Implications for the children

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Background

Metformin is increasingly used in pregnancy; in polycystic ovary syndrome (PCOS), GDM and obesity. It passes the placenta, with limited information on consequences for the offspring.

Aim: to explore possible effects of intrauterine metformin exposure on metabolic health, in children of women with PCOS

Method

Follow-up of 141 children from the PregMet-study1, an RCT comparing metformin (2000 mg daily) to placebo during PCOS pregnancies

• Primary end-point: age-and-gender adjusted BMI
• Secondary end-points: other age-and-gender adjusted anthropometric measurements, bioimpedance measurements, BMI categories, blood lipids, fasting glucose, HbA1c and blood pressure

Anthropometric measurements were converted to z-scores2,3

Results

Mean age at inclusion was 7.4 ± 1.2 SD in the placebo group and 7.6 ± 1.3 SD in the metformin group

Metformin exposed children had higher BMI z-score, waist-to-height ratio z-score and waist circumference z-score.

There was no difference in biochemical analyses or blood pressure.

The effect of metformin on offspring BMI z-score increased by 0.05 SD (95% CI 0.00 to 0.11, p=0.052) with every unit increase in maternal pre-pregnancy BMI

Body composition, biochemical markers and blood pressure of metformin and placebo exposed offspring

Birth weights were converted to z-scores, and cut-off levels. Offspring BMI z-score at follow-up

Maternal baseline characteristics

Metformin n=67
Placebo n=70
Mean (Mean SD)

<table>
<thead>
<tr>
<th>Maternal baseline characteristics</th>
<th>Metformin n=67</th>
<th>Placebo n=70</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>29.5 ± 3.9</td>
<td>30.1 ± 4.1</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>28.8 ± 6.8</td>
<td>28.5 ± 6.3</td>
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<td>Systolic blood pressure (mmHg)</td>
<td>118 ± 12</td>
<td>118 ± 12</td>
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<tr>
<td>Fasting plasma glucose (mmol/L)</td>
<td>4.6 ± 0.5</td>
<td>4.7 ± 0.6</td>
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<tr>
<td>2 h plasma glucose (mmol/L)</td>
<td>5.3 ± 1.5</td>
<td>5.4 ± 1.7</td>
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<tr>
<td>Cholesterol (mmol/L)</td>
<td>4.8 ± 1.1</td>
<td>4.4 ± 0.7</td>
</tr>
<tr>
<td>High Density Lipoprotein (mmol/L)</td>
<td>1.6 ± 0.4</td>
<td>1.6 ± 0.3</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.2 ± 0.5</td>
<td>1.1 ± 0.5</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>4 (6.0)</td>
<td>3 (4.6)</td>
</tr>
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</table>

No difference (p-value < 0.05) between the groups, except cholesterol (p=0.009)

Conclusion

• Children exposed to metformin in utero had increased risk of obesity and central adiposity
• The metformin effect was more pronounced when mothers had high pre-pregnancy BMI
• Our results endorse cautious use of metformin in PCOS pregnancies

1Venk E, et al. Metformin versus placebo from first trimester to delivery in polycystic ovary syndrome: a randomized, controlled multicenter study. J Clin Endocrinol Metab. 2010;95(9):4648-4656

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