Easing the burden of obesity in pregnancy: a UK perspective

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Scotland has one of the highest obesity rates of all OECD countries

Obesity in pregnancy

Obese women are more likely to die in pregnancy

- 49% of women who died had BMI ≥ 25
- 27% of women who died had BMI ≥ 30
- Thromboembolism - 78%
- Cardiac causes – 61%
  - Were overweight or obese

- Issues
  - Equipment (eg BP cuff)
  - Logistical
Maternal obesity - what are the problems (annual UK impact)

- Deaths of 9 women
- Stillbirth of 2,520 babies
- Macrosomia (birthweight > 4kg) of 11,200 babies
- 25,200 extra Caesarean sections
- Increased costs to the health service – £550 to £1035 per woman (Denison et al, 2014, BJOG)

Maternal obesity increases risk of infant mortality

Metabolic antenatal clinic in Edinburgh

Pregnant women with BMI ≥ 40

Metabolic antenatal clinic in Edinburgh

Protocol
- Regular weight / dietetic advice
- Encourage exercise
- High dose folate
- Screening for GDM
- Measure BP using appropriate sized cuff
- Growth scans
- Anaesthetic review
- Discussion re. delivery
- Post term fetal monitoring
- Post delivery oxytocin infusion
- Post natal thromboprophylaxis
Maternal obesity increases all cause death in offspring after adjustment

Reynolds R et al 2013 BMJ;347:f4539 doi: 10.1136/bmj.f4539

Maternal obesity during pregnancy and premature mortality from cardiovascular event in adult offspring: follow-up of 1 323 275 person years

Population studies

Reynolds R et al 2013 BMJ;347:f4539 doi: 10.1136/bmj.f4539

Maternal obesity increases all cause death in offspring after adjustment

Reynolds R et al 2013 BMJ;347:f4539 doi: 10.1136/bmj.f4539
HAPO shows a direct relationship between adverse pregnancy outcomes and glucose intolerance.

Obese pregnant women are more insulin resistant

<table>
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<tr>
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<th>Obese</th>
<th>Lean</th>
<th>P-value</th>
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<tbody>
<tr>
<td>HOMA (mean SEM)</td>
<td>4.3 (0.5)</td>
<td>1.2 (0.3)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Insulin (median IQR)</td>
<td>14.2 (11.3–27)</td>
<td>6.15 (4.47–9.5)</td>
<td>&lt; 0.0001</td>
</tr>
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Challier 2008

And high birthweight, 3636 (37) g versus 3556 (43) g, p = 0.04 after adjustment

Forbes SF et al 2015 Diabetologia 58:2615

Obese women have higher blood glucose and are more insulin resistant


Obese women have higher blood glucose and are more insulin resistant

HOMA (mean SEM)

Challier 2008

Insulin (median IQR)

Ramsay 2002

Ramsay JE 2002 JEM 87: 4231

Challier JC 2008 Placenta 29 : 274
Obesity, maternal glucose and insulin sensitivity

- Obese women have higher blood glucose and poorer insulin sensitivity
- High maternal blood glucose and poor insulin sensitivity correlate with a variety of adverse outcomes including caesarean section and high birthweight
- Does reduction of blood glucose and improvement in insulin sensitivity improve outcome?

Interventional study with metformin EMPOWaR

- Well established drug used to treat type II diabetes
- Biguanide that decreases hepatic glucose production
- Increases glucose uptake in liver and skeletal muscle
- Mechanism via inhibition of the mitochondrial respiratory chain and a consequent increase in AMP activated protein kinase

Primary objective

- What is the efficacy of metformin (up to 2500mg daily), given to obese pregnant women from 12 - 16 weeks gestation until delivery in reducing birthweight centile of the baby?

Chiswick C et al 2015 Lancet Diabetes and Endocrinology 3(10):77
### Primary outcome

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<th>Placebo (n=220)</th>
<th>Metformin (n=214)</th>
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<tr>
<td>Birthweight</td>
<td>3463g 660g</td>
<td>3462g 548g</td>
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<tr>
<td>Birthweight centile</td>
<td>57.3 27.1</td>
<td>56.9 28.6</td>
</tr>
<tr>
<td>Z score of Birthweight centile</td>
<td>0.2680 1.0055</td>
<td>0.2464 1.0179</td>
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Adjusted mean difference (95% CI) of birthweight centile:

\[-0.029 (-0.217 to 0.158), p = 0.7597\]

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**Effect of metformin on maternal and fetal outcomes in obese pregnant women (EMPOWAll): a randomised, double-blind, placebo-controlled trial**

Chiwick C et al 2015 Lancet Diabetes and Endocrinology 3(10):77

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**Lifestyle interventions in obese pregnant women**

Summary

- Obese women have increased risk of a variety of adverse outcomes
- Emerging evidence of long term offspring effects
- Pathophysiology behind adverse outcomes uncertain
- Exercise and treatment with glucose lowering drugs unhelpful
- Further research needed.

Acknowledgements

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