Exposure to phthalates and phenols in relation to gestational blood glucose homeostasis

B. G. Fisher[a], H. Frederiksen[b], A. M. Andersson[b], A. Juul[b], A. Thankamony[a], K. K. Ong[c], D. B. Dunger[a], I. A. Hughes[a], C. L. Acerini[a]

[a]Department of Paediatrics, University of Cambridge, Cambridge, United Kingdom; [b]Department of Growth and Reproduction and EDMaRC, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [c]MRC Epidemiology Unit, Institute of Metabolic Science, Cambridge, United Kingdom

Introduction

- Late pregnancy is characterised by insulin resistance, which can lead to gestational diabetes mellitus (GDM)[1].
- Endocrine disrupting chemicals (EDCs), such as phthalates and bisphenol A (BPA), have been associated with insulin resistance and type 2 diabetes in non-pregnant adults[2-5].
- By contrast, recent studies of pregnant women have found:
  - Negative relationships between phthalates and stimulated blood glucose[6];
  - No association between phthalates or BPA and GDM[7,8].
- No studies have examined triclosan (TCS) in relation to GDM, or gestational insulin resistance (IR) or secretion in relation to EDC exposure.

Method

- 232 mothers without type 1/2 diabetes with singleton male pregnancies were recruited from a single UK centre as part of a large prospective study (Cambridge Baby Growth Study).
- Serum was collected at 10-17 weeks of gestation.
- 18 EDCs (16 metabolites of 9 phthalate diesters, 9 phenols) were measured using liquid chromatography/tandem mass spectrometry.
- GDM was diagnosed from an oral glucose tolerance test at 28 weeks of gestation using IADPSG criteria.
- Homeostasis Model Assessment (HOMA)-IR and β-cell function were calculated.
- Regressions controlled for age, BMI, deprivation index, ethnicity, smoking, and parity.

Objective

- To investigate the relationship between maternal phthalate and phenol exposure at 10-17 weeks of gestation and glucose homeostasis at 28 weeks of gestation.

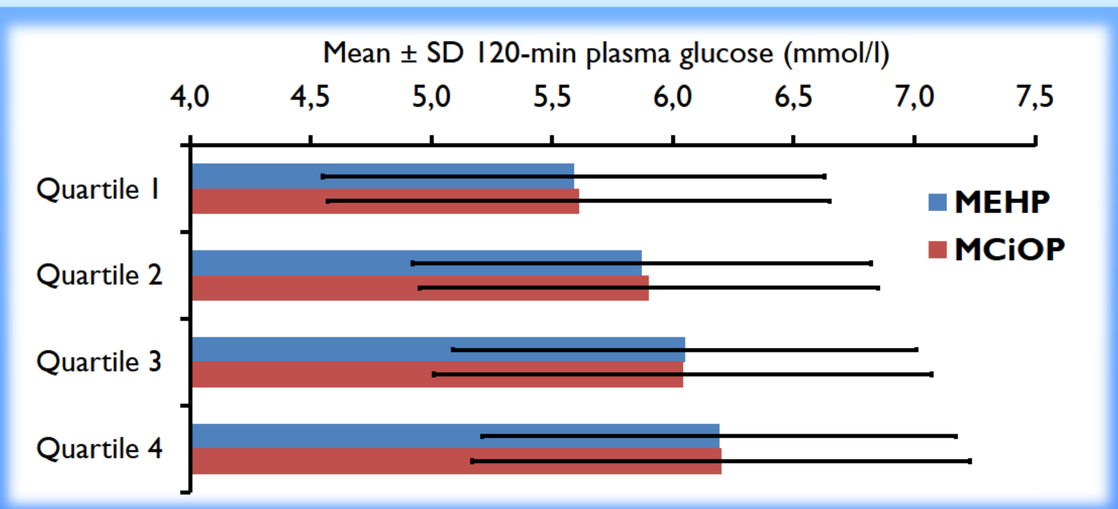
Results

Maternal characteristics (mean ± SD)

	Mothers with GDM (n = 47, 20.3%)	Mothers without GDM (n = 185, 79.7%)	P value
Age (years)	33.1 ± 4.4	33.7 ± 3.8	0.30
Pre-pregnancy BMI (kg/m²)	25.4 ± 5.1	23.7 ± 3.7	0.051
Ethnicity			
White	28 (100%)	119 (96.7%)	0.75
Other	0 (0%)	4 (3.3%)	
Current smoker	1/47 (2.1%)	4/185 (2.2%)	0.99
Parity			
0	22 (46.8%)	88 (47.6%)	0.99
1	19 (40.4%)	75 (40.5%)	
≥2	6 (12.8%)	22 (11.9%)	
Index of Multiple Deprivation (units)	9.43 ± 3.48	9.35 ± 4.27	0.90

Associations with parameters of glucose homeostasis

- Amongst mothers without GDM, mono-(2-ethylhexyl) phthalate (MEHP)† and mono(carboxyisooctyl) phthalate (MCiOP)† were associated with 120-min plasma glucose (adjusted β = 0.297 and 0.238, p = 0.002 and 0.013).



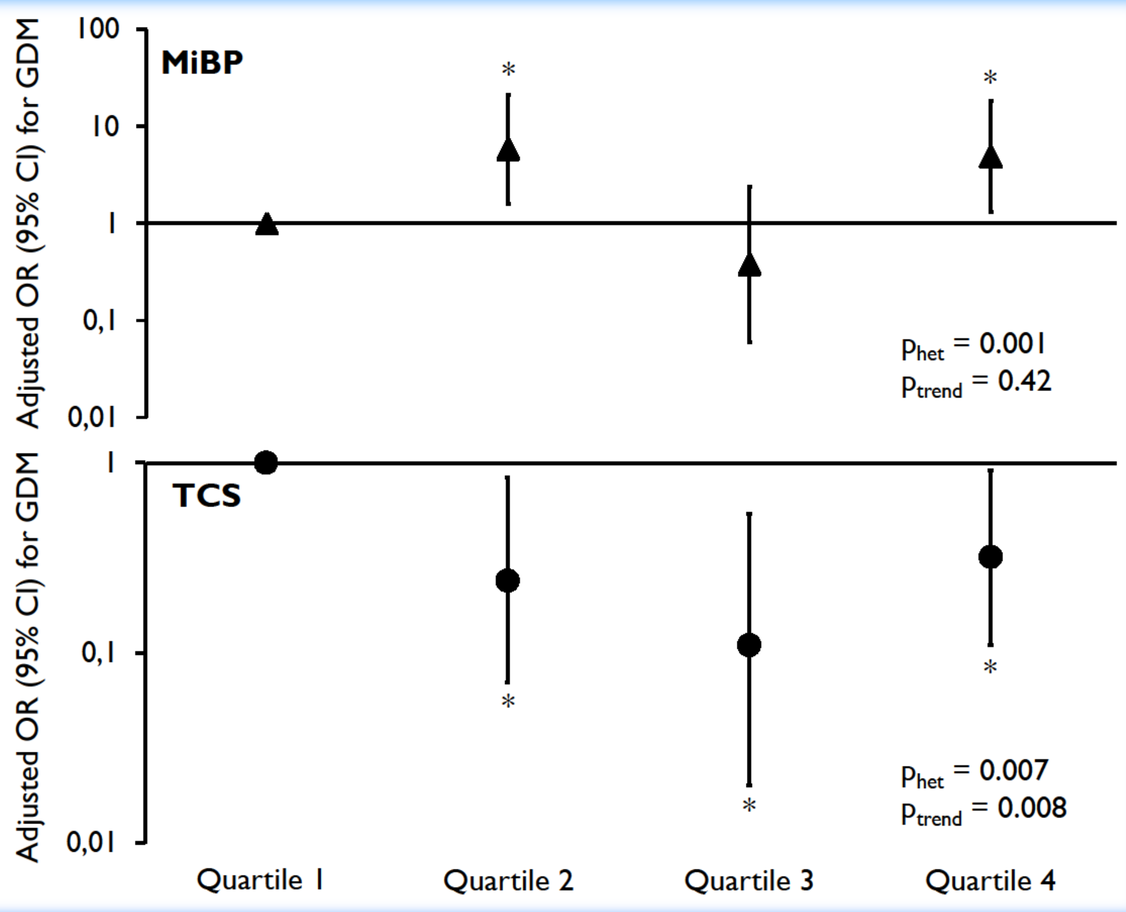
- No EDCs were associated with HOMA-IR, HOMA-β-cell function, or disposition index.

EDC characteristics

- 6 phthalate metabolites (MEP, MiBP, MnBP, MEHP, MECPP, MCiOP) and 3 phenols (BPA, TCS, BP-3) were detectable in >60% serum samples.
- Median concentrations were 1.56, 3.78, 1.34, 1.14, 0.52, 0.18, 1.76, 0.93, and 0.34 µg/l, respectively.

Associations with incident GDM

- Only mono-isobutyl phthalate (MiBP)† and TCS were significantly associated with incident GDM in continuous and quartile analyses.



† Phthalate metabolite parent compounds: MiBP: di-isobutyl phthalate; MEHP: di-(2-ethylhexyl) phthalate; MCiOP: di-isononyl phthalate.

Conclusion

- Our results provide further evidence of a diabetogenic effect of phthalates, and suggest for the first time a possible ameliorating effect of TCS.

References

1. National Collaborating Centre for Women's and Children's Health, 2015. http://www.nice.org.uk/guidance/ng3/evidence/full-guideline-3784285
2. James-Todd, T. et al., 2012. Environmental Health Perspectives, 120(9), pp.1307–1313.
3. Beydoun, H.A. et al., 2014. Annals of Epidemiology, 24(2), pp.90–97.
4. Dirinck, E. et al., 2015. Environmental Research, 137, pp.419–423.
5. Aekplakorn, W., Chailurkit, L.-O. & Ongphiphadhanakul, B., 2015. Journal of diabetes, 7(2), pp.240–9.
6. Robledo, C.A. et al., 2015. International Journal of Hygiene and Environmental Health, 218(3), pp.324–330.
7. Robledo, C. et al., 2013. Journal of toxicology and environmental health. Part A, 76(14), pp.865–73.
8. Shapiro, G.D. et al., 2015. Environment International, 83, pp.63–71.

ESPE 2015
256--P2
Diabetes and Insulin
Benjamin Fisher
DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: ESPE 2015 BARCELONA