BPA exposure during pregnancy: risk for gestational diabetes and diabetes following pregnancy

Paloma Alonso-Magdalena
Applied Biology Department and CIBERDEM, Miguel Hernández University, Elche, Spain
palonso@umh.es
Pregnancy transiently drives women into a metabolic stress scenario that can determinate their health status in later life.
- Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.

- Approximately 7% of all pregnancies are complicated by GDM resulting in more than 200,000 cases annually.
RISKS FACTORS FOR GDM

- Age
- History of gestational diabetes
- Obesity
- Ethnicity
- Sedentary lifestyle
- History of smoking
CONSEQUENCES OF GESTATIONAL DIABETES IN THE LONG TERM......
During post-partum most of the women return to euglycemic state, however carbohydrate intolerance can return with age.

- Women with GDM are at increased risk for the development of diabetes, usually type 2, after pregnancy.

Glucose intolerance during pregnancy as a predictor of maternal long-term health
“{**ENDOCRINE DISRUPTORS**} have been defined as exogenous substances that alter function(s) of the endocrine system and consequently cause adverse health effects in an intact organism, its progeny, or subpopulations”

The International Program for Chemical Safety
WHAT HAPPEN IF MOTHERS ARE EXPOSED TO THESE COMPOUNDS DURING PREGNANCY?
RISKS FACTORS FOR GDM AND LONG-TERM COMPLICATIONS

- Age
- History of gestational diabetes

ENDOCRINE DISRUPTOR CHEMICALS

- Sedentary lifestyle
- History of smoking
- PCOs
The case of bisphenol A: What is and where is found BPA?

Welshons, W. V. et al. Endocrinology 2006
BPA has been detected in 93% of the urine samples in USA (Calafat et al, 2008)

0.3-4.4 ng/ml (1.3-19.4 nM) unconjugated BPA in human blood from adult men and women (Vandenberg et al, EHP 2010)

BPA levels detected in amniotic fluid, neonatal blood, placenta, cord blood and human breast milk.
Bisphenol-A action on pregnant mice

End points measured at pregnancy days 17 and 18

BPA 10 μg/kg/day
BPA 100 μg/kg/day

Alonso-Magdalena et al, EHP 2010
Pregnancy

End points measured at pregnancy days 17 and 18

**GLUCOSE TOLERANCE TEST**

Alonso-Magdalena et al, EHP 2010
Insulin signaling in BPA-10 pregnant treated mice

Liver

Bisphenol-A alters glucose and lipid metabolism during pregnancy

Alonso-Magdalena et al, Environ Health Perspect 2010
EVOLUTION OF THE MOTHER AFTER DELIVERY

- 3 Months after labor
- 4 Months after labor
- 5 Months after labor
- 6 Months after labor
- 7 Months after labor
GLUCOSE TOLERANCE TEST in the mother after labor

A  3 MONTHS POSTPARTUM

B  4 MONTHS POSTPARTUM

C  5 MONTHS POSTPARTUM

D  6 MONTHS POSTPARTUM

Alonso-Magdalena P. et al Endocrinology 2015
INSULIN TOLERANCE TEST in the mother after labor

A 3 MONTHS POSTPARTUM

Time (min)

% Glycemia (mg/dL)

Control

BPA10

BPA100

B

4 MONTHS POSTPARTUM

Time (min)

% Glycemia (mg/dL)

B

C

5 MONTHS POSTPARTUM

Time (min)

% Glycemia (mg/dL)

D

6 MONTHS POSTPARTUM

Time (min)

% Glycemia (mg/dL)

Alonso-Magdalena P. et al Endocrinology 2015
Seven months after labor mothers that have been treated with BPA show a decline of pancreatic β-cell function.

A) Plasma insulin levels

B) Glucose-stimulated insulin secretion

C) Insulin secretion (% Insulin content)

D) Insulin content

Alonso-Magdalena P. et al Endocrinology 2015
Seven months after labor mothers that have been treated with BPA show reduced β-cell mass, reduced β-cell proliferation and increase rate of apoptosis

Alonso-Magdalena P. et al Endocrinology 2015
BPA exposure in mice during pregnancy resulted in an impairment of glucose tolerance and decreased insulin sensitivity in mothers.

Alterations on glucose metabolism were resolved after parturition but were triggered again some months later.

Six months after delivery those moms that have been treated with BPA during pregnancy exhibited marked glucose intolerance and insulin resistance.

Seven months after delivery they showed decrease β-cell function, β-cell mass and increased apoptosis.

They also showed an altered expression of several cell cycle regulators.

BPA exposure during pregnancy could be considered a new risk factor for the deterioration of maternal glucose metabolism and the increased occurrence of diabetes.
Figure 1 Pregnancy-like actions of endocrine disrupting chemicals on islet function and glucose homeostasis

Alonso-Magdalena, P. et al. (2011) Endocrine disruptors in the etiology of type 2 diabetes mellitus
Nat. Rev. Endocrinol. doi:10.1038/nrendo.2011.56
Acknowledgements

Ángel Nadal
Marta García-Arévalo
Iván Quesada
Sergi Soriano
Mª Luisa Navarro
Salomé Ramón

Elaine Vieira
Deborah Burks and Lorena Menes (Instituto Príncipe Felipe, CSIC, Valencia)

Grant support:

EFSD, MINECO, Generalitat Valenciana and ISCarlos III