Environmental Research 147 (2016) 71–81

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Exposure to organophosphorus and organochlorine pesticides, perfluoroalkyl substances, and polychlorinated biphenyls in pregnancy and the association with impaired glucose tolerance and gestational diabetes mellitus: The MIREC Study

Gabriel D. Shapiro [a,b], Linda Dodds [c,*], Tye E. Arbuckle [d], Jillian Ashley-Martin [c], Adrienne S. Ettinger [e], Mandy Fisher [d], Shayne Taback [f], Maryse F. Bouchard [b], Patricia Monnier [a], Renée Dallaire [g], Anne-Sophie Morisset [g], William Fraser [b,h,i]

[a] McGill University, Montreal, QC, Canada
[b] CHU Sainte-Justine Research Centre, Université de Montréal, Montreal, QC, Canada
[c] Dalhousie University, Halifax, NS, Canada
[d] Health Canada, Ottawa, ON, Canada
[e] Yale University, New Haven, CT, USA
[f] University of Manitoba, Winnipeg, MB, Canada
[g] Laval University, Québec City, QC, Canada
[h] Centre de recherche du CHUS, Sherbrooke, QC, Canada
[i] Université de Sherbrooke, Sherbrooke, QC, Canada

ARTICLE INFO

Article history:
Received 26 October 2015
Received in revised form
6 January 2016
Accepted 26 January 2016

Keywords:
Pesticides
Perfluoroalkyl substances
Polychlorinated biphenyls
Gestational diabetes mellitus
Pregnancy

ABSTRACT

Background: Studies report increases in rates of gestational diabetes mellitus (GDM) over recent decades. Environmental chemicals may increase the risk of diabetes through impacts on glucose metabolism, mitochondrial dysfunction, and endocrine-disrupting mechanisms including effects on pancreatic β-cell function and adiponectin release.

Objectives: To determine the associations between pesticides, perfluoroalkyl substances (PFASs) and polychlorinated biphenyls (PCBs) measured in early pregnancy and impaired glucose tolerance (IGT) and GDM in a Canadian birth cohort.

Methods: Women enrolled in the Maternal-Infant Research on Environmental Chemicals (MIREC) Study were included if they had a singleton delivery and did not have pre-existing diabetes. Exposure variables included three organophosphorus (OP) pesticide metabolites detected in first-trimester urine samples, as well as three organochlorine (OC) pesticides, three PFASs, and four PCBs in first-trimester blood samples. Gestational IGT and GDM were assessed by chart review in accordance with published guidelines. Adjusted logistic regression models were used to calculate odds ratios (ORs) and 95% confidence intervals (CI) for the association between quartiles of environmental chemicals and both gestational IGT and GDM.

Results: Of the 2001 women recruited into the MIREC cohort, 1274 met the inclusion criteria and had outcome and biomonitoring data available. Significantly lower odds of GDM were observed in the third and fourth quartiles of dimethylphosphate (DMP) and in the fourth quartile of dimethylthiophosphate (DMTP) in adjusted analyses (DMP Q3: OR=0.2, 95% CI=0.1–0.7; DMP Q4: OR=0.3, 95% CI=0.1–0.8; DMTP: OR=0.3, 95% CI=0.1–0.9). Significantly elevated odds of gestational IGT was observed in the second quartile of perfluorohexane sulfonate (PFHxS) (OR=3.5, 95% CI=1.4–8.9). No evidence of associations with GDM or IGT during pregnancy was observed for PCBs or OC pesticides.

Conclusions: We did not find consistent evidence for any positive associations between the chemicals we examined and GDM or IGT during pregnancy. We observed statistical evidence of inverse relationships between urine concentrations of DMP and DMTP with GDM. We cannot rule out the influence of residual

Abbreviations: CHMS, Canadian Health Measures Survey; DDE, p,p′-dichlorodiphenyldichloroethylene; DEP, diethylphosphate; DMP, dimethylphosphate; DMTP, dimethylthiophosphate; GDM, gestational diabetes mellitus; IGT, impaired glucose tolerance; LOD, limit of detection; MIREC, Maternal-Infant Research on Environmental Chemicals; OC, organochlorine; OP, organophosphorus; OR, odds ratio; PCB, polychlorinated biphenyl; PCB118, 2,3′,4,4′,5-pentachlorobiphenyl; PCB138, 2,2′,3,4,4′,5′-hexachlorobiphenyl; PCB153, 2,2′,4,4′,5,5′-hexachlorobiphenyl; PCB180, 2,2′,3,4,4′,5,5′-heptachlorobiphenyl; PFAS, perfluoroalkyl substance; PFHxS, perfluorohexane sulfonate; PFOA, perfluorooctanoic acid; PFOS, perfluorooctane sulfonate

* Correspondence to: Perinatal Epidemiology Research Unit, 7th Floor Women's Site, IWK Health Centre, 5980 University Ave., PO Box 9700, Halifax, NS, Canada B3H 6R8.
E-mail address: L.Dodds@dal.ca (L. Dodds).

http://dx.doi.org/10.1016/j.envres.2016.01.040

confounding due to unmeasured protective factors, such as nutritional benefits from fruit and vegetable consumption, also associated with pesticide exposure, on the observed inverse associations between maternal OP pesticide metabolites and GDM. These findings require further investigation.

1. Introduction

Diabetes is a substantial and growing public health problem (International Diabetes Federation, 2013), and increasing rates of gestational diabetes mellitus (GDM) form part of this trend (Davenport et al., 2010; Feig et al., 2014; Galtier, 2010). Evidence suggests that the etiology of diabetes is likely multifactorial (Public Health Agency of Canada, 2011) and that environmental chemicals may play a role along with more traditional risk factors such as excess caloric consumption, lack of physical activity and increased BMI (Bezek et al., 2008; Kuo et al., 2013; Thayer et al., 2012). However, examination of the environmental chemical hypothesis with regards to GDM has been more limited (Ettinger et al., 2009; Robledo et al., 2013; Saldana et al., 2007; Saunders et al., 2014). The potential health effects of perinatal chemical exposures (Newbold, 2011) and GDM (Aerts and Van Assche, 2006; Osgood et al., 2011) are a concern for subsequent maternal and offspring metabolic health.

Organophosphates (OPs) are the most widely used class of pesticides for agricultural and landscape pest control (Rezg et al., 2010). The primary route of exposure is via ingestion of contaminated food (Lu et al., 2008). These pesticides are metabolized relatively quickly and are not persistent in the environment (Lambert et al., 2005). The dialkyl phosphate metabolites, rather than the parent compounds, are used as non-specific biomarkers of exposure in urine. Evidence from human and animal studies supports a potential role for OPs in the development of obesity and type 2 diabetes (Rahimi and Abdollahi, 2007; Rezg et al., 2010).

Epidemiologic studies have also shown associations between organochlorine (OC) pesticides and diabetes (Azandjeme et al., 2014; Cox et al., 2007; Gray et al., 2013; Hectors et al., 2011; Lee et al., 2011a; Philibert et al., 2009; Rignell-Hydbom et al., 2009, 2007; Son et al., 2010; Turyk et al., 2009a, 2009b; Ukropec et al., 2010). While OC pesticides are no longer registered for use in Canada, they are persistent in the environment, and trace amounts may still be found in food products. Finally, epidemiologic evidence also suggests a potential role for other classes of chemicals including perfluoroalkyl substances (PFASs) (Lin et al., 2009; Steenland et al., 2010; Zhang et al., 2015) and polychlorinated biphenyls (PCBs) (Carpenter, 2008; Everett et al., 2011) in the development of diabetes.

The above-mentioned chemical classes are hypothesized to increase risk of diabetes through modulation of glucose metabolism (OP compounds and PFAS) (Hectors et al., 2011; Lv et al., 2013; Rahimi and Abdollahi, 2007), mitochondrial dysfunction (OC pesticides and PCBs) (Lee et al., 2014), and endocrine-disrupting mechanisms (OC pesticides and PCBs) (Lee et al., 2014) including effects on pancreatic β-cell function (PCBs) (Gray et al., 2013; Hectors et al., 2011) and adiponectin release (OC compounds) (Howell and Mangum, 2011). However, exploration of these chemicals in relation to GDM has been limited (Saldana et al., 2007; Saunders et al., 2014). In light of the current literature, we speculated that exposure to the above-mentioned chemical classes may be associated with GDM or impaired glucose tolerance (IGT) during pregnancy. Using data from a Canadian birth cohort, the present study sought to determine whether exposure to OP or OC pesticides, PFAS or PCBs, measured early in pregnancy in maternal blood and urine, was associated with increased risk of GDM or IGT during pregnancy.

2. Materials and methods

2.1. Study sample

The Maternal-Infant Research on Environmental Chemicals (MIREC) Study is a longitudinal birth cohort study conducted in Canada. Further details concerning inclusion and exclusion criteria and study objectives and procedures have been published elsewhere (Arbuckle et al., 2013). The present analysis used the same subset of the MIREC study sample as our previous work looking at GDM and gestational IGT in relation to metals and phthalates (Shapiro et al., 2015). Briefly, participants were included if they gave birth to a live singleton, had sufficient data from the glucose challenge test (GCT) and/or oral glucose tolerance test (OGTT) to determine a diagnosis of GDM and gestational IGT, and had exposure data available for at least one of the chemicals investigated (PCBs, OC pesticides, OPs, and PFASs). All participants signed informed consent forms and the study received ethical approval from Health Canada and all the study centres.

2.2. Chemical Biomonitoring data

First trimester urine samples were analysed for six OP pesticide metabolites (diethylphosphate (DEP), diethyldithiophosphate (DEDTP), diethylthiophosphate (DETP), dimethylphosphate (DMP), dimethylthiophosphate (DMTP), dimethyldithiophosphate (DMDTP)). Eleven OC pesticides (p,p′-dichlorodiphenyldichloroethylene (DDE), oxychlordane, trans-nonachlor, aldrin, alpha-chlordane, gamma-chlordane, cis-onachlor, gamma-hexachlorocylcohexane (γ-HCH), p,p′-dichlorodiphenyltrichloroethane (p,p′-DDT), hexachlorobenzene (HCB), mirex)), three PFASs (perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), perfluorohexane sulfonate (PFHxS)), and 24 PCBs were measured in first trimester plasma samples. We focused our analyses on exposures for which there were detectable levels in $>75\%$ of subjects. This included three OP pesticide metabolites (DEP, DMP, DMTP), three OC pesticides (p,p′- DDE, oxychlordane, trans-nonachlor), all three PFASs and four PCB congeners (2,3′,4,4′,5-pentachlorobiphenyl (PCB118), 2,2′,3,4,4′,5′-hexachlorobiphenyl (PCB138), 2,2′,4,4′,5,5′-hexachlorobiphenyl (PCB153), 2,2′,3,4,4′,5,5′-heptachlorobiphenyl (PCB180)).

All chemical analyses were carried out at the Toxicology Centre of the Quebec Institute of Public Health (Institut national de santé publique du Québec), accredited by the Standards Council of Canada under ISO 17025 and CAN-P-43. The accuracy and precision of the analyses are evaluated on a regular basis through the laboratory's participation in external quality assessment programs (Arbuckle et al., 2013). OC pesticides and PCBs were analyzed by gas chromatography—mass spectrometry using the Agilent 6890N/5973. Plasma samples were enriched with internal standards and halogenated organic compounds were retrieved by liquid-liquid extraction with a mixture of ammonium sulfate:ethanol:hexane (1:1:3). Extracts were concentrated, automatically purified on florisil column and then analyzed by gas chromatography coupled