Letter to Editor

iMedPub Journals
http://www.imedpub.com/

Journal of Clinical and Molecular Endocrinology
ISSN 2572-5432

2016
Vol.1 No.2:13

DOI: 10.21767/2572-5432.10013

Polychlorinated Biphenyl Exposure Induces Early End-Points of Type 2 Diabetes Mellitus: A Matter of Public Health Concern

Rodrigo Azevedo Loiola[1] and Sandra Farsky[2]

[1]William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University, London, United Kingdom

[2]Faculty of Pharmaceutical Sciences, University of São Paulo, São Paulo, Brazil

Corresponding author: Farsky S, Professor, Faculty of Pharmaceutical Sciences, University of São Paulo, São Paulo, Brazil, Tel: 55-11-30911193; E-mail: sfarsky@usp.br

Rec date: Jun 15, 2016; **Acc date**: Jun 23, 2016; **Pub date:** Jun 28, 2016

Citation: Loiola RA, Farsky S (2016) Polychlorinated Biphenyl Exposure Induces Early End-Points of Type 2 Diabetes Mellitus: A Matter of Public Health Concern. J Clin Mol Endocrinol 1: 13.

Letter to Editor

Polychlorinated biphenyls (PCBs) are persistent organic pollutants (POPs), which accumulates in the food chain due to their lipophilicity, bioaccumulation and biomagnification properties [1]. Despite the industrial production of PCBs being banned since late 1980s because of their negative impact on the human body and environment, high concentrations of PCBs still can be detected on air, food, water and human samples [1]. Although recent epidemiological studies have reported a body of evidences suggesting that chronic PCB exposure has contributed to a rising risk of metabolic disorders, especially obesity and type 2 diabetes mellitus (T2DM) [2], the underlying mechanisms involved in the metabolic side-effects of PCB exposure are still not clear.

Studies carried on by our group over the last years have revealed important aspects regarding the effects of PCB126 intoxication on metabolic function. The PCB126 is considered the most toxic among PCBs congeners and its biological effects are mediated by binding and activation of the cytoplasmic aryl hydrocarbon receptor (AhR), inducing the transcription and expression of AhR target genes [3]. Recently, our group has reported that long-term intranasal exposure to low doses of PCB126 impaired G protein coupled receptor (GPCR) signalling in circulating leukocytes and impaired innate immunological functions related to the host's defence to infections on rats [4]. Intriguingly, PCB126 exposure resulted in PC126 accumulation on liver and up-regulated AhR expression on liver and visceral adipose tissue, which are tissues that are important for regulating the glucose and lipid metabolism [4].

Based on such findings, we hypothesized that PCB126 intoxication and consequent upregulation of AhR-dependent signalling on target tissues, especially liver, adipose tissue and pancreas, can underlie the metabolic imbalance associated to obesity and T2DM. In order to test this hypothesis, further studies were carried to investigate the effects of PCB126 exposure on metabolic parameters and pancreatic function. Interestingly, PCB126 exposure increased body mass gain despite reduction in the mass of visceral adipose tissue. The PCB126-induced body mass gain was possibly associated to alteration to renal function and consequent hydric retention, since PCB126 exposure upregulated kidney AhR expression, and increased serum creatinine levels and total protein in urine. Although this was the first study to show *in vivo* renal intoxication induced by PCB126 exposure, further studies are necessary to elucidate the effects of PCB126 intoxication on kidney.

The PC126-dependent reduction of adipose tissue mass was associated to elevation of serum triglycerides and cholesterol levels, up-regulation of insulin-dependent glucose transporter GLUT4 expression, and reduction of interleukin 6 (IL-6) and nitric oxide (NO) production [5].

In conjunction with our previous observation that PCB126 exposure induces upregulation of AhR expression on adipose tissue [4], these findings clearly confirm that adipose tissue is a target of PCB126 intoxication. Additionally, PCB126 exposure increased serum levels of gamma-glutamyl transpeptidase (GGT), an early biomarker of hepatic toxicity and T2DM. Although PCB126 exposure had no effect on glucose tolerance, impairment of insulin sensitivity and elevation of circulating insulin levels, both common hallmarks of T2DM, were detected in rats following PCB126 intoxication.

Further *ex vivo* studies revealed that freshly isolated islets from rats exposed to PCB126 showed up-regulated AhR expression accompanied by exacerbated production of reactive oxygen species (ROS), an early sign of pancreatic dysfunction. Moreover, proteomic analysis of freshly isolated Langerhan's islets demonstrated that PCB126 exposure modified expression of several proteins linked to oxidative stress and failure of the following pancreatic β cells : heat shock protein 90 kDa; electron transfer flavoprotein subunit alpha; 78 kDa glucose-regulated protein; nucleoside diphosphate kinase A and B; and ribonuclease inhibitor.

To our knowledge, this is the first study reporting that intranasal PCB126 exposure induces oxidative stress and pancreatic βcell dysfunction. The up-regulation of AhR expression on liver, adipose tissue and pancreas, accompanied

by alteration of organ function and consequent metabolic imbalance highlights the involvement of AhR pathways on carbohydrate and lipid metabolism.

Taken all together, our recent studies report important findings indicating that long-term intranasal exposure to low doses of PCB126 induces toxic systemic alterations which are associated with early end-point of T2DM, including insulin resistance, hypertriglyceridemia, hyperinsulinemia and oxidative stress on pancreatic islets. Such findings reveal new evidences supporting the hypothesis that chronic exposure to POPs contributes to genesis and/or progression of T2DM and confirm previous evidences suggesting that chronic PCB exposure is a risk factor to T2DM [2]. In summary, our recent studies contribute to identify some of the mechanisms underlying the deleterious effects of chronic PCB exposure on metabolic function and support the adoption of new health public policies in order to prevent and/or minimize the exposure of population to environmental pollutants.

References

1. Mrema EJ, Rubino FM, Brambilla G, Moretto A, Tsatsakis AM, et al. (2013) Persistent organochlorinated pesticides and mechanisms of their toxicity. Toxicology 307: 74-88.
2. Lee DH, Porta M, Jacobs DR, Vanderberg LN (2014) Chlorinated persistent organic pollutants, obesity, and type 2 diabetes. Endocr Rev 35: 557-601.
3. Stockinger B, DiMeglio P, Gialitakis M, Duarte JH (2014) The aryl hydrocarbon receptor: multitasking in the immune system. Annu Rev Immunol 32: 403-432.
4. Shimada AL, Cruz WS, Loiola RA, Drewes CC, Dörr F, et al. (2015) Absorption of PCB126 by upper airways impairs G protein-coupled receptor-mediated immune response. Sci Rep 5: 14917.
5. Loiola RA, Anjos FM, Shimada ALB, Cruz WS, Drewes CC, et al. (2016) Farsky SHP. Long-term *in vivo* polychlorinated biphenyl 126 exposure induces oxidative stress and alters proteomic profile on islets of Langerhans. Sci Rep 6: 27882.