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Review

Adverse effects of weight loss: Are persistent organic pollutants a potential culprit?

M. Cheikh Rouhou [a], A.D. Karelis [b,*], D.H. St-Pierre [b], L. Lamontagne [a]

[a] *Department of Biological Sciences, Université du Québec à Montréal, H3C 3P8 Montréal, Canada*
[b] *Department of Exercise Science, Université du Québec à Montréal, C.P. 8888, Succursale centre-ville, H3C 3P8 Montréal, Canada*

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Abstract

Health professionals commonly recommend weight loss to individuals with obesity. However, unexpected adverse health effects after a weight-loss program have been reported in several studies. The factors that could explain this phenomenon are currently poorly understood. However, one potential factor that has emerged is persistent organic pollutants (POPs). Due to their lipophilic nature, POPs are known to accumulate in the adipose tissue and their concentrations are found to be higher in obese individuals than lean subjects. There is evidence to suggest that weight loss induces a significant increase in POPs levels in the bloodstream. Furthermore, the increases in plasma POPs levels after weight loss are even greater with an intensive weight loss. Thus, a critical question that remains unresolved is whether POPs released from the adipose tissue to the bloodstream during intensive weight loss could increase the risk of cardiometabolic disturbances. In turn, the accumulation of POPs released in response to an intensive weight loss may impair energy metabolism and stimulate a subsequent weight regain. Thus, the purpose of this review is to provide insights about the role of POPs on cardiometabolic risk factors during weight loss and weight regain that could potentially explain, at least in part, the adverse effects observed in certain weight-loss studies. We will also discuss the potential synergistic or antagonistic POPs-dependent risks following weight-loss programs. Ultimately, this may lead in establishing new therapeutic boundaries to minimize potential health hazards related to weight loss.

Keywords: Cardiometabolic risk factors; Dioxins; Organochlorine pesticides; Polychlorinated biphenyls; Weight regain

1. Introduction

Obesity has become a global epidemic [1]. Accordingly, the prevalence of adults with a body mass index (BMI) of 25 kg/m^2 and above has significantly increased from ∼29 to ∼38% between 1980 and 2013, worldwide [1]. It is now well established that obesity is associated with the development of cardiometabolic disorders such as insulin resistance, dyslipidemia, inflammation, hypertension, non-alcoholic fatty liver, type 2 diabetes and cardiovascular diseases [2]. Moreover, obesity is recognized to significantly decrease life expectancy and is the fifth leading cause of death, worldwide [3]. Weight loss between 5–10% of initial body weight is associated with improvements of cardiometabolic risk factors [4]. Accordingly, Canadian national weight management guidelines have recommended that all obese adults should lose weight [4].

Recently, there have been considerable concerns towards potential health effects of particular environmental chemicals such as persistent organic pollutants (POPs) [5]. Examples of POPs include dioxins, organochlorine pesticides (OCs), polybrominated diphenyls (PBDEs) and polychlorinated biphenyls (PCBs). POPs, once released in the environment, persist in the air, water, soil and living organisms [6]. The lipophilic nature of POPs promotes their capacity to accumulate in any type of fat [6]. Accordingly, humans are mainly exposed to POPs through

Abbreviations: POPs, Persistent organic pollutants; OC, Organochlorine pesticides; PBDEs, Polybrominated diphenyls; PCBs, Polychlorinated biphenyls; DDD, Dichloro-diphenyl-dichloroethane; DDE, Dichlorodiphenyl-dichloroethylene; DDT, dichlorodiphenyltrichloroethane; TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

* Corresponding author. Tel.: +001 514 987 3000x5082; fax: +001 514 987 6616.
E-mail address: karelis.antony@uqam.ca (A.D. Karelis).

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the consumption of contaminated foods such as fatty fish, meat and milk products but some workers can also be exposed through inhalation [6,7]. Consequently, detectable amounts of POPs are present in most human beings on the planet (> 85%) [8].

POPs are primarily known to accumulate in the adipose tissue and their concentrations are higher in obese individuals than lean subjects [9]. Several groups have reported that weight loss significantly increases POPs levels in the bloodstream [10,11]. In addition, circulating concentrations of POPs are directly correlated with the degree of weight loss [11]. Thus, a critical question that remains unresolved is whether high concentrations of POPs released from the adipose tissue to the bloodstream during intensive weight loss could promote the development of cardiometabolic dysfunctions. Interestingly, increases in plasma POPs levels may also impair energy homeostasis (by altering resting metabolic rate and the levels of oxidative enzymes) and in turn, promote subsequent weight regain after intensive weight loss [12]. If confirmed, this would be of important clinical relevance since it would suggest that major weight loss could potentially support the development of adverse health effects. Accordingly, several studies have reported deleterious health effects after weight loss (see review [13]). In addition, numerous studies have shown that weight cycling could be associated with an increased risk of cardiometabolic risk factors and mortality [14–19]. Therefore, the purpose of this review is to provide insights into the role of POPs on cardiometabolic risk factors during weight loss and weight regain that could potentially explain, at least in part, the adverse effects observed in certain weight loss interventions. We will also discuss the potential synergistic or antagonistic POPs-dependent risks since interactions between POPs are likely to occur following weight loss interventions, which could induce important modulations and affect health outcomes.

2. Persistent organic pollutants (POPs)

Obesity, cardiometabolic risk factors and type 2 diabetes develop in the presence of a host of factors such as overeating, physical inactivity and genetic predispositions [20]. However, although extensively studied by the scientific community in the last few decades, these causes appear to not fully explain the current obesity and type 2 diabetes epidemics. Therefore, it is rather appealing to consider other non-traditional biomedical risk factors that may emanate from unsuspected sources. One potential key avenue for novel risk factors that seems to be gaining attention is POPs. It should be noted that previously published reviews have reported that high levels of POPs in the bloodstream could be associated with an increased risk of cardiometabolic risk factors, obesity as well as type 2 diabetes [5,12,21–25] and will not be further summarized or discussed in this review.

2.1. Toxicokinetics of main POPs and their metabolites

PCBs are a family of high molecular weight, entirely synthetic, chlorinated organic compounds that are among the most common type of POPs known [6]. The PCBs family includes 209 congeners, which differ by the number of chlorine atoms attached to the molecule and their position on the biphenyl nucleus. They were initially developed in 1929 and were gradually banned in the late 1970s [26,27]. Humans can be exposed to PCBs by breathing contaminated air [28], dermal contact [29,30] and ingestion of contaminated water or food [31]. After exposure, PCBs are easily absorbed from the gastrointestinal tract by passive diffusion across lipophilic cell membranes [31]. When in the blood, PCB concentrations influence its solubility-based partition with red blood cells, albumin and lipoproteins [32,33]. Hence, lipoproteins allow PCB transport towards lipid rich tissues such as adipose, brain and liver [34]. Following their biotransformation, PCBs and their metabolites are eliminated primarily via feces and bile whereas approximately 5% of their by-products are excreted in urine [26]. It is noteworthy that PCB biotransformation rates are specie dependent and their average half-life ranges from 2.6 to 4.6 years [35].

Dichlorodiphenyltrichloroethane (DDT) is the most prevalent OC and will be the only one of this group that is discussed in this review. This substance was widely used around the world but because of its toxic effects, DDT was banned in several countries since 1972 [26] and its utilization is restricted to locations where major outbreaks such as malaria need to be prevented. However, even decades after being banished, its metabolites are still presents in human blood. Oral exposure and subsequent absorption by the organism through the stomach and intestines are considered as the most important route of entry of DDT in humans. Then, DDT and its metabolites are transported *via* binding to blood plasma proteins and distributed in all body tissues based on their fat content [36–39]. DDT is primarily bio-transformed by the liver into two main intermediate metabolites: dichlorodiphenyldichloroethylene (DDE) [40,41] and dichloro-diphenyl-dichloroethane (DDD) [42]. DDT can also be converted into biomethylsulfonyl metabolites, which are known to be potent toxic agents, particularly when reaching the adrenal gland. In addition, there is evidence to suggest that DDT plays an important role in the development of obesity [5,43,44]. DDT and its metabolites are thereafter eliminated mainly via urine and to a lesser extend in feces [45] as well as in breast milk [46].

Finally, PBDEs are a new group of POPs [47,48] that are used in many products such as stuffed articles (e.g. sofas, mattresses), building materials, electronics and textiles [49]. There are also 209 possible PBDEs congeners, which can be differentiated by the number and position of bromine atoms. Although PBDEs are among emerging and most concerning POPs, only few research studies have investigated the toxicological kinetics of these substances. To date, only information derived from experiments in rodents or aquatic organisms (some fish) are available. In rodents the absorption rate varies between 10 and 26% regardless of the route of exposure (e.g. respiratory, oral, or dermal) [50–52]. Following their transport into the organism, PBDEs appear to be metabolized by oxidative pathways and generate hydroxylated and methoxylated by-products [53]. Degradation depends on the degree of bromination and the route of exposure. The mechanisms underlying PBDE biotransformation still remain to be elucidated but they are primarily eliminated in feces [50,52].