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Reduction of the body burden of PCBs and DDE by dietary intervention in a randomized trial[☆],[☆☆],[★]

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Abstract

Serum polychlorinated biphenyls (PCBs) in Anniston, AL, residents have been associated with hypertension and diabetes. There have been no systematic interventions to reduce PCB body burdens in Anniston or other populations. Our objective was to determine the efficacy of 15 g/day of dietary olestra to reduce PCBs in Anniston residents. Blood PCBs and 1,1-*bis*-(4-chlorophenyl)-2,2-dichloroethene were measured at baseline and 4-month intervals in a double-blind, placebo-controlled, 1-year trial. Participants with elevated serum PCBs were randomized into two groups of 14 and received potato crisps made with olestra or vegetable oil (VO). Elimination rates during the study period were compared with 5-year prestudy rates. Eleven participants in the olestra group and 12 in the VO group completed the study. Except for one participant in the VO group, reasons for dropout were unrelated to treatments. The elimination rate of 37 non-coplanar PCB congeners during the 1-year trial was faster during olestra consumption compared to the pretrial period (-0.0829 ± 0.0357 and -0.00864 ± 0.0116 year^{-1}, respectively; $P=.04$), but not during VO consumption (-0.0413 ± 0.0408 and -0.0283 ± 0.0096 year^{-1}, respectively; $P=.27$). The concentration of PCBs in two olestra group participants decreased by 27% and 25% during the trial. There was no significant time by group interaction in change from baseline. However, group main effects for total PCBs and PCB 153 were of borderline significance. This pilot study has demonstrated that olestra can safely reduce body burdens of PCBs and supports a larger intervention trial that may also determine whether reduction in PCBs will reduce the risk of hypertension and diabetes.
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Keywords: PCBs DDE; Olestra; Dietary intervention

1. Introduction

Polychlorinated biphenyls (PCBs) are persistent, environmental toxicants and/or carcinogens. PCBs were manufactured for 40 years in Anniston, AL, resulting in environmental contamination and high body burdens of PCBs that were associated with increased risk of hypertension and diabetes as assessed by the Anniston Community Health Study (ACHS) [1–3]. No systematic interventions have been made to reduce PCBs in Anniston residents.

In addition to the studies in Anniston, the analysis of NHANES data disclosed a strong association between the serum level of non-coplanar PCB 153 and diabetes [4]. Although there is an apparent relationship between risk of disease and level of PCBs, there is minimal evidence that reducing the levels of PCBs will alter this risk. To our knowledge, only a single case report study has demonstrated that reducing PCBs will reduce the markers of disease, specifically blood glucose and lipid levels [5]. Presumably, this paucity of data is the result of not having a suitable method for removing PCBs from the body. We therefore undertook the

study to determine if it is possible to reduce PCB levels as a first step toward determining whether disease risk might then be altered.

PCBs are lipophilic and associated with stored triglycerides and serum lipids. The concentration of PCB levels in serum lipids thus reflects the total body burden as an estimate of the concentration in adipose tissue [6–8]. The measurements of PCBs in Anniston residents noted above have utilized lipid-corrected serum levels as a measure of exposure. Although direct measurements of concentration in adipose tissue and total body fat would have provided a more exact determination of body burden, we opted to use the lipid-normalized serum levels because of concerns about participant compliance in this exploratory trial.

PCBs and their metabolites enter the intestine by biliary or nonbiliary secretion and are reabsorbed by enterohepatic circulation. Reducing organochlorine reabsorption hastens removal from the body as demonstrated by administering cholestyramine to remove kepone [9]. Following the same strategy, we used the nonabsorbable lipid olestra, which reduces 1,1,1-trichloro-2,2'-bis(4-chlorophenyl) ethane (DDT) absorption and enhances 1,1-*bis*-(4-chlorophenyl)-2,2-dichloroethene (DDE) excretion in animals [10,11]. When added to the diet of mice exposed to hexachlorobenzene (HCB), olestra increased HCB excretion 30-fold [12]. Remarkably, in a study of a single patient who had high PCB exposure, a regimen of olestra decreased adipose PCBs from 3200 to 56 mg/kg over 2 years [5].

These previous preliminary studies have demonstrated that olestra can increase the rate of excretion of organochlorines from the body. However, there has not been a controlled randomized clinical trial to determine if olestra is effective in reducing the body burden of organochlorines in humans. In addition to the preliminary data that demonstrated effects of olestra on organochlorines in animals, we believed that olestra would provide a low-risk dietary intervention with high probability of compliance during a year of study.

Olestra is approved by the Food and Drug Administration for use in foods in the United States, and it is also approved for food uses in 24 other countries. Potato crisps of uniform size containing olestra provide a readily measurable dose form. We report here the results of a 1-year placebo-controlled intervention with olestra to reduce PCBs in residents of Anniston, AL. In addition to the measurement of changes in serum PCBs, we measured serum DDE levels, which had been previously reported to be reduced by olestra in animals [11].

2. Subjects and methods

2.1. Study participants

Study participants from Anniston were identified from the ACHS with serum PCB levels (37 non-coplanar congeners) above the national 50th percentile reported in the 2005–2007 National Health and Nutrition Examination Survey [13]. Recruitment from this pool ensured measurement of PCB levels during the trial and during the 4–6-year period prior to the trial. Recruitment took place from December 2010 to March 2011. All participants began the trial on April 27 or April 28, 2011.

The study size was based on the expected standard deviation of 4.5% for within-group error for PCB analyses [14]. A group size of 10, 80% power and alpha of 0.05 predicted that we would be able to see a reduction in body burden in the olestra group of 7% relative to a 1% change in the control group in a year. We recruited 14 participants in each group with the goal of completing the parallel trial with 10 in each group.

Exclusion criteria included pregnancy, lactation, intolerance of the test products, current use of weight-loss medications, gastrointestinal or eating disorders, history of bariatric surgery and kidney stones. All participants were given verbal and written explanation of the study, questions concerning its risks and details were solicited, and written informed consent statement was obtained.

2.2. Test products

Crisps made with either olestra or vegetable oil (VO) were purchased commercially. Olestra crisps were Pringles Light Original, and VO crisps were Pringles Original. Both crisps were then produced by Procter & Gamble and are now produced by Kellogg. The daily dose of 24 olestra crisps provided 15 g of olestra. The crisps were provided in individually sealed and labeled packets that contained half of the daily dose (12 olestra crisps; 6 VO crisps). The dose of both crisps provided 112 kcal/day. A month's supply of crisps was packaged in a sealed opaque box, and the study coordinator who dispensed the boxes was not aware of the contents. The participants were also unaware of their treatment assignment. Participants recorded daily ingestion of crisps in diaries, and they returned boxes containing unused product. Compliance was assessed as percent of provided dose.

2.3. Study design

Participants were randomized *a priori* by the Cincinnati Children's Hospital biostatistician into VO and olestra groups of 14 each and enrolled using a stratified design based on body mass index (BMI) split at 30 kg/m^2 and sex. Within each stratum, the subjects were put in random order using a random number generator in SAS. Then, group assignment was generated using random block sizes of 2 and 4 due to the small sample size.

Subjects visited the Anniston clinical site monthly for 12 months. Every 2 months, they were weighed, received nutritional counseling and were given a 2-month supply of crisps. At each visit, participants returned diaries recording crisp consumption. At months 0, 4, 8 and 12, fasting blood samples were taken for PCB and lipid analyses. Serum glucose and insulin were measured at 0 and 12 months.

The study was approved by Institutional Review Board (IRB) of the Cincinnati Children's Hospital Medical Center. This study included use of a US Food and Drug Administration's Investigational New Drug Application (IND #109 636) for olestra-containing crisps. At the Centers for Disease Control and Prevention (CDC), analyses were conducted as technical assistance and in compliance with Research Determination procedure; an exemption from the CDC IRB was obtained. Data collection in the original ACHS was approved by the IRB of the University of Alabama at Birmingham. The study is registered with ClinicalTrials.gov (NCT01261338). Adverse events were reported to the Anniston Coordinator, and a medical consultant in Anniston was available at all times to evaluate any report of referral for medical care.

2.4. Serum measurements

Serum lipids were measured using a CDC-certified method (Medpace Reference Laboratories, Cincinnati, OH). Serum glucose (Trinder modified Emerson method), insulin (radioimmunoassay) and vitamin E (high-performance liquid chromatography) were measured at the CTRC Core Laboratory, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

2.5. Organochlorine analysis

Serum was analyzed for PCB non-coplanar congeners, consisting of 35 individual congeners and 2 sets of coeluting peaks (congeners 138–158 and 196–203), at the CDC as described previously [14]. This set of congeners was previously studied in the Anniston ACHS and allowed us to utilize pretrial concentrations from that study. The method also provided measurements of nine pesticides including DDE, and we analyzed DDE in addition to the PCBs. PCB and DDE concentrations were normalized to serum lipids as previously

described (2.27×total cholesterol+triglycerides+62.3) and expressed as ng/g lipid [6–8].

2.6. Statistical considerations

RedCap software was used for data management and EXCEL for data capture. SAS version 9.3 (SAS Institute, Cary, NC) was used for analysis unless otherwise noted. Outliers and distributional properties were assessed by univariate analysis. Analysis of the PCB congeners and DDE incorporated a log transformation. Baseline differences between groups were analyzed using t test and Wilcoxon rank sum or χ^2 and Fisher's Exact Test, as appropriate. Analysis of the PCBs and DDE over the year used the fraction of their lipid-normalized values at the first visit. Changes over the 1-year period between the olestra and VO groups were assessed with a generalized linear random-effects mixed model to account for the repeated nature of the design. Of initial interest was the interaction between visit and group, and if this was nonsignificant, the main effects model was examined. Baseline values of the PCBs and DDE, as appropriate, were retained in the model.

Elimination rate constants were determined from the natural logarithms of these fractions (described below). Since we hypothesized that olestra crisps, relative to VO crisps and to each individual's own prior elimination rate of PCBs, would result in accelerated PCB loss, comparisons were based on one-tailed tests. Individual regression analysis plots of the logarithms of the fractions versus time were performed for each participant using Sigmaplot. Data are presented as mean±standard error or geometric mean [95% confidence interval (CI)], the latter reported when the data were skewed and a logarithmic transformation was used for analysis. Analysis of the PCBs included congener 153; the sum of congeners 153 180, 194, 196–203, 206 and 209 (higher-chlorinated congeners); and the total of 37 congeners.

We used a first-order decay model assuming the elimination rate of PCBs from the body was proportional to the amount in the body so that $dA/dt = -kt$ and $\mathrm{Ln}(A/A_\mathrm{o}) = -kt$, where A_o is the amount at time 0 and A is the amount remaining at time t. Time is expressed in years, and the rate constant, k, as year^{-1}. The natural logarithms of A/A_o were plotted against time to determine the elimination rate constant using linear regression analysis. Concentrations of lipid-normalized PCBs obtained 4 to 6 years before the study and at time 0 for each participant were used to calculate individual pretrial elimination rates, and these rates were compared with each participant's elimination rate during the trial by paired t test. Each individual's pretrial elimination rate was also compared with the rate during the trial by a one-tailed t test based on the standard error calculated from the regression analysis of each individual's change during the trial. Values are presented as means and standard errors with significance determined by $P<.05$.

Half-lives cannot be calculated when elimination rate constants are ≥0. Therefore, half-life estimates for each group were based on the mean of the group's elimination constant.

3. Results

The baseline characteristics of the groups and final visit measurements are presented in Table 1. Eleven of 14 participants in the olestra group and 12 of 14 in the VO group completed the trial. One participant in the olestra group started at the 4-month visit and completed 8 months of treatment. There were no statistically significant differences between groups at the initial visit (Table 1). Changes from baseline from the participants who completed the trial are presented in Table 2. There were no statistically significant changes in BMI, consistent with the nutritional counseling that was provided to maintain body weight during the trial.

Table 1
Baseline characteristics of the participants who started the study

Variable	Olestra $n=14$	VO $n=14$	P value
Age (years)	59.9±2.6	61.0±1.5	.70
Female	8 (57.1%)	9 (64.3%)	.70
Race/ethnicity			
African American	11 (78.6%)	10 (71.4%)	.65
White	2 (14.3%)	4 (28.6%)	
Native American	1 (7.1%)	0 (0%)	
BMI	31.3±1.9	35.6±2.9	.23
Total cholesterol (mg/dl)	175.2±9.3	191.5±10.8	.26
LDL cholesterol (mg/dl)	96.9±8.6	111.0±9.6	.29
HDL cholesterol (mg/dl)	54.4±4.5	58.7±3.5	.47
Triglycerides (mg/dl)	119.1±12.4	109.4±12.9	.59
Glucose (mg/dl)	111.4±10.3	118.0±13.1	.70
Insulin (U/ml)	24.4±4.5	23.2±3.4	.82
α-Tocopherol (μg/ml)	14.2±1.2	15.3±2.5	.68

Data are presented as mean±S.E.M. or n (%). HDL, high-density lipoprotein.

3.1. Serum PCB levels

There were no statistically significant differences in total PCBs, PCB 153 or a group of higher-chlorinated congeners (153 180, 194, 196–203, 206 and 209) at baseline between the olestra and VO groups. The baseline values for total PCBs [geometric mean (95% CI)] as ng/g lipid were 1448 (960, 2184) and 1341 (1001, 1978) for the olestra and VO group, respectively. For the higher-chlorinated congeners, these values were 709 (470, 1072) and 629 (475, 834); and for PCB, 153, 247 (144, 424) and 253 (168, 381), respectively.

The percent change from baseline was used to analyze the effect of study group on serum PCBs (Fig. 1). The P value for the overall group effect was .06. There was no statistically significant interaction of time by group for PCB 153 or for total PCBs. The P value for the overall group effect was .09. For the higher congeners, the interaction was not statistically significant. The P value for the overall group effect was .16. In all analyses, baseline level was retained as a covariate in the model, although not statistically significant.

The total lipid-normalized serum PCBs [37 congeners; mean (95% CI)] at the beginning of the trial were 1341 (1001, 1798) and 1448 (960, 2184) ng/g lipid (parts per billion) for the VO and olestra groups, respectively. The concentrations on a wet weight basis were 8.4 (6.4, 11.2) and 9.3 (5.9, 14.8) ng/g serum for the VO and olestra groups, respectively.

Elimination rate constants were calculated for the 37 congeners, a group of higher-chlorinated congeners (PCBs 153 180, 194, 196–203, 206, 209) and PCB 153 alone. The higher-chlorinated congeners were selected because of prevalence. Congener 153 was analyzed separately because of prevalence and its measurement in previous studies. Serum PCB levels (ng/g lipid) measured 3.7 to 6.2 years (mean of 5.2 ±0.1 years) before the trial for each individual were compared with

Table 2
BMI and serum measurements at the end of the 1-year trial and change from baseline

Variable	VOlestra $n=11$ [a]		VO $n=12$	
	Final visit	Change from baseline	Final visit	Change from baseline
BMI (kg/m²)	32.8±2.0	−0.07±0.31	35.0±3.3	−0.27±0.43
Total cholesterol (mg/dl)	213.1±15.8	35.7[b]±8.8	190.0±11.2	−1.4±6.0
LDL cholesterol (mg/dl)	124.5±15.7	28.3[b]±8.0	109.4±10.0	0.42±5.11
HDL cholesterol (mg/dl)	60.0±4.8	5.9±3.3	59.9±4.3	−0.33±2.92
Triglycerides (mg/dl)	143.1±14.9	8.5±16.7	104.0±9.1	−6.8±8.1
Glucose (mg/dl)	117.1±14.7	7.4±9.3	105.5±9.6	−4.0±6.4
Insulin (U/ml)	37.8±8.4	9.9±6.1	31.6±6.7	8.1±6.5
α-Tocopherol (μg/ml)	15.4±1.1	0.32±1.00	13.0±1.1	−2.5±1.8

[a] One subject in the olestra group started late, so final visit was at 8 months.
[b] Statistically significant change from baseline.
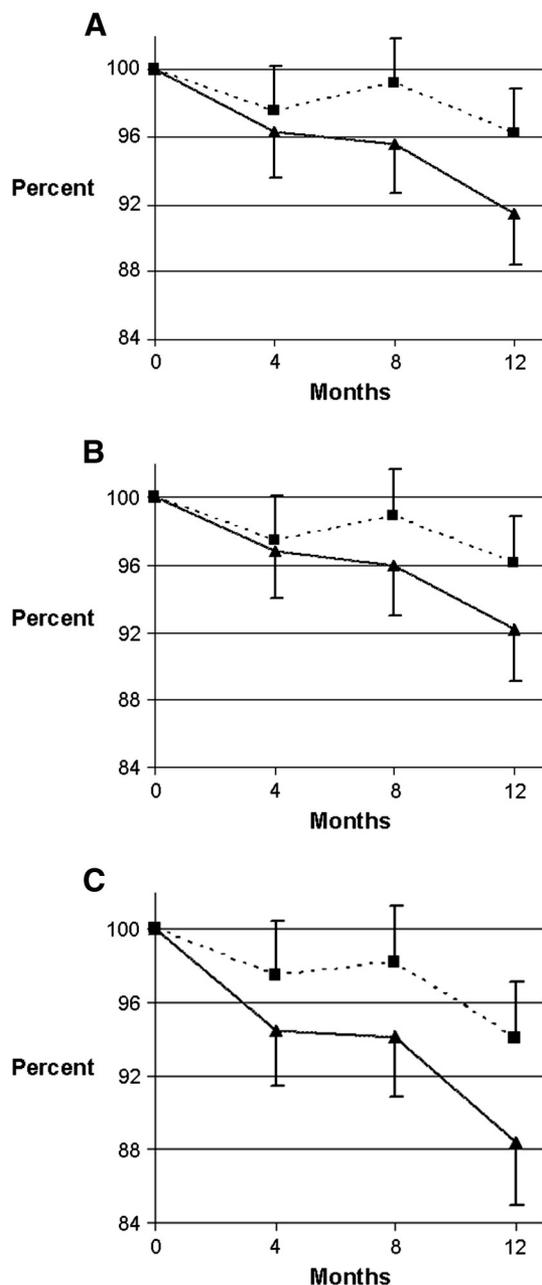
A

B

C

Fig. 1. Change from baseline for total PCBs (A), higher-chlorinated congeners (B) and PCB 153 (C) for the olestra group (solid line) and the VO group (dotted line). Standard errors are indicated by the vertical bars.

time 0 levels to calculate pretrial elimination rates. Rates were calculated from values at 0, 0.33, 0.67 and 1.0 years (Table 3).

Half-lives were estimated from the mean elimination rate constants. Total PCB half-lives were 80.2 and 24.5 years for the olestra and VO groups, respectively. During the trial, these decreased to 8.4 and 16.8 years, respectively. Higher-chlorinated congener pretrial values of 280.1 and 33.4 years decreased to 8.6 and 23.4 years for the olestra and VO groups, respectively, during the trial. These values for PCB 153 were 33.3 and 23.2 years during the pretrial period and 5.6 and 10.6 years during the trial for the olestra and VO groups, respectively.

Percent change in body burden was calculated from elimination rate constants for pretrial and trial periods. The predicted change during the year of the trial was determined from the pretrial elimination rate. This predicted change compared with the observed

Table 3
Elimination rate constants for total PCBs (37 congeners), higher-chlorinated congeners and PCB 153 in the VO and olestra groups for the pretrial and trial periods

Period	Measurement	Olestra (year^{-1})	VO (year^{-1})
Pretrial	Total PCBs	−0.00864±0.0116	−0.0283±0.0096
Trial	Total PCBs	−0.0829[a]±0.0357	−0.0413±0.0408
Pretrial	Higher congeners	−0.00247±0.0110	−0.0208±0.0062
Trial	Higher congeners	−0.0809[b]±0.0356	−0.0296±0.0425
Pretrial	PCB 153	−0.0282±0.0146	−0.02987±0.0084
Trial	PCB 153	−0.1234[c]±0.0566	−0.06546±0.0404

Letters indicate significant difference from pretrial value: a, $P=.04$; b, $P=.03$; c, $P=.06$.

change is presented for all PCBs during the trial for the VO and the olestra groups in Fig. 2. During the trial, the VO group's PCB concentrations decreased to 96% of baseline, compared with a 1-year decrease to 97% predicted by the pretrial measurements. The olestra group's concentration decreased to 92% of baseline, compared with a predicted value of 99%. The decrease during the trial period was significantly greater ($P<.05$) than that predicted from the pretrial elimination rate for the olestra group.

3.2. DDE

Of nine analyzed pesticides, the most prevalent was DDE, DDT's principal metabolite. Baseline lipid-normalized levels were elevated relative to the general population, with 383 (171, 857) ng/g lipid in the olestra group and 466 (279, 779) ng/g lipid in the VO group,
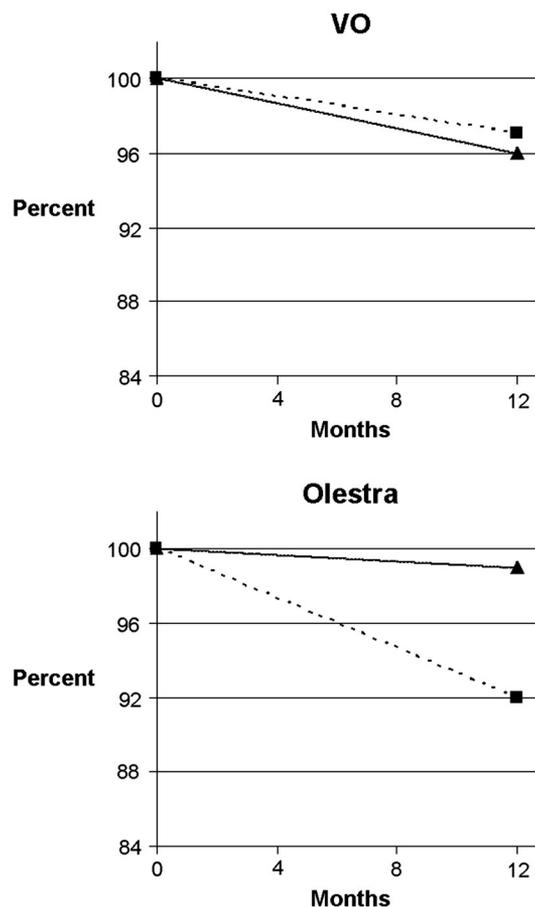
VO

Olestra

Fig. 2. A comparison of the observed (dotted line) and predicted (solid line) changes in total PCB body burden based on elimination rate constants calculated for the VO and olestra groups. The decrease during the trial period was significantly greater than the change predicted from the pretrial elimination rate for the olestra group.

corresponding to the 75th to 90th percentile values for the US population over 20 years [13]. The change in DDE levels during the pretrial period was extremely variable. In the olestra group, there was a mean increase of 84.3%±66.2% in DDE, and in the VO group, there was an increase of 17.3%±46.6%. This high variance is consistent with highly variable exposure during the pretrial period, which prevents a comparison of the elimination rate during the pretrial with that during the trial. During the trial, the mean elimination rate constant for the DDE in the VO group was -0.053 ± 0.0460 year^{-1}, and that for the olestra group was -0.175 ± 0.064 year^{-1} ($P=.067$).

3.3. Changes from baseline

No difference in PCB concentrations was found between the olestra and VO groups at baseline. For PCBs, the analysis examined the percent change from baseline. The visit by group interaction was not significant ($P=.70$), and the baseline term was borderline ($P=\cdot06$). The main effects model showed a significant group effect ($P=.02$), and the baseline level was of borderline significance ($P=.06$). Baseline (geometric mean, 95% CI, ng/g) concentrations of DDE were 383 (171, 857) and 466 (279, 779) for the olestra and VO groups, respectively. At 12 months, the concentrations were 84.1%±4.0% and 94.9%±3.6% of the baseline values for the olestra and VO groups, respectively.

3.4. Adverse events and dropouts

Five participants dropped out of the study: two in the VO group and three in the olestra group. In the VO group, one was due to weight gain and diarrhea, and the other was due to hypertension. In the olestra group, one was hospitalized during the first month of the trial with diabetic complications, one was lost to follow up, and one had an infection.

Four participants reported adverse events that may be related to the trial. Two participants in the olestra group and one in the VO group reported loose stools. For one participant in the olestra group, crisp consumption was temporarily discontinued, the symptoms stopped, and the participant continued the study regimen without recurrence of loose stools. One participant in the olestra group reported gas and bloating.

3.5. Compliance

Returned containers were checked and found to be consistent with the diaries that were kept by the participants. The VO group consumed 96.7%±1.2% of provided crisps; and the olestra group, 92.9%±2.2%.

4. Discussion

In this placebo-controlled trial, intervention with 15 g of olestra per day for 1 year significantly reduced lipid-normalized PCBs more than that predicted by pretrial measurements. These results are consistent with olestra increasing the rate of reduction of the body burden of PCBs, and they suggest a feasible intervention to reduce associated health risks.

There was high variance in the response to olestra. For example, total PCB levels in participants 13 and 19 decreased by 27% and 25%, respectively, during the trial, yielding half-lives of 2.2 and 2.4 years, values that are markedly greater than their respective reductions of 0.2% and 0.9% per year in the pretrial period. PCB elimination rates during the trial were significantly different from pretrial rates ($P<.05$) for participants 13 and 19 and for 5 of 11 olestra group participants. In the VO group, the rates during the trial differed from pretrial rates in only 2 of 12 participants.

Wide variations in serum concentration and elimination rates are typical of PCB biomonitoring. PCB half-life estimates varied considerably within treatment groups, among pretest and in-test estimates, as well as when compared between pretest and in-test estimates. Given these realities, we acknowledge that even more variability is likely to be observed when determining half-lives based on a 1-year timeframe for biomonitoring (as done in this study) compared to estimations based on longer timeframes. This analytical consideration indicates the value of a longer trial.

A large adipose mass limits the proportion of the body's PCBs that are available to the blood for direct intestinal excretion. The half-life of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) has been shown to double when body fat increased from 20 to 30 kg, suggesting that an individual will more likely respond to olestra when the adipose tissue compartment is small [15]. Consistent with this possibility is the observation that the BMIs of participants 13 and 19, who experienced large increases in elimination rates, were 24.1 and 27.6, respectively, which were less than that of the group mean ($32\cdot8$) and were maintained during the study. It seems likely that health benefits that may result will be determined by the mass of adipose tissue that stores these compounds. A large adipose depot may limit the fraction of PCBs that are available for removal through interruption of enterohepatic circulation.

Ideally, this trial would have measured adipose tissue mass throughout the study along with adipose concentrations of PCBs so that body burden would be the product of adipose tissue mass and PCB concentration. However, given this trial's exploratory nature and our concerns about participant compliance, we opted to measure serum PCB concentrations. It has been shown that lipid-normalized serum organochlorine concentrations are good approximations of the adipose tissue levels [16,17]. Our "window" on PCB body burden was PCBs in the blood serum lipid fraction coupled with constant body weight.

The VO was not an inert placebo since it provided dietary fat, and this might have accounted for the observed decrease in the half-life of blood PCBs in some VO individuals. Partial malabsorption of dietary fat can reduce the absorption of organochlorines in enterohepatic circulation [18].

Previous studies of the effects of olestra on organochlorine metabolism in humans have been reported. Blood levels of organochlorines were measured during 3 months of weight loss to determine olestra's effect on increases in blood organochlorines that accompany weight loss [19]. In that trial, olestra altered β-hexachlorocyclohexane but not other organochlorines. The subjects lost body weight during that trial so that total organochlorine body burdens were not measured. Geusau et al. reported a "relatively small effect" of olestra on another organochlorine, the dioxin TCDD, in two subjects [20]. The small effect of olestra was attributed to the short half-life of TCDD and poor compliance with the olestra dose during the 3-year trial. Moser and McLachlan reported enhancement of fecal excretion rates of dioxin when olestra was fed to four subjects [21].

Increases in total and low-density lipoprotein (LDL) cholesterol in the olestra group at 12 months observed during the trial were unexpected since olestra has previously been reported to modestly reduce these levels [22–24]. There was not, however, a significant increase in these lipids based on regression analysis of their concentration over time.

Minimal risk resulted from treatment with 15 g/day of olestra. Modest and transient gastrointestinal effects were reported by only two participants in the olestra group. With the regimen of a daily normal multivitamin supplement, there was no effect on fat-soluble vitamin status based on serum α-tocopherol levels.

Our findings suggest that nonabsorbable dietary lipid can hasten the removal of PCBs. Because the trial was exploratory in nature, the sample size was small and the duration was short in terms of PCB half-

lives. Finally, we do not know if exposure to PCBs in foods continued in some individuals during the trial.

5. Conclusion

Interruption of enterohepatic circulation of PCBs and their metabolites by a nonabsorbable lipid can reduce body burdens of PCBs. Modest, transient adverse events related to the regimen were observed, consistent with a low risk-to-benefit ratio. Extension of this study to a cohort with normal ranges of BMI and to subjects who are undergoing weight loss will expand our understanding of this novel and potentially useful treatment strategy.

Acknowledgments

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jnutbio.2014.01.002.

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