

Dietary cadmium intake and fecundability in a North American preconception cohort study

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BACKGROUND

- Cadmium (Cd) is a toxic heavy metal.
- Dietary cadmium (D-Cd) is a primary source of exposure in non-smoking populations.
- In animal studies, Cd exposure alters oocyte meiotic progression, inhibits oocyte meiotic maturation *in vivo* and *in vitro*, and impairs trophoblast development.
- In a preconception cohort of 501 women, high concentrations of Cd in whole blood were associated with lower fecundability.
- There have been no studies of D-Cd intake and fecundability.

OBJECTIVE

To examine the association between dietary cadmium intake and fecundability among 4,768 women participating in Pregnancy Study Online (PRESTO)

METHODS

- PRESTO: North American preconception cohort study.
- Eligibility criteria:
 - Resident of United States or Canada
 - Females: age 21-45 y
 - Planning a pregnancy
 - ≤6 months attempt time at study entry
 - Not using fertility treatment
- Baseline questionnaire on demographics, lifestyle, medical history, anthropometrics, and measures of SES
- Ten days after enrollment, participants completed a validated food frequency questionnaire (FFQ): National Cancer Institute's Diet History Questionnaire (DHQ) II
- D-Cd intake was estimated by combining FFQ responses with US Food & Drug Administration data on D-Cd content.
- Females completed bimonthly follow-up questionnaires for up to 12 months or until conception.
- The analysis was restricted to women attempting to conceive for ≤6 cycles at study entry to avoid selection bias.
- Proportional probabilities models estimated the fecundability ratio (FR) and 95% confidence interval (CI).

TABLES AND FIGURES

Table 1. Baseline characteristics of 4,768 PRESTO participants by quintiles of D-Cd intake

D-Cd intake (µg/day)	Q1	Q2	Q3	Q4	Q5
	<6.8	6.8-7.6	7.7-8.4	8.5-9.5	≥9.6
Number of women (N)	953	954	954	954	953
Age, years(mean)	29.6	30.1	30.0	30.2	30.5
BMI, kg/m ² (mean)	28.4	27.1	26.9	26.9	26.5
Healthy Eating Index score (mean)	60.0	65.2	66.9	68.3	70.5
Energy intake, kcal/day(mean)	1531	1603	1602	1616	1546
Smoking status					
Current regular (%)	7.3	4.5	4.7	2.9	3.2
Current occasional (%)	3.8	2.4	2.9	3.0	3.9
Past (%)	14.4	14.2	12.6	15.4	13.9
Parous (%)	37.7	33.0	30.5	25.1	24.5
Alcohol intake, drinks/week	3.4	3.5	3.2	3.3	2.8
Physical activity METs/week					
<10 (%)	16.1	14.4	9.9	8.4	8.5
>40 (%)	25.8	29.2	32.5	37.4	45.1
Last method of contraception					
Hormonal (%)	40.7	41.8	37.3	39.1	34.0
Barrier (%)	40.0	38.5	42.0	41.3	44.7
Intercourse frequency, times/week					
<1 (%)	22.2	20.9	22.2	20.9	19.8
≥4 (%)	15.5	14.7	13.4	13.2	14.8
Using method to improve pregnancy chances (%)	73.6	80.4	74.3	75.3	77.8
Daily use of multivitamins (%)	81.3	83.9	83.3	86.3	85.5
Education					
≤High school (%)	4.6	3.0	2.8	2.3	2.1
≥Graduate school (%)	36.2	41.7	47.0	48.8	47.9
Income (USD)					
<50 K (%)	21.2	17.0	15.1	13.8	15.4
≥150K (%)	13.4	18.5	17.5	19.2	20.0

Table 2. Association between increasing quintile of D-Cd intake and fecundability

			Unadjusted		Adjusted ^a		Adjusted ^b	
D-Cd intake (µg/day)	No. of pregnancies	No. of cycles	FR	95% CI	FR	95% CI	FR	95% CI
All women								
Q1	550	3,987	1.00	Ref	1.00	Ref	1.00	Ref
Q2	594	3,889	1.09	0.98-1.21	1.04	0.94-1.16	1.03	0.92-1.14
Q3	622	3,836	1.16	1.05-1.29	1.09	0.98-1.21	1.07	0.96-1.18
Q4	620	3,869	1.14	1.03-1.27	1.09	0.98-1.22	1.07	0.96-1.19
Q5	623	3,778	1.18	1.06-1.31	1.11	1.00-1.24	1.08	0.97-1.20
Never smokers with no current passive smoke exposure								
Q1	409	2,710	1.00	Ref	1.00	Ref	1.00	Ref
Q2	461	2,833	1.06	0.94-1.20	1.03	0.92-1.16	1.02	0.90-1.15
Q3	486	2,909	1.12	0.99-1.26	1.07	0.95-1.20	1.05	0.93-1.18
Q4	488	2,842	1.12	0.99-1.26	1.09	0.96-1.22	1.06	0.94-1.20
Q5	477	2,857	1.10	0.97-1.24	1.05	0.93-1.19	1.02	0.90-1.16

^aModel a' is adjusted for age, female BMI, energy intake, smoking history, parity, physical activity per week, hormonal last method of birth control, daily use of multivitamins, race/ethnicity, education, income, geographic region; ^bModel b'= 'Model a' + Healthy Eating Index.



RESULTS

- Median D-Cd was 8.0 µg/day (interquartile range: 7.0-9.1).
- Top 5 contributors to D-Cd: nuts & seeds, fried potatoes, dark green lettuce, cooked greens and white potatoes.
- D-Cd intake was inversely associated with BMI, current smoking, and parity, and positively associated with Healthy Eating Index scores, physical activity, education, and multivitamin use (**Table 1**).
- FRs for quintiles 2-5 vs. quintile 1 of D-Cd intake were 1.03, 1.07, 1.07, and 1.08, respectively (**Table 2**).
- Results did not differ appreciably among never smokers with no current passive smoke exposure, for whom Cd exposure from other sources (e.g., cigarettes) would be lower.
- Results did not differ materially by age (<30 vs. ≥30 years), BMI (<30 vs. ≥30 kg/m²), total fiber intake (<25 vs. ≥25 g/day), geographic region of residence (West, Midwest, Northeast, South, Canada), or attempt time at study entry (<3 vs. ≥3 cycles) (data not shown).

DISCUSSION

- Despite evidence of its toxicity *in vitro* and animal studies, we found little evidence of an association between increased D-Cd intake and fecundability.
- Study limitations include non-differential misclassification of D-Cd intake and potential for unmeasured or residual confounding by healthy lifestyle.

CONCLUSIONS

Dietary intake of cadmium, as measured via FFQ, was not appreciably associated with fecundability.

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