

Research and Practice Innovations

A Novel Dietary Intervention to Optimize Vitamin E Intake of Pregnant Women to 15 mg/Day

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ABSTRACT

Associations have been reported between suboptimal maternal vitamin E intake during pregnancy and childhood asthma. This pilot study conducted in 2008/2009 investigated the feasibility and acceptability of a food-based randomized controlled trial in pregnant women to optimize dietary vitamin E intake to 15 mg/day. A food-based intervention using “food exchanges” to individually optimize dietary vitamin E intake to 15 mg/day was developed and included in an advice booklet. Forty-three pregnant women with a personal/partner history of asthma were recruited at 12 weeks gestation and randomized to food-based intervention or a control group until 20 weeks gestation. A registered dietitian assessed the vitamin E intake of 22 women and provided tailored advice on food-based exchanges to optimize their intake to 15 mg/day. The 21 control women were not given dietary advice. The food-based intervention was completed by 19 women and increased mean vitamin E intake: food diary data, 7.13 mg/day (95% confidence interval: 5.63 to 18.6) to 17.4 mg/day (95% confidence interval: 14.4 to 20.5) ($P < 0.001$). This pilot study demonstrates the feasibility and acceptability of a food-exchange–based intervention to optimize dietary vitamin E intake during pregnancy. Additional work is required to determine whether this intervention,

if sustained for the rest of pregnancy, reduces the likelihood of childhood asthma. The methodology used in the design of this novel food-based intervention could be transferred to other nutrients.

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It has been hypothesized that changes in diet have contributed to the recent marked increase in asthma (1,2), with a recent systematic review concluding that there is strong supportive evidence to prioritize trials of increasing maternal vitamin E intake during pregnancy as a potential population-based intervention to reduce childhood asthma (3). This article describes the development of a novel food-based intervention to optimize maternal vitamin E intake during pregnancy to 15 mg/day and the results of piloting the intervention in a short-term randomized controlled trial.

The possibility of conducting a trial of vitamin E modification in pregnancy in relation to childhood asthma is being considered. Several considerations support the notion of using a food-based intervention to optimize maternal vitamin E intake to 15 mg/day in preference to vitamin E supplementation. Firstly, previous antioxidant supplementation trials have failed to demonstrate beneficial effects on cardiovascular disease, cancer, and all-cause mortality, despite reports of beneficial associations from observational studies (4). Recently, a pre-eclampsia trial of vitamin E supplementation during pregnancy reported that supplements of vitamin E (133 mg/day) during pregnancy did not reduce the incidence of respiratory outcomes in children up to 2 years (5). These studies suggest that supplements of maternal vitamin E during pregnancy are unlikely to have a beneficial effect on childhood asthma. Secondly, the use of a food-based intervention to enhance a dietary pattern that increases vitamin E intake embraces the complexity of diet by pragmatically accepting that the intervention not only increases vitamin E intake, but also the intake of naturally associated nutrients. A strength of such an intervention is that other nutrients (eg, polyunsaturated fatty acid [PUFA], vitamin D), or the nutrient composition of the overall dietary pattern, can be essential for any beneficial effect. Finally, although in the United Kingdom there are no explicit recommendations for vitamin E intake, the US recommended daily allowance for women is 15 mg/day, and is unchanged by pregnancy (6).

Because of the innovative nature of such a food-based intervention, it was considered necessary to pilot the

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randomized controlled trial (RCT) of the food-based intervention in pregnancy to assess the feasibility of a larger definitive RCT. A secondary aim was to confirm that the food-based intervention not only increases vitamin E intake, but also the intakes of other naturally associated nutrients.

METHODS

Participants

It is envisaged that a future RCT investigating whether vitamin E modification during pregnancy reduces the likelihood of childhood asthma would focus on women pregnant with a child at high risk for developing asthma. These women are likely to be more motivated to participate and comply with the intervention; a further advantage is that the sample size is minimized because of the higher incidence of asthma in their offspring. Therefore, in this pilot study, pregnant women with a personal and/or partner history of asthma attending the Aberdeen Maternity Hospital for routine antenatal care were recruited at 12 weeks gestation. The aim of this study was to recruit and randomize 40 subjects; 20 intervention and 20 controls. Subjects were allocated in accordance with a prerecruitment computer-generated randomization sequence. Vitamin E supplement use was an exclusion criterion. All participants provided written informed consent and ethical approval was granted by the North of Scotland Research Ethics Service (08/S0802/130).

Procedures

Local obstetric practice is for all pregnant women to undergo an ultrasonographic examination of the fetus at 12 and 20 weeks gestation. These scan visits were used to recruit and follow-up subjects. All participants had their dietary and serum vitamin E status assessed at 12 and 20 weeks gestation by validated semi-quantitative food frequency questionnaire (FFQ) (Scottish Collaborative Group version 6.5) (7) and measurement of serum α -tocopherol.

Control Group

Control group participants received no dietary advice, but also met with the registered dietitian at 12 and 20 weeks gestation for blood sampling and completion of FFQs.

Intervention Group

In addition to the 12- and 20-week FFQ and blood sampling, the intervention-group women received the food-based intervention to individually optimize vitamin E intake to 15 mg/day.

The registered study dietitian developed the food-based intervention by using food composition tables to identify vitamin E-rich foods and portion sizes containing 2 mg vitamin E. It was also believed important that the intervention should be designed with the pregnant woman, her family, and national recommendations for dietary intakes during pregnancy, in mind. An illustrated advice booklet was developed containing information on food portions with 2 mg vitamin E, including breakfast cereals, spreads, cooking oils, vegetables, fruit, fish, sauces,

snacks, nuts, and seeds. Practical examples of breakfast, lunch, and dinner options to increase vitamin E intake by 2 mg were also included. At recruitment, intervention-group women were instructed on how to complete a 4-day nonweighed diet diary (3 weekdays, 1 weekend day) using photographic examples of food measures. The diary was analyzed using WINDIETS (Univation Ltd, Aberdeen, UK) and in a subsequent face-to-face consultation the registered dietitian provided feedback on macro- and micronutrient intakes and addressed any issues raised (eg, body weight, intakes of iron, calcium). The diet diary was used to highlight existing dietary sources of vitamin E, enabling the registered dietitian to suggest ways each woman could increase her vitamin E intake using foods already included in her diet. This tailoring of individual diets minimized the impact of the dietary intervention on the rest of the family. Suggested changes were reinforced by the advice booklet that contained pictures of exchanges of foods containing vitamin E and the amount needed to provide 2 mg vitamin E (eg, 1 tablespoon potato salad, 1 medium portion of whole-grain breakfast cereal). The number of times per day any of these food exchanges should be eaten was tailored to increase the baseline intake to 15 mg/day, eg, a woman consuming 7 mg/day vitamin E would be advised to add four 2-mg exchanges each day. Overweight or obese women were advised not to include high-energy vitamin E sources in their diet. Common suggestions included changing/increasing breakfast cereals, changing brands of soft margarine and/or cooking oil, adding nuts/seeds to cereals, including coleslaw or potato chips in lunches. Intervention-group women were contacted by telephone at 15 to 16 weeks gestation to assess progress, identify problems, and provide further advice. At 18 weeks gestation, these women completed a second 4-day diet diary, the analysis of which was provided at the 20-week scan visit by the registered dietitian. All women were asked not to take supplements during the study.

Qualitative Subject Study Evaluation

At the end of the study, participating women were invited to take part in a semi-structured interview conducted by one of the researchers to discuss the study, the dietary intervention, any concerns about the study, and suggestions to improve the study. Interviews were digitally recorded, transcribed, and analyzed for key themes.

Statistical Considerations

Study statistical power was based on a previous study of pregnant women (8,9). With a mean vitamin E intake of 9.3 mg/day (standard deviation=8.7), 20 subjects in each arm were needed to detect an increase in vitamin E intake of 5.7 mg/day (ie, to 15 mg/day) with 80% power at the 5% level of significance.

RESULTS AND DISCUSSION

In total, 172 women were approached, 61 (35%) had a personal and/or partner history of asthma. Eighteen (30%) of these eligible women declined, 43 were randomized: 21 to the control group and 22 to the intervention. Participants tended to be older than those declining (me-

Table. Summary of vitamin E parameters from food diaries, food frequency questionnaire, and serum for control and intervention groups at 12 and 18/20 weeks gestation, as appropriate

	Control (n=20)		Dietary Intervention (n=19)	
	12 wk	18/20 wk	12 wk	18/20 wk
	←—————mean (95% confidence interval)—————→			
Food diary				
Vitamin E (mg/d)			7.13 (5.63-8.63)	17.4*** (14.4-20.5)
Energy (kcal/d)			1719 (1576-1863)	2128*** (1914-2342)
Energy-adjusted vitamin E (mg/d)			6.41 (5.30-7.52)	17.0*** (14.0-20.0)
Food frequency questionnaire				
Vitamin E (mg/d)	12.3 (10.4-14.1)	12.4 (10.1-14.8)	10.9 (8.50-13.3)	15.9** (12.4-19.4)
Serum				
α -Tocopherol (μ mol/L) ^a	26.3 (23.0-25.6)	29.4** (25.9-32.7)	25.3 (23.5-27.7)	28.7** (26.5-30.8)
Cholesterol (mmol/L) ^b	4.90 (4.50-5.30)	5.70*** (5.19-6.21)	4.59 (4.33-4.86)	5.68*** (5.43-5.93)
α -Tocopherol/cholesterol (μ mol/mmol)	5.34 (4.97-5.71)	5.19 (4.69-5.69)	5.54 (5.17-5.91)	5.05 (4.72-5.37)
Change α -tocopherol 12 and 20 weeks, (μ mol/L) ^a	3.05 (1.48-4.62)		3.29 (0.95-5.64)	

^aTo convert μ mol/L α -tocopherol to mg/dL, multiply μ mol/L by 0.04307. To convert mg/dL α -tocopherol to μ mol/L, multiply mg/dL by 23.2. α -Tocopherol of 26.3 μ mol/L=1.13 mg/dL.

^bTo convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.026. Cholesterol of 4.90 mmol/L=189 mg/dL.

** $P<0.01$, 12 vs 18/20 weeks.

*** $P<0.001$, 12 vs 18/20 weeks.

dian age=29.0 years; interquartile range [IQR]=26.0 to 34.0 years vs median age=25.5 years; IQR=22.0 to 30.5 years, respectively) and of higher socioeconomic status (Scottish Index of Multiple Deprivation (10); median decile=8; IQR=5 to 9 vs median decile=5; IQR=3 to 9), none of these differences were statistically significant ($P>0.2$). Thirty-nine (91%) women completed the study: 20 (95%) control and 19 (86%) intervention.

Results of the vitamin E analyses from the diet diaries, FFQs, and serum are provided in the Table.

Diet Diary

The food-based intervention increased mean dietary vitamin E intake from 7.13 mg/day (95% confidence interval [CI]: 5.63 to 8.63) at 12 weeks gestation to 17.4 mg/day (95% CI: 14.4 to 20.5) at 18 weeks gestation ($P<0.001$). Energy-adjusted dietary vitamin E intake increased from 6.41 mg/day (95% CI: 5.30 to 7.52) to 17.0 mg/day (95% CI: 14.0 to 20.0) ($P<0.001$). In analysis on an intention-to-treat basis, assuming no dietary change for noncompleters, mean vitamin E intake increased from 7.13 mg/day (95% CI: 5.93 to 8.33) to 15.6 mg/day (95% CI: 12.5 to 18.6) ($P<0.001$) and mean energy-adjusted vitamin E intake increased from 6.41 mg/day (95% CI: 5.52 to 7.30) to 15.1 mg/day (95% CI: 12.1 to 18.1) ($P<0.001$). At 18 weeks gestation, four (21%) participants had a vitamin E intake <14 mg/day and five (26%) had a vitamin E intake >20 mg/day. This finding suggests that any proposed pregnancy vitamin E RCT should include additional diet diary assessments between 18 weeks gestation and delivery to ensure that the food-based intervention is sustained throughout pregnancy, and to further tailor dietary intake to 15 mg/day, thus optimizing vitamin E intake and preventing excessive vitamin E intake.

In addition to vitamin E, associations have been reported between maternal PUFAs (particularly n-3

PUFA), selenium, and zinc status during pregnancy and childhood wheeze and asthma (9,11-16). In this pilot study, the food-based intervention not only increased vitamin E intake, but also increased mean intakes of PUFAs from 10.2 g/day (95% CI: 8.7 to 11.7) to 23.1 g/day (95% CI: 20.1 to 26.1) ($P<0.001$), selenium from 33.6 μ g/day (95% CI: 28.1 to 39.1) to 48.7 μ g/day (95% CI: 39.7 to 57.8) ($P=0.001$), and zinc from 7.30 mg/day (95% CI: 6.36 to 8.34) to 8.58 mg/day (95% CI: 7.37 to 9.78) ($P=0.014$). This finding suggests that the previously reported associations between childhood asthma and maternal intake of these individual nutrients should not be viewed in isolation and that they might reflect an association with overall dietary pattern. It seems likely that an advantage of the food-based intervention is that by promoting a dietary pattern it also increases the intake of other nutrients that have been reported to be associated with childhood wheeze and asthma. Although the focus of the chosen dietary intervention was vitamin E, it might be that any potentially beneficial effect of the dietary intervention is dependent on the complex mixture of naturally associated nutrients.

The qualitative study evaluation suggested that the food-based intervention was more acceptable than a supplement intervention. Only three of 39 women commented that they would be happy to take a supplement, many women (21 of 39; 54%) mentioned needing reassurance that there would be no adverse effects of taking supplements to themselves or the baby and that they would prefer the more natural option of changing their diet.

FFQ

FFQ estimates of nutrient intake were used to support the food diary data and to compare intervention and control groups. The FFQ demonstrated that mean vita-

min E intakes of the control and intervention groups did not differ at recruitment, 12.3 mg/day (95% CI: 10.4 to 14.1) and 10.9 mg/day (95% CI: 8.50 to 13.3), respectively ($P=0.21$). FFQ data from the control group revealed no significant change in vitamin E intake between 12 weeks (mean=12.3 mg/day; 95% CI: 10.4 to 14.1) and 20 weeks gestation (12.4 mg/day; 95% CI: 10.1 to 14.8) ($P=0.899$), suggesting that informing women of a vitamin E intervention study does not change dietary behavior, a finding pertinent to any future RCT using a food-based vitamin E intervention. Consistent with the food diary, the FFQ demonstrated that the food-based intervention increased vitamin E intake from 10.9 mg/day (95% CI: 8.50 to 13.3) to 15.9 mg/day (95% CI: 12.4 to 19.4) ($P=0.008$). Analysis on an intention-to-treat basis demonstrated that the intervention was associated with an increase in mean vitamin E from 11.0 mg/day (95% CI: 9.0 to 12.9) to 15.0 mg/day (95% CI: 12.1 to 18.0) ($P=0.009$) and mean energy-adjusted vitamin E intake from 9.8 mg/day (95% CI: 8.7 to 10.8) to 13.5 mg/day (95% CI: 12.4 to 14.6) ($P<0.001$).

The FFQ further supported the food diary data by demonstrating that the food-based intervention increased mean PUFA acids from 15.1 g/day (95% CI: 11.4 to 18.8) to 19.4 g/day (95% CI: 14.9 to 23.9) ($P=0.047$). In addition, the composition tables used in the analysis of the FFQ also enabled estimation of n-3 and n-6 PUFA intakes, making possible an exploratory investigation of the nature of the PUFA increase associated with the intervention. These FFQ data suggested that for energy-unadjusted n-6 and n-3 PUFA intakes, the food-based intervention was associated with nonsignificant increases in n-6 PUFA (1.80 g/day [95% CI -1.22 to 4.83]; $P=0.23$) and n-3 PUFA (0.39 g/day [95% CI -0.35 to 1.13]; $P=0.28$). However, for energy-adjusted intakes, the food-based intervention was associated with a significant increase in n-3 PUFA (0.28 g/day [95% CI 0.08 to 0.48]; $P<0.001$), but not in n-6 PUFA (0.79 g/day [95% CI -0.26 to 1.85]; $P=0.30$).

Serum α -Tocopherol

There were no significant differences in serum α -tocopherol between control and intervention groups at 12 and 20 weeks gestation. Mean serum α -tocopherol increased in both groups between 12 and 20 weeks gestation: control increased from 1.13 mg/dL (95% CI 0.99 to 1.10) [26.3 μ mol/L (95% CI 23.0 to 25.6)] to 1.27 mg/dL (95% CI 1.11 to 1.41) [29.4 μ mol/L (95% CI 25.9 to 32.7)] ($P=0.001$) and intervention increased from 1.09 mg/dL (95% CI 1.01 to 1.19) [25.3 μ mol/L (95% CI 23.5 to 27.7)] to 1.24 mg/dL (95% CI 1.14 to 1.33) [28.7 μ mol/L (95% CI 26.5 to 30.8)] ($P=0.009$). These results are consistent with the reported physiological increase in maternal serum α -tocopherol from 12 weeks of pregnancy onward (17). The increase in serum α -tocopherol between 12 and 20 weeks gestation did not differ between the control and intervention groups. Thus, although the food-based intervention increased vitamin E intake, there was minimal effect on serum α -tocopherol. One of the limitations of vitamin E intervention is that there is no suitable biomarker that accurately reflects dietary intake or tissue stores of vitamin E (18). To illustrate this, a previous study that supplemented pregnant women with 133 mg/day vita-

min E resulted in an approximately 40% difference in plasma α -tocopherol between control and intervention subjects at 20 weeks gestation (19). Extrapolation to the present study suggests that a 10-mg/day increase in vitamin E intake would increase serum α -tocopherol by about 3% to 5%. The current small pilot study was powered to detect changes in dietary vitamin E intake and, consequently, did not have the power to detect small changes in serum α -tocopherol. Any future vitamin E RCT would need to be of sufficient size and power to detect small changes in serum α -tocopherol or consider using an alternative biomarker of vitamin E status (eg, buccal mucosa, platelets) (20).

This pilot study demonstrates that pregnant women are willing and able to increase their dietary vitamin E intake between 12 and 20 weeks gestation. The qualitative study evaluation suggested that pregnant women would be willing to maintain the dietary changes until delivery, with 17 of 19 women saying that they would have been willing to maintain the changes for a longer period, and the remaining 2 women saying they would have been willing to try to maintain the changes for a longer period. However, any future RCT investigating the effects of vitamin E modification during pregnancy on childhood asthma would need the intervention to continue from 12 weeks gestation to delivery, therefore, additional studies are needed to confirm the sustainability of the food-based intervention for the duration of pregnancy.

CONCLUSIONS

This study demonstrates for the first time that pregnant women with a personal and/or partner history of asthma are able to use a novel food-based exchange intervention to increase their dietary vitamin E intake to 15 mg/day. The study demonstrates the feasibility and acceptability of the food-based intervention to increase dietary vitamin E intake, but further work is required to ascertain the sustainability throughout pregnancy and whether it reduces the likelihood of childhood asthma. Although the focus of this pilot study was vitamin E, the process of identifying exchanges of foods containing specified quantities of nutrients and the subsequent development of an individually tailored food-based intervention could be transferred to other nutrients or combinations of nutrients for use in food-based rather than supplement-based intervention trials, which may be more acceptable to women during pregnancy.

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