Prostaglandins, Leukotrienes and Essential Fatty Acids 177 (2022) 102399

Contents lists available at ScienceDirect

Prostaglandins, Leukotrienes and Essential Fatty Acids

journal homepage: www.elsevier.com/locate/plefa

Original research article

Utility of a 7- question online screener for DHA intake

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ARTICLE INFO

Keywords:
DHA intake
Pregnancy
Preterm birth

ABSTRACT

The secondary analyses of two large, recently completed randomized clinical trials of DHA supplementation in pregnancy found that women with a low baseline DHA status benefited from randomization to a higher dose (800 vs 0 and 1000 vs 200 mg/day DHA). To obtain DHA status, it is necessary to obtain a blood sample and conduct an analysis using gas chromatography (GC) or GC-mass spectrometry (GCMS), both barriers to clinics where pregnant women receive advice on nutrition. Participants consuming less than 150 mg/day of DHA at baseline in our recent trial had a lower risk of early preterm birth and preterm birth when assigned to 1000 vs 200 m/day DHA. DHA intake was determined using a 7-question food frequency questionnaire administered by a trained nutritionist. Because the need for trained personnel to administer the questionnaire would be a barrier to implementing this finding in clinical management of pregnancy, the goal of this study was to determine if an online version of the questionnaire could be validly completed without assistance.

Abbreviations

ADORE	(Assessment of DHA On Reducing Early Preterm Birth)
EPB	(Early preterm birth)
DHA	(Docosahexaenoic acid)
FFQ	(Food frequency questionnaire)
NICHD	(National Institute of Child Health and Human Development)
PANDA	(Prenatal Autonomic Neurodevelopmental Assessment)
PP	(Bayesian posterior probability)
PTB	(Preterm birth)
RCT	(Randomized clinical trial)
US	(United States)

1. Introduction

Two recent randomized clinical trials (RCTs) found that pregnant women with low DHA status, determined by measuring DHA in blood lipids, and who were randomly assigned to 800 or 1000 mg/d of supplemental DHA had significantly lower early preterm birth (EPB, <34 weeks gestation) and preterm birth (<37 weeks gestation) than those assigned to 0 or 200 mg/d of DHA [1, 2]. To implement these findings, obstetricians and others who care for pregnant women would need to obtain a measure of DHA status to best advise women who enter prenatal care if they could benefit from a higher dose of DHA.

A clinically pragmatic way to know who could benefit from supplementation would be to administer a 7-question screener designed to capture DHA intake (DHA Food Frequency Questionnaire, DHA-FFQ) [3]. We administered the DHA-FFQ and measured DHA status (DHA as a weight percent of fatty acids in red blood cell phospholipids) at baseline in 1400 women enrolled in one of two RCTs [2, 4]. We found that the DHA-FFQ had good validity in predicting DHA status [5]. Even more importantly, participants who were consuming less than 150 mg/day of DHA from food and supplements and who were assigned to 800 or 1000 mg/d of DHA had significantly less early preterm birth (EPB, <34 weeks gestation, pp = 0.99) and preterm birth (PTB, <37 weeks gestation, pp = 0.97) [6]. Another desirable feature of the DHA-FFQ is that it requires less than 5 min to complete, and it is available through an on-line platform.

An estimation of DHA intake at the first prenatal visit would be an efficient and pragmatic way for obstetricians and others who care for pregnant women to rapidly identify women who could benefit from a higher dose of DHA than in most prenatal supplements. One barrier remains in that the DHA-FFQ was administered by trained study personnel [5] in our RCTs [2, 4], and it cannot be assumed that the

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https://doi.org/10.1016/j.plefa.2022.102399
Received 27 October 2021; Received in revised form 6 January 2022; Accepted 6 January 2022
Available online 8 January 2022

results would be reliable if pregnant women were to complete it independently. Moreover, the utility of the DHA-FFQ would be reduced if clinics needed to train additional personnel to administer the questionnaire. The goal of this quality improvement study was to determine if pregnant women could reliably complete the DHA-FFQ online compared to completing it with a trained interviewer.

2. Methods

Women scheduled for their first obstetrical appointment at the University of Kansas Medical Center were asked to complete a modified version of the DHA-FFQ in REDCap. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Kansas Medical Center [7, 8]. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources.

Those who completed the DHA-FFQ were then invited to take the survey again over the phone with a trained interviewer. We planned to interview 100 women who completed the survey independently. In fact, a total of 101 women completed the DHA-FFQ independently and with an interviewer.

2.1. Modified DHA-FFQ: a self-administered questionnaire

The original version of the DHA-FFQ consists of 7 questions that ask participants how many 3-ounce servings of fish (there are three categories based on DHA content of the fish consumed - high, medium or low high) and liver they consumed monthly in the past 2 months; and how many 3-ounce servings of poultry and the number of egg yolks they consumed weekly. Another question asks about dietary supplements and functional foods containing DHA, including brand name, the dose or serving size consumed, number of days per week it was consumed [3].

The format of the DHA-FFQ was modified slightly to create an electronic survey with branching logic that could be completed without a trained interviewer. The first three fish questions were put into a matrix format that ask the subject to mark off each fish consumed in the past two months with an option to select "I have not consumed any of the fish listed above in the past 2 months." For each fish selected, a new field appeared to ask for the number of 3-ounce servings consumed of that fish in the past two months. Each serving size question included a note reminding the subject that a 3-ounce serving is approximately the size of a deck of cards. To automatically calculate monthly intake for each of the three fish questions, a formula was created on a form separate from the survey. For each question, the total number of servings reported in the past two months is added together, then divided in half to provide the number of servings consumed monthly. The liver question also asks for total servings in the past two months and is then divided by two on the back end to get monthly intake. Questions five and six remain the same as the original format, asking for weekly intake of egg yolks and poultry respectively.

Question seven asks "Are you taking a prenatal vitamin with DHA in it or a fish oil supplement?" If the subject answers "Yes", two additional fields appear asking the amount of DHA in the supplement and the number of days per week the supplement is taken. These two pieces of information are multiplied together and then the product is divided by seven to estimate daily DHA exposure from the supplement. If multiple DHA-containing supplements are consumed, the question asks to report total mg of DHA combined and averages frequency of intake. Functional foods containing DHA were omitted because these were rarely reported in the validation study (1.62% of participants in the validation study reported consuming DHA-containing functional foods) [5].

Estimated total daily DHA intake is calculated the same way as the original questionnaire, multiplying the number of servings reported for each question by the factor specified by the questionnaire, then adding together the product of each question with daily DHA exposure from supplements to get the total estimated daily DHA intake as mg/day. The number of monthly servings reported for question one is multiplied by 22, the number of servings for question two is multiplied by 10 and question three multiplied by five. The number of weekly servings reported for questions five and six are multiplied by three and five, respectively.

The link below shows the survey which could be easily modified for remote use or for use in clinical practice with a message going to caregivers. We have currently using the survey in our Department of Obstetrics and Gynecology as part of a quality improvement study. https://redcap.kumc.edu/surveys/?s=XLP7DJDWF4

2.2. Participants

The link to the electronic survey was distributed by nurses in the University of Kansas Health System Obstetrics and Gynecology clinic via a patient portal in the electronic medical record system prior to a woman's initial prenatal doctor's appointment. Women were asked to complete the survey online as part of a quality insurance program conducted in the department clinics. A trained nutritionist received the results of each completed survey and contacted women who completed the survey to ask if they would be willing to complete the DHA-FFQ in the original interviewer-administered format. The survey was offered to 239 women. Of the 140 women (58.5%) who completed the survey on their own, 101 of 140 (72.1%) agreed to complete the DHA-FFQ with a nutritionist, thereby completing both surveys. Five women who completed the survey in both formats were excluded from the analysis because they began taking a DHA-containing supplement after completing the survey on their own and before being interviewed. **Table 1** contains characteristics of the 96 women included in the analysis to evaluate the self-administered instrument.

2.3. Nonparticipants

Of the 138 (58%) who were not interviewed, 39 (16%) completed only the self-administered survey and did not respond to a request for an interview; and 99 did not complete the survey and were not contacted. **Table 1** includes characteristics of women who completed the self-administered survey, but either declined or did not respond to requests to complete the interview. It also includes women who were sent the link and invited to complete the independent survey, but who did not complete it.

2.4. Statistical analysis

To investigate the validity of the DHA-FFQ as a self-administered instrument, Pearson's correlation coefficients between the self-administered DHA-FFQ completed online and interview-administered DHA-FFQ were computed. Reliability was estimated between the two using intra class correlation coefficient, values closer to 1 indicate strong agreement between variables [9]. A Bland Altman plot investigated a visual of the reliability of the two variables (called x and y) [10]. This plotted the difference on the vertical axis (x-y) and the average on the horizontal axis $[(x + y)/2]$. Visualized is shift in the measurement and the variability in the measurement. With no measurement error the Bland-Altman is expected to be 0 on the vertical. However, it is expected to have some variability. For visualizing this, we scaled the largest possible difference in the vertical axis. For example, in this study since there is a scale from 0 to 1200 mg of DHA, we placed the vertical axis on a scale from -1200 to 1200. The horizontal axis is on the possible values of $(x + y)/2$ (the average). The plotted vertical is a measure of the technical error and if it is wide and short, has small error. The sensitivity

Table 1
Subject Characteristics .

Characteristic	N (%) or Mean ± SD		
	Both Complete[a] *N* = 96 (41. 03%)	Independent Only[b] *N* = 39 (16. 67%)	Neither Complete[c] *N* = 99 (42. 31%)
Self-Administered DHA-FFQ – TOTAL DHA mg/d[†]	260. 05 ± 224. 07	240. 31 ± 221. 37	
Interviewer-Administered DHA-FFQ – TOTAL DHA mg/d[†]	238. 73 ± 194. 16		
Maternal Age (years) [†]	30. 79 ± 4. 81	29. 64 ± 4. 93	29. 22 ± 5. 00
Maternal Race*			
Non-Hispanic or Latino	88 (91.67)	34 (87.18)	86 (86.87)
Asian	3 (3.13)	1 (2.56)	2 (2.02)
Black or African American	11 (11.46)	4 (10.26)	20 (20.2)
Other	4 (4.17)	1 (2.56)	3 (3.03)
Bi- or Multi- Racial	1 (1.04)	1 (2.56)	1 (1.01)
White or Caucasian	69 (71.88)	27 (69.23)	60 (60.61)
Hispanic or Latino	5 (5.21)	5 (12.82)	10 (10.1)
Other	4 (4.17)	5 (12.82)	8 (8.08)
White	1 (1.04)	0 (0)	2 (2.02)
Unknown	3 (3.13)	0 (0)	3 (3.03)
Bi- or Multi- Racial	0 (0)	0 (0)	1 (1.01)
Other	1 (1.04)	0 (0)	0 (0)
Unknown	1 (1.04)	0 (0)	2 (2.02)
White	1 (1.04)	0 (0)	0 (0)
Taking a DHA-Containing Supplement*			
Yes, DHA Supplement	68 (70. 83)	27 (69. 23)	
No, DHA Supplement	28 (29. 17)	12 (30. 77)	
Insurance Type *			
Private	88 (91. 67)	32 (82. 05)	77 (77. 78)
Public	7 (7. 29)	7 (17. 95)	18 (18. 18)
Uninsured	1 (1. 04)	0 (0)	4 (4. 04)
Mean Income based on Zip Code *			
Mean Income <185% Poverty Level	23 (23. 96)	12 (30. 77)	38 (38. 38)
Mean Income >185% Poverty Level	73 (76. 04)	27 (69. 23)	61 (61. 62)

*Values are presented as total and percent. [†]Values are presented as mean ± standard deviation.

[a] Both the self-administered and interviewer-administered surveys were completed.

[b] Only the self-administered survey was completed. Subjects either did not respond to or declined interview request.

[c] Subjects were sent the link, but did not complete the self-administered survey.

of using the self-administered DHA-FFQ for identifying low DHA intake (<150 mg) and specificity of high DHA intake (≥150 mg) from the interviewer-administered DHA-FFQ were calculated. We also summarized agreement between low and high intakes using kappa agreement, a kappa close to 1 is perfect agreement after adjusting for chance.

3. Results

There was a strong correlation (r = 0. 88; 95% CI: 0.83–0.92) between DHA intake estimated by the independent survey and by interview. The self-administered DHA-FFQ was shown to be reliable based on the intraclass coefficient (ICC = 0.869; 95% CI: 0.81–0.91). Further reliability visualization is suggested from the wide and short Bland-Altman graph (Fig. 1). The sensitivity of the independent survey for identifying low DHA intake (<150 mg/d) and specificity for identifying high DHA intake (≥150 mg/d) from interview responses were 92.1% and 91.4%, respectively. Additionally, the kappa agreement between the two formats was strong (0.827; 95% CI: 0.71–0.94).

Although statistical comparisons were not made, the women who completed the survey but who did not give permission for an interview appear to have similar characteristics. Women who chose not to complete the questionnaire appeared somewhat more likely to be racially or ethnically diverse (Black and Hispanic/Latina) and more likely to live in a zip code with a mean income ≤185% of the poverty level.

4. Discussion and conclusion

The results of our analysis demonstrate that independent completion of the DHA-FFQ online is a valid and reliable way to estimate average daily DHA intake and to categorize intake as low (<150 mg/day). Women with low intake in our previous RCTs benefited from assignment to 800 or 1000 mg/day of DHA compared to 200 mg/day with lower rates of EPB and PTB [5]. Of the 96 participants included in the analysis, only 5 (5%) with an intake <150 mg/day were not identified correctly based on their independent completion of the DHA-FFQ. Because pregnant women can complete the DHA-FFQ without a trained interviewer and reliably be identified as having an intake <150 mg DHA per day, the DHA-FFQ could be implemented in prenatal care and used by clinicians as a pragmatic way to identify patients who have low DHA intake and who have been shown to benefit from a higher DHA intake in the range of 800 to 1000 mg with less EPB and PTB.

A limitation of the study was that not all patients completed the DHA-FFQ as requested by the clinic. Those who did not were more likely to be racial or ethnic minorities (Black and Hispanic/Latina) or to live in a zip code with a mean income ≤185% of the poverty level. Because the questionnaire was administered in English and on-line, those who did not complete the survey may not have been able to access and/or understand the DHA-FFQ. We don't know if they also may have been less able to complete it independently. In addition, we do not know their daily DHA intake. It is possible, therefore, that women at the highest risk of PTB and EPB were not included in our analysis. For the DHA-FFQ to be most useful, all women entering prenatal care would need to complete the questionnaire and future work should examine ways to be more inclusive of populations who are in most need of supplementation. One possible future strategy might include offering patients access to the survey in their preferred language through a clinic-owned tablet or to provide a QR code that they could complete on their telephone while they are in the waiting area prior to their prenatal appointment where accessibility to the internet is readily available.

In conclusion, patients can reliably complete the DHA-FFQ without professional assistance. The survey could easily be modified for remote use and/or to provide the result to clinicians who care for pregnant women or to pregnant women themselves so that they could share the result and a recommendation for DHA supplementation with their caretaker. We are currently doing a quality improvement project with the Department of Obstetrics and Gynecology at the University of Kansas Medical Center to determine how best to implement the survey in the care of pregnant women.

Funding

This work was supported by a grant from The National Institutes of Health Child Health and Human Development (NICHD) (ADORE: R01HD083292). The NICHD had no role in study design, data collection, data analysis, data interpretation, or writing of this article.

CRediT authorship contribution statement

DN Christifano: Methodology, Data curation, Writing – review & editing. **SA Crawford:** Methodology, Data curation, Writing – review & editing, Data curation. **G Lee:** Conceptualization, Methodology, Writing – review & editing. **BJ Gajewski:** Software, Validation, Methodology, Formal analysis, Writing – review & editing. **SE Carlson:** Conceptualization, Methodology, Supervision, Writing – original draft, Writing –

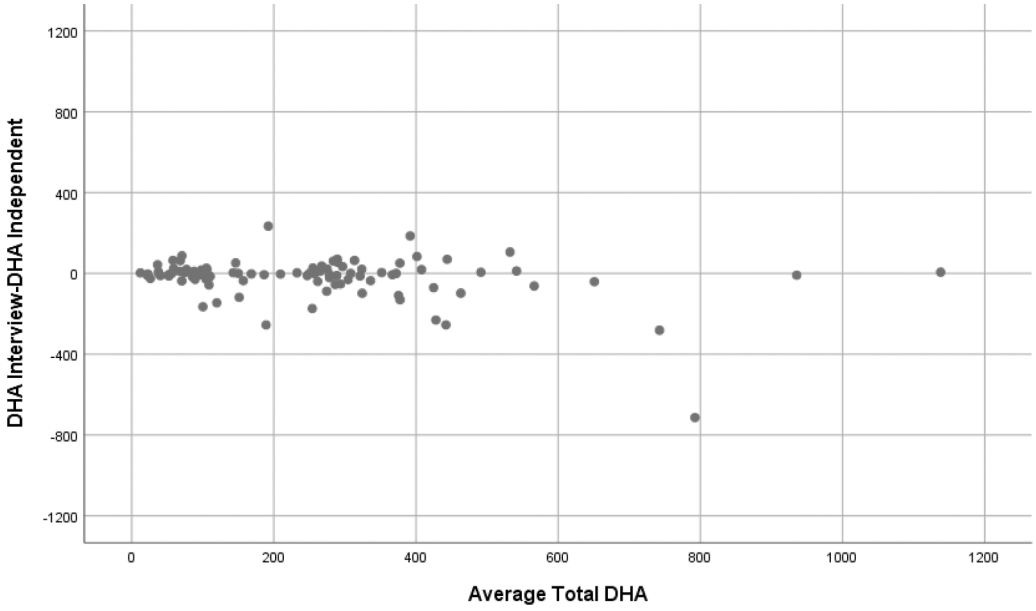

Fig. 1. Bland Altman plot showing agreement between the DHA-FFQ self-administered on-line and interviewer-administered DHA-FFQ in estimating DHA intake.

review & editing, Visualization, Resources.

Declaration of Competing Interest

S.E.C. has received honorariums for presentations about DHA in infancy and pregnancy. S.E.C. and B.J.G. were PIs of R01HD083292. The other authors have no competing interests.

Acknowledgements

G.L., D.N.C., and S.A.C. developed the modified REDCap survey instrument that was completed online. G.L. directed the quality improvement project. B.J.G. conducted the statistical analysis. S.A.C. interviewed participants who completed the DHA-FFQ independently and who agreed to complete it again. S.E.C. and S.A.C. wrote the original draft of the manuscript, however, all authors contributed to the writing and reviewed and approved the final version of the manuscript. We thank the pregnant women who participated in the trials. Support for this research came from The National Institutes of Health Child Health and Human Development (NICHD) (ADORE: R01HD083292).

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