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Original research

Acceptability and side effects of omega 3 in pregnant women with deficient intake

Indalecio Gustavo Martinez Velasco[ab1]*, Roman Jimenez Lopez[c2], Maria Fernanda Gallego Mora[b3], Oliver Arciniega Mancilla[c4], Diana Isabel Castro Luna[bd5], Deny Guadalupe Gonzalez Guzmán[b6], Esmeralda Galarza de la Cruz[b7]

[a] Hospital Comunitario de Tecomatlán, Servicios de Salud del Estado de Puebla. Puebla, México.
[b] Centro de Investigación en Nutrición y Educación Perinatal, Departamento de Nutrición Perinatal. Chapulco, Puebla, México.
[c] Renacimiento General Hospital, IMSS-Bienestar Hospital, Guerrero, México.
[d] Universidad Anáhuac-Campus Puebla, Facultad de Ciencias de la Salud, Cholula, Puebla, México.

ID ORCID:

[1]https://orcid.org/0000-0003-4443-2190, [2]https://orcid.org/0000-0003-4911-1003, [3]https://orcid.org/0009-0009-5056-6372, [4]https://orcid.org/0009-0007-5843-1566, [5]https://orcid.org/0009-0006-9299-5376, [6]https://orcid.org/0009-0003-5103-354X, [7]https://orcid.org/0009-0003-5422-4886

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ABSTRACT

Introduction: Omega-3 polyunsaturated fatty acids, such as EPA and DHA, are essential during pregnancy because of their benefits for maternal health and fetal development. In pregnant women with omega-3 deficiency, assessment of tolerability, acceptability and potential side effects is crucial to optimize treatment adherence. **Objective:** To determine the tolerability and main side effects in a group of pregnant women with inadequate fish intake in a rural community. **Materials and methods:** A dietary survey was carried out in a group of pregnant women attending their antenatal check-ups at a private Gyneco -obstetric facility, to investigate the need for omega-3 supplementation in a population of pregnant women using a simplified questionnaire. Two capsules containing 760 mg of EPA and 520 mg of DHA were prescribed from the 20th week of pregnancy. The presence of side effects and adherence to the prescription were documented. **Results:** Tolerance was 100.0%. Side effects included nausea 19.2%, belching 4.6%, fishy breath 2.3%, vomiting 1.5% and no cases of allergic reaction. No patient discontinued supplementation. **Conclusions:** The side effects of omega-3 PUFAs in this study were very low, resulting in excellent compliance.

Key words: preterm birth; omega-3; pregnancy; food frequency questionnaire; fish; docosahexaenoic acid.

* *Corresponding author*: Indalecio Gustavo Martinez Velasco. Hospital Comunitario de Tecomatlán, Servicios de Salud del Estado de Puebla, Mexico. Email: Indaleciomvgine@outlook.com

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RESUMEN

Introducción: Los ácidos grasos poliinsaturados n-3, como el EPA y el DHA, son esenciales durante el embarazo por sus beneficios para la salud materna y el desarrollo fetal. En mujeres embarazadas con deficiencia de omega-3, es crucial evaluar la tolerabilidad, aceptabilidad y posibles efectos secundarios para optimizar la adherencia al tratamiento. **Objetivo:** Determinar la tolerabilidad y los principales efectos colaterales en un grupo de embarazadas con ingesta deficiente de pescado en una comunidad rural. **Material y métodos:** Se realizó una encuesta nutricional en un grupo de embarazadas que asistían a su control prenatal a una institución privada de Ginecoobstetricia para investigar la necesidad de suplementación con omega-3 mediante un cuestionario simplificado en una población de embarazadas. Se prescribieron 2 cápsulas conteniendo EPA 760 mg y DHA 520 mg a partir de las 20 semanas. Se documentó la presencia de efectos colaterales y la adherencia a la prescripción. **Resultados:** Se encontró un porcentaje de tolerabilidad del 100.0%. Los efectos colaterales fueron náusea 19.2 %, eructos 4.6 %, aliento a pescado 2.3 %, vómito 1.5 % y ningún caso de reacción alérgica. Ninguna paciente abandonó la suplementación. **Conclusiones:** Los efectos colaterales de los AGPI n-3 en el presente estudio fueron muy bajos, resultando en una excelente adherencia al tratamiento.

Palabras clave: parto pretérmino; omega-3; pregnancy; food frequency questionaire; fish; docosahexanoic acid.

INTRODUCTION

Long-chain omega-3 polyunsaturated fatty acids (n-3 PUFAs), specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) promote fetal neural and brain development when there is adequate intake of these nutrients during pregnancy.[1-4] Fish and other seafood, as well as plant-based foods such as chia seeds, are the primary sources of EPA and DHA in the diet during gestation in the Mexican population.[5-6]

Due to different studies showing that DHA requirements are insufficient in pregnant women in Latin America, including Mexico,[7-8] it is extremely important to supplement this population for two reasons: the first is that the placenta has a low conversion capacity (from 2% to 10%), which is insufficient to produce the necessary amount for fetal brain development, and the second is the low accessibility and cost in rural communities.[9-10]

The use of supplements is widely marketed in other countries;[11] however, few published articles on this topic worldwide make it essential to explore this area at the national level and even more so in communities with low accessibility and poverty.

Different side effects have been reported in the literature, including dizziness, diarrhea, nausea, belching, difficulty swallowing the capsule, fishy breath, and fatigue.[12]

This study aims to investigate the acceptability and side effects of omega-3 in a population with low fish intake in a rural Mexican community.

MATERIAL AND METHODS

Pregnant patients who attended their first prenatal visit at the Center for Nutrition Research and Perinatal Education from January 2022 to December 2023 were included. Each patient was invited to participate in the study and provided written information through a brochure and a video about the importance of consuming fish and/or supplements with n-3 PUFA to prevent preterm birth. Patients who agreed to participate in the study were asked to sign a consent form and complete a questionnaire during the first consultation, which included demographic, gynecological-obstetric, and fish intake frequency data (Annex 1).

Patients with low fish intake (never or only once a month) were given a supplement containing 760 mg of EPA and 520 mg of DHA per capsule (Herbalifeline, Herbalife Nutrition USA), prescribed twice daily, starting in week 20 of gestation. After one month, the patient was scheduled for a follow-up appointment to collect acceptability and side effects data. Inclusion criteria were age 18 to 35 years, gestational age of 14 to 19 weeks, and low fish consumption according to a simplified questionnaire. Exclusion criteria: Patient with a fish, shrimp, or other seafood allergy and intake of any vitamin containing any n-3. Elimination criteria: Patients with hyperemesis gravidarum and patients who discontinued treatment for another reason.

This project was carried out following the ethical principles established in the Declaration of Helsinki and with the approval of the local research committee (CLIS003) and the ethics of the institution's research committee.

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RESULTS

During the period, 138 were included, corresponding to the group with deficient fish intake, meaning those who never consumed it or only once a month. Eight patients were excluded from the group with deficient intake: 6 due to a history of fish allergy and two due to hyperemesis gravidarum, resulting in 130 patients who entered the group that received the supplement (Figure 1).

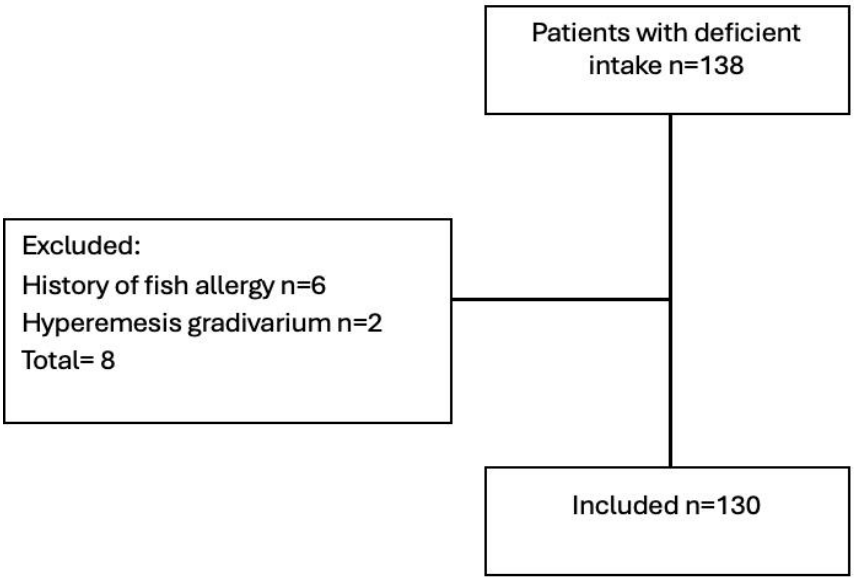

Figure 1. Flow diagram

The supplement's tolerability was 100.0%. 27.6% of the group reported side effects, the most common of which were nausea, belching, fishy breath, and vomiting (Table 1). There were no reported cases of allergy. No side effect prompted the discontinuation of the supplement.

Table 1. Side effects

TYPE OF EFFECT	No.	%
Nausea	25	19.2
Burping	6	4.6
Fishy breath	3	2.3
Vomit	2	1.5
Skin rash	0	0
TOTAL	36	27.6

Some patients experienced two side effects simultaneously.

DISCUSSION

After more than three decades of study, the benefits of omega-3 PUFA intake during pregnancy have been more clearly defined, primarily regarding DHA and EPA. Derived from the latest Cochrane review on the action of omega-3 during pregnancy published in 2018, which included over 70 controlled studies conducted by Middleton et al.,[13] strong evidence was found in qualitative studies. Pregnant women assigned to the group with fish, fish oil, DHA, or EPA intake or who were recommended to consume foods with omega-3 had an 11% reduction in the risk of preterm birth before 37 weeks and a 42% reduction in the risk of early preterm birth before 34 weeks.

Current guidelines recommend a regular consumption of 224-336 g, or 2 to 3 servings of fish per week during pregnancy, to consume an average of 200 mg/day of DHA.[14] Recent data shows that nearly a quarter of pregnant women in the United States do not consume fish, and only 16% take supplements.[15]

It has been shown that the requirements for omega-3 during pregnancy are insufficient in our country. Al-Hinai, in a cohort of pregnant women where the consumption of n-3 PUFAs was quantified using a standard food questionnaire during the different trimesters of pregnancy, demonstrated that in the first and second trimester, the 50th percentile of consumption was reported at 20 mg/day of EPA and 40 mg/day for DHA, and in the third trimester, the 50th percentile of consumption was reported at 10 mg/day of EPA and 40 mg/day for DHA, demonstrating the low consumption of PUFAs and consequently a higher risk of preterm birth.[16]

There are biochemical studies to determine the amount of omega-3 fatty acids through blood; however, they are not yet available in our country, making it very important to know the requirements through daily food frequency records (DFR). The DFR is a simple and inexpensive method, with its main drawback being the complexity involved in carrying it out and the time required by both the interviewer and the interviewee.[17] An important aspect to consider is knowing its degree of correlation. A correlation is considered low when it is < 0.30, moderate or acceptable between 0.30-0.49, and high if it is > 0.50.[18-19] Several studies have been published on the correlation between food frequency questionnaires and omega-3 levels in pregnant women. In Mexico, Parra et al. reported a good correlation between α-linolenic acid, DHA and EPA in erythrocyte membranes in a population of pregnant women, which was 0.32, 0.35 and 0.36, acceptable correlation.[20]

Reports from different countries in Europe (Norway and Switzerland) and Asia (China and Japan) have shown a good correlation between the level of n-3 AGPI and the food frequency consumption questionnaire.[21-24]

To skip lengthy questionnaires, Crawford at the Kansas Medical Center validated a simplified 7-question questionnaire called DHA-FFQ, also using graphical support in 1,355 pregnant patients, achieving an acceptable result when comparing the extensive questionnaire of the National Cancer Institute Diet Questionnaire II (DHQ II) with a shortened questionnaire, reporting a correlation level of 0.52 with the level of DHA in red blood cells versus 0.35 from the DHQ II.25 More recently, a study by Christifano et al. was published in which the DHA-FFQ was modified to create an electronic format of consecutive responses that can be completed by the respondent without the need for a trained interviewer, aiming to make it more practical for health personnel.[26]

Within the safety and tolerability aspect of current marine oil preparation prescription, a low frequency of adverse events has been found. According to the British National Formulary (BNF), side effects are classified as follows: common (burping, constipation, diarrhea, gastrointestinal discomfort, gastrointestinal disorders, nausea, vomiting), uncommon (dizziness, gout, bleeding, headache, hyperglycemia, hypotension, skin reactions, altered taste) and rare (liver disorders).[27] In a recent article on the clinical use and efficacy of EPA-DHA, Elgar describes that most studies involving omega-3 use in humans, have documented mild side effects, however, she mentions evidence of more serious effects, such as an increased risk of bleeding, possibly due to the inhibitory effect of marine oils on platelet aggregation in healthy patients, despite this, no cases of postoperative bleeding in patients undergoing surgery were found in 20 reviewed studies,[28] which is a relevant consideration given the potential need for cesarean section in a percentage of pregnant patients.

Adverse effects have been reported in the non-pregnant population, with a relative risk of dysgeusia 4.2, fatigue 3.6, constipation 3.2 and vomiting 2.2.[29] In the pregnant population, literature describing adverse effects is limited. According to Freeman, in a case series of 59 patients, 13 (22%) reported uncommon side effects, including dizziness, diarrhea, nausea, burping, reflux, difficulty swallowing capsules, bad breath and fatigue. The most common effect were difficulty breathing, bad taste and reflux; however, no patient discontinued the medication due to intolerance.[12] Given the increasing use of omega-3 supplements among pregnant women, both with and without a prescription, it is

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important to remain aware of the potential adverse effects associated with their use.

The main weakness of our study is that it was based on only one question about supplementation; however, we believe that it is practical and feasible for general practitioners or specialists to implement, because of the lack of availability of a nutrition specialist in their care center and, above all, because of the workload and extensive information provided during obstetric consultations, which makes it difficult to adequately assess this issue in prenatal consultations.[30]

One of the strengths of our study is that it was conducted in a rural area where fish is not available. The study found that the surveyed pregnant women have a deficient consumption rate of 53%, which is higher than that of the United States, where a percentage of 24.6% is reported, and in Australia, at 19.3%.[31-32]

CONCLUSIONS

Our data suggest that omega-3 supplementation during the perinatal period is well tolerated, with very low side effects, consequently improving the health of both the mother and the newborn.

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CONFLICT OF INTEREST

The authors of the article declare that they have no conflict of interest.

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ANNEX 1. QUESTIONNAIRE

1. What is your age?
2. What is your highest educational level?
   a) Primary
   b) Secondary
   c) Junior High School
   d) Professional
3. What is your obstetric history?
   a) First pregnancy
   b) Second pregnancy
   c) Multiple pregnancies
4. What is your marital status?
   a) Single
   b) Free union
   c) Married
5. How often do you consume fish?
   a) Never or less than once per month
   b) Less than once per week
   c) 1 or 2 times per week
   d) More than 3 times per week
6. Have you experienced any of the following side effects?
   a) Nausea
   b) Burping
   c) Fishy breath
   d) Vomiting
   e) Skin rash