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Expert Opinion

Omega-3 fatty acid supply in pregnancy for risk reduction of preterm and early preterm birth: A position statement by the European Board and College of Obstetrics and Gynaecology (EBCOG)

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ABSTRACT

Pre-term birth is associated with significant neonatal morbidity and mortality. Pre-term births are associated with significant health and neuro-developmental risks in childhood and adulthood. Women with multiple pregnancies are at much higher risks. Low levels of omega-3 long-chain polyunsaturated fatty acids (PUFAs), such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are associated with higher risk of pre-term labour and increased consumption of foods rich in omega-3 PUFA or supplements are associated with a 11 % and 42 % risk reduction of early and late preterm births, respectively.

Introduction

Preterm births in Europe currently account for about 4.0 (Lithuania) to 8.2 % (Cyprus) of all singleton live births, with significantly much higher rates for multiple pregnancies ranging from 42.1 % (Latvia) to 74.8 % (Cyprus) of all multiple live births. These births are associated with a higher morbidity and mortality with 22–27 weeks gestation births accounting, in 2019, for 47.3 % of neonatal deaths and 28–36 weeks births accounting for 27.1 %. Term pregnancies only accounted for 25.6 % of all neonatal deaths in Europe [1]. In addition, preterm births are also associated with health and developmental risks in childhood and risks for the development of adult onset metabolic and chronic diseases.

In contrast to physician-indicated preterm births for fetal or maternal-indicated conditions, the causes of spontaneous preterm birth are heterogeneous and are often unidentified. There is a substantial proportion that can be attributed to either multiple pregnancies or the choice to deliver early as a result of fetal or maternal obstetric complications [2]. Spontaneous preterm births have been associated with a number of socio-biological risk factors [3]. Improvements in neonatal support management over the last decades have resulted in improved survival prospects for these infants. However, few effective interventions have been developed to actually prevent spontaneous preterm births. A 2019 Cochrane Review including 35,212 women showed high grade evidence suggesting that low-dose aspirin reduces preterm births by about 10 % [4]. Progesterone has been shown to reduce the risks of spontaneous singleton preterm births in cases with a mid-trimester sonographic short cervix. There is no convincing evidence to support its use to prevent recurrent singleton preterm births [5,6]. New prevention strategies need to be identified and introduced into clinical practice.

Omega-3 fatty acids

A recent review of the literature has shown compelling evidence correlating preterm births with low levels of omega-3 long-chain polyunsaturated fatty acids (PUFAs), such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) [7]. A 2018 Cochrane Review (70 RCTs involving 19,927 women) evaluating omega-3 polyunsaturated fatty acids (PUFAs) supplementation during pregnancy showed strong evidence that increased consumption of foods rich in omega-3 PUFA or supplements were associated with a 11 % and 42 % risk reduction of early and late preterm births respectively [8]. Similar findings were reported in a follow-up review [9]. It has been proposed that the

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safeguarding effect against preterm births may be linked to the inhibitory effects of PUFAs on the production of dienoic prostaglandins, primarily PGF2α and PGE2, that act as mediators for the onset of labour [10].

Omega-3 PUFA intake appears to be safe during pregnancy and no potentially harmful limit has been established. The 2018 Cochrane Review concluded that omega-3 PUFA probably increased the incidence of post-term pregnancies. There was however no evidence for an increase in serious adverse events for mothers or the offspring.[8] The European Food Safety Authority (EFSA) do not raise any safety concerns with the daily intake of up to 5 g EPA+DHA, 1.8 g of EPA alone or 1.0 g/d of DHA alone.[11] PUFAs, such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are naturally available in high quantities in oily fish such as anchovies, herring, mackerel, black cod, salmon, sardines, bluefin tuna, whitefish, striped bass and cobia. They are also accesible in some form of nuts and seeds such as walnuts, flaxseeds and sunflower seeds.

Recommendations

A consortium of expert medical-scientific associations supported by the charitable Child Health Foundation (Stiftung Kindergesundheit, www.kindergesundheit.de) based at the LMU University of Munich Hospitals, after reviewing the available evidence, proposed a number of recommendations in an effort to reduce the number of spontaneous singletom preterm births by increasing the maternal intake of omega-3 fatty acids. As a partner to this onsortium, the European Board & College of Obstetrics and Gynaecology (EBCOG) fully endorses these recommendations [7].

- Women of childbearing age should be encouraged to obtain a regular supply of omega-3 fatty acids from foods rich in these fatty acids. The daily target intake during pregnancy should aim to reach within the range of 350–450 mg, in accordance with the recommendations by the European Food Safety Authority.
- Pregnant women at increased risk of preterm births due to inadequate DHA intake should receive a regular supply of about 600–1000 mg/day of DHA plus EPA, or DHA alone. Prematurity risk from insufficient DHA intake can be assessed through the use of a dietary questionnaire and/or DHA measurement in the blood lipid component.
- Commencing supplementation is advisable during the second trimester of pregnancy before 20 weeks of gestation, and should be sustained until approximately 37 weeks.
- Additional research efforts should be directed towards to develop simple and practical screening digital approaches to allow for automatic categorization of risk based on low DHA intake.

This paper has been peer reviewed by Professor Juriy Wladimiroff, Cambridge, Professor Fionnuala McAuliffe, Dublin and Dr Sofia Tsiapakidou, Thessaloniki.

CRediT authorship contribution statement

Charles Savona-Ventura wrote the first draft of the position statement and all the other authors reviewed and made substantial contributions to the text.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Euro-Peristat Project. European Health Report : Core indicators of the health and care of pregnant women and babies in Europe from 2015 to 2019. Inserm, Paris, 2020. Available https://www.europeristat.com/index.php/reports/ephr-2019.html.
[2] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371(9606):75–84. https://doi.org/10.1016/S0140-6736(08)60074-4. PMID: 18177778; PMCID: PMC7134569.
[3] Savona-Ventura C, Buttigieg GG, Felice N, Gulliamier RA, Gatt M. Risk factors for prematurity in the Maltese Islands: 1999–2006. Int J Risk Saf Med 2009;21(4):177–84.
[4] Duley L, Meher S, Hunter KE, Seidler AL, Askie LM. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database Syst Rev 2019;2019(10):CD004659. https://doi.org/10.1002/14651858.CD004659.pub3. PMID: 31684684; PMCID: PMC6820858.
[5] Romero R, Conde-Agudelo A, Da Fonseca E, O'Brien JM, Cetingoz E, Creasy GW, et al. Vaginal progesterone for preventing preterm birth and adverse perinatal outcomes in singleton gestations with a short cervix: a meta-analysis of individual patient data. Am J Obstet Gynecol 2018;218(2):161–80. https://doi.org/10.1016/j.ajog.2017.11.576. PMID: 29157866; PMCID: PMC5987201.
[6] Conde-Agudelo A, Romero R. Vaginal progesterone to prevent preterm birth in pregnant women with a sonographic short cervix: clinical and public health implications. Am J Obstet Gynecol 2016;214(2):235–42. https://doi.org/10.1016/j.ajog.2015.09.102. PMID: 26450404; PMCID: PMC5703061.
[7] Cetin I, Carlson SE, Burden C, Fonseca EBD, Renzo GCD, Hadjipanayis A, et al. Omega-3 fatty acid supply in pregnancy for risk reduction of preterm and early preterm birth. Am J Obstet Gynecol MFM 2023;7:101251. https://doi.org/10.1016/j.ajogmf.2023.101251. PMID: 38070679.
[8] Middleton P, Gomersall JC, Gould JF, Shepherd E, Olsen SF, Makrides M. Omega-3 fatty acid addition during pregnancy. Cochrane Database Syst Rev 2018;11(11):CD003402. https://doi.org/10.1002/14651858.CD003402.pub3. PMID: 30480773; PMCID: PMC6516961.
[9] Best KP, Gibson RA, Makrides M. ISSFAL statement number 7 - Omega-3 fatty acids during pregnancy to reduce preterm birth. Prostaglandins Leukot Essent Fatty Acids 2022;186:102495. https://doi.org/10.1016/j.plefa.2022.102495. PMID: 36228573.
[10] Lee SA, Kim HJ, Chang KC, Baek JC, Park JK, Shin JK, et al. DHA and EPA Down-regulate COX-2 expression through suppression of NF-kappaB activity in LPS-treated human umbilical vein endothelial cells. Korean J Physiol Pharmacol 2009;13(4):301–7. https://doi.org/10.4196/kjpp.2009.13.4.301. PMID: 19885014; PMCID: PMC2766710.
[11] EFSA-Panel-on-Nutrition-Novel-Foods-and-Food-Allergens. Scientific Opinion on the Tolerable Upper Intake Level of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA). EFSA Journal. 2012;2012(7):2815.