



PUFA treatment in patients with gestational diabetes mellitus: Lights and shadows

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The systematic review and meta-analysis published by Liu et al. summarizes existing evidence and suggests potential metabolic benefits of treatment with polyunsaturated fatty acids (PUFA) in pregnant women with gestational diabetes.¹ According to the findings of this study, treatment with PUFA is able to decrease fasting plasma glucose (FPG) and fasting insulin levels and improves insulin resistance, with a positive effect also on inflammation and a number of lipid fractions, including triglycerides and very-low density lipoprotein cholesterol. These promising results can be reached in the included clinical studies with PUFA daily dose up to 2000 mg, that are very high dosages of PUFA for which human teratogenic risk has not been proven nor has it been ruled out. This is of course a critical issue that should be always considered when evaluating findings from clinical trials involving pregnant women, mainly due to the difficulties of assessing the drug-associated risk of teratogenesis.²

The European Food Safety Authority (EFSA) currently recommends for pregnant women a daily dietary intake of 250 mg of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), or 100–200 mg daily of DHA in addition to the consumption of two servings of fish per week.³ Even if the average dietary intake of PUFA in patients with gestational diabetes is 200–300 mg/day lower than recommended,⁴ these doses are very far from those tested in the clinical studies included in the meta-analysis by Liu et al. Despite this, in patients with gestational diabetes mellitus, treatment with PUFA even at lower doses historically associates to increased insulin sensitivity, lower preterm delivery, reduced risk of developing hypertension, pre-eclampsia and other cardiovascular diseases in mothers and normal fetal growth and fetal brain

development.⁵ Moreover, PUFA could also lower the risk of the child to develop type 1 diabetes due to their immunomodulatory effect and anti-inflammatory properties.⁶

What discussed above is indeed critical, since gestational diabetes is currently one of the most common pregnancy complications, being associated with short- and long-term adverse health outcomes in women and their offspring.⁷ It should be also mentioned that several factors contribute to the ethnic differences in prevalence and outcomes of gestational diabetes mellitus, including screening strategies in the different countries, genetics, body composition, gestational weight gain as well as cultural attitudes and practices.⁸ In this light, great consideration should be given to the geographical location, since all the clinical studies included in the meta-analysis by Liu et al. were carried out in Iran.¹ Even if medical nutrition therapy (MNT) is the cornerstone for the treatment of gestational diabetes mellitus,⁹ it is variably applied across countries. A challenge in the prescription and adherence to MNT is the impact of cultural traditions as regards to food and meal times.¹⁰ For example, many women of the Islamic faith observe fasting during the month of Ramadan, despite being excused by their faith from participating while pregnant,⁹ and it is likely to have had an impact on the final observations of the clinical studies included in the meta-analysis.

Despite these issues and limitations, the work by Li et al. is quite interesting and links existing knowledge with new insights and valuable information.¹ Furthermore, this study suggests future research paths for overcoming existing challenges and cones of shadow. Pharmacotherapy for pregnant women with gestational diabetes is still under debate^{11,12} and the use of nutraceuticals is strongly encouraged for their safety,¹³

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with the ultimate goal to traduce the risk for adverse pregnancy outcome and the long-term cardiometabolic complications for both the mother and the child.^{14,15} Yet, this is complicated by the fact that available data is often contradictory; for instance, the supplementation of fish oils during the last trimester of pregnancy has shown no effects on plasma lipids and lipoproteins in the offspring, as well as on their adiposity.¹⁶ Therefore, further research are expected to clarify what is the best EPA/DHA to use in women with gestational diabetes mellitus, in order to obtain a clinically significant reduction in the risk of developing maternal and fetal complications, with both short and long-term consequences. Finally, the research of new and pharmaceutical forms of PUFA is needed in order to detect the one with the best bioavailability and efficacy, and with a parallel reduction in the production costs to face the progressive fish stocks dwindling.

CRediT authorship contribution statement

Federica Fogacci: Conceptualization, Methodology, Writing- Original draft preparation.

Manfredi Rizzo: Conceptualization, Methodology, Writing- Reviewing and Editing, Supervision.

Arrigo F.G. Cicero: Conceptualization, Methodology, Writing- Original draft preparation, Supervision.

Declaration of competing interest

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