RESPONSE TO COMMENT ON FARREN ET AL.

The Prevention of Gestational Diabetes Mellitus With Antenatal Oral Inositol Supplementation: A Randomized Controlled Trial. Diabetes Care 2017;40:759–763

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We thank Drs. Pintaudi and Di Vieste for their comments (1) on our article (2). They highlight diversity among our study cohort. However, we believe this does not explain the ineffectiveness of inositol in preventing gestational diabetes mellitus (GDM). First, of the 240 women, 151 had a family history of diabetes as their only risk factor, with 74 in the intervention group and 77 in the control group. The incidence of GDM was 17.6% in the intervention group compared with 10.4% in the control group ($P = 0.2$). The authors highlight that most women in the study were Irish-born. The Irish population is increasingly diverse, and 39 women were of an ethnicity that is considered high risk. Again, there was no difference between the two groups when ethnicity was compared ($P = 0.13$).

Five women in total had a history of macrosomia: two in the intervention group and three in the control group. Macrosomia was defined as a birth weight ≥4.5 kg. The authors state that daughters of persons with type 1 diabetes were at greater risk of developing GDM compared with daughters of those with type 2 diabetes. In our cohort, 35 women had a parent with type 1 diabetes: 19 in the intervention group and 16 in the control group. There was no difference between the groups in any of the baseline characteristics of the women studied. Therefore, in our view the ineffectiveness of inositol cannot be attributed to the demographics. Further research is required to examine the relationship between inositol and ethnicity.

The authors (1) have highlighted the differences in the dose of *myo*-inositol (MI) and *D*-chiro-inositol that we used as compared with previous studies. As reported, this dose was extrapolated from a study that showed improvement in the metabolic parameters in women with polycystic ovary syndrome (3). We have suggested that a higher dose of MI may be required to prevent GDM. The literature to date suggests that MI is safe up to doses of 12 g per day (4). It is also our view that as there is a lack of consensus regarding optimal dose, combination, and even stereoisomer, consequently inositol should not be added to antenatal vitamin supplementation until future pharmacokinetics demonstrate what regimen improves clinical outcomes.

Last, the authors highlight the difference between the Irish and Italian diets. Grains and beans are the highest sources of inositol in the diet (5). As 98% of the population of Ireland consumes bread on a regular basis, the ingestion of inositol is high in the Irish diet (6). Therefore, if dietary intake was effective, this should have positively affected the rate of GDM. The evidence, however, is that GDM rates in Ireland are increasing (7). Also, it is worth noting that inositol does not come from diet alone, as levels are maintained within the body by de novo synthesis from glucose (4).

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References

1. Pintaudi B, Di Vieste G. Comment on Farren et al. The prevention of gestational diabetes mellitus with antenatal oral inositol supplementation: a randomized controlled trial. Diabetes Care 2017;40:759–763 (Letter). Diabetes Care 2017;40:e172. https://doi.org/10.2337/dc17-0847
2. Farren M, Daly N, McKeating A, Kinsley B, Turner MJ, Daly S. The prevention of gestational diabetes mellitus with antenatal oral inositol supplementation: a randomized controlled trial. Diabetes Care 2017;40:759–763
3. Nordio M, Proietti E. The combined therapy with myo-inositol and D-chiro-inositol reduces the risk of metabolic disease in PCOS overweight patients compared to myo-inositol supplementation alone. Eur Rev Med Pharmacol Sci 2012;16:575–581
4. Carlomagno G, Unfer V. Inositol safety: clinical evidences. Eur Rev Med Pharmacol Sci 2011;15:931–936
5. Clements RS Jr, Darnell B. Myo-inositol content of common foods: development of a high-myo-inositol diet. Am J Clin Nutr 1980;33:1954–1967
6. Irish Universities Nutrition Alliance. National Adult Nutrition Survey, Summary Report, March 2011 [Internet]. Available from http://www.iuna.net/wp-content/uploads/2010/12/National-Adult-Nutrition-Survey-Summary-Report-March-2011.pdf. Accessed 27 June 2017
7. Ali FM, Farah N, O'Dwyer V, O'Connor C, Kennelly MM, Turner MJ. The impact of new national guidelines on screening for gestational diabetes mellitus. Ir Med J 2013;106:57–59

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