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EDITORIAL

Gestational diabetes: Is it time to change cardiovascular risk in women?☆

Diabetes gestacional: ¿es tiempo de cambiar el riesgo cardiovascular en las mujeres?

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Obesity and gestational diabetes (GD) are the two most important risk factors for the development of type 2 diabetes mellitus (DM2).[1]

We know from a recent study conducted in Spain that mortality due to all causes, adjusted for age and gender, is more than twice as high in adults with DM2 than in those without DM2, and that this risk is, moreover, considerably higher in women with DM2.[2]

Gestational diabetes is one of the most common medical complications during pregnancy. Women with GD and their descendants have a higher risk of short- and long-term complications, including – in the case of the mothers – the subsequent development of DM2 and cardiovascular disease (CVD). The offspring in turn are at a lifelong increased risk of suffering obesity, DM2 and metabolic syndrome.[3]

A recent review has shown that GD, even if DM2 does not develop, implies a two-fold increase in the risk of CVD.[4] This is why GD is considered an ''emerging'' cardiovascular risk factor.

Although there are differences in the screening tests and diagnostic cut-off points, it is generally accepted that the identification and early treatment of women with GD reduces complications in pregnancy and during the perinatal period. Results from the HAPO study have shown a continuous relationship between maternal hyperglycemia and adverse outcomes.[5] Recently, the HAPO follow-up study also found that adolescent offspring of mothers with GD present higher levels of blood glucose and insulin resistance in childhood, regardless of the maternal and child body mass index (BMI) or a family history of DM2, and that this relationship is, moreover, continuous.[6]

At our hospital, we adopted the HAPO criteria in 2012 and conducted a study comparing two female cohorts: one based on the old Carpenter and Coustan (CC) criteria, and the other based on the HAPO criteria. This was a retrospective study, though except for the difference in criteria, both cohorts were comparable and were treated at the same unit, by the same staff and with the same treatment protocol being applied. The aim was to compare maternal and fetal morbidity after the introduction of the new criteria. The use of the new criteria was associated with a 3.4-fold increase in the prevalence of GD in our population (10.6% CC versus 35% HAPO). Despite this increase in the number of cases, however, the clear benefits in terms of fetal and maternal health resulted in significant economic savings.[7] This work has been referenced in the Standards of Care of

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the American Diabetes Association (ADA) from 2015 to the present.[8,9]

In addition, a study estimating the cost-benefit ratio in the diagnosis of GD, comparing no universal testing versus two- or one-step testing with a diagnosis of GD, concluded that the one-step approach is cost-effective if the patients receive counseling and postpartum care to prevent the future development of diabetes.[10] In this regard, the ADA recommends reviewing women with GD 6–12 weeks after delivery. In addition, women with a history of GD should be monitored at least every three years for life, due to the risk of developing DM2, and should receive lifestyle recommendations or even metformin treatment to prevent DM2 from developing.[9]

However, in this recent retrospective study,[3] although women with GD were 20 times more likely to develop DM2, almost three times more likely to develop ischemic heart disease and twice as likely to develop arterial hypertension, less than 60% of the women diagnosed with GD were assessed in primary care to rule out DM2 in the first year after delivery, and the proportion, moreover, decreased rapidly after this period. Given this fact, it is the responsibility of the specialists involved in the management of the disorder to transmit the fact that these women constitute an identifiable risk group and are ideal targets for preventive interventions. Are we going to?

A retrospective study is published in this same issue of the journal, involving 305 women seen for postpartum control in Spain. It comprised a multiethnic cohort: 47% Caucasian, 22% Asian, 12% Hispanic and 10% Moroccan, presenting GD with National Diabetes Prevention Program (NDDP) criteria. In the first year of monitoring, 41% of the patients showed changes in carbohydrate metabolism, with this risk being three times higher in non-Caucasian women.[11]

At our hospital, while still using the CC criteria, we conducted a randomized, prospective postpartum study of 260 women with a history of GD and normal baseline blood glucose at 6–12 weeks postpartum. The patients were divided into two parallel groups: 130 women subjected to standard follow-up, and 130 women enrolled in a nutrition and physical activity program, monitored over a period of three years. After follow-up, the control group had a prevalence of altered glucose metabolism of 56.7% versus 42.8% in the intervention group ($p < 0.05$). Despite the high percentage of altered glucose metabolism in postpartum, lifestyle intervention proved effective in terms of prevention among the women with previous GD. Increased body weight and unhealthy fat intake were the strongest predictors of the development of glucose disorders.[12]

Finally, the Atlantis cohort study of an Irish population of women with GD based on the HAPO criteria also involved a three-year follow-up of 295 pregnant women with previous GD versus 378 without GD in the same period, paired by age and the BMI. Metabolic syndrome (MS) was seen to be three times more frequent in the women with GD. The prevalence of MS was 25% in the patients with previous GD and only 6% in the patients without GD. This is particularly worrying in a population of young women belonging to a low-risk ethnic group.[13]

These three postpartum follow-up studies show that regardless of the criteria used, women with GD have a greater future cardiovascular risk, and moreover constitute a population that is easy to identify and target for preventive interventions, as was shown by our interventional and follow-up study, where a clear improvement was observed after nutritional and lifestyle intervention.

More than 80% of the women with GD are controlled by dietary measures; as a result, diet remains the first indicated treatment. Multiple interventions have been proposed, though data regarding the optimum diet for achieving euglycemia and the best perinatal outcomes are limited. A recent meta-analysis of different dietary interventions has shown favorable results in terms of maternal blood glucose and birth weight. This indicates that there is room for improving standard dietary advice for women with GD.[14]

At our hospital we conducted a retrospective study analyzing lifestyle during the first months of our two female cohorts (CC and HAPO), using a semi-quantitative nutritional consumption questionnaire. We identified a protective pattern, with statistical significance being reached only in the HAPO cohort – probably because screening was better in this cohort – and this difference, moreover, persisted after adjusting for age and the BMI.[15] Based on these data, we designed a prospective, randomized interventional study involving 440 women in the control group (CG) and 434 in the intervention group (IG). The CG received the standard nutritional recommendations with regard to a Mediterranean diet, with total fat reduction, while the IG received a Mediterranean diet supplemented with extra virgin olive oil (EVOO) and nuts (pistachios), which were provided free of charge to ensure compliance. Early nutritional intervention in the first weeks of pregnancy[8–12] involving a Mediterranean diet supplemented with EVOO and pistachios, resulted in an almost 30% decrease in the development of GD by week 24, based on the new criteria. The incidence of GD was reduced from 35% initially to 23% (CG) and 17% (IG) after the intervention. Moreover, many adverse events were seen to improve in the intervention group.[16]

These results can easily be incorporated into clinical practice, and afford a simple approach for reducing the burden of an increasing incidence of GD. In addition, early nutritional intervention prior to DG diagnosis can improve differences in maternal-fetal adverse outcomes between women with and without GD.[17]

We have thus demonstrated that there are protective nutritional effects regarding both primary prevention (avoiding the development of GD) and secondary prevention (avoiding adverse events after the diagnosis of GD). All these data indicate that it is crucial to control diabetes ''from the beginning.'' As endocrinologists, it is our duty to promote strategies that require a multidisciplinary approach from primary care onwards, with the collaboration of obstetricians and pediatricians in order to deal with this pandemic. It is also crucial that we invest in trained nurses who can conduct group sessions involving nutritional and lifestyle recommendations, and identify those women who are in need of such recommendations. Clearly, if we do not diagnose these cases, patient treatment will not be possible.

We must act now in order to ensure that these changes will take place, and join together in efforts to protect the health of these women, emphasizing ''whole life''

prevention and adopting a straightforward approach in order to prevent future adverse events, both in these patients and in their offspring.

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