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COMMENTARY

Prevention of perinatal death with low-dose aspirin in developing countries

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Prevention of perinatal death, mainly related to eclampsia in developing countries, is a priority for the WHO. The study by Bakthi and Vaiman[1] raises the possibility that low-dose aspirin could be part of the solution.

PREECLAMPSIA

Hypertensive disorders of pregnancy (HDP), and particularly preeclampsia, remain a major source of adverse pregnancy outcomes worldwide, being one of the major causes of maternal, fetal and neonatal morbidity. Delivery of the placenta is the sole cure of preeclampsia. Left untreated, preeclamptic mothers can suffer from several complications, such as generalized seizures (eclampsia), HELLP syndrome and placental abruption, which could result in maternal and fetal death.

Usually defined as the new-onset hypertension after 20 weeks' gestation, gravidic hypertension becomes preeclampsia when associated with proteinuria. The physiopathology of HDP and preeclampsia remains unclear, but involves placental and endothelial dysfunction. Inadequate invasion and transformation of uterine spiral arteries by trophoblastic cells are common findings and most likely have a key role in pathologic processes. These changes culminate in systemic endothelial dysfunction, vasoconstriction, reduced plasma volume and decreased blood flow, affecting virtually all organs of preeclamptic women.[2]

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PREECLAMPSIA IN DEVELOPING COUNTRIES

HDP and preeclampsia are the second leading cause of maternal death worldwide.[3,4] Most of these deaths occur in developing countries and are related to eclampsia. Eclampsia is 30 times more common in developing countries than in developed countries, reaching close to 1% of pregnancies in the most affected regions.[5] The WHO estimates that preeclampsia and eclampsia account for 25% of stillbirths, 25% of neonatal deaths and an unknown number of long-term neurological disabilities in developing countries.[3] Although women in several developing countries are significantly menaced by preeclampsia, their risk of eclampsia and other serious complications is underscored by the dearth of antenatal care.

FAILURE OF PREVENTION STRATEGIES

Several interventions during pregnancy, including vitamins, calcium, fish oil, aspirin and heparin, have been proposed for the prevention of HDP and preeclampsia, but most large, randomized trials have failed to demonstrate a significant effect of these potential preventive measures. Until recently, low-dose aspirin and calcium were the only two treatments that were recognized to have a significant, but modest impact in lowering the incidence of HDP and preeclampsia, both of them being coupled with a 15–20% reduction in selected populations.[6] However, a recent meta-analysis indicated that when started early in pregnancy, the benefits of low-dose aspirin could be much more significant.[7] If commenced before 16 weeks' gestation, low-dose aspirin could prevent more than half of preeclampsia and intrauterine growth restriction cases. To improve the efficiency of prevention strategies, great efforts, combining maternal, biochemical and ultrasonographic markers, are currently being expended to identify women at high-risk for preeclampsia, early in pregnancy.[8]

PREVENTION STRATEGIES IN DEVELOPING COUNTRIES

Strategies for the prevention of HDP, preeclampsia and their complications in developing countries have to consider the very high rate of the disease. When more than 10% of pregnancies are affected by preeclampsia, additional screening for a high-risk subgroup would most likely be unnecessary. In fact, the real challenge would be to have a first contact with the women early in pregnancy and preferentially during the first trimester, to propose new strategies of prevention.

Bakthi and Vaiman[1] recruited 164 women at the time of first trimester ultrasound and randomized them to low-dose aspirin or no treatment. They discerned that low-dose aspirin was linked with a reduction of gravidic hypertension, preeclampsia and HELLP syndrome. However, the most important finding was the decrease in perinatal death, which was 9% in the untreated group, compared with no case in the low-dose aspirin group. Their results indicate that perinatal death could be prevented by low-dose aspirin. Interestingly, even if the rate of preterm birth was higher than expected, low-dose aspirin was also associated with a very significant diminution in its rate (91 *vs.* 41%), suggesting that it could also obviate other obstetrical syndromes related to placental disorders.[9,10]

FUTURE STUDIES

We believe that future studies aimed at preventing HDP, preeclampsia and their complications in developing countries, should use original data from those countries. Considering that the women characteristics, the care

facilities and the therapeutic stakes are very different than developed countries, the impact of any intervention, such as low-dose aspirin, could differ tremendously. However, based on the observations of Bakthi and Vaiman[1], recruitment of pregnant women in early gestation would most likely be a major condition for intervention's success in developing countries, as well as in developed countries. Whether low-dose aspirin, calcium or both prophylaxes should be favoured remains unclear, but we believe that endeavours in this direction should be embraced.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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