Aspirin delays the metabolic clock of gestation in women at risk of preeclampsia: abridged secondary publication

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KEY MESSAGES

1. Aspirin significantly delays the metabolic clock according to estimated gestational age.
2. Aspirin treatment partially reverses a wide range of metabolic changes during gestation.
3. These results strongly support the aspirin-related delay hypothesis.

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Introduction

Low-dose aspirin treatment can reduce the rate of preterm preeclampsia in high-risk women, but the mechanism underlying the prophylactic response is unknown. Exploratory analyses have suggested that aspirin can delay placental ageing and thus the onset of preeclampsia. We aim to investigate the effects of aspirin on gestational age advancement and the risk of preeclampsia using a molecular estimator specific to high-risk pregnant women.

Methods

This study used plasma samples from the ASPRE trial involving pregnant women at high risk for preterm preeclampsia. Plasma samples were collected at 11 to 13 weeks (before treatment) and at 20 to 23 weeks (after treatment). Untargeted metabolomics profiling was performed on plasma samples from 58 women in the aspirin group and 58 women in the placebo group. Each treatment group contained 30 women who eventually developed preeclampsia and 28 women who did not. Samples from each of the four treatment/outcome combinations were matched approximately 1:1:1:1 according to predicted preeclampsia risk scores.

Results

Metabolic effects of aspirin and metabolic differences were potentially associated with variation in the treatment response. Aspirin treatment resulted in a strong drug-associated metabolomics signature, and the preeclamptic or non-preeclamptic outcome in response to treatment was associated with the level of internal aspirin exposure (P=0.0083). Comparing women with and without preeclampsia after aspirin treatment revealed differences in 73 metabolites, some of which are involved in pathways with regulatory importance in pregnancy and placental functions such as glycerophospholipid metabolism, polyunsaturated fatty acid metabolism, and steroid hormone biosynthesis. To explore the hypothesis that aspirin delays gestational age advancement and thus the onset of preeclampsia, we constructed a metabolic clock to estimate gestational age in pre-treatment and placebo-treated samples. The results showed that aspirin significantly slowed metabolic gestational ageing by 1.27 weeks (95% confidence interval, 0.66-1.88 weeks) and partially reversed one-fourth of the metabolic changes during gestation.

Conclusion

Aspirin significantly delays the metabolic clock according to estimated gestational age. Aspirin treatment partially reverses a wide range of metabolic changes during gestation. These results strongly support the aspirin-related delay hypothesis.

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Disclosure

The results of this research have been previously published in:

1. Li X, Milosavljevic A, Elsea SH, et al. Effective aspirin treatment of women at risk for preeclampsia delays the metabolic clock of gestation. Hypertension 2021;78:1398-410.