endometritis was significantly lower in the women treated with antibiotics than in those who were not. In contrast, the offspring of the antibiotic-treated group expressed a higher ratio of neonatal antibiotic administration, higher neonatal intensive care unit admission rates, and a higher rate of 5-minute Apgar<7 than the nonantibiotic treated group, with the etiology of this finding remaining unclear. Antibiotics are among the most critical, yet common, medications prescribed during pregnancy, and they should be used carefully. It has been mentioned that the administration of antibiotics, especially in the absence of any infection, could affect the gut microbiota and cause endotoxins to be released from it; this could lead to endotoxemia. The endotoxemia, in turn, causes inflammation and the release of proinflammatory cytokines. Moreover, some antibiotics themselves could cause the release of proinflammatory cytokines from the white blood cells of peripheral blood. In a recent in vivo study, we have shown that antibiotic administration during pregnancy in a noninfectious condition could cause an inflammatory state and lead to the release of proinflammatory cytokines such as interleukin 1 B (IL-1B), IL-6, and tumor necrosis factor α, depending on the type of antibiotic consumed. Thus, we should be careful regarding both the administration of antibiotics and the type of the antibiotic administered during pregnancy.

In the study by Bank et al., it seems that the inflammation caused by bacterial degradations (in case of infection), gut-induced endotoxemia, and/or direct proinflammatory cytokine release caused an inflammatory state in the offspring of the treatment group. This inflammatory state mimicked an infectious condition and led to their admission in the neonatal intensive care unit, and therefore, antibiotic administration.

Altogether, antibiotics are very crucial during pregnancy, and as stated by Bank et al., “The American College of Obstetricians and Gynecologists currently recommends that antibiotic treatment be considered for women with isolated maternal fevers in labor.” Considering the adverse neonatal effects stated by Bank et al. and the recommendations of the American College of Obstetricians and Gynecologists, we suggest that studies focus on finding antibiotics with the lowest inflammation-provoking properties to reduce the inflammatory reactions in neonates.

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REFERENCES

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Intrapartum antibiotic administration and associated neonatal inflammation

We appreciate the interest in our article “Outcomes associated with antibiotic administration for isolated maternal fever in labor” expressed by Drs Norooznezhad, Aliabad, and Hantoushzadeh. We agree with their call for research on the fetal effects of intrapartum antibiotics and developing approaches to minimize neonatal inflammation. The most common antibiotic combination used in our cohort was ampicillin and gentamicin; in mouse models, ampicillin has been associated with increased blood corticosterone, interleukin 6, and lipopolysaccharide levels, whereas gentamicin has been associated with the formation of reactive oxygen species, leading to risks of nephrotoxicity and ototoxicity. It is unclear if this inflammation has a clinically apparent effect on neonates treated with ampicillin and gentamicin intrapartum or how antibiotic treatment may mediate infection-driven inflammation in such neonates.

We caution against fully attributing our findings to an antibiotic-induced inflammatory process among the neonates studied. At our institution, if a concern is raised for suspected intra-amniotic infection and inflammation, pediatric presence at delivery is requested, and the threshold for admission to the neonatal intensive care unit is lower for an infant
Impaired cerebral autoregulation, cerebral perfusion pressure, and intracranial pressure in eclampsia

TO THE EDITORS: The article published by Bergman et al in a recent issue of the American Journal of Obstetrics and Gynecology reported altered dynamic cerebral autoregulation and cerebral perfusion pressure (CPP) in eclampsia. The estimation of CPP based on the formula proposed by Belfort et al raises a few concerns related to the findings and interpretations of this study. The CPP is a difference in the mean arterial pressure (MAP) and intracranial pressure (ICP) or cerebral venous pressure. In the eclampsia group, the CPP exceeded MAP (mean CPP = 109.5 mm Hg; MAP = 103.6 mm Hg), which is physiologically implausible. According to the data provided in this study, the ICP (MAP−CPP) would be −5.9 mm Hg (negative), 6.9 mm Hg, 24.7 mm Hg, and 8.9 mm Hg in eclampsia, preeclampsia with severe features, preeclampsia without severe features, and normal pregnancy, respectively. Although the authors convincingly demonstrated a lower autoregulatory index in eclampsia, suggesting impaired autoregulation, the derived ICP value does not support impaired autoregulation in eclampsia. The abolition of cerebral autoregulation increases cerebral blood volume and ICP. In addition, a rise in ICP may also impair cerebral autoregulation. The derived ICP data indicate a maximum ICP level (24.7 mm Hg) in women with preeclampsia without severe features. Moreover, ICP levels appear normal in eclampsia, preeclampsia with severe features, and normal pregnancy. Accordingly, the impairment in cerebral autoregulation should have been at a maximum in preeclampsia without severe features. In patients with intact cerebral autoregulation, the ICP remains constant until a CPP of 150 mm Hg, and the CPP reflects a change in the MAP only. In this study, women with eclampsia had a mean CPP of 109.5 mm Hg, and the authors also noted impaired autoregulation. Therefore, a negative ICP level in eclampsia is indeed surprising. This apparent contradiction in the values of the autoregulatory index and ICP is difficult to explain if we believe that the CPP estimation based on the formula by Belfort et al is correct. A constant cerebral blood volume is maintained by cerebrovascular resistance (CVR). A rise or fall in CPP is accompanied by an increase or decrease in CVR. The majority of women in the eclampsia group were receiving magnesium (75%) and antihypertensive medications (50%). The potent vasodilatory effects of magnesium and antihypertensive therapy could have reduced the CVR despite a higher CPP or MAP. Arguably, the cerebral blood flow velocity in all 3 phenotypes of preeclampsia and normal healthy controls could have been different because of cerebral vasodilatation. In addition, blood flow velocity may differ because of the extent of cerebral vasodilatation at constant CPP or MAP. Therefore, the estimation of autoregulatory index and CPP is based on the change in MAP, CPP, and blood flow velocity in the middle cerebral artery and their estimation based on the complex formula in different patient groups may not be ideal for comparison. To conclude, we suggest a revision in the formula for calculation of CPP or replicating the findings of this study by invasive estimation of ICP in these phenotypes of preeclampsia.

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