Reply: Search for a predictive relationship between ultrasound thickness of the lower uterine segment and rupture of the uterus in women with a prior cesarean does not make biological sense

We would like to thank Drs Ragusa and Svelato for their comments regarding our recent article titled “Evaluation of the usefulness of ultrasound measurement of the lower uterine segment before delivery of women with a prior cesarean: a randomized trial.”

We are happy to have the opportunity to stress the need for another randomized controlled trial (RCT). Drs Ragusa and Svelato state that further studies on the subject are “totally useless, because the strength of a muscle tissue is proportional to its thickness, but this is not necessarily true of a fibrous tissue, which can break despite its thickness.” Their comment, however, is simply an assertion made without evidence. More precisely, they cite a study from 1924 as evidence of the presence of fibrous tissue but seem to think that “this (that the strength of a muscle tissue is proportional to its thickness) is not necessarily true of a fibrous tissue” is affirmative evidence that further studies are useless. We respectfully disagree.

A high level of evidence is difficult to obtain in clinical research. According to the US Preventive Services Task Force, only properly powered and conducted RCTs ensure the highest level of evidence. Unfortunately, our RCT was underpowered, which did not allow for a formal conclusion. Identifying the women who have had a previous cesarean delivery and who are at a real risk for uterine rupture remains, as Drs Ragusa and Svelato agree, an important aim in obstetrical care, and a definitive conclusion on the usefulness of ultrasound or the lack thereof, for predicting this risk would be helpful for physicians and their patients. Certainly, the concern of all the authors (and their reviewers and editors) who have considered this topic cannot be brushed aside as being devoid of “biological, and consequently, clinical sense.”

Finally, even if our trial was positive, another trial would be necessary to confirm our results. As the US Federal Food, Drug, and Cosmetic Act, which provides the legal standard in the United States for establishing the efficacy necessary for drug approval by the US Food and Drug Administration, wisely states, “Substantial evidence” is based on positive findings from 2 or more adequate and well-controlled trials.

We definitely need more RCTs in clinical research.

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REFERENCES

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Broad-spectrum antibiotics in pregnancy: role of inflammation in neonatal outcomes

TO THE EDITORS: We read the article titled “Outcomes associated with antibiotic administration for isolated maternal fever in labor” by Bank et al with great interest. They have investigated the role of antibiotic therapy on maternal and fetal outcomes in pregnancies associated with fever but “without evidence of infection.” According to their results, postpartum
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.1

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.2,3 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 1B (IL-1B), IL-6, and tumor necrosis factor α, depending on the type of antibiotic consumed.4 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,1 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,1 “The American College of Obstetricians and Gynecologists currently recommends that antibiotic treatment be considered for women with isolated maternal fevers in labor.”5 Considering the adverse neonatal effects stated by Bank et al1 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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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 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 risks of nephrotoxicity and ototoxicity.2 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...