A dilemma of antenatal corticosteroids for long-term consequences

TO THE EDITORS: Antenatal corticosteroids (ACS) are known to accelerate fetal lung maturation and prevent preterm neonatal mortality, respiratory distress syndrome, and brain injury. The American College of Obstetricians and Gynecologists has expanded its recommendations for the use of ACS to late preterm and early term deliveries.\(^1\) Under such guidelines, the proportion of infants who are exposed to synthetic corticosteroids has substantially increased. In the setting of a large infant population being involved, it is imperative to evaluate the long-term safety of ACS, especially after a population-based cohort study that reported a hazard ratio of 1.47 of any mental or behavioral disorder in children born at term who were exposed to ACS.\(^2\)

For this purpose, Osteen et al\(^3\) recently determined the long-term outcomes in term-born children ≥5 years old who were born to mothers receiving ACS compared with controls whose mothers were also evaluated for threatened preterm labor but did not receive ACS. They found that the former babies have increased odds of being in a lower growth percentile than those not exposed; the rates of diagnoses such as asthma, developmental delay, and attention deficit disorders were not different. This study indicates a need for more judicious use of ACS in women who may not be likely to deliver until term. However, this study raises some important issues that should be addressed.

There were statistically significant differences between the 2 groups for their birth characteristics regarding birth length, head circumference, and birthweight. The authors said none of these differences were clinically significant. In that case, considering no statistically significant difference for height or length percentile, why is the weight percentile (<10%) difference between the 2 infant groups clinically significant (<10%)? Furthermore, the retrospective study design could not exclude the confounding factors of the mothers.\(^4\) For example, for the ACS-exposed group, the mothers were younger and had higher rates of diabetes and hypertensive disorders. The abnormal pregnancy events that lead clinicians to administer steroids might also predispose the exposed children to have a lower growth percentile. This study lacked information about steroid type, dosing, or timing of exposure, making it impossible to determine whether these factors were relevant.

Nevertheless, we agree with Osteen et al that though the benefits of ACS outweigh the risks in those vulnerable infants, this may not be suitable for all infants. Continued efforts are needed to select true high-risk cases among women considered to be at risk for preterm labor to ensure that ACS therapy is offered with more benefit than harm (Figure).

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The authors report no conflict of interest.

No funding was obtained for this work.

**FIGURE**

Antenatal corticosteroids treatment for women with threatened preterm labor

Women considered at risk for preterm labor

Evaluation
(Symptoms, ultrasound, biomarkers, etc)

Women with true high risk for preterm deliveries within 1 week

Antenatal corticosteroids

Follow-up

Women with low risk for preterm deliveries

Uterine necrosis in obstetrics after emergency surgical procedure: the dark side of hypogastric artery ligation

TO THE EDITORS: Karoui et al, in their report about uterine necrosis after artery ligation, described an interesting and rare case of surgical complication of the treatment of postpartum hemorrhage following the failure of medical therapy. Moreover, we appreciate the authors’ interest in reporting these surgical adverse events of postpartum hemorrhages, and we take the opportunity to highlight the problem and the consequence of uterine vascular deprivation. In our center, patients presented with analog cases of postpartum hemorrhage caused by traumatic lesion of uterine vessels following cesarean delivery. The patients underwent abdominal delivery for breech presentation, and during surgery, agenesis of the peritoneal tissue of the broad ligament was observed with exposure of the uterine arterial and venous vessels bilaterally; intraoperative hemorrhage following performance of bilateral ligation of the hypogastric artery was also observed. The patient reported uterine necrosis 40 days after the surgical procedure, and laparotomic hysterectomy was performed for sepsis. The women reported fever, abdominal pain, and purulent lochia belatedly, remaining asymptomatic during the puerperium. Literature shows limited cases of uterine necrosis after surgical uterine compression sutures, artery ligation, or artery embolization for the management of postpartum hemorrhages; the incidence and casual factors remain unknown. We may suppose that the onset of uterine necrosis could be the sum of 2 different pathways. First, in patients who underwent artery ligation, the ischemic damage derives from inadequate collateral circulation (round uterine ligament arteries) that do not allow sufficient blood supply to the uterus. Hormonal status, proinflammatory cytokine and chemokine pathway activation, and immune response probably play a key role in the uterine reperfusion mechanism. Artery ligation may cause an unpredictable modification in the endothelial tissue of uterine vessels, resulting in more severe ischemic damage. On the other hand, agenesis of the peritoneum could induce excessive laxity of the peritoneal tissue, and concomitant physiological changes in the connective and extracellular matrix during pregnancy increase the risk of modified physiological uterine involution of postpartum with an increased risk of ischemic injury. The distinctive traits of these 2 cases lie in the development of uterine necrosis after artery ligation and not following uterine compression sutures, as reported in literature data. Finally, uterine necrosis may represent a tardive event without early symptoms, as demonstrated by our cases.

In conclusion, uterine necrosis after artery ligation may be an indicative event in obstetrics to conduct counseling of postsurgical emergency procedures properly, because incomplete knowledge of the timing of uterine reperfusion represents a challenge.

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The authors report no conflict of interest.
No funding was availed for this work.

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