Breif response to ORACLE study

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Objective

To compare the release of endotoxins and inflammatory cytokines and pregnancy outcomes in septic and non-septic rats after administration of antibiotics.

Methods

Thirty-six pregnant Wistar rats were divided into six groups. Group A (control) received intraperitoneal saline on the 17th gestational day, Group B received 300 µg/kg intraperitoneal lipopolysaccharide (LPS) on the 17th gestational day, Groups C and D received 20 mg/kg/day intravenous ceftazidime and ceftriaxone, respectively, between the 18th and 20th gestational days, Groups E and F received intraperitoneal E. coli on the 17th gestational day followed by 20 mg/kg/day intravenous ceftazidime and ceftriaxone, respectively, between the 18th and 20th gestational days. Four and six hours after the last injections, maternal blood samples were drawn to determine endotoxin, tumor necrosis factor α (TNF-α), interleukin 1β (IL-1β), and interleukin 6 (IL-6) levels. The rats were then followed until birth.

Results

At four and six hours post-injection, maternal serum endotoxin and TNF-α levels were highest in LPS-treated and non-septic antibiotics-treated rats ($p=0.005$). IL-1β levels were highest in LPS-treated septic antibiotics-treated rats ($p=0.02$). IL-6 levels in maternal serum at four hours were not significantly different between the groups; however, at six hours, they were highest in both the LPS and ceftriaxone-treated groups ($p=0.01$). The LPS group and both groups of non-septic antibiotic-treated rats exhibited shorter gestational duration than others ($p=0.01$). The stillbirth rates were highest in all antibiotics-treated groups ($p=0.02$).

Conclusion

Antibiotic administration in pregnant rat models, especially in non-septic state, is associated with significantly elevated production of endotoxin and inflammatory cytokines, which might induce preterm birth and increase adverse pregnancy outcomes.