

41 Evidence for involvement of the receptor for advanced glycation end products (RAGE) axis in pathogenesis of fetal intra-uterine growth restriction (IUGR)

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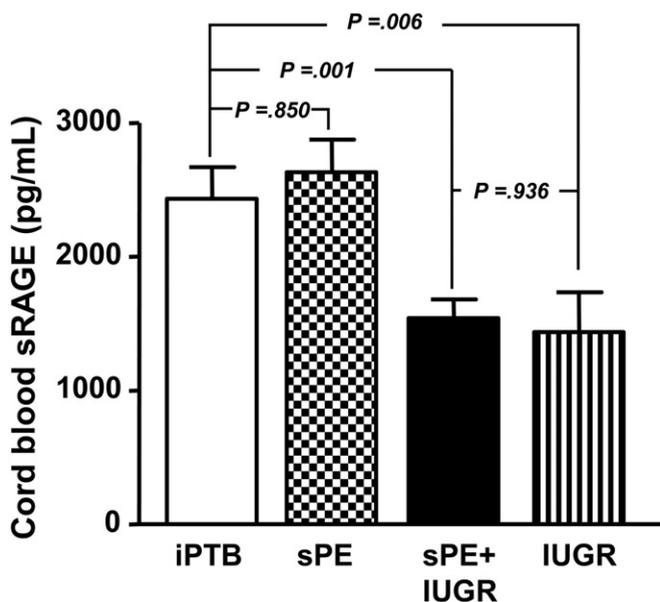
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OBJECTIVE: Identification of relevant pathogenic pathways that may be responsible for the increased morbidity and mortality of fetuses with IUGR is critical. Recent advances have provided an improved understanding of the mechanisms of chronic cellular injury following engagement of RAGE (membrane cell receptor) and soluble RAGE (sRAGE, competitive inhibitor) in complex diseases such as preterm birth (PTB) and preeclampsia (PE). The objective of this study was to investigate the fetal serum levels of total sRAGE and endogenous secretory RAGE (esRAGE, alternative spliced RAGE isoform) in fetuses with IUGR and correlate with neonatal death as the adverse outcome.

STUDY DESIGN: In a case-control study, cord blood serum sRAGE and esRAGE were measured by specific immunoassays in 84 consecutive preterm singleton newborns in the following groups: (i) idiopathic PTB (iPTB, n=27, GA: median [IQR] 31 [30-32] wks); (ii) severe PE (sPE) without IUGR (n=23, GA: 31 [28-32] wks); (iii) sPE+IUGR (n=22, GA: 28 [25-33] wks); (iv) idiopathic IUGR (n=12, GA: 29 [27-32] wks). Established criteria were used to define iPTB, sPE, IUGR (<10%) and abnormal Dopplers.

RESULTS: 1) There was a significant difference in birthweight (P<0.001) but not GA among groups; 2) IUGR fetuses had lower total sRAGE levels independent of sPE (2-way ANOVA P<0.001, Figure); 3) The contribution of esRAGE to total sRAGE was similar (~40%) with no differences in esRAGE levels between groups; 4) sRAGE and esRAGE levels were not impacted by GA, Doppler indices or acid-base status at delivery; 5) IUGR newborns who died (n=9) had significantly lower total sRAGE (P<0.05) at birth.

CONCLUSIONS: This study demonstrates involvement of RAGE pathway in the pathogenesis of IUGR and related neonatal death. Similar levels of esRAGE suggest that the transcriptional mechanism responsible for sRAGE production remains intact. The cause for sRAGE deficiency in IUGR fetuses may be either lack of post-translational RAGE processing or excessive consumption by RAGE ligands.



42 Effects of maternal obesity on tissue concentrations of prophylactic cefazolin during cesarean delivery

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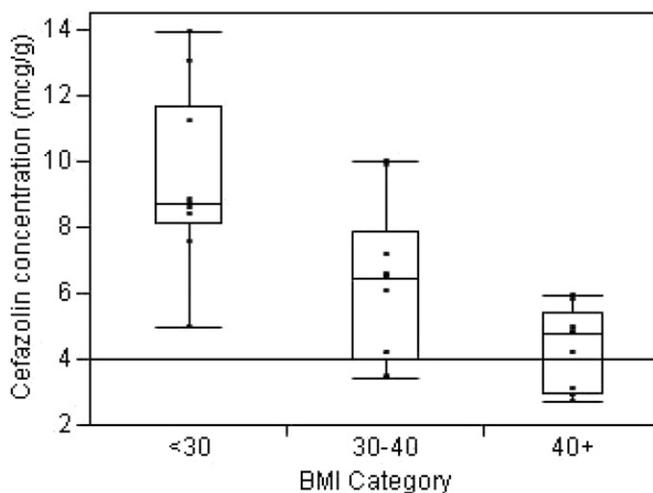
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OBJECTIVE: Surgical site infections remain a frequent complication of cesarean delivery despite antimicrobial prophylaxis, causing increased mortality, morbidity, and costs. No prior investigations have evaluated the tissue penetration and concentrations of preoperative antibiotics at the time of cesarean delivery as a function of maternal obesity.

STUDY DESIGN: 29 patients scheduled for elective cesarean delivery were stratified according to body mass index (BMI) category, with 10 study participants classified as lean ("BMI <30"), 10 as obese ("BMI 30-39.9") and 9 as extremely obese ("BMI ≥40"). All patients were given the standard preoperative dose of 2 grams cefazolin 30-60 minutes prior to skin incision. Antibiotic concentrations from adipose samples, collected after skin incision and prior to skin closure, along with myometrial and serum samples were analyzed via microbiological agar diffusion assay.

RESULTS: Cefazolin concentrations within adipose tissue obtained at the skin incision were inversely proportional with maternal BMI (r=0.67, p<0.001). The mean adipose concentration was 9.37±2.7 mcg/g in the lean group of women compared to 6.37±2.3 mcg/g in the obese group (p=0.005) and 4.35±1.2 mcg/g in the extremely obese group (p<0.001). Significant portion of specimens from obese and extremely obese subjects did not achieve minimal inhibitory concentrations (≥4mcg/g) for most potential wound pathogens in adipose samples at skin incision (20% and 33.3% respectively) or closure (20.0% and 44.4% respectively). No significant difference in cefazolin concentration was observed in mean closure adipose, myometrial or serum specimens across the BMI categories.

CONCLUSIONS: Pharmacokinetic analysis suggests that present dosing strategies may fail to provide adequate antimicrobial coverage in obese patients during cesarean delivery.



43 Response to 17-α-hydroxyprogesterone is affected by progesterone receptor polymorphisms

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OBJECTIVE: Although 17-α-hydroxyprogesterone (17-OHP) reduces recurrence of preterm birth (PTB), a substantial proportion of women who receive this treatment still deliver preterm. We examined SNPs in the progesterone receptor gene in women with prior sponta-