

INFLUENCE OF SEX STEROIDS ON UTERINE ARTERY REACTIVITY TO PLACENTAL GROWTH FACTOR (PlGF)

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Preeclampsia, a disorder characterized by hypertension and decreased uterine vascular perfusion, occurs in 5% of pregnant women. A potent vasodilator, placental growth factor (PlGF), has been shown to play a key role in increasing uteroplacental blood flow during normal pregnancy. Furthermore, reduced PlGF signaling has been postulated to be the underlying cause of preeclampsia although the exact mechanism is not known. In this study, we hypothesized that sex steroids (estrogen and progesterone) play a key role in modulating the vasodilatory effects of PlGF in the uterine circulation during pregnancy. The hypothesis was tested by using an *in vitro* approach that allowed us to directly evaluate the reactivity (sensitivity and efficacy) of the main uterine artery to PlGF. Adult Sprague-Dawley rats were oophorectomized and implanted with subcutaneous pellets by Innovative Research of America (Sarasota, FL) prior to shipment to the University of Vermont, resulting in continuous release of 17 β estradiol (0.5 mg; n=10), progesterone (100 mg; n=10), or a combination thereof (n=8) for up to three weeks; the control group consisted of age-matched oophorectomized animals (n=10) without hormone replacement. Following 21 days of treatment, rats were weighed, killed, and trunk blood collected for determination of steroid concentrations determined by ELISA. The uterus was dissected out, weighed, and its vascular dimensions measured. A segment of the main uterine artery was cannulated, pressurized (50 mmHg) and studied using a video-electronic vessel perfusion system. Circulating hormone levels were much lower than expected, indicating a malfunction of the pellets, for reasons likely related to manufacturer's error, as implantation sites appeared to be normal. The analysis of variance (ANOVA) revealed no significant differences in PlGF reactivity between groups, although this was not unexpected in view of the failure of pellet hormone release. Thus, this experiment will have to be repeated before our hypothesis can be confirmed or rejected.