Pregnant rats treated with a serotonin precursor have reduced fetal weight and lower plasma volume and kallikrein levels

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Abstract

Pregnant women with preeclampsia have increased serotonin levels, suggesting a possible role of this amine in abnormal pregnancy. With the hypothesis that an increase in serotonin would reduce volume expansion and cause fetal growth restriction, we evaluated the maternal and fetal effects of the administration of the serotonin precursor 5-hydroxytryptophan (5-HTP) to Sprague-Dawley rats. At pregnancy day 13 (n=19) or in random cycle nonpregnant rats (n=10), animals were assigned to a single injection of 5-HTP (100 mg/kg IP) or to a control group. Animals were studied at day 21, after overnight urinary collection. Additional pregnant rats received ketanserin (1 mg/kg), a 5-HT2 receptor antagonist, 1 hour before 5-HTP injection. In pregnant rats, 5-HTP lowered plasma volume (control: 221.1; 5-HTP: 170.7 mL; P<0.001) and creatinine clearance, whereas serum creatinine and urinary protein excretion were increased; no changes were observed in nonpregnant rats. Systolic blood pressure did not change significantly. Urinary kallikrein activity and plasma aldosterone levels decreased only in pregnant animals. Fetal (control: 5.5±0.1; 5-HTP: 4.2±0.2 g; P<0.001) and placental weights were reduced. In nonpregnant and pregnant animals, 5-HTP caused profound renal morphological alterations and decreased kallikrein immunostaining. Preadministration of ketanserin abolished all of the changes associated with the use of 5-HTP. These data indicate that the administration of a serotonin precursor to pregnant rats limits plasma volume expansion and fetal growth via 5-HT2 receptors, suggesting a possible role for serotonin in abnormal pregnancy. We postulate that an increased vascular resistance, both at the placental and renal levels, mediates these effects.

Keywords: Preeclampsia/pregnancy, experimental models, acute kidney failure, kallikrein, aldosterone, plasma volume, serotonin.