The purpose of this study was to test the hypothesis that pregnancy may influence the pharmacodynamics of cocaine. Fifteen chronically catheterized term pregnant (P) and 18 nonpregnant (NP) female Sprague-Dawley rats were used. Cocaine (5mg/kg) was infused intravenously over a 15 min period to each adult animal. Arterial pressure and heart rate were monitored throughout. Cardiac output and organ blood flow were measured using the microsphere method, prior to and at the end of cocaine infusion. Additional blood samples were also withdrawn at the end of infusion for cocaine determinations. All animals were killed and several organs examined. Fetal blood was sampled by cardiac puncture, and brain, heart and liver were obtained. Cocaine concentrations in all blood and tissue samples were determined, using a gas chromatographic procedure. In a separate study, blood was obtained from 5 P and 6 NP rats for colorimetric measurement of plasma cholinesterase activity (1). ANOVA and t test were performed, where applicable, for statistical analyses. A p value of less than 0.05 was considered significant.

Cocaine infusion resulted in hypertrophy associated with a fall in cardiac output from 35.9±1.1 to 26.3±1.8 ml/min/100g in P, and from 31.6±1.3 to 27.2±1.4 ml/min/100g in NP rats. These changes were statistically significant in the P group. In general, cocaine infusion decreased regional blood flow; the decrease was statistically significant in the heart in both P and NP animals, while it was significant in the heart and placenta in the P group. A decrease in placental blood flow (from 1.42±0.16 to 0.72±0.17 ml/min/g) was striking. The mean plasma cocaine concentration in the P group was significantly lower; 1.65±0.12 vs. 2.18±0.20 ng/ml in the NP animals. Overall tissue concentrations were similar, while tissue to plasma concentration ratios were higher in the P group. Cocaine concentration in fetal plasma was 366±21 ng/ml, resulting in a fetal to maternal concentration ratio of 0.23±0.05. Drug concentrations in the fetal heart and brain were 11 and 8 times lower than corresponding maternal organs. Tissue to plasma concentration ratios in these fetal organs were also significantly lower than in the mother. Plasma cholinesterase activity in P (2.16±0.197 ml/μmol) was significantly higher than in NP animals (1.44±0.134 ml/μmol).

These observations indicate that pregnancy enhances the hemodynamic effects of cocaine. The lower blood concentrations of the drug in P rats were probably due to the greater volume of distribution and higher plasma cholinesterase activity. The overall values for the tissue to plasma concentration ratios of cocaine in the P were higher than those in the NP group indicating that pregnancy increases tissue uptake of the drug. Low fetal plasma and tissue concentration of cocaine were probably related, in part, to a severe reduction in the placental blood flow induced by the drug.

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Reference