POSTER DISCUSSION X

A1075

TITLE: COCAINE INDUCED HYPERTENSION IN THE EWE AND RESPONSE TO TREATMENT WITH LABETALOL

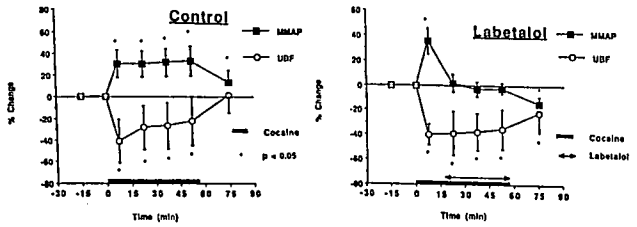
AUTHORS: Hughes SC, Vertommen JD, Rosen MA, Messer CP,Espinoza MI, Parer JT, Shnider SM

AFFILIATION: University of California, San Francisco, Department of Anesthesia

Introduction: With the increase of cocaine abuse in the United States, it's use among women of reproductive age has also increased.[1] Acute effects of cocaine abuse in the parturient include hypertension, placental abruption, fetal distress requiring cesarean section, rupture of maternal intracranial aneurysms, and peripartum seizures. Cocaine administered to the pregnant ewe increases maternal mean arterial pressure (MMAP) and reduces uterine blood flow (UBF). A previous study demonstrated that hydralazine administration to cocaine intoxicated ewes controls blood pressure but does not improve cocaine induced decrease in UBF.[2] The purpose of the present study was to determine the effects of labetalol treatment of cocaine-induced maternal hypertension on the maternal-fetal cardiovascular system, blood gas and acid base status, UBF and catecholamine response.

Methods: With approval of the UCSF Committee on Animal Research we studied chronic maternal-fetal sheep preparation (120 days gestation). MMAP, UBF, MHR, fetal mean arterial pressure and heart rate were measured. Fetal and maternal arterial samples were obtained for cocaine serum concentrations, acid-base status, and catecholamine analyses. Cocaine was administered intravenously to the ewe for 55 min to induce and maintain both increased MMAP and reduced UBF. A control group (n=11) received cocaine alone, while the study group (n=10) also received intravenous labetalol 15 min after cocaine administration. Both drugs were discontinued 55 min after the start of the cocaine infusion and followed by a 35 min recovery period. Statistical analyses were performed using repeated measures ANOVA and Dunnett t-testing ($P<0.05$).

Results:



Cocaine administration resulted in a 32 ± 13(SD)% increase in MMAP and a 26 ± 21% reduction in UBF. In the group which received labetalol, MMAP was restored quickly to base line values, but UBF remained reduced 37 ± 16(SD)% during cocaine infusion and during the recovery period reduced 22 ± 16(SD)%. MHR increased significantly (14 ± 21%) in the control group but labetalol restored MHR to base line values. FHR and FMAP increased significantly in response to cocaine administration. Labetalol reduced FHR below base line values but had little effect on FMAP. Fetal pH and O_2 saturation declined significantly after cocaine administration and remained reduced in the recovery period. Labetalol did not alter fetal pH or O_2 saturation. Maternal and fetal cocaine and catecholamine levels will be reported.

Discussion: Hydralazine, often used in the hypertensive parturient, controls cocaine induced maternal hypertension. However, in the ewe, this results in a potentially catastrophic increase in MHR (121%).[2] Labetalol more rapidly controls maternal blood pressure and controls MHR. However UBF is not improved and fetal status continues to show the effects of decreased UBF. While the applicability of this data to humans is uncertain, labetalol may be preferable to hydralazine for treatment of the acutely cocaine intoxicated parturient.

References:

1. Am J Obstet Gynecol 163:1535-42, 1990.
2. Anesthesiology 73:A928, 1990.

A1076

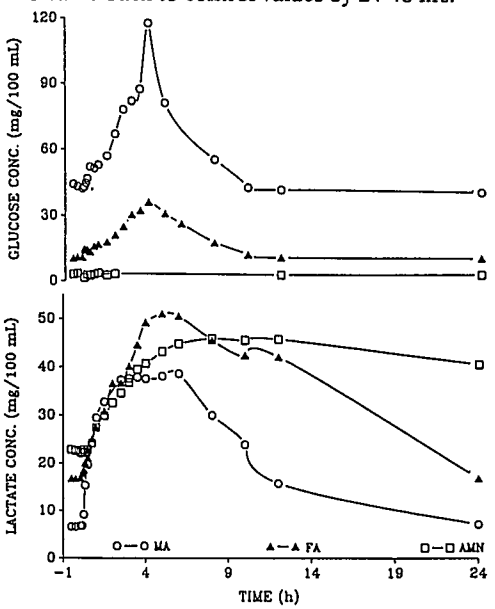
TITLE: ACUTE METABOLIC ACIDOSIS IN THE FETAL LAMB FOLLOWING MATERNAL LABETALOL ADMINISTRATION.

AUTHORS: K. Yeleswaram, M.Pharm., D.W. Rurak, D.Phil., C. Hall, A.H.T., G.H. McMorland, M.B. & J.E. Axelson, Ph.D.

AFFILIATION: Faculties of Pharmaceutical Sciences & Medicine, The Children's Variety Research Centre, University of British Columbia, Vancouver, B.C. V5Z 4H4 CANADA.

The metabolic effects of the antihypertensive drug labetalol (L) in pregnancy, and the fetal metabolic effects of L in particular, are not well documented. We studied the maternal-fetal pharmacokinetics and pharmacodynamics of L in pregnant sheep at 125-140 days gestation following a 100 mg i.v. bolus to the ewe. Serial samples were obtained from the maternal artery (MA), fetal artery (FA) and amniotic fluid (AMN) for 48 hrs following L administration. Blood gas, lactate (LAC), glucose (GLU) and L measurements were made in those samples. Maternal and fetal heart rate and arterial and amniotic pressures were monitored continuously.

No significant changes were seen in the maternal or fetal cardiovascular parameters. Maternal and fetal pO_2 and pCO_2 remained unchanged. However, marked increases were seen in the fetal and maternal LAC and GLU, associated with a significant decrease in the fetal arterial blood pH. A representative plot of the LAC and GLU changes are shown below. In identical control experiments, no changes were seen in any of the metabolic indices. Even though the placental transfer of L was less than 20%, the fetal LAC changes were more pronounced than that in the ewe. Also, significant accumulation of LAC was seen in the amniotic fluid, which may at least partly be responsible for the persistence of the LAC in the fetus for several hours. In all the animals studied (n=9), the fetal pH and LAC came back to control values by 24-48 hrs.



While L has been reported to cause elevated GLU concentrations in man, possibly through its partial ß-agonist activity, the exact mechanism involved in the development of acute lactic acidosis in the fetal lamb is not yet clear.

Supported by a 'Medical Research Council of Canada Program Grant'. K.Y. is a recipient of B.C. & Yukon Heart Foundation Research Traineeship.