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MORPHINE'S SITE OF ACTION FOR ANALGESIA TO UTERINE CERVICAL DISTENSION IS CENTRAL AND ANTAGONIZED BY ESTROGEN Eisenach, J.C., Sandner-Kiesling, A. *Anesthesiology*, Wake Forest University, Winston-Salem, NC Introduction. Mu opioid receptor agonists are commonly administered to relieve the pain of uterine cervical distension (UCD), such as occurs during labor. Whether these agents have a purely central action, or also work through peripheral mechanisms has not been studied. We therefore investigated morphine's site of action to inhibit responses to UCD in a new animal model. We have greatly simplified this model by beginning with adult, non-pregnant, ovariectomized rats. As a next step towards eventual study of labor pain, we examined the effect of estrogen replacement in ovariectomized rats on morphine's efficacy. Methods. Ovariectomized adult female rats were anesthetized and UCD induced by manual separation of two fine metal rods. This results in a reflex contraction of the abdominal wall musculature, which is quantified using the rectified, integrated EMG. Following determination of a baseline stimulus-response to UCD, animals received IV morphine by cumulative dosing, with dose range and timing determined in preliminary experiments. To determine the site of effect of IV morphine, animals received either naltrexone (centrally active) or methylnaltrexone (peripherally restricted). In other experiments, animals received subcutaneous pellet implants with placebo or 17-beta-estradiol, to achieve physiologic, nonpregnant circulating concentrations. Data were analyzed by two way analysis of variance, with $p < 0.05$ considered significant. Results. UCD induced rectus abdominus contraction, with a threshold of 25 g, and an accelerating response up to 100 g. This was accompanied by an increase in blood pressure. IV morphine inhibited both EMG and blood pressure responses to UCD, with a threshold of 10 mcg/kg, a 50% maximum inhibition dose (ID50) of 30 mcg/kg, and complete inhibition at 300 mcg/kg. In contrast, morphine was ineffective in animals with estrogen replacement. The effect of 300 mcg/kg IV morphine was dose-dependently inhibited by the centrally acting naltrexone (ID50 of 120 mcg/kg), whereas methylnaltrexone was without effect. Discussion. Systemically administered morphine inhibits response to UCD at doses one to two orders of magnitude less than those required to inhibit responses to noxious heat (such as tail flick or hot plate). Estrogen reduces morphine's effect, consistent with psychophysical studies in women. Of course, extrapolation of these results to women in labor may be hazardous, but the results offer an explanation for the poor potency of IV opioids for the treatment of labor pain. Antagonist studies are consistent with a central site of morphine action and with previous work showing no functional mu opioid receptors on visceral afferent terminals. Supported in part by NIH grant GM35523 and NS41386.

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SPECTRAL ECG ANALYSIS PREDICTS LABOR OUTCOME IN NULLIPAROUS INDUCED-LABOR PATIENTS Leighton, B.L., DiMaria, L.J.; Whittaker, M.S.; Malhotra, S.; Kligfield, P.D. Weill Cornell Medical College, New York, NY Introduction Adrenergic tone affects labor outcome. Beta-agonists are tocolytic, while propranolol decreases the dystocia cesarean delivery rate.(1,2) Power spectral analysis of Holter ECG data, an easy and noninvasive test, reflects cardiac autonomic balance.(3) Increases in the ratio of the normalized low to high frequency ECG components (LF/HF ratio) correlate with increased cardiovascular sympathetic tone.(3) We hypothesized that the autonomic balance of the heart and the uterus might be similar. Thus, this prospective survey looks for correlations between the normalized LF/HF ratio and labor outcome. Methods Healthy nulliparas with BMI < 35 consented to participate in this IRB-approved study before scheduled labor inductions. We recorded the ECG using a digital 12-lead Holter monitor and analyzed the data using the H-Scribe system (Mortara Instrument, Milwaukee).(3) Patients sat quietly during the 15 min ECG recording period. We recorded age, ht, wt, cervical exams, infant wt, delivery time, delivery mode, and indication for C/S. Pts with infants > 4 kg wt or C/S for fetal indications were excluded. Results In the 1st 26 patients, labor outcome correlated with normalized LF/HF. Median normalized LF/HF ratios were 0.79 in vaginal vs. 1.02 in cesarean delivery pts. C/S rates were 6% vs. 50% in pts with normalized LF/HF less than vs. greater than 0.9 ($p=0.02$, Fisher's exact test). Discussion In slim healthy nulliparous induction pts with normal wt infants, dystocia cesarean delivery correlated with normalized LF/HF. Research is needed to a) verify these results, b) determine whether these results also apply to spontaneously laboring women, and c) find safe ways to alter autonomic tone to minimize the dystocia C/S risk. Dr. Leighton is a 1999 FAER/SOAP-OAPEF Clinical Research Starter Grant Recipient. 1. *Obstet Gynecol* 1999;94:869-77 2. *Obstet Gynecol* 1996; 88:517-20 3. *Circulation* 1996;93:1043-65

Normalized LF/HF Ratios in Sitting Induced-Labor Pts				
LF/HF:	<0.7	0.7-0.89	0.9-1.1	>1.1
Pts who delivered vaginally (n)	6	11	3	1
Pts who delivered by C/S (n)	0	1	3	1