Title: EFFECT OF NITROPRUSSIDE, HYDRALAZINE AND TRIMETHAPHAN ON CONTRACTILITY IN HUMAN UTERINE ARTERIES

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Introduction. A hypertensive emergency of pregnancy requires immediate antihypertensive treatment to reduce maternal blood pressure without substantially decreasing placental perfusion and compromising the fetus. Hydralazine and trimethaphan are extensively used for the treatment of preeclampsia/eclampsia. Hydralazine lowers blood pressure by a direct vasodilatory action; trimethaphan lowers blood pressure primarily by ganglionic blockade, although it has been suggested that this drug also produces direct vasodilation. Nitroprusside is also used in the treatment of a hypertensive emergency of pregnancy. The purpose of this study was to determine the effectiveness of nitroprusside, hydralazine and trimethaphan on the contractile response to norepinephrine (NE) in isolated, perfused uterine arteries from nonpregnant patients. Uterine arteries were chosen for this study because these blood vessels supply blood to the utero-fetal unit during pregnancy and because it has been suggested that there is a decreased uteroplacental perfusion in pregnancy-induced hypertension. (1)

Methods. Uterine arteries from nine patients were examined. The arteries were obtained after hysterectomy. The use of human uterine arteries for this study was approved by the Human Research Committee at the University of Texas Medical Branch, Galveston, Texas. Ring sections of arteries (2 mm in length) were mounted in chambers (5 ml-volume) and superfused at a constant flow rate (4 ml/min) with a polystaltic pump (Gilson Instruments). See Figure 1 for a schematic drawing of the superfusion chamber. The superfusate was oxygenated Krebs-bicarbonate solution (pH 7.4) maintained at 37°C. Drugs were administered in the inflowing superfusate. Increases in isometric tension were measured by force-displacement transducers (Statham), calibrated with 1 gram tension, and recorded on a Gould recorder (2400 Brush Model). The arterial rings with resting tension of 1 gram were allowed to equilibrate for one hour before commencement of the experiment.

Results. Both nitroprusside (10^{-9} - 10^{-7}M) and hydralazine (10^{-9} - 10^{-5}M) produced concentration-dependent inhibition of the contraction induced by NE (10^{-5}M). The log concentration-effect curves for nitroprusside, hydralazine, and trimethaphan are shown in Figure 2. The concentration of the drugs that inhibited the contractile response to NE (10^{-5}M) by 50% (IC_{50}) was 4.2 ± 1 x 10^{-9}M (n=6) and 2.6 ± 0.8 x 10^{-6}M (n=5) for nitroprusside and hydralazine, respectively. Trimethaphan, at concentrations up to 10^{-4}M, produced only partial inhibition (21 ± 10%; n=3) of the response to NE.

Discussion. These results indicate that nitroprusside is about 600 times more potent than hydralazine in inhibiting the contractile response to NE in isolated uterine arteries and that trimethaphan was an ineffective vasodilator. In view of the clinical doses used for these drugs, nitroprusside appears to be a very effective dilator of uterine arteries.

Reference.

1. Page EW: On the pathogenesis of pre-eclampsia and eclampsia. J Ob and Gyn of Brit Commonwealth 79:883-894, 1972.

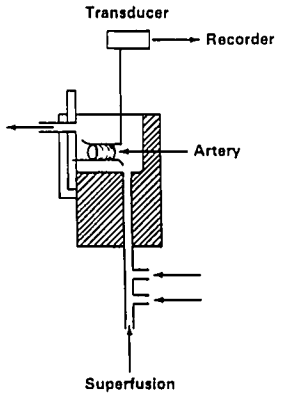

Figure 1. Schematic drawing of superfusion chamber.

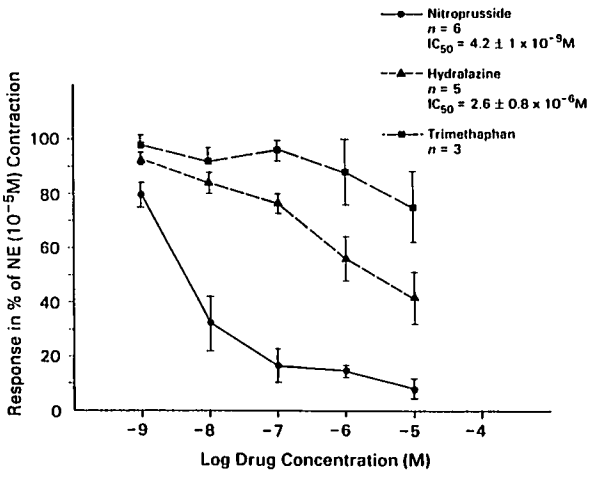

Figure 2. Log concentration-effect curves for nitroprusside, hydralazine and trimethaphan in isolated human uterine arteries. NE (10^{-5}M) induced a contraction which was about 90% of the maximal contractile response to NE. Vertical bars represent the standard error of the mean.