Title : NITROGLYCERIN AND THE UTERINE VASCULATURE IN GRAVID EWES

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Introduction. Severe hypertension often accompanies tracheal intubation in preeclamptic patients given general anesthesia for cesarean section. Intracranial hemorrhage and cardiac failure are possible sequellae. Hypertension can be controlled with intravenous antihypertensive drugs, but none of the commonly used agents is ideal when considering maternal and fetal effects. Nitroglycerin may be a suitable agent, however its effects on the uterine vasculature are unknown. We studied changes in uterine blood flow and vascular conductance when nitroglycerin and nitroprusside were given to counteract norepinephrine-induced hypertension.

Methods. Seven ewes (119-139 days gestation) were anesthetized with i.v. ketamine. A mammary artery and vein were cannulated for mean aortic blood pressure (MAP) measurments and for intravenous norepinephrine infusions. An electromagnetic flow probe was implanted around a uterine artery, and a pressure balloon was placed between the chorion and uterine wall. After a minimum of 3 post-operative days and following stabilization for 30 minutes, control values of MAP, uterine blood flow (UBF), intrauterine pressure (IUP), and pulse rate (PR) were recorded from awake ewes. Norepinephrine (NE) was infused alone for 2 minute periods at rates of 0.1, 0.2, 0.5, 1.0μg/Kg/Min.; parameters returned to control between doses. After stabilization, nitroglycerin (NTG) or nitroprusside (SNP), selected randomly, was infused to reduce MAP by 15-25%. Ten minutes later, while continuing the antihypertensive agent, the above sequence of NE doses was repeated. This was repeated with the other hypertensive drug. At a later time, when MAP and UBF were stable, NE was infused to increase MAP by 20% for 10 minutes. While continuing the NE, NTG or SNP was infused to return MAP to control. Both drugs were discontinued and the sequence was repeated with the other antihypertensive agent. Following the study, uterine vascular conductance was calculated: UVC = UBF/MAP.

Results. Eleven studies were performed in seven ewes. Changes in MAP, PR, UBF, UVC seen with the 2 higher doses of NE alone are presented in table 1. NTG alone (mean dose 19μg/Kg/Min) reduced MAP from control by 20%, increased PR (33%), decreased UBF (6%), and increased UVC (18%). In comparison SNP (mean dose 3μg/Kg/Min) decreased MAP by 21%, increased PR (43%), reduced UBF (12%), and increased UVC (11%). NTG and SNP similarly lessened the effects of NE on MAP, UBF, and UVC (table 1). Intrauterine pressure was not changed by NE, NTG, or SNP. A continuous infusion of NE increased MAP by 22%, reduced UBF by 42%, and decreased UVC by 52%. The addition of NTG reduced MAP to 4% below control while increasing UBF and UVC to 25% and 21% below control, respectively. Similar results occurred with SNP which brought MAP to 5% below control; UBF and UVC were increased to 27% and 23% below control, respectively.

Discussion. If a reliable way to control the hypertensive response to tracheal intubation could be devised, the safety of general anesthesia would be increased in preeclamptic patients. Although they may not be applicable to preeclamptic humans, our data from gravid ewes show that NTG and SNP equally counteract norepinephrine induced hypertension. Uterine vascular conductance, the reciprocal of resistance, defines the conducting property of the uterine vascular bed. The similar increase in conductance produced by NTG and SNP alone indicates that uterine vasodilatation occurred in our awake preparation. This accounts for the smaller actual reductions in UBF than would be predicted from changes in MAP. Conductance determinations additionally show that NTG and SNP similarly attenuate the vasoconstrictive action of norepinephrine on the uterine vascular bed. As a result, UBF is improved by NTG and SNP. Due to their rapid onset of action and short duration of effect, both NTG and SNP allow precise, rapid control of hypertension. The concern about the neonatal metabolic effects of nitroprusside makes nitroglycerin an attractive alternative for controlling maternal hypertension.

Table 1. Mean Percent change in parameters from control

| | NE Alone* | | NE + NTG+ | | NE + SNP** | |
|---|---|---|---|---|---|---|
| | 0.5 | 1.0 | 0.5 | 1.0 | 0.5 | 1.0 |
| MAP | +19 | +38 | -2 | +14 | -3 | +13 |
| PR | -23 | -34 | -9 | -20 | -5 | -18 |
| UBF | -51 | -72 | -29 | -55 | -36 | -48 |
| UVC | -54 | -76 | -21 | -55 | -29 | -47 |

*NE at 0.5 and 1.0μg/Kg/Min. for 2 minutes
+NTG infused at 19μg/Kg/Min.
**SNP infused at 3μg/Kg/Min.