Title : PLACENTAL TRANSFER OF EPHEDRINE

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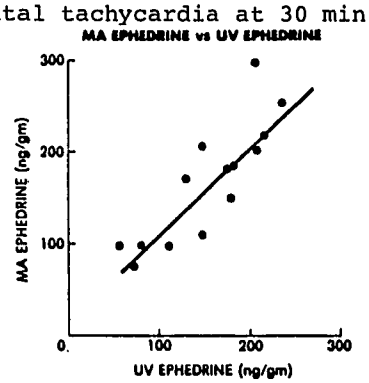
Introduction: Ephedrine is used widely in parturients to prevent and treat spinal and epidural hypotension. Last year we presented evidence that fetal heart rate and beat-to-beat variability increased in the human parturient given ephedrine.[1] We speculated that fetal heart rate changes were due to a direct action of ephedrine or its metabolites following placental transfer. The present study describes a technique for measurement of blood ephedrine levels, documents the placental transfer of the drug, and reports the fetal and neonatal effects of this transfer.

Method: We developed a combined gas chromatography-mass spectrometry assay for ephedrine and its metabolite norephedrine. A derivative of ephedrine served as an internal standard and carrier, which consisted of a stable isotope-labelled variant of ephedrine itself using deuterium. In order to ensure unequivocal identification of ephedrine, the method of specific ion recording was employed utilizing the internal standard. Fetal blood ephedrine was extracted and its derivative synthesized. The mass spectrometer peak of the derivative of the extracted material was identical to the peak of the derivative of ephedrine. An inverse isotope dilution procedure was employed such that the internal standard acted as a carrier and simultaneously provided accurate quantitation.

The study was approved by the Committee on Human Research and informed consent was obtained from all participants.

Twenty-one patients for cesarean section received 25 or 50 mg of ephedrine intramuscularly within 20 min preceding injection of epidural anesthesia. Each patient also received the usual fluid administration and left uterine displacement. Maternal cardiovascular status was stable throughout the duration of the anesthetic. Fetal heart rate was determined before and 15 min and 30 min after ephedrine administration. At delivery, Apgar scores were measured and blood was drawn from the maternal artery, umbilical vein and umbilical artery; ephedrine levels and acid base status were measured. Neonatal heart rate and blood pressure were measured at 5 min and 30 min of life and compared to a control group which received no ephedrine. Blood pressure was measured using a Marion Scientific Corporation Infrasonde.

Results: The maternal blood levels at birth of ephedrine ranged from 75 nanograms/gram (ng/gm) of plasma to 298 ng/gm while the umbilical vein concentrations ranged from 56 to 236 ng/gm. The fetal blood level was directly related to the maternal level. (See figure) The mean drug concentration in umbilical venous blood was 93% of maternal artery levels and was not related to the time following ephedrine administration (range 38-98 min). Apgar scores and acid base status were within normal limits regardless of ephedrine levels. Neonatal systolic blood pressures at 5 and 30 min and heart rate at 5 min were also within normal limits. There was a tendency toward neonatal tachycardia at 30 min.



Discussion: Our results demonstrate a fetal blood level at delivery approximately equal to the maternal level indicating that ephedrine does cross the placenta when administered to the parturient. Previous work using continuous fetal heart rate monitoring showed that fetal heart rate increased at about 45 min following intramuscular administration of ephedrine to the mother. Our samples were drawn from 38 to 98 min after ephedrine administration and document the presence of ephedrine during the period of expected fetal effects. The presence of ephedrine had no measurable deleterious effects on fetal well-being or neonatal outcome. Minimal neonatal tachycardia may result from the maternal administration of ephedrine, but neonatal systolic blood pressure and umbilical vein acid base status are normal. Changes in fetal heart rate, beat-to-beat variability, and neonatal heart rate may occur, but do not appear to be associated with any adverse effects. Therefore, despite placental transfer of ephedrine, we believe ephedrine is a safe vasopressor for treatment and prevention of maternal hypotension.

Reference:

[1]Wright RG, Rolbin SH, Shnider SM, et al: Maternal administration of ephedrine increases fetal heart rate and variability. (Abstr). American Society of Anesthesiologists Annual Meeting, 1977, p 131.

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