Title : ENFLURANE AND HALOTHANE: EFFECTS OF PLACENTAL TRANSFER

Authors : T. Abboud, M.D.; E. Henriksen, M.D.; S.H. Kim, M.D.; T.C. Chen, M.D.; G. Levinson, M.D.; and S.M. Shnider, M.D.

Affiliation: Department of Obstetrical Anesthesia, University of Southern California, Los Angeles County General Hospital, Los Angeles, California 90033 and Department of Anesthesia, Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, California 94143

Introduction: Neonatal depression following nitrous oxide anesthesia for cesarean section is related to the duration of anesthesia. Low-dose halothane or enflurane frequently is added to nitrous oxide to allow higher inspired maternal oxygen concentrations and to decrease maternal awareness. The neonatal effects of the placental transfer of enflurane or halothane have not been fully evaluated. The present study reports the relationship between fetal blood levels of these halogenated agents at time of delivery and maternal blood levels, fetal acid base status, Apgar scores and early neonatal neurobehavioral scale (ENNS).

Method: Forty-seven healthy parturients undergoing elective cesarean section were studied. Informed consent and approval by the research committee of the Professional Staff Association and the University of Southern California Health Sciences were obtained. Patients were randomly assigned to four groups defined by anesthetic and dose: 0.25% halothane, 0.5% halothane, 0.5% enflurane and 1.0% enflurane. Fifty per cent nitrous oxide and oxygen was added in each case. All patients were premedicated with i.v. glycopyrrolate and antacid by mouth. Maternal blood pressure and heart rate were monitored and left uterine displacement applied. Anesthesia was induced with 4 mg/kg thiopental followed by 1.5 mg/kg succinylcholine and endotracheal intubation. Ventilation was controlled with a tidal volume of 10 ml/kg at a rate of 10 breaths per min to provide normal maternal $PaCO_2$. At delivery blood was drawn from the maternal radial artery and from the umbilical vein and artery of a cord segment doubly clamped prior to the infant's first breath. Enflurane or halothane blood levels were measured by gas chromatography. Maternal arterial and umbilical venous and arterial blood gases were determined. The condition of the neonate was evaluated by cord acid base status, Apgar scores at 1 and 5 min, and the ENNS at 2 and 24 hours of age. Results on the ENNS were compared with results from 22 patients who received nitrous oxide 50% without a halogenated agent. Blood loss was estimated by the anesthesiologist and by Hgb and Hct measured on the third post-operative day. All patients were interviewed 24 hours postpartum to determine the incidence of recall.

Results: Higher inspired anesthetic concentrations produced higher blood levels (Table) but within the time range studied (6 to 21 min) were not related to duration of anesthesia. Umbilical vein concentration was 54 to 68% of maternal blood level and overall also was unrelated to the duration of anesthesia. However, 6 babies had one minute Apgar scores of 6 or less. These babies all had higher than average anesthetic blood levels and also had prolonged durations of anesthesia or uterine incision to delivery time. With both halothane and enflurane the umbilical artery/umbilical vein ratio was approximately 0.5 and did not vary with time suggesting continued fetal uptake of anesthetic. Maternal and fetal acid base status were normal in all groups and not related to either maternal or fetal anesthetic blood levels. All five-minute Apgar scores were 8 or more. Babies with higher than average halothane or enflurane blood levels did not have lower ENNS scores at 2 and 24 hours of age than babies with either no halogenated agent or with lower than average blood levels of halogenated agent. The incidence of maternal recall in patients who received nitrous oxide alone was 7%. There was no recall in any of the patients who received a halogenated agent. Blood loss, as indicated by comparison of the pre-operative hematocrit to the hematocrit on the third post-operative day was not affected by the addition of the halogenated agent.

Discussion: The present study shows that fetal uptake of either halothane or enflurane occurs rapidly with 54 to 68% equilibration occurring within 6 min. Presumably, therefore, the increased incidence of neonatal depression that occurs with longer durations of anesthesia antepartum is due to the nitrous oxide and not to the halogenated agent. The addition of low-dose halogenated agent did not adversely affect the Apgar scores or ENNS at 2 or 24 hours of age.

PLACENTAL TRANSFER OF HALOTHANE AND ENFLURANE

	Halothane		Enflurane		N_2O
	0.25%	0.5%	0.5%	1.0%	50%
n	6	17	18	6	22
MA*	2.1	3.1	3.4	6.3	--
UV*	1.4	1.7	2.2	4.3	--
UA*	0.7	0.8	1.0	---	--
UV/MA	.63	.54	.64	.68	--
Hematocrit					
Pre-op	36	38	37	37	36
Post-op	32	30	33	31	31

* Mean enflurane or halothane blood concentration in mg/100 ml