229

MATERNAL AND FETAL HEMODYNAMIC AND FETAL BRAIN FUNCTION(EEG)EFFECTS OF MATERNAL INFUSION OF DIAZOXIDE(D). Jahangir Ayromlooi (Spon.by P.Lipsitz),SUNY Med.Sch.at Stony Brook,Long Island Jewish-Hillside Med.Ctr.,Dept.Ob-Gyn,New Hyde Park, N.Y.

D has been used to stop premature labor. D(4mg/kg) was infused over 5 minutes to 7 anesthetized ewes at mean gestation of 141±1.5SE days. Post-infusion changes± SE of baseline maternal blood pressure(MBP), fetal carotid(FC)pH,pO_2,O_2 saturation(O_2%),cerebral blood flow(CBF) and % increase(Δ%) are presented in this table:

Time	0	5 Min.	15 Min.	30 Min.
MBP	72.4 ±4.70	45.9 ±7.42 *	37.2 ±6.71 *	34.0±5.66 *
pH	7.34±0.034	7.28±0.320*	7.23±0.061*	7.17±0.780*
O_2	22.0 ±2.5	17.2 ±2.26 *	15.3 ±1.06 *	14.1±1.40 *
O_2%	63.6 ±7.71	40.3 ±6.57 *	32.2 ±6.70 *	26.8±6.65 *
CBF	181.9±25.86	222.0±43.40	251.0±84.25	298 ±73.15
Δ%		+32%	+61%	+65%

*p < 0.05

Fetal BP showed no significant change. Fetal EEG showed either reduction of amplitude and frequency or isoelectricity in 3 of 5 non-hypoxic fetuses studied. Conclusion: D causes maternal hypotension,fetal hypoxia, acidosis, EEG changes and increased Δ% of CBF.

230

EFFECT OF PHOTOTHERAPY ON THE ELIMINATION (β) PHASE OF RIBOFLAVIN AND GENTAMICIN. Cheston M. Berlin, Maryann Gushue, and Cheryl Lee. (Spon. by Nicholas M. Nelson). Penn State Univ Coll Med, M. S. Hershey Med Ctr, Dept Ped, Hershey, PA.

Phototherapy is widely used for treatment of hyperbilirubinemia. Other substances circulating in the blood might be affected by such exposure to light. Two compounds were studied in the rabbit: gentamicin and riboflavin. The latter possesses a conjugated double bond structure which fluoresces at 445 nm (similar to bilirubin). Gentamicin is a commonly used antibiotic in neonates. Adult rabbits were shaved over back, flanks, and upper legs (>60% surface area). Riboflavin (50 mg) was injected I.P., gentamicin (2 mg/kg) I.V. Venous blood samples were obtained hourly for 6-8 hrs. During sampling periods animals were exposed to ambient light (control) and to a white light bank (6-7 μ watts/cm^2 at 18 inches) as "phototherapy". 4 weeks separated control and phototherapy period. Plasma concentrations were analyzed by least squares method for slope of line of best fit; β and $t_{1/2}$ was calculated.

Rabbit	Riboflavin Half Lives (Hrs.) No Light	Riboflavin Light	Gentamicin No Light	Gentamicin Light
1	1.66	2.70	- -	- -
2	1.82	2.18	- -	- -
3	- -	- -	0.42	0.36
4	4.73	4.63	1.26	0.55
5	6.12	2.85	0.63	0.73
6	3.23	3.73	1.14	1.26

These data indicate no consistent alteration with phototherapy in vivo in the elimination phase of drug metabolism.

231

PHARMACOKINETICS OF AQUEOUS PENICILLINS IN CEREBROSPINAL FLUID OF NEONATES. Betty Bernard, Larry Tinsley*, John Mapp. (Spons. by Paul Y.K. Wu.) Dept. of Pediatrics, Univ. of So. California School of Medicine, Los Angeles County-USC Medical Center.

If central nervous system (CNS) involvement is suspected in congenital syphilis, both aqueous penicillin G (APG) and aqueous procaine penicillin G (APP) are recommended for treatment. To study pharmacokinetics after administration of APG and APP, single samples of cerebrospinal fluid (CSF) and serum of 21 infants treated for congenital syphilis were obtained 1½ to 6 hrs. following a single IM dose of 50,000 units/kg body weight. Only one baby was symptomatic. Serum levels and half-lives of APG and APP were within the ranges reported for term infants. Treponemacidal levels after APG (≥.03 ug/ml) were detected in 11 CSF specimens in the first sample at ½ hr. and persisted through the 6 hr. study. A peak CSF level of 0.17 ug/ml was found at 2½ to 3 hrs. with an estimated half-life of 1½ hrs. After APP, penicillin activity was not detected in 5 CSF samples between ½ to 1 hr., but was present by 1½ hrs. Only 2 of 9 samples reached APP levels of ≥.03 ug/ml; in these two, a peak of 0.08 ug/ml was reached at 2½ hrs. These preliminary data show that both penicillins will provide treponemacidal levels in the serum, but APG reaches a higher CSF level and persists for a longer time. APG appears to be a more appropriate drug for treatment of congenital syphilis with suspect or proven CNS involvement.

(*Current address: UCLA Sch. of Med., Dept. of Pediatrics)

232

EFFECTS OF MATERNAL ISOXSUPRINE (VASODILAN) ADMINISTRATION ON PREMATURE INFANTS. Jane E. Brazy and Marcos J. Pupkin (Spon. by George W. Brumley). Duke University School of Medicine, Division of Perinatal Medicine, Durham, North Carolina.

A retrospective one year study of all inborn infants of ≤35 weeks' gestation was undertaken to determine neonatal effects of maternal Isoxsuprine (I) administration. Mothers of 43 infants received I. within 48 hours of delivery and mothers of 107 received no I. When divided into gestational age groups, there were no significant differences in infants' birthweights, Apgar scores, pulse rates, hematocrits, or the incidence of respiratory diseases. Hypocalcemia, hypoglycemia, abdominal symptoms of ileus, hypotension and death were all significantly higher in infants whose mothers received I. Hypotension and death occurred predominantly in very pre-term infants.

	I. (%)	No I. (%)	p-value
Abdominal symptoms	40	10	<.01
Blood sugar <40 mg%	14	5	<.05
Calcium <7 mg%	59	31	<.01
Hypotension	60	41	<.05
Death	16	6	<.05

Significant ileus and metabolic derangements appear to be related to maternal I. administration. The high mortality and incidence of hypotension deserves further investigation.

233

INCREASED FETAL BREATHING WITH PILOCARPINE IN FETAL LAMBS. E.R.Brown, E.E.Lawson, H.W. Taeusch and V.Chernick Dept. of Pediatrics, Harvard Medical School, Boston, Ma.

Rapid irregular fetal breathing (FB) is present 35% of the time in the fetal lamb and 70-80% of the time in the human fetus near term. Several pharmacologic agents affect FB patterns. CNS stimulants, such as epinephrine, doxapram, and caffeine,increase fetal breathing, while depressants, such as phenobarbitol, depress it. Pilocarpine (PC), a cholinergic drug, has known CNS excitatory action. To study the effect of PC (3 mg/kg fetal weight) on FB, tracheal pressure(TP) was monitored in three chronically catheterized fetal lambs between 139 and 147 days gestation. Drugs were infused directly into the fetal jugular vein.

Drug	n	latent period(sec)	f(Breath/min)	$\bar{X}$ TP/Br (cmH_2O)
Saline	3	no response	12 ± 17	10 ± 4
Pilocarpine	3	11 ± 2	18 ± 12	41 ±16
Epinephrine	2	122 ± 80	19 ± 9	22 ± 5
Atropine+PC	2	113 ± 72	29 ± 15	17 ± 6

The effect of PC on FB may be mediated through one of two mechanisms or both: the short latent period suggests a direct cholinergic mechanism; the longer latency seen in atropine pretreated fetuses resembles that of epinephrine, consistent with a nicotinic action at the sympathetic ganglia.

234

EFFECT OF FREE FATTY ACIDS AND OF SERUM ULTRAFILTRATES ON BILIRUBIN DISPLACEMENT IN NEONATAL SERUM. W.J. Cashore, R. Brodersen, W. Oh. Brown Univ. Program in Med., Women & Infants Hosp., Dept. of Ped., Prov., R.I. and Institute for Medical Biochemistry, Aarhus, Denmark.

Free fatty acids (FFA) are strong bilirubin displacers from Albumin (A) at FFA:A ratio >3:1. A model of bilirubin displacement using FFA:A ratio to predict free bilirubin was tested in 21 sera from 14 newborns (8 sick, 6 well). Concentration of FFA was 0.64 ± 0.40 mEq/l, A 0.41 ± 0.09 mEq/l, and FFA:A was 1.6 ± 1.0 (Mean ± S.D.); FFA:A was <3:1 in 20 of 21 sera, regardless of clinical condition. Free bilirubin (peroxidase assay, pH 7.4, serum dilution 1:40, 25°C) correlated with bilirubin: albumin molar ratio ($r = 0.845$, $p < 0.01$), but was higher than predicted from the FFA:A ratios, even without a history of displacing drugs, suggesting the presence of other displacers. To reduce the effect of dilution in the peroxidase assay and restore the free serum concentrations of weak displacers, protein-free ultrafiltrates of 10 sera were made by centrifugation. Incubation of the 10 sera with their ultrafiltrates gave a 1.5 to 4 fold further displacement of bilirubin, proportional to the amount of ultrafiltrate added in the test. The data suggest that neonatal sera contain bilirubin displacers other than FFA or drugs whose effect on free bilirubin is reduced by dilution during the assay. Use of ultrafiltrates allows re-equilibration of serum albumin with weak displacers and a more accurate assessment of their potential clinical significance.