PI-83

AMETHOCAINE VS LIDOCAINE — PRILOCAINE LOCAL ANAETHETIC OINTMENTS, FOR PROCEDURAL PAIN IN CHILDREN. R. Bishai, MD, M.H. Freedman, MD, and G. Koren, MD, Div of Cl Pharmacol and Hemat/Onc, Hospital for Sick Children, Univ of Toronto.

Objective: To compare the effect of Amethocaine (Ametop) and Lidocaine-Prilocaine (EMLA), in children with cancer undergoing Port-a-Cath puncture. **Study design:** A randomized, double-blind, cross over design. **Patients:** Thirty nine children completed the study: The mean age was 10 years and 4 months and all were treated with various chemotherapy protocols. **Methods:** Every child received 1g of amethocaine gel for 30 min, preceded by a placebo gel for 30 min or 1 g of EMLA cream for 60 min, which was checked at 30 min to guarantee blindness. The dressing was removed after 60 min, and the procedure was done within 5-10 min. Children rated the pain using the "faces" visual analogue scale (VAS), scoring from 0 to 5. Parents and attending nurse operators rated the pain on a 10 cm scale VAS. **Results:** There were no differences in mean VAS scores with amethocaine vs EMLA as rated by the children, parents or nurse operators. No serious side effects were detected with either ointment. **Conclusion:** Our results indicate that for Port-a-Cath application in children, 30 min of amethocaine gel is clinically equivalent to 60 min of EMLA.

PI-84

THE EFFECTS OF INTRAUTERINE COCAINE EXPOSURE ON NEURODEVELOPMENT OF ADOPTED CHILDREN: THE TORONTO ADOPTION STUDY. I. Nulman, MD, J. Rovet, PhD, R. Greenbaum, BSc, M. Loebstein, MA, J. Wolpin PhD, P. Pace-Asciak, BA, G. Koren, MD, Motherisk Program, Div of Clin Pharmacol/Toxicol, Dept of Pediatrics and Psychology, Hospital for Sick Children, Univ of Toronto, Toronto, Canada.

Studies of children's neurodevelopment following in utero cocaine exposure have not separated intrauterine from postnatal environmental effects because cocaine-using mothers cluster in low socioeconomic classes and have other risk factors. To overcome this limitation, we assessed physical and neurodevelopmental characteristics of 52 children, 26 adopted by parents who during the process of adoption sought counseling in the Motherisk program for parental cocaine exposure and 26 controls matched for maternal IQ, SES, and gestation age. The study group had (a) smaller head circumferences (34th versus 54th percentiles, p=0.009) but did not differ in height or weight, (b) lower McCarthy GCI scores (102.8 versus 114.2 p=0.002), (c) poorer receptive and expressive language performance on the Reynell, and (d) higher activity levels, less persistence, and increased distractibility on temperament tests. In multivariate analysis, cocaine exposure was significantly associated with lower IQ and poorer language development independent of intrauterine growth retardation and other potential confounders.

PI-85

PERINATAL OUTCOME FOLLOWING GESTATIONAL EXPOSURE TO ANTIDEPRESSANTS; SEPARATING THE EFFECTS OF DEPRESSION, PHARMACOTHERAPY AND OTHER CONFOUNDERS. I. Nulman, MD, J. Wolpin, PhD, J. Theis, MD, D. Stewart, MD, G. Koren, MD, The Motherisk Program, Div of Clin Pharmacol, Dept of Pediatrics, The Hospital for Sick Children, Research Institute, The Center of Women Health, The Toronto Hospital, Univ of Toronto, Toronto, Canada.

To separate the effects of tricyclic antidepressant drugs (TCA) and fluoxetine taken during pregnancy on measures of perinatal outcome, from the effects of maternal depression and other confounders. A prospective, controlled, observational study of mother-child pairs exposed in utero to TCA, fluoxetine and unexposed controls. The statistical model adjusted for independent variables which may affect the outcomes of interest, including length of therapy (first trimester vs throughout pregnancy), smoking, socioeconomic class, and severity of depression. Neither TCA nor fluoxetine taken either during the first trimester or throughout pregnancy, affected birth weight, gestational age, or the risk for neonatal complications when severity of maternal depression was considered in the model. Without controlling for the severity of maternal depression, birth weight was affected by antidepressant therapy. These observations are explained by the fact that women who continued fluoxetine throughout gestation had significantly more severe depression. TCAs and fluoxetine do not increase fetal risk for prematurely, lower birth weight or perinatal complications. Conversely, the level of clinical depression does affect fetal well being.

PI-86

POPULATION PHARMACOKINETICS OF METHYLPHENIDATE. R.I. Shader, J.S. Harmatz,* J.R. Oesterheld,* D.X. Parmalee,* F.R. Sallee,* and D.J. Greenblatt, Tufts University, Boston, MA.

A single plasma methylphenidate (MP) concentration was determined in each of 273 children and adolescents aged 5-18 years (mean 11.1 years) who were clinically good responders to methylphenidate for the treatment of attention-deficit hyperactivity disorder. Of the 273 patients, 109 (40%) were receiving MP on a twice-daily dosage schedule (mean total daily dose: 25 mg); the other 164 (60%) were receiving 3-times-daily dosage (mean total daily dose: 39.3 mg). A nonlinear regression model was applied to estimate overall population values of MP clearance and elimination half-life ($t_{1/2}$), assuming a one compartment model with first-order absorption and elimination, and further assuming that clearance is linearly related to body weight. The model incorporated each patient's dosage size and schedule, body weight, and time of plasma sample. Since age and body weight were significantly intercorrelated via an exponential function (r^2=0.54, p<.001), their contributions to variations in clearance were not independent. Iterated solutions of best fit were: $t_{1/2}$, 4.5 hours (95% confidence interval (CI): 3.1-8.1 hours), and apparent clearance, 90.7 ml/min/kg (95% CI: 74.6-106.7 ml/min/kg). The model explained 43% of the overall variance in MP concentrations (r^2=0.43, p<.001). The kinetic parameters are consistent with those reported in traditional multiple-sample kinetic studies of MP. In a small subsample (N=16), a second plasma sample was drawn one month later at the same time of day and at the same dose. For these 16 children, the correlation between the two samples was highly significant (r=0.83). The relatively noninvasive approach used in this study allows assessment of pharmacokinetic properties of medications under conditions of appropriate clinical use in special populations such as adolescents and children.