

OI-B-4

NEURODEVELOPMENT OF CHILDREN EXPOSED TO FLUOXETINE(FL) IN UTERO: A PROSPECTIVE LONGITUDINAL STUDY. L. Nulman,* MD, J. Rovet,* Ph.D., D. Stewart,* MD, N.A. Kulin,* BSc, G. Koren, MD. Divs. of Clin. Pharm, Hosp. for Sick Children, Toronto General Hosp., and Univ of Toronto, Toronto, Canada.

FL is frequently used by women of childbearing age. Because half of the pregnancies in North America are unplanned, fetal exposure cannot be avoided. FL has not yet been found to be teratogenic. The aims of this study were to assess the effects of FL on fetal neurodevelopment and to address the safety of using this drug throughout pregnancy. Thirty-six mother-child pairs who were exposed to FL during the first trimester of pregnancy and another 19 mother-child pairs who were exposed throughout pregnancy were compared to 81 mother-child pairs who were exposed to tricyclic antidepressants (TCA) and 87 mother-child pairs exposed to non-teratogenic drugs (NTD). Potential confounding characteristics did not differ between the groups. The primary outcome measure was global IQ, assessed by either the Bayley (<30 mo) or McCarthy(>30 mo) Scales. Mean global IQ scores for younger FL children was 116 ± 17 (n=40), and for the McCarthy group the mean was 114 ± 16 (n=14). The mean global IQs across tests in the TCA group (n=81) and the NTD group (n=84) were 118 ± 13 and 114 ± 13, respectively, which did not differ from FL scores. Children exposed to FL only in the first trimester were not different from those exposed throughout pregnancy (116 ± 17, n=35 and 115 ± 17, n=19, respectively, p < 0.7) Our results on FL use in pregnancy are reassuring.

PII-2

CHLOROQUINE-MEDIATED VASODILATION IN HUMAN HAND VEIN. A. Abiose, MD* O. Tangphao, MD*, M. Grossmann, MD*, T.F. Blaschke, MD and B.B. Hoffman, MD. Division of Clinical Pharmacology, Stanford University Medical Center, Stanford, CA., and GRECC, VA Medical Center, Palo Alto, CA.

Chloroquine-induced hypotension is a common and serious side effect of parenteral administration. Our aim was to investigate whether chloroquine produces venodilation in the human hand vein in vivo and to explore the underlying mechanism. In 19 healthy volunteers (16 ♂ and 3 ♀) dose-response curves were constructed by infusing chloroquine (0.75-50 µg/min) into hand veins precontracted with phenylephrine. 9 subjects had the dose-response curves repeated in the presence of 1-NMMA (47 µg/min). Infusion of chloroquine into precontracted veins produced venodilation in a dose-dependent manner. The venodilatory response ranged from 15±19% at an infusion rate of 0.75 µg/min to 61±24% at 48 µg/min. In the presence of 1-NMMA, the response to chloroquine at 48 µg/min decreased to 44 ± 32% (p=0.08). Thus, chloroquine causes venodilation at infusion rates achieving concentrations similar to those observed after clinically-relevant IV doses, and suggests a possible role for nitric oxide.

PII-1

POST-MARKETING ADVERSE EVENTS ASSOCIATED WITH THE NICOTINE PATCH AND POLACRILEX RESIN IN THE UNITED STATES. Spyker DA, Alderfer RJ, Goetsch RA, Armstrong GD, Longmire AW, Kramer ED, FDA, Rockville, MD.

We compared the post-market surveillance adverse event (AE) reports for nicotine polacrilex resin (gum) and the transdermal patch. **Methods:** We examined the FDA's Spontaneous Reporting System (SRS) for all AEs related to these products. AE rates for groups of COSTART terms for each route were reported: 1) % of total AE reports, and 2) AEs / million prescriptions (Rx).

Results:

Adverse Event Group	Gum			Patch		
	Num	% of 1,281	MRx 12.3	Num	% of 3,848	MRx 11.8
Dermatologic, local or generalized	39	3.0%	3.2	1533	40%	130
Addiction or Dependence	475	37%	39	24	0.62%	2.0
Gastrointestinal, Hiccups	163	13%	13	522	14%	44
Oral problems (mouth, teeth)	289	23%	23	141	3.7%	12
Withdrawal, no effect, headache	156	12%	13	442	11%	38
Nervous system, CNS	75	5.9%	6.1	384	10%	33
Sleep & dream disturbance	17	1.3%	1.4	416	11%	35

Discussion: There are no reports of primary nicotine dependence to the gum or the patch. The higher rate of dependence/addiction (long term use) with the gum may reflect greater user volition and/or different pharmacokinetics (T_{peak} = 20 min vs. 2-8 hr for the gum vs. patch). Limitations of using SRS or Rx data are well known.

PII-3

SERIOUS ADVERSE REACTIONS INDUCED BY MINOCYCLINE: L. Shapiro *MD, S. Knowles* BScPhm and N.H. Shear MD, Division of Clinical Pharmacology, Sunnybrook HSC, Toronto, CANADA

Background: Minocycline, a frequently used drug in the treatment of acne vulgaris, has well reported side effects which include nausea, emesis, dizziness, photosensitivity, pigmentation and fixed drug eruptions. Serious adverse drug reactions are not well recognized.

Objective: To identify serious adverse reactions attributed to minocycline specifically hypersensitivity syndrome, (HSS), serum sickness-like reaction (SSLR), and drug-induced lupus syndrome(DILS).

Methods: The files of our hospital based Adverse Drug Reaction (ADR) Clinic from January 1985 to June 1995 and the records of the Health Protection Branch, ADR reporting section from 1966 until 1995 were reviewed for serious reactions possibly induced by minocycline i.e. HSS, SSLR and DILS.

Results: Eleven patients with serious adverse reactions attributable to minocycline were identified. A complete literature review retrieved an additional 16 events. The groups were comparable with regard to sex, age, average daily dose of minocycline. The interval to onset(mean±sd) for the SSLR was 15.7±9.9 days, for the HSS 23.6±6.9 days (p=0.1). For DILS it was 757.6±245.0 days. It behooves prescribing physicians to be aware of these potentially life-threatening adverse reactions to minocycline.