O'Callaghan, Michael E.; MacLennan, Alastair Harvey
Brain damage and maternal medication
American Journal of Obstetrics and Gynecology, 2013; 208(2):160-161

DOI: 10.1016/j.ajog.2012.11.022

Brain Damage and Maternal Medication

Dear Sir,

The paper by Tyler *et al*[1] provides novel data on the important issue of brain damage and maternal medication on which currently there is little published literature.

The authors report a positive association between maternal aspirin use during pregnancy and quadriparesis and between maternal NSAIDs use during pregnancy and quadriparesis and diparesis in infants delivered very preterm[1]. Tyler *et al*'s discussion highlights the possibilities for confounding by indication and the need for replication in larger cohorts.

Using an already recruited cerebral palsy cohort[2] we were able to replicate part of these analyses is 145 quadriplegics, 149 diplegics and 191 hemiplegics, a cohort with 3-11 times the number of each cerebral palsy subtype reported by Tyler *et al* but recruited from deliveries at all gestational ages. Our cohort had insufficient power to independently replicate the associations reported by Tyler *et al* in very preterm infants (68 cases of cerebral palsy born at <28 weeks) but for all gestational ages no association was apparent with Aspirin and NSAID use and cerebral palsy outcomes.

In contrast, we report negative associations of maternal antibiotic use with diplegia and hemiplegia (see table 1) which was unexpected as perinatal infection is a risk factor for cerebral palsy[3].

Retrospective analysis of rare outcomes such as cerebral palsy is required to achieve large sample sizes. Our data was collected using a maternal health questionnaire administered at the time of participation and may be subject to recall bias. Time between birth and study participation may account for the low reported use of Aspirin and NSAIDs compared to the report of Tyler *et al*. Our analysis adjusts for similar, but not identical confounders. It is possible that NSAID and Aspirin use is higher amongst mothers who deliver very preterm infants when compared to mothers delivering at term. The interesting results of Tyler *et al* described in infants born before 28 weeks may not generalize to cerebral palsy children born at later gestational ages.

The question of over-the-counter medications and cerebral palsy is difficult to answer as prospective studies with high quality data provide small samples, yet larger cohorts from retrospective studies provide less reliable data.

DISCLOSURE: The authors report no conflict of interest.

(357/400 words)

ME O'Callaghan, PhD

AH MacLennan, MD

Discipline of Obstetrics and Gynaecology, School of Paediatrics and Reproductive Health, Robinson Institute, The University of Adelaide, Australia.

1. Tyler CP, Paneth N, Allred EN, et al. Brain damage in preterm newborns and maternal medication: The elgan study. Am J Obstet Gynecol 2012;207:192 e1-9.
2. O'callaghan ME, Maclennan AH, Gibson CS, et al. The australian cerebral palsy research study--protocol for a national collaborative study investigating genomic and clinical associations with cerebral palsy. J Paediatr Child Health 2011;47:99-110.
3. Wu YW, Colford JM. Chorioamnionitis as a risk factor for cerebral palsy: A meta-analysis. JAMA 2000;284:1417-24.

Table 1. Maternal medications and association with cerebral palsy subtypes

Maternal Medication	**Controls (1,154)**	**Quadriplegia (145)**		**Diplegia (149)**		**Hemiplegia (191)**		**All CP Cases (587)**	
	n (%)	n (%)	OR (95% CI), p value	n (%)	OR (95% CI), p value	n (%)	OR (95% CI), p value	n (%)	OR (95% CI), p value
Antibiotics	58 (5)	7 (4.8)	0.3 (0.09-1.01), 0.052	11 (7.4)	**0.17 (0.06-0.52), 0.002**	15 (7.9)	**0.17 (0.07-0.41), < 0.001**	40 (6.8)	**4.08 (2.08-8), < 0.001**
Aspirin	4 (0.3)	0 (0)	-	1 (0.7)	-	1 (0.5)	-	5 (0.9)	0.94 (0.11-8.18), 0.95
NSAIDs	9 (0.8)	1 (0.7)	1.57 (0.11-22.4), 0.74	1 (0.7)	1.6 (0.11-22.97), 0.73	3 (1.6)	0.41 (0.1-1.69), 0.217	9 (1.5)	1.41 (0.4-4.91), 0.59
Paracetamol	265 (23)	25 (17.2)	1.26 (0.68-2.33), 0.465	29 (19.5)	0.7 (0.4-1.23), 0.215	51 (27)	0.66 (0.44-1.01), 0.056	125 (22)	1.25 (0.91,1.72), 0.17

* Adjusted for gestational age, birth weight centile and evidence of maternal infection in perinatal notes.