



Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Congenital Anomalies Cork & Kerry

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EUROCAT and pharmacovigilance: Lamotrigine study

To assess the safety of drugs in pregnancy, data from a large population is required. The EUROCAT registries survey over a million births per year, a quarter of all births in Europe. At least half the registries in the EUROCAT network collect information on first trimester drug use. Drug information is got from obstetric records or by interview with the mother. The percentage of cases with drug exposure (excluding vitamins/minerals) varies from 4.4% to 26.0% among registries.

EUROCAT was asked to carry out a case-control study of lamotrigine exposure (an anti-epileptic drug) and orofacial clefts. The request followed an FDA alert (September 2006), issued when the North American Antiepileptic Drug Pregnancy Registry reported an unexpectedly high prevalence (relative risk of approx. 15) of isolated non-syndromic, cleft palate and/or cleft lip in infants exposed to lamotrigine monotherapy during the first trimester of pregnancy (Holmes et al 2006). A UK study (Morrow et al 2006) and a study based on the GSK register did not replicate this finding.

The EUROCAT study aimed to investigate whether intrauterine exposure to lamotrigine monotherapy in the first trimester of pregnancy is associated with an increased risk of isolated orofacial clefts relative to other malformations, using a case-control design. Nineteen EUROCAT registries contributed data for some or all of the period 1995-2005 giving a study population of 3.9 million births. There were 5,511 non-syndromic orofacial cleft (OC) registrations. 4,571 were isolated OC, and 1,969 had cleft palate of whom 1,532 were isolated. There were 72 lamotrigine exposed (40 mono- and 32 polytherapy) registrations. The study found no evidence of an increased risk of oral clefts relative to other malformations with lamotrigine exposure. The study excluded a more than three-fold risk of isolated OCs relative to other non-chromosomal malformations due to lamotrigine monotherapy.

Anti-epileptics are an important teratogenic risk. There is little information about new generation anti-epileptics. The EUROCAT study helps fill this gap.

Methodological approaches to the Assessment of Risk of Congenital Anomaly due to Environment Pollution Workshop, Budapest, 2007

EUROCAT is under EU contract for the European Surveillance of Congenital Anomalies. This workshop harnessed expertise on congenital anomaly risk from environmental exposure. Break out sessions involved small groups identifying areas for priority attention and study. EU and WHO policy direction on the prevention of birth defects from environmental pollution was explored. EUROCAT as a coordinating centre for the WHO, can interact officially with any other WHO programme. The European regulatory framework for teratogens and current teratogenic screening was presented. The potential of population based biomonitoring for exposure assessment was discussed. The EU funded INTERESE project will develop biomarkers for exposure, for effects and for susceptibility. The first project on biomarkers of exposure will test hair for lead and mercury, and urine for cadmium and cotinine. The feasibility of collaborative working and a co-ordinated approach throughout the EU will be assessed.

Presentations on recent incidents explored epidemiological methods to investigate environmental exposures in relation to congenital anomalies. Many involved case control studies. Others focussed on the pathway of exposure and examined exposure dose. The use of routine environmental data for modelling population exposure is being developed.

A EUROCAT statistical methodology detects time clusters using scan methods and is incorporated into EDMP (EUROCAT Data Management Programme). EUROCAT registers now have two years experience of routine cluster detection and investigation. The use of Satscan to detect spatial clusters in five regions of Britain was presented and discussed. <http://www.eurocat.ulster.ac.uk/announcements.html>

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Dr Mary O'Mahony,
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Ms Benvon Deasy
Public Health Surveillance Scientist

Ms Christine O'Driscoll
Congenital Anomaly Nurse

We would like to welcome 2 new Congenital Anomaly Registry staff:
Ms Maria Ryan replacing Ms Christine O'Driscoll; Ms Aline Brennan replacing Ms Benvon Deasy

Epidemiology: 2002-2003 Cork & Kerry Registry Data

2002:

There were 8454 births in Cork and Kerry in 2002 (4410 males, 4044 females). The number of babies with a birth defect was 225 (2.6%), 213 singleton, 10 twin and 1 triplet deliveries. There were 216 livebirths and 9 stillbirths. There were 104 male and 120 female infants born with a birth defect. In one case gender was not recorded. The age of mothers who gave birth to a child with a congenital anomaly in 2002 ranged from 17-44 years. Prevalence of congenital anomaly increases with maternal age with the rate per 1000 increased in 40-44 age group. 69% of cases were discovered by first week of birth. In those with a congenital anomaly, 17.3% were under 37 weeks gestation compared to 5% nationally. Also, in those with a birth defect, 15% were under 2500g compared to 5% nationally.

2003:

There were 8383 births in 2003 (4416 males, 3967 females). The number of babies with a birth defect was 210 (2.5%), 202 singleton and 8 twin deliveries. There were 200 livebirths, 9 stillbirths and 1 termination of pregnancy in the UK. There were 94 males and 115 females born with a birth defect. In one case gender was not recorded. The age of mothers ranged from 17-44 years. Rate per 1000 was high (48.9) in 40-44 age group compared to 24.2 in 30-34 year age group and 16.6 in 25-29 year age group. 13% of defects were discovered prenatally. A further 69% were found by the end of the 1st week of life. 1% were diagnosed after 1 year of age. 20% of infants were under 37 weeks gestation compared to 5% nationally. 18% were under 2500g compared to 5% nationally.

Table 1: Cases of congenital anomaly and prevalence per 10,000 births from Cork and Kerry Registry Data compared to Eurocat Full Member Registry Data , 2002-2003 (includes Live Births, Foetal Deaths and Terminations of Pregnancy where data available)

Anomaly	Cork & Kerry cases 2002	Cork & Kerry prevalence 2002	Eurocat cases 2002	Eurocat prevalence 2002	Cork & Kerry cases 2003	Cork & Kerry prevalence 2003	Eurocat cases 2003	Eurocat prevalence 2003
All anomalies	208	244.45	20431	240.45	188	223.15	16087	226.13
Nervous System	10	11.75	1906	22.43	22	26.11	1667	23.43
Eye	4	4.7	277	3.26	5	5.93	211	2.97
Ear, face & neck	2	2.35	259	3.05	1	1.19	149	2.09
Congenital Heart Disease	76	89.32	6425	75.61	75	89.02	4838	68.01
Respiratory	3	3.53	421	4.95	6	7.12	357	5.02
Oro-facial clefts	15	17.63	1195	14.06	11	13.06	974	13.69
Digestive System	5	5.88	1067	12.56	9	10.68	896	12.59
Abdominal wall defects	4	4.7	428	5.04	3	3.56	395	5.55
Urinary	10	11.75	2590	30.48	5	5.93	1965	27.62
Genital	8	9.4	1571	18.49	7	8.31	1088	15.29
Limb	57	66.99	3213	37.81	41	48.66	2576	36.21
Musculo-skeletal	6	7.05	656	7.72	9	10.68	547	7.69
Other malformations	2	2.35	850	10	1	1.19	455	6.4
Teratogenic syndromes with malformations	1	1.18	52	0.68	0	0	50	0.79
Genetic syndromes & microdeletions	7	8.23	401	4.72	4	4.75	317	4.46
Chromosomal	34	39.96	2774	32.65	33	39.17	2445	34.37
Other anomaly out of range/not a case	13				15			
Total	221				203			

Table 2: Cases and prevalence per 10,000 births of Congenital Heart Disease from Cork and Kerry Registry Data compared to Eurocat Full Member Registry Data , 2002-2003 (includes Live Births, Foetal Deaths and Terminations of Pregnancy where data available)

Anomaly	Cork & Kerry	Cork & Kerry prevalence	Eurocat cases	Eurocat prevalence	Cork & Kerry	Cork & Kerry	Eurocat cases	Eurocat prevalence
Congenital Heart Disease	76	89.32	6425	75.61	75	89.02	4838	68.01
Common arterial truncus	0	0	71	0.9	1	1.19	49	0.75
Transposition of great vessels	4	4.7	247	3.12	5	5.93	198	3.04
Single ventricle	0	0	41	0.48	0	0	38	0.53
Ventricular septal defect (VSD)	33	38.78	2581	30.37	37	43.92	1964	27.61
Atrial septal defect (ASD)	19	22.33	2081	24.49	23	27.3	1432	20.13
Atrioventricular septal defect (AVSD)	6	7.05	274	3.22	5	5.93	232	3.26
Tetralogy of Fallot	3	3.53	280	3.3	3	3.56	207	2.91
Tricuspid atresia and stenosis	3	3.53	50	0.59	0	0	42	0.59
Ebstein's anomaly	1	1.18	36	0.42	0	0	30	0.42
Pulmonary valve stenosis	5	5.88	279	3.28	1	1.19	252	3.54
Pulmonary valve atresia	2	2.35	58	0.68	0	0	72	1.01
Aortic valve atresia/stenosis	1	1.18	90	1.18	1	1.19	68	1.07
Hypoplastic left heart	1	1.18	196	2.31	3	3.56	186	2.61
Hypoplastic right heart	1	1.18	26	0.34	0	0	32	0.5
Coarctation of aorta	3	3.53	302	3.55	5	5.93	217	3.05
Total anomalous pulm venous return	1	1.18	38	0.45	1	1.19	33	0.46

NOTE: Data in Tables above extracted from EUROCAT website November 2007. Due to data validation/cleaning there are some discrepancies with Regional Registry Data described in text above.