Birth Defects´ Occurrence in Offspring of Mothers Taking 1st Trimester Medication in the Czech Republic

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Introduction:

To prove that any agent is teratogenic means to give an evidence that either a maternal exposure to this agent increases the incidence of a congenital malformation beyond its normal level in a given population (monitoring, prospective methods) or that in the personal history of malformed babies an exposure to this agent occurs significantly more frequently than in the history of unmalformed ones (retrospective methods).

Both types of data are not easy to obtain and usually not possible without a well-established birth defects registration system.

Material and methods:

Data on birth defects in the Czech Republic from the Institute of Health Information and Statistics - National Register of Congenital Anomalies from the 1996 – 2003 period were used. The analysis of birth defects incidences of selected types of malformations registered in offspring of mothers taking 1st trimester medication was performed and the data were compared to a control group data on healthy children born to mothers taking medications from the same time period.

An equality test of two Poisson distributions (Sachs, 1994) was used.

Material and methods II:

There were 25,580 children born with a birth defects registered in the period under the study. Out of them, 1,004 were born to mothers taking 1st trimester medication making a total of 1,288 particular birth defects. A control group covered 1,321 exposed women giving birth to a child without any birth defect.

Results I:

Number of children with birth defect(s) in particular years

Year	Number	%
1996	196	19.52
1997	151	15.04
1998	110	10.96
1999	136	13.55
2000	91	9.06
2001	96	9.56
2002	111	11.06
2003	113	11.25
Total	1004	100.00

Results II:

Number of registered defects in particular years

Year	Number	%
1996	237	18.40
1997	193	14.98
1998	152	11.80
1999	188	14.60
2000	126	9.78
2001	115	8.93
2002	135	10.48
2003	142	11.02
Total	1288	100.00

Tab. 1

Occurrence of congenital malformations (CM) in a general population compared to that in children of mothers taking 1st trimester medication, Czech Republic 1996 – 2003, absolute numbers

Type(s) of congenital anomaly (CA)	CA with medication	other CA	CA total
CA of nervous system (Q00-Q07)	56	686	742
CA of eye, ear, face and neck (Q10-Q18)	71	1701	1772
CA of circulatory system (Q20-Q28)	427	12947	13374
CA of respiratory system (Q30-Q34)	9	355	364
Cleft palate and cleft lip (Q35-Q37)	68	1197	1265
CA of upper alim. track and digestive system(Q38-Q45)	49	1393	1442
CA of genital organs(Q50-Q56)	146	3621	3767
CA of urinary system (Q60-Q64)	91	2289	2380
CM and deform. of musculoskeletal system (Q65-Q79)	259	6630	6889
Other CM (Q80-Q89)	80	1948	2028
Chromosomal abnormalities (Q90-Q99)	32	728	760
Total	1288	33495	34783

Results III:

Statistically significantly increased risk was found in following diagnoses:

- Anencephaly
- Spina bifida
- Congenital hydrocephalus
- Anophthalmos/microphthalmos
- Malformations of cardiac septa
- Cleft palate and cleft lip
- Reduction defects of upper limb

Tab. 2

Statistical significance of incidences of selected types of CM in child population with medication in its prenatal history (1st trimester) compared to that without it (Czech Republic 1996 – 2003)

Dg	Congenital malformation	Significance
Q00	Anencefaly	$p < 0.001$
Q03	Congenital hydrocephalus	$p < 0.05$
Q05	Spina bifida	$p < 0.001$
Q11	Anophthalmos, micro- and macrophthalmos	$p < 0.01$
Q71	Reduction defects of upper limb	$p < 0.01$

Results IV:

The distribution of a number of reported drugs in use in the control group of 1 321 women taking 1st trimester medication and giving birth to a child without any birth defect:

	Number	%
1 drug	836	63.29
2 drugs	329	24.91
3 drugs	105	7.95
4+ drugs	51	3.86
total women	1321	100.00
(total drugs 2 013)		

Tab. 3

Statistical significance of the frequency of maternal use of different drug groups - comparison of the population of children born with a birth defect to the population of healthy children

Group	Characteristics	Significance
J	Antiinfectivs for general use	$p < 0.0001$
J01	Antibacterial drugs for general use	$p < 0.0001$
N	Nervous system (antiepileptics)	$p < 0.0001$

Conclusions I:

A significantly increased incidences in children born to mothers taking 1st trimester medication compared to general population was found for following defects: anencephaly, spina bifida, congenital hydrocephalus, anophthalmia/microphthalmia, some types of congenital hearth defects, cleft lip with cleft palate and limb reduction defects. A significantly higher risk resulting from these incidences was found also in following 5 types of drugs: anticoagulants, antihypertensivs, peripheral vasodilatants, urologics and antiepileptics.

Conclusions II:

Although the results are not always unambiguous and are probably influenced by both information and recall bias, they contribute to our knowledge on adverse effects of drugs in pregnancy in the Czech Republic. They also stress the need for a high preliminary caution in drug prescription and for a complex risk assessement. It is obvious that much more data are needed for any future decision in this sensitive field.

This study was supported by an IGA MZ CR grant # 7516-3