Opipramol for antidepressant therapy in early pregnancy

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Introduction: The tricyclic antidepressant opipramol is used in Europe for more than 50 years. Nevertheless references on possible reproductive effects of opipramol are missing. The present study aimed to compare outcomes of pregnancies exposed to opipramol with no or non-teratogenic medication during first trimester of pregnancy.

Methods: In a prospective follow-up study we collected data of pregnancy outcomes after medication with opipramol (n = 243) between 1989 and 2015. Our Teratology Information Service (TIS) was contacted by physicians and patients after exposure to opipramol in the first trimester. We compared the results with a control group (n = 901) of our TIS in the same interval, which was not or not severely exposed. Statistical evaluation was performed by Fisher’s Exact Test. The gestational age at call did not differ between both groups (day 49 vs day 51; p = 0.80), the maternal age however was higher in the exposed group (33 years vs 30 years; p < 0.001).

Results: After treatment with opipramol 22 patients (22/243 = 9.1%) preferred early termination of pregnancy. The incidence of elective terminations of pregnancy was higher (p = 0.00002) after therapy with opipramol than in the control group (22/901 = 2.4%). The other 221 documented pregnancies ended with spontaneous abortions in 33 cases and ongoing pregnancies in 188 cases. The rate of spontaneous abortions (33/221 = 14.9%) did not differ significantly from the control group (89/879 = 10.1%, p = 0.054). 14 congenital anomalies were reported after intrauterine exposure to opipramol in early pregnancy: severe developmental delay (n = 3), cleft lip (n = 2), hydronephrosis (n = 2), choanal atresia, inguinal hernia, corpus callosum agenesis, trisomy 18 (n = 3), trisomy 21. After exclusion of chromosomal aberrations in both groups the overall rate of congenital anomalies was not significantly increased when patients had been treated with opipramol in early pregnancy (10/184 = 5.4% vs 27/787 = 3.4%; relative risk 1.58; 95% confidence interval 0.73, 3.34). A consistent pattern of anomalies could not be confirmed.

Conclusions: Our prospective controlled follow-up study does not support the assumption of a teratogenic effect of opipramol.

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Collaborative ENTS study of the fetal effects of maternal varenicline use in pregnancy

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Introduction: Varenicline (ATC code: N07BA03) is a smoking cessation aid for which limited published pregnancy safety data currently exist [1].

Methods: This multicentre prospective observational comparative cohort study was performed using data collected from eight member organizations of the ENTS network, and included pregnancies occurring between 2001 and 2014. The study sample consisted of eighty-nine varenicline exposed pregnancies and two matched comparator groups consisting of 267 non-teratogen exposed (NTE) controls and 78 exposed to nicotine replacement therapy or bupropion (NRT/B) for smoking cessation. Crude rates of any, major and minor non-genetic congenital malformations were compared between exposed and comparator groups using exact methods. We also estimated hazards ratios for live birth, spontaneous abortion, elective termination and intrauterine fetal death.
death/stillbirth using time-dependent Cox proportional hazards models.

**Results:** For all exposed pregnancies, varenicline use occurred in the first trimester only, with a considerable proportion discontinuing use early in pregnancy (72.1% <6 gestational weeks). No significant increased risk of overall (i. vs. NTE: OR 1.54, 95% CI 0.508 to 4.25, ii. vs. NRT/B: OR 1.02, 95% CI 0.280 to 3.87), major (i. OR 3.03, 95% CI 0.217 to 42.4, ii. OR 1.76, 95% CI 0.090 to 10.6), or minor (i. OR 1.26, 95% CI 0.339 to 4.00, ii. OR 0.87, 95% CI 0.192 to 3.94) non-genetic congenital malformation was observed following first trimester varenicline exposure. No significant increase in spontaneous abortion or intrauterine fetal death/stillbirth was identified between exposed and comparator groups. A statistically significant increase in the rate of elective termination was identified following maternal varenicline use in comparison with NTE controls (aHR 4.57, 95% CI 1.66 to 12.6), although this was not replicated in the comparison with NRT/B exposed controls (aHR 1.65, 95% CI 0.564 to 4.83).

**Discussion:** No evidence of an increased risk of congenital malformation was identified in this study, but the findings are limited by early therapy discontinuation and the small sample size. In view of these limitations and the lack of additional published safety data, routine use of varenicline as a smoking cessation aid in pregnancy cannot currently be recommended.

**Reference**


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**Anogenital distance as a marker of reproductive toxicity**

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**Background:** Increasing evidence suggests that exposures to man-made chemicals found in commonly used products, such as personal care products, the lining of cans used for food-stuffs and others, are endocrine disruptors. Further evidence suggests that endocrine disruptors are associated with adverse child development, especially neurodevelopment, development of the reproductive system and obesity. Here, we report results examining associations between exposure to polychlorinated diethyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) and anogenital distance (AGD), a measure influenced by androgen exposure.