

J Clin Psychiatry. 2005 Mar;66(3):317-22.

Safety of haloperidol and penfluridol in pregnancy: a multicenter, prospective, controlled study.

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OBJECTIVE: To assess the safety of the butyrophenone neuroleptics haloperidol and penfluridol in pregnancy.

METHOD: The rate of major anomalies was compared between a cohort of pregnant women counseled for gestational exposure to haloperidol or penfluridol and a control group counseled for nonteratogen exposure. This multicenter, prospective, controlled study was conducted within the European Network of Teratology Information Services (ENTIS) and included women who contacted 1 of 4 teratology information services for counseling between January 1989 and December 2001.

RESULTS: We followed up on the outcomes of 215 pregnancies exposed to haloperidol (N = 188) or penfluridol (N = 27)-78.2% (of 206) were in the first trimester-and compared to outcomes of 631 ENTIS controls. The rate of congenital anomalies did not differ between the haloperidol/penfluridol-exposed group and the control group (6/179 = 3.4% vs. 22/581 = 3.8%, $p = .787$). No difference was found by limiting the analysis to those exposed to butyrophenones during the first trimester. There were 2 cases of limb defects in the butyrophenone-exposed group (1 after haloperidol and 1 after penfluridol exposure) and none in the controls. A higher rate of elective terminations of pregnancy (8.8% vs. 3.8%, $p = .004$), a higher rate of preterm birth (13.9% vs. 6.9%, $p = .006$), a lower median birth weight (3155 g vs. 3370 g, $p < .001$), and a lower median birth weight of full-term infants (3250 g vs. 3415 g, $p = .004$) were found in the butyrophenone-exposed group compared to the controls.

CONCLUSION: This study suggests that haloperidol and penfluridol do not represent a major teratogenic risk. Since a possible association between butyrophenone exposure and limb defects cannot be ruled out with this sample size, a level II ultrasound with emphasis on the limbs should be considered in pregnancies with first trimester exposure.