

MOTHERISK UPDATE

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Are the new SSRIs safe for pregnant women?

ABSTRACT

QUESTION More and more of my female patients are switching to the new selective serotonin reuptake inhibitors. Are they safe during pregnancy?

ANSWER Our data suggest these drugs do not increase the malformation rate, but there are no data on neurodevelopment. Because such data do exist on fluoxetine and tricyclic antidepressants, those drugs should be considered first.

A decade after introduction of the first selective serotonin reuptake inhibitor (SSRI), fluoxetine (eg, Prozac), into clinical use, this class of antidepressants is being used by millions of men and women worldwide. Because more than half of all pregnancies are unplanned, and because an estimated 8% to 20% of all women suffer from depression, fetal safety is a primary concern when antidepressants are prescribed.

During the last few years, new SSRIs with purportedly fewer adverse effects than fluoxetine have been introduced into the market.¹⁻³ While many women of reproductive age use the newer SSRIs for depression and other indications (such as obsessive-compulsive disorder), no data on whether they are safe to use during pregnancy have been collected. The Motherisk Program has recently completed the first prospective, controlled, cohort study of pregnancy outcome following fetal exposure to the new SSRIs.⁴

Patients and methods

The prospective cohort included all women who

contacted one of nine participating Teratology Information Services regarding exposure to fluvoxamine (eg, Luvox), sertraline (Zoloft), or paroxetine (Paxil) during the first trimester of pregnancy. The primary end point of interest was rate of major malformations defined as structural or functional anomalies that have serious medical or social consequences.

A total of 267 women met the study inclusion criteria: 92 from Toronto; 66 from Tampa, Fla; 46 from Philadelphia, Pa; 32 from Farmington, Conn; 11 from Salt Lake City, Utah; seven from Burlington, Vt; six from London, Ont; four from Chicago, Ill; and three from Indianapolis, Ind. Of these 267 women, 147 used sertraline,

97 paroxetine, and 26 fluvoxamine; 49 women used SSRIs throughout pregnancy. Most women used sertraline at 50 mg/d (range 25 to 250 mg), paroxetine at 30 mg/d (range 10 to 60 mg), and fluvoxamine at 50 mg/d (range 25 to 200 mg).

Research findings

Women exposed to SSRIs were significantly less likely to be primigravid, and significantly more likely to smoke cigarettes and to have had previous therapeutic abortions (**Table 1**). These trends were similar for the three SSRIs.

Pregnancy outcome did not differ among the groups. There were similar rates of major malformations, spontaneous and elective abortions, and stillbirth. Mean birth weights were similar, as was gestation age (**Table 2**). Outcomes for women who took SSRIs throughout pregnancy were similar to outcomes of those who took the drugs only during the first trimester. Smokers and non-smokers using SSRIs had similar outcomes (data not shown).

Do you have a question about the safety of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to Dr Gideon Koren by fax at (416) 813-7562; they will be addressed in future Motherisk Updates.

Published Motherisk Updates are available through a link on the College of Family Physicians of Canada website (www.cfpc.ca). Some articles are published in *The Motherisk Newsletter* also.

Motherisk questions are prepared by the **Motherisk Team** at the Hospital for Sick Children in Toronto and edited by **Dr G. Koren**, Professor of Pediatrics in Pharmacology, Pharmacy, and Medicine at the University of Toronto. **Ms Kulin** and **Ms Pastuszak** are members of the Motherisk Team.

Our study confirms the results of animal experiments in showing that, when used in recommended doses, the new SSRIs do not appear to increase the risk of congenital malformations. Our sample was large enough to detect a relative risk of 2.5 for major malformations with a power of 80% and an α of .05. ♣

References

1. Solvay Kingswood. *Product information. Luvox*. Scarborough, Ont: Solvay Kingswood; 1991.
2. SmithKline Beecham Pharmaceuticals. *Product information. Paxil*. Oakville, Ont: SmithKline Beecham Pharmaceuticals; 1995.
3. Pfizer Pharmaceuticals. *Product information. Zoloft*. Kirkland, Que: Pfizer Pharmaceuticals; 1994.
4. Kulin NA, Pastuszak A, Sage SR, Schick-Boschetto B, Spivey G, Feldcamp M, et al. Pregnancy outcome following maternal use of the new selective serotonin reuptake inhibitors. A prospective controlled multicenter study. *JAMA* 1998;279:609-10.

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Table 1. Characteristics of women exposed to SSRIs compared with controls

CHARACTERISTIC	WOMEN EXPOSED TO SSRIS N = 267	CONTROLS N = 267	P VALUE
Gravidity			<.005
• 1	57	90	
• 2 or more	199	177	
Parity			.07
• 0	95	125	
• 1 or more	152	142	
Previous spontaneous abortion			.91
• 0	157	205	
• 1 or more	49	61	
Previous therapeutic abortion			.03
• 0	166	235	
• 1 or more	40	31	
Smoker	74	43	<.001
Non-smoker	129	224	
Consumed alcohol	75	98	.94
Did not consume alcohol	130	169	
Age at conception	31.3 (\pm 4.8)	30.8 (\pm 4.9)	.29

Table 2. Pregnancy outcomes of women exposed to SSRIs compared with outcomes of controls

OUTCOMES	WOMEN EXPOSED TO SSRIS N = 267	CONTROLS N = 267	P VALUE
Live births	222 (83.1%)	235 (88.0%)	.14
Spontaneous abortions	30 (11.2%)	21 (7.9%)	.24
Therapeutic abortions	15 (5.6%)	9 (3.4%)	.30
Stillbirths	0	2 (0.7%)	.50
Major malformations (% of live births)	9 (4.0%)	9 (3.8%)	.91
Birth weight (g)	3439 (SD \pm 505)	3445 (SD \pm 609)	.91
Gestation age (wk)	39.4 (SD \pm 1.7)	39.4 (SD \pm 1.9)	.71