

Adverse Effects in Neonates Exposed to SSRIs and SNRI in Late Gestation

Gideon Koren¹ and Nina Boucher²

¹The Motherisk Program, The Hospital for Sick Children, Toronto; ²Laval University, Faculty of Pharmacy, Québec City, Québec

ABSTRACT

Neonates exposed at term to selective serotonin (SSRI) or serotonin-norepinephrine reuptake inhibitors (SNRI) medications may encounter symptoms such as irritability, rigidity, tremor and respiratory distress. Most available data suggest that these self limited symptoms are due to discontinuation of the drug, although there are

documented cases of symptoms associated with high serum concentrations in the neonate that subsided when levels fall. Preliminary evidence suggests that the very early respiratory symptoms may not be part of discontinuation but rather part of a reversible form of persistent pulmonary hypertension of the newborn (PPHN).

INTRODUCTION

Adults discontinuing SSRI or SNRI medications have been often reported to experience a withdrawal syndrome characterized by irritability, insomnia, mental instability, tremors and even seizures.¹ It is not surprising, therefore, that the neonatal brain may react similarly after birth, when the steady intrauterine exposure to these drugs has subsided. Epidemiological studies have documented that up to 30% of neonates exposed to SSRI and SNRI near term may suffer from symptoms which include irritability, sleep disturbances, rigidity, tremor, limpness or similar signs.² While kinetically it is reasonable to assume that, with elimination of these medications, a discontinuation syndrome is expected, Knoppert and colleagues documented a case of neonatal symptomatology associated with high serum concentrations of paroxetine that has subsided with decreasing levels, suggesting serotonin toxicity, as part of the well known serotonergic syndrome.³

One characteristic of the adverse neonatal effects of SSRI and SNRI is varying degrees of respiratory distress, which may in severe cases necessitate respiratory support.² Recent epidemiological studies have documented that near term exposure to SSRI confers an increased risk for persistent pulmonary hypertension of the newborn (PPHN), which is often associated, among other symptoms, with respiratory distress.^{4,5} Recently Fornaro and colleagues confirmed PPHN in experimental animals exposed to fluoxetine.⁶ While in all previous studies the respiratory symptoms have been lumped as part of the “poor neonatal adaptation syndrome”, be it withdrawal or serotonergic syndrome, preliminary data may suggest that the respiratory insufficiency may in fact be part of PPHN, and its resolution may signal resolution of the PPHN. Upon the first descriptions of SSRI-SNRI neonatal symptomatology, regulatory agencies in

different countries called upon physicians to consider discontinuation of these drugs near term to avoid neonatal morbidity.

This advice has been very unfortunate, as it neglects some serious arguments in this risk-benefit analysis:

- 1) The worse predictor of post partum depression is depression at term. Maternal morbidity due to suboptimally treated depression should be avoided.
- 2) The neonatal morbidity is self limited and, in most cases, mild. Moreover, there is no proof that with discontinuing these medications near term the baby will escape the discontinuation syndrome.

Conclusion

We believe that women with depression and their babies should be kept in the obstetric ward for several days, to encounter and effectively manage the possible neonatal syndrome, to establish breastfeeding and to ensure that maternal mental status is stable.

Funding Source: *Supported in part by Jonathan's Alert*

Corresponding Author: vkoren@sickkids.ca

REFERENCES

1. Haddad PM, Dursun SM. Neurological complications of psychiatric drugs: clinical features and management. *Hum Psychopharmacol* 2008; 1: 15-26.
2. Koren G, Matsui D, Einarson A, Knoppert D, Steiner M. Is maternal use of selective serotonin reuptake inhibitors in the third trimester of pregnancy harmful to neonates? *CMAJ* 2005; 172: 1457-9.
3. Knoppert DC, Nimkar R, Principi T, Yuen D. Paroxetine toxicity in a newborn after in utero exposure: clinical symptoms correlate with serum levels. *Ther Drug Monit* 2006; 28: 5-7.
4. Chambers CD, Hernandez-Diaz S, Van Marter LJ, Werler MM, Louik C, Jones KL, Mitchell AA. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. *N Engl J Med* 2006; 354: 579-87.
5. Kallen B, Olausson PO. Maternal use of selective serotonin re-uptake inhibitors and persistent pulmonary hypertension of the newborn. *Pharmacoepidemiol Drug Saf* 2008; 17: 801-6.
6. Fornaro E, Li D, Pan J, Belik J. Prenatal exposure to fluoxetine induces fetal pulmonary hypertension in the rat. *Am J Respir Crit Care Med* 2007; 176: 1035-40.