Fluoxetine Withdrawal Syndrome in the Newborn

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A term baby was admitted to our neonatal unit with jitteriness, hypertonia, sneezing and fever. Her mother was on 20 mg of fluoxetine throughout her pregnancy. These symptoms which were possibly due to fluoxetine withdrawal lasted only for a short while. We attempt to look at the reported prevalence of this condition in the literature.

Key words: Fluoxetine withdrawal, Neonate, SSRI withdrawal.

Selective Serotonin Re-uptake Inhibitors (SSRI’s) such as fluoxetine are increasingly being used to treat depression in pregnant women as they are shown to be relatively harmless to the developing fetus. However, symptoms of SSRI withdrawal have been occasionally reported. Here we describe a neonate who presented with symptoms possibly due to fluoxetine withdrawal.

Case report

A term infant was born with a birth weight of 3200 g to a 28-year-old mother. The APGAR scores were 9 at 1 and 5 minutes and...
she was nursed in the post natal ward. At 6 hours of age she was noticed to be jittery on handling. As she was otherwise well with normal blood glucose (2.6 mmol/L) she was nursed under close observation in the post natal wards. However she gradually started sneezing and developed a temperature of 37.9 degrees centigrade. Her full blood count, C reactive protein, liver functions and blood culture were within normal limits. Her other blood tests undertaken were blood glucose 4.5 mmol/L, serum calcium 2.36 mmol/L, serum magnesium 0.73 mmol/L, serum sodium 135 mmol/L, potassium 5.4 mmol/L, urea was 4.4 mmol/L and creatinine was 42 µmol/L. By 15 hours of age, she developed increasing jitteriness, vomiting and poor feeding. Her tone was increased in all four limbs. She was admitted to the neonatal unit for further management. At this stage it was found that the mother had been on 20 mg per day of fluoxetine throughout her pregnancy for depression. There was no history of any other drug intake including recreational drugs. She was started on 10% dextrose infusion. Her feeds were stopped transiently and were gradually restarted within few hours, which she tolerated well. By 2 days of age the jitteriness improved and she was transferred to the post natal ward and thereafter discharged home on day 3. Urine drug screen, which included amphetamines, benzodiazepines, cocaine metabolites, methadone and its metabolites, cyclizine, opiates, phenothiazines and tricyclic antidepressants, was negative in the mother and infant. A provisional diagnosis of fluoxetine withdrawal syndrome was made. She was reviewed again at 1 week of age. On examination she was well with only mild jitteriness. Repeat serum electrolytes and blood glucose continued to be within normal limits. The mother was reassured and the baby was sent home. The jitteriness resolved within few days and the infant has been well since.

Discussion

Fluoxetine is a widely used antidepressant drug in pregnancy. It is also used to treat anxiety, panic disorder and obsessive compulsive disorder. Several studies have shown that it could be safely used in pregnancy. Intrauterine exposure of fluoxetine may lead to neonatal syndrome, which includes withdrawal or toxicity. Most of the data on neonatal problems after maternal SSRI exposure come from case reports, pharmacovigilance updates and systematic follow up studies of SSRI exposed pregnancies.

To date at least 7 isolated case reports on fluoxetine withdrawal or toxicity has been published(1-7). Databases of adverse drug event reports(8-10) and small case series reports(11) provide additional sources of information on the SSRI-related neonatal withdrawal syndrome including fluoxetine. Sanz, et al.(8) in their recent analysis of the adverse drug event database of the World Health Organisation (WHO) Collaborating Centre for International Drug Monitoring reported a total of 74 SSRI-related neonatal withdrawal syndrome cases of which 10 were due to fluoxetine (others paroxetine = 51, sertraline = 7, citalopram = 6). The US Food and Drug administration (FDA) Adverse Event Reporting System(9) recorded 57 instances of SSRI-related neonatal withdrawal syndrome by November 2001. Of these 4 were due to fluoxetine (others paroxetine = 35, sertraline = 8, citalopram = 5, fluvoxamine = 2 and venlafaxine = 3). By August 2003, out of the 26 SSRI-related neonatal withdrawal syndrome cases, the Australian Adverse Drug Reaction bulletin(10) reported 7 neonates with symptoms due to maternal third trimester ingestion of fluoxetine. In the United Kingdom
(UK) the National Teratology Information Service (NTIS) to date have recorded 8 cases of possible neonatal withdrawal following maternal fluoxetine use in 513 pregnant women (NTIS, Regional Drug & Therapeutics Center, Newcastle, UK, unpublished data 2004).

The clinical presentation of fluoxetine withdrawal depends on the timing and amount of last maternal use, maternal and infant metabolism and excretion. The most commonly reported neonatal symptoms include agitation, irritability, impending seizures, hypotonia or hyper tonia, hyperreflexia, drowsiness, jitteriness, feeding problems, persistent crying, tachypnoea, temperature instability, acrocyanosis and tremors. In addition fluoxetine toxicity has been observed as scattered petechiae over the face and trunk along with cephalhaematoma(5), marked motor automatism and skin manifestations(6). It has also been associated with colic(3), lipo meningocele(4), and cardiac arrhythmia(7). Due to its longer half life (2-3 days) the withdrawal symptoms due to fluoxetine are usually mild and self limiting compared to other SSRI’s. Moreover it is obvious from the published work that majority of the reported cases of suspected SSRI-induced neonatal withdrawal syndrome are due to Paroxetine and fluoxetine(9).

Management of these infants should include a detailed maternal history and thorough clinical examination in addition to various laboratory tests. A good maternal drug history is vital as the physician who is unaware of a mother’s ingestion of the drug may mistake the signs of withdrawal for other neonatal problems like central nervous system infections, hypocalcemia, hypoglycaemia, other electrolyte abnormalities and colic. Also it is equally important that no clinical sign should be attributed solely to drug withdrawal without appropriate assessment and diagnostic tests to rule out other causes. Most of the neonates need only supportive care and could be nursed in the postnatal ward or admitted to neonatal unit for observation, as seen in our patient. More essentially the withdrawal symptoms could be minimised by using the lowest effective maternal dose of fluoxetine.

It is probable that the prevalence of neonatal withdrawal syndrome due to maternal ingestion of fluoxetine might be much more than what’s been purported in published medical literature. Although, fluoxetine produces no identifiable major malformations in the developing fetus; obstetricians, midwives, psychiatrists and paediatricians should be more aware of the existence of this self-limiting illness. This would enable them to better inform and counsel all pregnant women on fluoxetine therapy of the possible adverse effects in the newborn period and assist them in identifying withdrawal symptoms in their newborn.

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CASE REPORTS


