

Neonatal intraventricular haemorrhage associated with maternal use of paroxetine

Yvonne C. M. Duijvestijn, Mathijs D. Kalmeijer,¹ Anneke L. M. Passier,² Peter Dahlem & Frans Smiers³

Department of Pediatrics, Emma Children's Hospital/Academic Medical Centre, Amsterdam, ¹Department of Clinical Pharmacy, Academic Medical Centre, Amsterdam, ²Netherlands Pharmacovigilance Centre Lareb, 's Hertogenbosch, and ³Department of Pediatric Hematology Oncology, Leiden University Medical Centre, Leiden, the Netherlands

Selective serotonin reuptake inhibitors (SSRIs) have been reported to inhibit serotonin uptake into platelets, resulting in decreased platelet function. We report a case of a large intraventricular haemorrhage in a 6-h-old boy, whose mother used paroxetine during pregnancy.

Keywords: intraventricular haemorrhage, newborn, selective serotonin reuptake inhibitors

Case report

After 40 weeks of uncomplicated pregnancy and labour a healthy boy with a birthweight of 4200 g was born at home under accompaniment of a midwife. The APGAR score after, respectively, 1 and 5 min was 9 and 10. The infant received vitamin K directly post partum (1 mg per os). There was no history of premature rupture of the membranes or meconium-stained amniotic fluid. The mother used paroxetine 20 mg daily during the last 5 years, continuing during pregnancy. Family history was unremarkable and in particular mentioned no bleeding disorders. Six hours postnatal the child became progressively lethargic and showed abnormal neurological responses. He was admitted to a regional hospital, where an irritated male neonate in hyperextension with a bulging fontanel was seen. The Glasgow Coma Scale was E4, M3, V2. A cranial computed tomography showed a large intraventricular haemorrhage with ventricular enlargement necessitating external ventricular drainage and transfer to a paediatric intensive care unit. Despite this intervention he developed apnoeas and severe convulsions for which he was intubated and was given multiple antiepileptic drug therapy.

Platelet count of the child and the mother, activated partial thromboplastin time, prothrombin time (PT) as well as factors VIII, IX, XI and XIII were within normal range. Platelet serotonin level in maternal plasma was 93 ng/10⁹ plts (normal range >400 ng/10⁹ plts). In the child platelet serotonin level was 143 ng/10⁹ plts. Platelet

aggregation using platelet-rich plasma of the mother in response to adenosine diphosphate (ADP), ristocetin, collagen and arachidonic acid was normal in the mother and was not performed in the child. Magnetic resonance imaging investigation showed an enlarged right ventricle and white matter atrophy at the right side. It did not reveal any vascular malformations. However, our patient remained dependent on continuous ventricular drainage. On follow-up after 7 weeks he still needed ventricular drainage and showed severe neurological abnormalities with stereotype movements, hypotony of the legs, epilepsy and abnormal eye movements with seriously disturbed visual evoked potentials.

Discussion

Selective serotonin reuptake inhibitors (SSRIs) have been reported to inhibit serotonin uptake into platelets, resulting in decreased platelet function [1]. The role of serotonin in SSRI-induced haemorrhage is not completely understood. SSRIs reduce uptake of serotonin by platelets, inducing reduction in granular storage of serotonin. This may cause decreased platelet activation. Increased bleeding tendency after use of SSRI has been described previously for users [2, 3] as well as for *in utero* exposed fetus [4].

The capacity of paroxetine to cross the placenta is illustrated by reports of neonatal symptoms associated with maternal use of paroxetine. Withdrawal symptoms in neonates after *in utero* exposure to paroxetine may be relatively slow compared with adults, due to possible immaturity of the liver in the newborn child [5, 6].

In our patient maternal use of SSRI during pregnancy might explain the severe intraventricular haemorrhage. No other predisposing factors could be discovered. More

Correspondence: J. L. M. Passier, Netherlands Pharmacovigilance Centre Lareb, Goudsbloemvallei 7, 5237 MH's-Hertogenbosch, the Netherlands. Tel.: + 31 73 646 9718; Fax: + 31 73 642 6136; E-mail: a.passier@lareb.nl

Received 8 April 2003, accepted 19 May 2003.

research needs to be done to elucidate the risks of use during pregnancy. Until utmost safety can be guaranteed, the use of SSRIs, especially during the last trimester of pregnancy, should be discouraged.

References

- 1 Hergovich N, Aigner M, Eichler HG, Entlicher J, Drucker C, Jilma B. Paroxetine decreases platelet serotonin storage and platelet functions in human beings. *Clin Pharmacol Ther* 2000; **68**: 435–442.
- 2 Cooper TA, Valcour VG, Gibbons RB, O'Brien-Falls K. Spontaneous ecchymoses due to paroxetine administration. *Am J Med* 1998; **104**: 197–198.
- 3 Walraven C, Mamdani MM, Wells PS, Williams JI. Inhibition of serotonin reuptake by antidepressants and upper gastrointestinal bleeding in elderly patients: retrospective cohort study. *BMJ* 2001; **323**: 655–658.
- 4 Stanford MS, Patton JH. *In utero* exposure to fluoxetine HCl increases hematoma frequency at birth. *Pharmacol Biochem Behav* 1993; **45**: 959–962.
- 5 Nijhuis IJ, Kok-Van Rooij GW, Bosschaart AN. Withdrawal reactions of a premature neonate after maternal use of paroxetine. *Arch Dis Child Fetal Neonatal* 2001; **84**: F77.
- 6 Nordeng H, Lindemann R, Perminov KV, Reikvam A. Neonatal withdrawal syndrome after *in utero* exposure to selective serotonin reuptake inhibitors. *Acta Paediatr* 2001; **90**: 288–291.