## Letter to the editor

## Clozapine and lorazepam administration in pregnancy

V Di Michele<sup>1</sup>, LA Ramenghi<sup>2</sup>, G Sabatino<sup>2</sup>

<sup>1</sup> Department of Psychiatry, Spirito Santo Hospital, via Fontra Romana, 65124 Pescara; <sup>2</sup>Neonatal Unit, University of Chieti, Italy

(Received 19 July 1995; accepted 4 October 1995)

Several successful pregnancies have recently been reported in women on clozapine treatment (Lieberman and Safferman, 1992; Waldman, 1993; Barnas et al, 1994). Due to the increasing use of this drug in schizophrenics, clinical psychiatrists now often have to manage patients taking clozapine plus benzodiazepine. This combination, although discouraged by some authors (Klimke and Klieser, 1994) has curiously produced beneficial effects in such patients (Konofsky and Lindenmayer, 1993).

We describe a successful pregnancy in a woman undergoing treatment with clozapine and lorazepam, but whose baby developed transient Floppy Infant Syndrome (FIS).

The woman, aged 37, had suffered from schizophrenia since she was 25. She was married, with one child aged 13, and had taken clozapine for 2 years before the present pregnancy. Due to subjective well-being, she had a strong desire for a child, and despite her mental disease and continuous treatment with psychotropic drugs, she became pregnant. She took clozapine at a dose of 200 mg/day, which was increased up to 300 mg/day three times during her pregnancy, according to her clinical condition. In addition she took lorazepam 2.5 mg three times daily, and frequently increased this dose up to five tablets a day.

Under obstetric supervision, the pregnancy was uneventful, and a male child was born by caesarean section at term (37 weeks of gestation). The Apgar score was 7 at 1 minute, and 9 at 5 minutes. The baby weighed 3.300 g. Arterial cord Ph was 7.3.

At physical examination, the child had benign tachipnoea and mild FIS, and was immediatly admitted to the Neonatal Unit Chieti University; hypotonia resolved five days later. Cerebral ultrasound, electroencephalography, abdominal ultrasound and lung X-ray were all normal.

On the basis of evidence in the literature that clozapine accumulates in breast milk (Barnas et al, 1993), the infant was bottle fed.

Pregnancy may be the consequence of impressive effect of clozapine in improving the quality of life and social functioning of schizophrenic woman (Meltzer et al, 1990). In fact, the present patient's strong wish for a child was the result of long-standing subjective well-being. We believe that with the increasing use of clozapine, psychiatrists will have to face this problem more frequently in the near future. Furthermore, women should be advised against combining clozapine and lorazepam during pregnancy because of the possible risk of FIS. To the best of our knowledge, FIS has not yet been reported in infants born to mothers who received clozapine alone during pregnancy, although caution is recommended in this condition (Barnas et al, 1994).

## REFERENCES

- Barnas C, Bergant A, Hummer M, Saria A, Fleischacker WW. Clozapine concentrations in maternal and fetal plasma, amniotic fluid, and breast milk (letter). Am J Psychiatry 1994;151:945
- Klimke A, Klieser E. Sudden death after intravenous application of lorazepam in a patient treated with clozapine (letter). Am J Psychiatry 1994;151:780
- Konofsky D, Lindenmayer JP. Relapse following Lorazepam withdrawal (letter). Am J Psychiatry 1993;150:348-9
- Lieberman J, Safferman AZ. Clinical profile of clozapine: adverse reactions and agranulocytosis, in clozapine. In: Lapierre Y, Jones B, eds. Treatment Resistant Schizophrenia: A Scientific Update. London: Royal Society of Medicine, 1992
- Meltzer HY, Burnett S, Bastani B, Ramirez LF. Effects of six months of clozapine treatment on the quality of life of chronic schizophrenic patients. *Hosp Comm Psychiatry* 1990;41:892-7
- Waldman MD, Safferman AZ. Pregnancy and clozapine (letter). Am J Psychiatry 1993;150:168-9