DOI:10.1111/j.1365-2125.2004.02163.x

Letter to the Editor

Ritodrine-induced transient neutropenia in newborn twins after *in utero* exposure: Report of first cases

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Ritodrine hydrochloride is a β_2 symphatomimetic agent and is used as an effective inhibitor of uterine contractions to treat premature labour. However its widespread use has resulted in some undesirable maternal complications, such as tachycardia [1], increased systolic blood pressure [2], pulmonary oedema [3] and neutropenia [4–6]. Ritodrine crosses the placental barrier and enters the fetal circulation readily, with cord serum ritodrine concentrations being reported as equal to or slightly lower than those in the maternal serum [7]. Effects in infants exposed *in utero* to ritodrine have included hyperinsulinaemia, hypoglycaemia [8], increased birth weight, and thickening of the interventricular septum [9]. This is the first report of two neonatal cases of transient neutropenia induced by maternal intravenous infusion of ritodrine.

A 23-year old woman who was 35 weeks pregnant with twins was admitted because of uterine contractions. She had no history of infection, early membrane rupture, fever, neutropenia or recent exposure to any drugs or toxins except ferrous sulphate and multivitamins during pregnancy. White blood cell count (WBC) was 9800/mm^3 and absolute neutrophil count (ANC) was 7402/mm^3. She was started on ritodrine at 120 μg min^{-1} intravenously on admission, and the rate of infusion was increased gradually over 48 h to 240 μg min^{-1} due to uncontrolled uterine contractions. In spite of ritodrine treatment for 48 h, at 35 weeks and 2 days gestation, she was delivered of two male infants weighing 2595 and 2270 g.

APGAR scores and physical examination of the infants were normal except for plethorea in the second newborn and we took blood samples for complete blood count (CBC) and venous haematocrit. WBCs and ANCs of infants were 4740/mm^3, 948/mm^3 and 4350/mm^3, 783/mm^3, respectively. Because of neutropenia, we did a sepsis workup and C-reactive protein was negative in both infants. Blood and urine cultures were taken. We did not do bone marrow aspiration from either of newborns because of the wishes of family and the general wellbeing of the infants. Antibody titres of TORCH were negative in both infants. Antibiotic therapy was not started.

We repeated CBCs of the infants and the mother at 3, 5, 7, 9 and 12 days. In a 2 week period, the neutropenia resolved spontaneously and the general condition of the infants was good (Figure 1). Blood and urine cultures were negative. Maternal WBC declined by the third day but returned to normal by the ninth day.

Mechanisms of drug-induced neutropenia are non-dose related immune-mediated toxic reaction and dose-related bone marrow suppression [5, 10]. The immune-mediated reaction causes a precipitous decline in granulocytes occurring only a short time after ingestion of a small amount of the drug [6]. Neutropenia due to anti-inflammatory drugs, semisynthetic penicillins and antiseizure medications is commonly seen in neonates but ritodrine-induced neutropenia in newborns has not been reported yet. Recovery from drug-induced neutropenia generally begins within several days after the offending agent is discontinued. The clinical courses of our cases indicated that the neutropenia was probably due to non-dose-related immune-mediated toxic reaction induced by ritodrine.

Ritodrine-induced neutropenia was reported first in 1986 [4]. Kobayashi & Ikushima also reported ritodrine-induced neutropenia cases but all were maternal neutropenia induced by ritodrine [5, 6]. Although, the exact mechanism of ritodrine-induced neutropenia is not known, this complication must be considered in patients to whom ritodrine is administered and in newborns whose mothers receive ritodrine.

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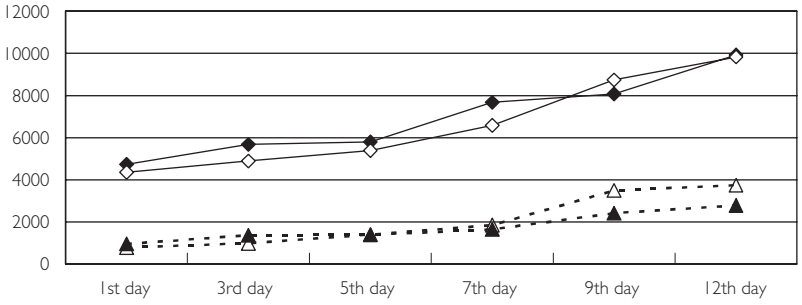


Figure 1
WBC (1st infant) (◆), WBC (2nd infant) (◇), ANC (1st infant) (▲), ANC (2nd infant) (△)

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Received
16 March 2004
Accepted
18 March 2004

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