Mild Toxicity after tenfold iatrogen overdose of doxapram in a preterm infant

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Objective: Doxapram is used as an analeptic in preterm infants. Intravenous loading doses range from 0.5 to 2.5 mg/kg, the intravenous maintenance dose is 1 mg/kg/h. The data on the onset of therapeutic effects range from 1–8 hours. Overdose experience in the literature is limited. Severe cases might have nausea, vomiting, tachycardia, hypertension, hyperpnea, seizures, hemolysis, coma and respiratory failure. We report a case of an iatrogen overdose which is to our knowledge the highest continuous infusion rate. Case Report: A preterm twin infant (born at 28 weeks gestation), 37 days old, 1.730 g, had been intubated and ventilated for about 10 days because of severe apnoea and bradycardia with superimposed pneumonia. After extubation the patient was first treated with therapeutic doses of doxapram and therapeutic doses of oral coffein, phenobarbital and clarithromycin. For prevention of apnea the patient was treated for 6.5 hours with Doxapram 0.95 mg/kg/h (1.62 mg/h) intravenously. While moving the child in the ICU, the infusion rate was accidently changed to 16.2 mg/h (9.5 mg/kg/h). This ten-fold dose continued for approximately 4.5 hours (± 15 min). The error was noted when the infusion was finished. The overall dose for 4.5 hours was 72.9 mg. There were no cardiovascular or neurologic effects during the infusion or afterwards. Blood pressure and heart rate remained stable. Seizures might have been prevented by phenobarbital. The only symptoms noted were nausea and increased gastric residuals. Some episodes of apnea occurred several hours later but could be explained by the prematurity of the infant. Conclusion: The only toxic effects of doxapram seen in a premature infant after the intravenous administration of 9.5 mg/kg/h for 4.5 hours were gastrointestinal disturbances. The margin of safety of doxapram might be wider than it has been thought. Since the infant did not respond well to therapeutic doses, there might also be an individual sensibility towards doxapram. Further case reports are needed to assess the toxicity of this substance.