Probable adverse reaction to a pharmaceutical excipient

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CASE REPORT

A baby boy was born to a primigravid mother at 24 weeks gestation weighing 710 g. He received poracartan (Curosurf) and mechanical ventilation for presumed surfactant deficiency lung disease. On the third day of life, he developed widespread erythema and sloughing of the skin associated with staphylococcal septicemia which was treated with fluvoxacinil and vancomycin. After he developed a red swollen right knee on day 17 and a swollen cheek on day 18, intravenous clindamycin was prescribed in place of vancomycin. The first two doses of clindamycin were given without a problem, but after the third and fourth doses, the baby suffered a profound desaturation and chest splinting requiring resuscitation. The clindamycin was discontinued in view of concerns that there may have been a causative association. The baby suffered no obvious sequelae, there was no radiological evidence of osteomyelitis three weeks later, and he was transferred back to his local hospital well at 11 weeks of age.

It is stated in the Summary of Product Characteristics that the benzyl alcohol component of clindamycin injection may cause "gasing syndrome" in premature neonates, but we have been unable to find any reports in the literature specific to clindamycin. The manufacturer's pharmacovigilance department had not received any reports of this syndrome.

Benzyl alcohol is used as a preservative in many pharmaceutical formulations. In the early 1980s reports started to appear about toxicity of benzyl alcohol in neonates. Gershman et al.2 reported a gasping syndrome in 10 premature infants. In the United States at this time, bacteriostatic water and NaCl injections contained 0.9% benzyl alcohol. The infants received multiple injections from flushes and NaCl injections containing 0.9% benzyl alcohol. The authors reported the gasping syndrome as the most striking feature, but there were other symptoms including metabolic acidosis, intraventricular haemorrhage, and neurological problems. Sixteen neonatal deaths were reported that were thought to be due to benzyl alcohol toxicity.

After this report, the Food and Drug Administration (FDA) recommended that fluids preserved with benzyl alcohol were not to be used in premature babies. In 1986, Hiller et al.3 found that, in their review of reports to the FDA, adverse reactions to drug therapy are a significant cause of death in infants and children. This case report illustrates the potential for serious adverse reactions to excipients to occur that may be difficult to distinguish from other medical problems. Clindamycin is rarely used in premature neonates and is not licensed in infants of less than 1 month of age. This reaction, which could have been fatal, provides further evidence for having medicines available that have been fully tested and are licensed in children and the importance of reporting adverse reactions in children particularly when the medicines are being used in an unlicensed or off label manner. Prescribers should be aware of the potential for excipients to cause adverse reactions in addition to the drug itself. These reactions should be reported to the UK's Committee on Safety of Medicines (CSM) using the Yellow Card Reporting Scheme in the usual way.

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Accepted 31 January 2003

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