



PIC QUESTION OF THE WEEK: 9/17/07

Q: Are there any risks associated with the use of ceftriaxone in combination with calcium salts?

A. Ceftriaxone (Rocephin), a third generation cephalosporin, is widely used in the treatment of many conditions including acute otitis media, gonorrhea, meningitis, and infections of the skin and lower respiratory tract. It is indicated for use in both adults and children. In July, 2007 the FDA along with the manufacturer issued a safety alert addressing new information regarding the concomitant use of intravenous (I.V.) ceftriaxone and calcium containing products in neonates. A small number of post-marketing reports had identified cases of fatal reactions in neonates caused by the precipitation of calcium-ceftriaxone complexes in the lungs and kidneys of both term and premature neonates. The patients had received I.V. doses of ceftriaxone and calcium solutions (sometimes even in different lines). More recently, a September 2007 MedWatch alert expanded the warning to include patients of all ages. In addition, it recommended avoiding the administration of ceftriaxone and calcium containing products within 48 hours of each other, even in different infusion lines or at different sites. There is currently no data on the risk of combining *intramuscular* (I.M.) ceftriaxone with I.V. or oral calcium salts. It has long been established that ceftriaxone can produce biliary sludge or pseudolithiasis (most commonly in children). *High* concentrations of ceftriaxone are known to bind with calcium and form insoluble stones. This has occurred not only in the biliary system, but in the kidneys as well. Several cases of ceftriaxone-induced nephrolithiasis have appeared in the literature. In one study, 4 of 51 children receiving I.M. or I.V. ceftriaxone developed small, asymptomatic kidney stones that resolved spontaneously in three of the four patients. The study did not describe use of concomitant calcium solutions or products. In another trial, kidney stones were reported in 4 of 284 pediatric patients receiving I.V. ceftriaxone. Again, little data was presented regarding concomitant administration of calcium salts. Based on recent FDA reports and previous documentation of the formation of insoluble precipitates, ceftriaxone should probably not be administered within 48 hours of calcium salts.

References:

- Avci Z, Koktener A, Uras N, et al. Nephrolithiasis associated with ceftriaxone therapy: a prospective study in 51 children. *Arch Dis Child* 2004;89:1069-72.
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- Mohkam M, Karimi A, Gharib A, et al. Ceftriaxone associated nephrolithiasis: a prospective study in 284 children. *Pediatr Nephrol* 2007;22:690-4.

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