

Prolonged Sedation Related to Erythromycin and Midazolam Interaction- A Word of Caution

Procedural sedation in children is a challenging endeavor. We report an interesting case of prolonged sedation probably due to an interaction between erythromycin and midazolam in a child.

A 6 year old, 24 kg boy was referred for do an outpatient magnetic resonance imaging of the pelvis and femur as he was suffering with fever and progressive pain in hip area and limping. The boy was otherwise healthy, with an unremarkable medical history and review of systems. He was taking some medicines for fever, and the details were not known. As he was having a fear of injection, oral midazolam suspension of 0.5 mg/kg was given and patient's cooperation was achieved throughout the procedure. His physiologic parameters remained well within age-adjusted normal values. At the termination of the study after 45 minutes, he remained deeply sedated with a Ramsay Sedation Score of 5 and was transferred uneventfully to the emergency department for monitoring. 30 minutes after completion of the imaging study, he remained profoundly asleep; hence intravenous flumazenil of 0.01 mg/kg bolus was given to shorten post procedure recovery time. Although he was satisfactorily aroused from sedation with a modified Aldrete score of 9, he was admitted to the intensive care unit for overnight continuous cardio-respiratory monitoring. The mother brought the remaining tablets which were erythromycin and paracetamol. A possibility of prolonged midazolam effect due to erythromycin was entertained. He remained hemodynamically and neurologically stable in the ICU throughout the night and discharged home without any sequelae.

Midazolam is the most commonly used drug in pediatric procedural sedation, as it can be delivered by all routes of administration. It has a rapid onset and a short elimination half-life (1.17 h) compared with other benzodiazepines, and thus makes it particularly suitable for brief procedures [2]. Unfortunately, injections are one of the most frightening, distressing and sometimes painful aspect, and hence, oral route is preferred. Both erythromycin and midazolam are substrates of the cytochrome P450 3A4 enzyme system and compete for

enzyme sites. Metabolism of midazolam is inhibited resulting in decrease in midazolam clearance, and an increase in the half-life and serum concentration of midazolam. The degree of inhibition of 3A4 enzyme varies among the macrolides. The reported frequency of interaction in descending order is erythromycin, clarithromycin, roxithromycin and azithromycin [3]. Olkkola, *et al.* [4] had demonstrated that sedation produced by single dose of midazolam was prolonged in patients receiving erythromycin. Hiller, *et al.* [5] had reported loss of consciousness following intravenous erythromycin administration due to interaction with oral midazolam administered.

As macrolides are prescribed in medical practice and these patients are likely to be seen by different practitioners for procedures requiring sedation, it is worth while to elicit clinical history and verify the drugs given before administering midazolam. This report illustrates the importance of avoiding midazolam for patients receiving erythromycin.

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