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Hypothermia from Azithromycin

To the Editor:

The clinical safety and tolerance of azithromycin for macrolide therapy of children is accepted.[1] Hypothermia in association with antibiotic therapy has been reported only in four cases of erythromycin treatment.[2-4] Seven other reports of hypothermia during erythromycin treatment are known to the World Health Organization, but details of the cases are not available for publication.[2] We report three pediatric cases of hypothermia that occurred during azithromycin treatment.

A 3.5-year-old girl with acute tonsillopharyngitis had a rectal temperature of 40°C. She received only azithromycin, 150 mg/d (10 mg/kg) in a single oral dose for three days. By the end of the treatment, the signs of tonsillopharyngitis had regressed but six hours after the third dose she became unresponsive and her skin was pale, cold and clammy. Rectal temperature was 34.4°C. On the fifth day after termination of azithromycin, rectal temperature became 36°C and the hypothermia and other symptoms disappeared.

In the second case, a 5-year-old girl had acute tonsillopharyngitis with a rectal temperature of 39.2°C. She received azithromycin, 200 mg/d as a single dose of an oral solution. She received no other medications. Twelve hours after the second dose her skin became pale and cold. Rectal temperature was 35°C. Azithromycin treatment was discontinued but hypothermia persisted for four days. At five days after discontinuation of treatment her rectal temperature was 36.5°C.

A 5-year-old boy was admitted to the hospital because of a rectal temperature of 39°C. He was diagnosed as having acute otitis media and azithromycin 200 mg/d was started as a single dose of oral solution (10 mg/kg/d). Twelve hours after the third dose, cold skin was noted and rectal temperature was 35.7°C. He had no symptom other than hypothermia. Over the next 24 hours his temperature returned to 37.5°C. Complete blood count, serum electrolytes, renal, liver, and thyroid function tests in all cases were normal.

Many drugs and toxins may interfere with normal thermoregulation and result in hypothermia. Clinical hypothermia relates to the membrane depressant effect resulting in ionic and electrical conduction disturbances in the brain, heart, peripheral nerves and other major organs. Although definitive attribution of the hypothermia of our cases to azithromycin is difficult, no other cause was evident.

The newly developed macrolides and macrolide-like antibiotics have safety profiles similar to those of the erythromycin derivatives.[5] It has been suggested that three day azithromycin therapy has a significantly lower risk of side effects and is less likely to be discontinued than standard antibiotic regimens used in the treatment of upper respiratory tract and skin infections in children.[1] In the literature the relationship between erythromycin and hypothermia as a consequence of central nervous system involvement has been suggested but there are no data concerning a possible cellular mechanism of

hypothermia in association with macrolides.[2-4,6]

The cases are considered important since hypothermia has not been previously related to azithromycin therapy even though the degrees of decrease in body temperature of our cases can not be defined as true hypothermia. Azithromycin may have an antipyretic effect resulting in a decreased body temperature in some patients; genetic susceptibility must also be considered. Further studies of the relationship between azithromycin and hypothermia seem indicated.

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