STUDY POPULATION. Forty-three children (mean age: 8.8 years) with a history of recurrent wheezing or asthma were enrolled when presenting to the emergency department of Children’s Medical Center (Dallas, TX) with an acute exacerbation of wheezing.

METHODS. Study participants were randomly assigned to receive oral clarithromycin or placebo for 5 days. All participants received systemic steroids for 5 to 6 days and aerosolized β agonists. On enrollment (visit 1), after 3 to 5 days (visit 2), and after 3 to 8 weeks (visit 3), children were clinically evaluated and respiratory samples (nasopharyngeal swab and aspirate) were obtained. Nasopharyngeal swabs were tested for *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. Nasopharyngeal aspirates were analyzed for cytokine and chemokine concentrations (tumor necrosis factor α [TNF-α], interferon γ, interleukin 1β [IL-1β], IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, granulocyte/macrophage colony-stimulating factor, regulated upon activation, normal T cells expressed and secreted [RANTES], eotaxin, macrophage inflammatory protein 1α, macrophage inflammatory protein 1β, and monocyte chemotactic protein 1). Serum was analyzed for cytokine concentrations (TNF-α, interferon γ, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, and granulocyte/macrophage colony-stimulating factor).

RESULTS. Evidence of *M pneumoniae* infection was found in 20 patients (48%), and *C pneumoniae* was found in 12 patients (28%). Nine patients had dual infection. No significant differences in nasopharyngeal aspirate or serum cytokine or chemokine concentrations were found between patients with evidence of *C pneumoniae* and/or *M pneumoniae* infection and those without evidence of infection before treatment with clarithromycin or placebo. No difference in asthma severity was found. No difference in resolution of symptoms was noted in patients treated with clarithromycin versus placebo. No correlation was identified between asthma severity and nasopharyngeal concentrations of cytokines and chemokines. Correlation was found between serum IL-10 concentration and asthma severity (P = .02). Nasopharyngeal concentrations of TNF-α, IL-1β, and IL-10 were significantly and persistently lower in children treated with clarithromycin compared with placebo. There tended to be a greater effect of clarithromycin on nasopharyngeal cytokine concentrations in patients with evidence of *M pneumoniae* or *C pneumoniae* infection. No significant differences were detected in serum cytokines.

CONCLUSIONS. Five days of clarithromycin therapy significantly decreased nasal concentrations of TNF-α, IL-1β, and IL-10 out to 3 to 8 weeks, indicating that macrolides may have a long-lasting effect on immune mediators beyond the time that therapy is completed.

REVIEWER COMMENTS. Clarithromycin is postulated to have immunomodulatory and antiinflammatory properties in addition to its antimicrobial activity. Clarithromycin had a greater effect diminishing cytokine concentrations in those children with evidence of *M pneumoniae* and/or *C pneumoniae* infection compared with those children without infection. However, in this small, short-term study, no obvious clinical improvement was seen with clarithromycin therapy, although half the children who presented with acute wheezing had evidence of atypical infection.

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The Use of Magnesium Sulfate in Acute Asthma: Rapid Uptake of Evidence in North American Emergency Departments


PURPOSE OF THE STUDY. Magnesium sulfate (MgSO₄) has been shown to be an effective acute bronchodilator in both children and adults with severe acute asthma, yet little is known about its actual clinical use.

STUDY POPULATION. Between 1997 and 2001, ~10 000 patients were enrolled onto observational asthma studies in the Multicenter Airway Research Collaboration, which is part of the Emergency Medicine Network (EMNet), a collaboration of 140 mostly academic medical institution emergency departments (EDs) in the United States and Canada. In 2001, a survey was conducted of all site investigators regarding MgSO₄ use in this patient group.

METHODS. At the time of the study, physicians were unaware of the study and did not use a particular protocol at each site. Chart review was conducted on patients 2 to 54 years of age who were currently having an asthma exacerbation. Patients were managed at the discretion of the treating physician, and cases in which intravenous MgSO₄ was used were identified. Pulmonary-function studies, usually peak expiratory flows (PEFs), were recorded as early during the ED evaluation as possible but were not attempted or recorded in all cases. The subsequent survey consisted of 2 parts: a preliminary survey of the use of intravenous MgSO₄ in the hospital and a second part regarding interest in research in this area.

RESULTS. From 10 169 ED visits, 9745 (96%) charts documented information regarding administration of MgSO₄ for the patients while in the ED. Of these, 240 (2.5%) patients received this drug. The use was 10 times higher among patients who were subsequently admitted versus nonadmitted patients. No specific data as to the number of children so treated were presented. Logistic regression identified several factors associated with MgSO₄ use:
increasing age, female gender, past history of intubation, duration of symptoms <24 hours, higher initial respiratory rate, low PEF or missing PEF data, and greater use of β agonists and systemic corticosteroids in the ED. In response to the survey, site leaders listed severity and failure to respond to initial β agonists as factors that would prompt MgSO₄ use. They disagreed with the use of MgSO₄ in all asthmatic patients in the ED. Site leaders also described far less use of this agent both prehospital and in the ICU.

CONCLUSIONS. Most ED physicians accept the efficacy of MgSO₄ in acute asthma, but its use remains relatively uncommon. In both practice and theory, these physicians seem to restrict its use to patients with severe acute asthma. Patterns of use will likely continue to evolve as knowledge of the efficacy and safety of MgSO₄ in acute asthma management disseminates.

REVIEWER COMMENTS. Because the use of MgSO₄ was so much higher in admitted patients, does this not beg the question as to whether it should be used even more aggressively in the ED and in the subsequently hospitalized child with status asthmaticus? Also, considering the apparent safety of MgSO₄ in either the intravenous or nebulized form, should this drug be part of the outpatient treatment protocol for the child with relatively severe bronchospasm who first presents in the office of the pediatrician or allergist?

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