Why do we give magnesium to kids with asthma exacerbations?

Ciarallo et al. Intravenous magnesium therapy for moderate to severe pediatric asthma: results of a randomized, placebo-controlled trial. J Pediatr 1996;129:809-14.

Take Home Message: Children having moderate to severe asthma exacerbations treated with intravenous magnesium in an emergency room had greater improvement in pulmonary function and a lower hospitalization rate compared to children treated with placebo.

Highlights: Prior to this trial, which was published by Ciarallo et al. in 1996[i], the use of magnesium had only been formally studied in adults with asthma. This was the first randomized, placebo-controlled trial evaluating the use of IV magnesium in children with asthma exacerbations. Children presenting to an urban academic emergency room with moderate to severe asthma (with a peak expiratory flow rate (PEFR) less than 60% predicted after receiving bronchodilators) were randomized to receive either 25 mg/kg of IV magnesium or placebo (normal saline). The children who received magnesium had significantly improved pulmonary function as compared to the children who received normal saline, as demonstrated by percent increases in PEFR, forced expiratory volume at 1 second (FEV1) and forced vital capacity (FVC). Additionally, the patients who received magnesium were more likely to be discharged home from the emergency room, though the decision to hospitalize patients was often made before entry into the study, so there may be a bias in favor of admission. There were no adverse effects from the magnesium.

Ciarallo et al. published a second study in 2000[ii] which compared a higher dose of magnesium (40 mg/kg) to placebo. This higher-dose magnesium group had similar trends in improvement in pulmonary function as did the lower-dose magnesium group from the first study; however, when the improvement between the two magnesium groups was compared, the higher-dose magnesium group had greater improvements in pulmonary

function than did the lower-dose magnesium group. These two studies helped lay the groundwork for intravenous magnesium of up to 40 mg/kg (with a maximum dose of 2 grams) becoming often standard-of-care in patients with moderate and severe asthma exacerbations.

The Nitty-Gritty:

- **Design:**
    - Randomized, double-blind, placebo-controlled trial
    - N= 31
        - Magnesium group (n=15)
        - Placebo group (n=16)
    - Setting: Boston Children's Hospital Emergency Room
    - Enrollment: 1993-1994
    - Primary outcome: change in pulmonary function
- **Population:**
    - **Inclusion Criteria:**
        - 6-18 years of age
        - Presenting to ED with an acute asthma exacerbation

- § PEFR < 60% of the predicted value after three nebulized albuterol treatments
- § IV access necessary for further medical management

- o **Exclusion Criteria**
  - § Body temperature > 38.5 degrees Celsius
  - § Systolic blood pressure less than 25th percentile for age
  - § Recent use of theophylline
  - § History of cardiac, renal, or pulmonary disease
  - § Pregnancy

- o **Baseline Characteristics –** data from magnesium group, no significant differences other than FEV1 as indicated
  - § Age: 10.8 +-3.6 years
  - § Male sex: 55%
  - § SaO2: 92.0+-3.7%
  - § RR: 35+-9
  - § PEFR: 143+-67 L/min

- § PEFR: 43.8+-13.6 % predicted
- § FEV1: 33.1+-11.4 % predicted (magnesium group) vs. 45.1+-12.2 % predicted (placebo group) (p=0.01)
- § FVC 41.8+-15.7
- § Systolic BP 120+-13 mm Hg
- § Baseline Mg 0.8+-0.1

- **Intervention**: Patients were randomized to receive magnesium sulfate (25 mg/kg, maximum 2 gm) or an equivalent volume of normal saline solution. Serial vital signs, physical examinations, pulse oximetry and results of pulmonary function studies were recorded at the start of the infusion, at 10 minutes, at the completion of the infusion (20 minutes) and then at 15-minute intervals for a total of 90 additional minutes. Albuterol was given as determined by the medical team

- **Outcomes:** comparisons are magnesium group vs. placebo groups
  - o **Primary outcome:** Change in pulmonary function
    - § Improvement in PEFR at:
      - 80 minutes after initiation of infusion: 46% vs. 16% (p=0.05)
      - 110 minutes: 59% vs. 20% (p=0.05)
    - § Improvement in FEV1 at:

- 80 minutes after initiation of infusion: 55% vs. 1% (p=0.01)
- 110 minutes: 75% vs. 5% (p=0.01)

- **Secondary outcomes:**
  - Rate of discharge home from the ED: 27% vs. 0% (p=0.03)
  - Duration of stay among patients admitted: no significant difference

- **Adverse Events:** none
- **Criticisms [iii]**
  - The study did not standardize the quantity or duration of care given in the ED before or after magnesium was given
  - Protocol depended on primary physician's assessment, but no objective data, that IV access was needed
  - FEV1 was significantly different at baseline between the two groups

[i] Ciarallo et al. Intravenous magnesium therapy for moderate to severe pediatric asthma: results of a randomized, placebo-controlled trial. J Pediatr 1996;129:809-14.

[ii] Ciarallo et al. Higher-dose intravenous magnesium therapy for children with moderate to severe acute asthma. Arch Pediatr Adolesc Med 2000;154:979-983.

[iii] Kattan M. Management of asthma: a continuing challenge. J Pediatr 1996;129:783-5.