Does magnesium sulfate have a role in the management of pediatric status asthmaticus?

Scenario
Jimmy was in the emergency department with his third severe asthma attack of the winter. He could tell he was going to be admitted... again. He was not improving much after one hour on continuous nebulized albuterol and intravenous steroids. The new pediatric registrar was running around asking for the magnesium. The senior consultant looked at him like he was a misplaced obstetrician. What evidence did he have to suggest magnesium might make Jimmy better and prevent admission?

Structured Clinical Question
In children with status asthmaticus, [patient] does acute administration of intravenous magnesium sulfate [intervention] reduce hospital admission rate? [outcome]

Search
Cochrane Database of Systematic Reviews - none with children (1). Medline - "magnesium" and "asthma" and "child" and [(double and blind) or placebo] - 4 pertinent trials in 18 hits. One additional meta-analysis was identified; hospital admission rate was not assessed as an outcome (2).

A further search conducted in July 2003 added three further studies on adults alone (see Summary Table 2) and no further trials in children.

Summary
Table 1

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Study type (level of evidence)</th>
<th>Outcome</th>
<th>Key Result</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Devi PR et al. 1997 (3)</td>
<td>47 children in ED with severe status asthmaticus</td>
<td>RCT (1b)</td>
<td>Admission to hospital</td>
<td>ARR 0.34 (95% CI 0.07, 0.61); NNT 3 (95% CI 2, 14)</td>
<td>0.2 cc/kg 50% MgSO4 given</td>
</tr>
<tr>
<td>Scarfone RJ et al. 2000 (4)</td>
<td>54 children in ED with moderate status asthmaticus</td>
<td>RCT (1b)</td>
<td>Admission to hospital</td>
<td>ARR 0.07 (95% CI –0.2, 0.34), NNT 14 (95% CI 3, ∞; NNH ∞ to 5)</td>
<td>75 mg/kg MgSO4 (max 2.5 gm)</td>
</tr>
<tr>
<td>Ciarallo L et al. 1996 (5)</td>
<td>31 children in ED with moderate-severe status asthmaticus</td>
<td>RCT (1b)</td>
<td>Admission to hospital</td>
<td>ARR 0.27 (95% CI 0.05, 0.49), NNT 4 (95% CI 2, 19)</td>
<td>25 mg/kg MgSO4 (max 2 gm)</td>
</tr>
</tbody>
</table>
Table 2

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Study type (level of evidence)</th>
<th>Outcome</th>
<th>Key Result</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silverman et al.</td>
<td>248 adults with FEV1 ≤ 30% predicted on ED arrival</td>
<td>RCT (1b)</td>
<td>FEV1</td>
<td>FEV1 mean difference 4.7% (95% CI 0.29 to 9.3%)</td>
<td>2 gm MgSO4 given; post-hoc: FEV1 ≤ 25% initially had better responses</td>
</tr>
<tr>
<td>Hughes et al.</td>
<td>52 adults in ED with FEV1 &lt; 50% predicted after salbutamol treatment</td>
<td>RCT (1b)</td>
<td>FEV1</td>
<td>FEV1 mean difference 0.37 liters (95% CI 0.13 to 0.61)*</td>
<td>151 mg MgSO4 nebulized with salbutamol Admission secondary endpoint</td>
</tr>
<tr>
<td>Bessmertny et al.</td>
<td>74 adults in ED with FEV1 40-80% predicted</td>
<td>RCT (1b)</td>
<td>FEV1</td>
<td>FEV1 mean difference 5% (95% CI –4 to 14%)</td>
<td>Three nebulized doses of 384 mg MgSO4 with albuterol at 20 min intervals</td>
</tr>
</tbody>
</table>

Commentary

Updating this topic report in July 2003 has added three adult studies which give consistent results with the previous report.

Three of these four studies of intravenous MgSO4 in pediatric ED patients with moderate-severe status asthmaticus showed significant reduction in hospitalization rates compared to controls. (A formal meta-analysis of these trials would give a better quality answer than to simply add up study numbers.) These patients had all already been treated with maximal inhaled beta-agonist therapy and corticosteroids. The rough similarly of the ARR in the three positive trials suggests a real and clinically significant improvement in an obvious clinical endpoint – hospitalization. MgSO4 is easy to administer, can be used in conjunction with other therapies, and appears to demonstrate a clinical effect within one to two hours.

The Cochrane review combines adults and children, was performed before two of the studies (the Scarfone and 2nd Ciarallo papers) noted above appeared, and did not separate out children in a subgroup analysis in terms of hospitalization rates. The other systematic review did not evaluate hospital admission as an outcome measure. Though difficult to compare
severity of patients across studies, all patients were “moderately to severely”
affected and very likely to require hospitalization. Furthermore, given the low
cost and lack of any side effects noted across the studies (of course it will
take thousands of patients studied to confidently conclude a drug is “safe”),
intravenous magnesium may be indicated in pediatric refractory status
asthmaticus. A formal systematic review of these studies is still needed.

Clinical bottom lines
1. Magnesium sulfate may reduce hospitalization rates of pediatric patients
   with severe status asthmaticus (NNT ~ 3)
2. The most severely affected patients stand to benefit the most; MgSO4
   should be considered in refractory patients with impending respiratory
   failure

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Citations:
1. Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr. Magnesium sulfate for
treating exacerbations of acute asthma in the emergency department. Cochrane Database Syst
2. Alter HJ, Koepsell TD, Hilty WM. Intravenous magnesium as an adjuvant in acute
3. Devi PR, Kumar L, Singhi SC, Prasad R, Singh M. Intravenous magnesium sulfate in acute
severe asthma not responding to conventional therapy. Indian Pediatr. 1997 May;34(5):389-
97.
4. Scarfone RJ, Loiselle JM, Joffe MD, Mull CC, Stiller S, Thompson K, Gracely EJ. A
randomized trial of magnesium in the emergency department treatment of children with
5. Ciarallo L, Sauer AH, Shannon MW. Intravenous magnesium therapy for moderate to severe
pediatric asthma: results of a randomized, placebo-controlled trial. J Pediatr. 1996
Dec;129(6):809-14.