Rebound symptoms in clinically isolated syndrome (CIS) or multiple sclerosis (MS) patients treated with intravenous methylprednisolone (IVMP) 1 g per day for 3 days vs. 1 g per day for 5 days.

A retrospective chart review.

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Introduction

Intravenous glucocorticoids have been used to treat MS exacerbations for the past 25 years. Although glucocorticoid use has not been found to have a long term benefit in MS, glucocorticoids have been found to accelerate recovery from MS exacerbations. The dosage and route of administration have been variable and there is weak evidence to support the use of a specific dose.

Numerous investigations have been undertaken to help determine the optimal dose of glucocorticoids in MS relapse treatment. In the optic neuritis treatment trial (ONTT), one study arm received IVMP 1 g/day for 3 days (250 mg every 6 hours) followed by a prednisone taper. This dose, compared to oral prednisone or placebo, was found to reduce the duration and severity of symptoms, but had no clear effect on long-term outcomes. The oral prednisone group rebounded more than the IVMP or the placebo groups suggesting that very low doses of prednisone may be insufficient or may even raise the risk of recurrent inflammation. A more recent study comparing IV and high dose (comparable to IV) oral glucocorticoids utilized a 5-day regimen and found similar clinical and MRI outcomes. Another study comparing IVMP 1 g/day for 5 days to a single 1 g dose demonstrated better recovery in the 5-day group. A small study of 31 patients comparing 500 mg/day for 5 days to 2 g/day for 5 days showed better MRI outcomes in the high dose group. Based upon the evidence, there is a suggestion that higher doses of glucocorticoids are more beneficial for clinical as well as MRI outcomes.

However, an optimal dose of glucocorticoids for the treatment of MS relapses is not established for the treatment of MS relapses. As glucocorticoids have numerous short and long-term side effects optimal dose needs to be established.

AIM

To investigate the occurrence of rebound neurological symptoms following treatment of a MS exacerbation with IVMP 1 g/day for 3 days vs. 1 g/day for 5 days.

Results

80 records were reviewed and 50 met inclusion criteria. 25 in each dosing group. All had a diagnosis of relapsing MS. There were no differences in the groups regarding age or the distribution of men and women. EDSS was slightly higher in the 5-day group. Disease duration was longer in the 3-day group.

A total of 7 patients out of the total of 50 experienced rebound symptoms. There were 4 patients in the 3-day IVMP group and 3 patients in the 5-day IVMP group who experienced rebound symptoms.

Logistic regression analyses revealed no difference in risk for having a rebound after 3 vs. 5 days of steroid therapy following the treatment of a relapse. Even when adjusting for age, sex, disease duration, EDSS and type of DMT. (p=0.51).^6

Conclusions

In this cohort of 50 RRMS patients there was no difference in the odds of having a rebound neurological symptoms after either three or five days of IV methylprednisolone. After adjusting for EDSS, sex, age, disease modifying treatment and disease duration, there were still no differences observed.

The results of this investigation are limited as this was a prospective and open label investigation with a small sample size. Overall, there were few individuals who experienced any rebound symptoms. Thus our ability to detect any differences was very limited.

However, IV methylprednisolone is a common treatment for MS exacerbations and little evidence regarding the optimal dose. Glucocorticoids have numerous short and long term side effects and thus it is important to determine the minimal effective dose. Additional investigation is warranted; ideally through a prospective, randomized clinical trial.

Population Characteristics

<table>
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<tr>
<th>Age (mean)</th>
<th>EDSS (mean)</th>
<th>Years Since Diagnosis (mean)</th>
<th>DMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>39.2 (20-54)</td>
<td>2.7 (1.0-6.0)</td>
<td>4.26 (0.5-30)</td>
<td>Glat acetate (GA)</td>
</tr>
<tr>
<td>36.8 (23-50)</td>
<td>3.2 (0-4.5)</td>
<td>5.71 (0.5-15)</td>
<td>IFN-beta 1a RM</td>
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<td>20 (80%)</td>
<td>2.0 (0-4.5)</td>
<td>2.0 (0-4.5)</td>
<td>IFN-beta 1a SC</td>
</tr>
<tr>
<td>20 (80%)</td>
<td>2.0 (0-4.5)</td>
<td>2.0 (0-4.5)</td>
<td>IFN-beta 1b SC</td>
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<td>20 (80%)</td>
<td>2.0 (0-4.5)</td>
<td>2.0 (0-4.5)</td>
<td>Natailizumab</td>
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<td>2.0 (0-4.5)</td>
<td>IFN-beta 1a IM-GA</td>
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<td>2.0 (0-4.5)</td>
<td>2.0 (0-4.5)</td>
<td>No DMT</td>
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</tbody>
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Bibliography


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