Treatment of Chronic Inflammatory Demyelinating Polyneuropathy With Pulsed Oral Steroids

Suraj Ashok Muley, MD; Praful Kelkar, MD; Gareth J. Parry, MD

Background: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune-mediated neuropathy that responds to various immunosuppressive treatments. Oral daily prednisone therapy is effective and inexpensive, but the long-term treatment that is usually necessary leads to serious adverse effects. Consequently, intravenous immunoglobulin and plasma exchange have been widely used to treat CIDP, making treatment expensive and inconvenient. A steroid regimen that reduces adverse effects but preserves efficacy would simplify treatment. Pulsed steroids have nongenomic actions not seen with low-dose steroids, including rapid inhibition of arachidonic acid release and of calcium and sodium cycling across plasma membranes of immune cells.

Objective: To study the efficacy, safety, and tolerability of pulsed oral methylprednisolone therapy in patients with CIDP.

Design: Open-label prospective study.

Setting: University of Minnesota Neuropathy Center, Minneapolis.

Patients: Ten patients (3 women and 7 men) with CIDP followed up for at least 22 months.

Main Outcome Measures: Neuromuscular score and Inflammatory Neuropathy Cause and Treatment (INCAT) disability score were used as outcome measures for efficacy; weight, blood pressure, changes in bone density, and steroid-related adverse effect questionnaire were used as outcome measures for safety.

Results: This steroid regimen leads to significant improvement in weakness and disability in all patients treated and to off-treatment remission in 60% of patients. Treatment was fairly well tolerated, and only 1 patient discontinued treatment because of adverse effects. Steroid-induced osteoporosis remained a problem, especially in older patients.

Conclusions: Pulsed oral methylprednisolone may be efficacious in the long-term treatment of CIDP and is relatively well tolerated. Remission can be induced in most patients, especially those with a shorter duration of disease.

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CHRONIC INFLAMMATORY demyelinating polyneuropathy (CIDP) is an immune-mediated neuropathy that can result in significant weakness, numbness, and sensory ataxia. In a study1 that followed up 53 patients for more than 7 years, only 2 recovered, 36 had mild to moderate disease, 6 were confined to a wheelchair or bed, and 6 died of the disease. Although treatment with prednisone is effective,2,3 the long-term treatment that is usually necessary leads to adverse effects.4 Consequently, intravenous immunoglobulin and plasma exchange (Plex) have been widely used, making treatment expensive and inconvenient. A steroid regimen that would preserve efficacy and improve tolerability would be convenient for patients and reduce the monumental cost of treatment. Preliminary studies indicate that treatment with pulsed oral dexamethasone5 and intravenous methylprednisolone6 is effective and reduces steroid-related adverse effects. Pulsed oral methylprednisolone, to our knowledge, has never been studied in CIDP. We report our experience in 10 patients with CIDP treated with pulsed oral methylprednisolone and followed up for a minimum of 22 months.

METHODS

An open-label prospective study was conducted in 10 (3 women and 7 men) patients with CIDP aged 22 to 84 years (mean [SD] age, 49 [16.27] years) treated with pulsed oral methylprednisolone at the University of Minnesota, Minneapolis. Duration of disease before treatment with pulsed oral methylprednisolone ranged from 2 months to 10 years. Four of the 10 patients were treated with intravenous immunoglobulin before enrollment into the study, but there was either no response to treatment or the response was short-lived, with significant intertreatment deterioration. One patient was treated with Plex and daily prednisone for a few weeks without a response. All

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Table 1. Clinical Characteristics of 10 Patients With CIDP

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y</th>
<th>Duration of Disease, mo</th>
<th>Baseline NMS</th>
<th>Baseline DS</th>
<th>3-mo NMS</th>
<th>Baseline NMS</th>
<th>1-y NMS</th>
<th>1-y DS</th>
<th>1-y NMS</th>
<th>1-y DS</th>
<th>2-y NMS</th>
<th>2-y DS</th>
<th>Time to Remission, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/54</td>
<td>12</td>
<td>106</td>
<td>Not available</td>
<td>111</td>
<td>119</td>
<td>0</td>
<td>120</td>
<td>0</td>
<td>14</td>
<td>NA</td>
<td>NA</td>
<td>26</td>
</tr>
<tr>
<td>2/F/49</td>
<td>3</td>
<td>87.5</td>
<td>7</td>
<td>119.5</td>
<td>120</td>
<td>3</td>
<td>120</td>
<td>0</td>
<td>14</td>
<td>NA</td>
<td>NA</td>
<td>14</td>
</tr>
<tr>
<td>3/M/84</td>
<td>10</td>
<td>100.5</td>
<td>5</td>
<td>106.5</td>
<td>113.5</td>
<td>2</td>
<td>111.5</td>
<td>4</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>4/M/46</td>
<td>72</td>
<td>118.5</td>
<td>1</td>
<td>118.5</td>
<td>119.5</td>
<td>0</td>
<td>115</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>29</td>
</tr>
<tr>
<td>5/M/54</td>
<td>4</td>
<td>93</td>
<td>6</td>
<td>118.5</td>
<td>120</td>
<td>0</td>
<td>120</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>29</td>
</tr>
<tr>
<td>6/M/58</td>
<td>120</td>
<td>104.5</td>
<td>5</td>
<td>111</td>
<td>116.5</td>
<td>1</td>
<td>114.5</td>
<td>3</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>29</td>
</tr>
<tr>
<td>7/M/41</td>
<td>2</td>
<td>120</td>
<td>Not available</td>
<td>120</td>
<td>120</td>
<td>0</td>
<td>120</td>
<td>0</td>
<td>27</td>
<td>NA</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>8/F/48</td>
<td>3</td>
<td>104</td>
<td>6</td>
<td>120</td>
<td>120</td>
<td>2</td>
<td>120</td>
<td>0</td>
<td>32</td>
<td>NA</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>9/M/22</td>
<td>3</td>
<td>107</td>
<td>3</td>
<td>109</td>
<td>120</td>
<td>0</td>
<td>119</td>
<td>0</td>
<td>34</td>
<td>NA</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>10/F/54</td>
<td>72</td>
<td>Not available</td>
<td>Not available</td>
<td>120</td>
<td>Stopped treatment early because of adverse effects</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; DS, disability score; NA, not applicable; NMS, neuromuscular score.

Table 2. Efficacy of Pulsed Oral Methylprednisolone Therapy in 10 Patients With CIDP at 1 and 2 Years

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (Range)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>1 y</td>
</tr>
<tr>
<td>Neuromuscular score</td>
<td>105.25 (93-120)</td>
<td>120 (113.5-120)</td>
</tr>
<tr>
<td>INCAT disability score</td>
<td>5 (1-7)</td>
<td>1 (0-3)</td>
</tr>
</tbody>
</table>

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; INCAT, Inflammatory Neuropathy Cause and Treatment.

RESULTS

One patient with a history of heartburn developed gastritis and duodenal ulceration after administration of the first dose of pulsed oral methylprednisolone, and treatment was stopped. The remaining 9 patients were treated for at least 2 years or until remission was achieved (range, 14-34 months). The mean (SD) dose at 1 year was 316 (141) mg/wk (range, 100-500 mg/wk) and at 2 years was 175 (153) mg/wk (range, 0-500 mg/wk). Only dosage of patients receiving medication was included in the calculation. None of the 9 patients discontinued treatment because of a perception of inefficacy or adverse effects.

Six of 9 patients treated with pulsed oral methylprednisolone went into remission after a mean (SD) of 27 (7.04) months of treatment (range, 14-34 months), and remission was sustained for a mean (SD) of 29 (9) months (17, 18, 31, 31, 37, and 39 months). The mean (SD) duration of disease in patients who went into remission was 4.5 (3.72) months (2, 3, 3, 3, 4, and 12 months) and in whom remission could not be induced was 68.5 (45) months (10, 72, 72, and 120 months) (Table 1). None of the patients in whom remission was induced had relapsed at the time of this publication.

The median NMS at baseline was 105.25 (range, 93-120). Of the 8 patients with weakness, the NMS increased in 7 at 3 months and in 1 at 6 months. At 1 year, the NMS increased in all of the patients to a median of 120 (range, 113.5-120) (P = .01). At 2 years, the median NMS was 120, and it was either stable or improved to 120 in 5 of 9 patients; it declined by a median of 2 points (range, 1-4.5 points) in 4 of 9 patients (Table 2). In the 6 patients in remission, the NMS was 120, indicating no weakness.

The median DS improved from a baseline of 5 (range, 1-7) to 1 (range, 0-3) (P = .01) at 1 year in 6 of 7 patients.
year, without additional treatments. In the remaining
existing type 2 diabetes mellitus had a reduction in the
tus after 9 months of treatment. One patient with pre-
patients. One obese patient developed diabetes melli-
pressure from a baseline of 130/77 mm Hg to 132/80 mm Hg
change was noted at 2 years. Median weight at 2 years
Table 3. Safety of Pulsed Oral Methylprednisolone Therapy in 10 Patients With CIDP at 1 and 2 Years

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>1 y</th>
<th>2 y</th>
<th>Baseline vs 1 y</th>
<th>1 y vs 2 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, lb</td>
<td>190 (153-264)</td>
<td>215 (158-300)</td>
<td>219 (148-243)</td>
<td>.01</td>
<td>NS</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
<td>130 (101-142)</td>
<td>132 (123-146)</td>
<td>129 (101-142)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic</td>
<td>77 (67-94)</td>
<td>80 (72-86)</td>
<td>75.5 (62-85)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; NS, not significant.
SI conversion factor: To convert pounds to kilograms, multiply by 0.45.

Table 4. Adverse Effects of Pulsed Oral Methylprednisolone Therapy in 10 Patients With CIDP

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Patients, No.</th>
<th>Duration, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>9</td>
<td>1-2</td>
</tr>
<tr>
<td>Unpleasant taste</td>
<td>9</td>
<td>1-2</td>
</tr>
<tr>
<td>Mood changes</td>
<td>8</td>
<td>1-2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5</td>
<td>1-2</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>3</td>
<td>1-3</td>
</tr>
<tr>
<td>Skin thinning</td>
<td>3</td>
<td>Long-term</td>
</tr>
<tr>
<td>Mild edema</td>
<td>3</td>
<td>Intermittent</td>
</tr>
<tr>
<td>Dyspopsia</td>
<td>3</td>
<td>1-2</td>
</tr>
<tr>
<td>Heart burn</td>
<td>2</td>
<td>1-2, with first few doses</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2</td>
<td>1-2</td>
</tr>
<tr>
<td>Moon facies</td>
<td>1</td>
<td>Long-term</td>
</tr>
<tr>
<td>Rash</td>
<td>1</td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

Abbreviation: CIDP, chronic inflammatory demyelinating polyneuropathy.

One patient had worsening of preexisting depression.

for whom data were available; for 1 patient it was 0 at
baseline, and there was no change at 1 year. At 2 years,
the DS was 0 in 6 of 8 patients for whom data were avail-
able; it increased by 2 points in the other 2 patients
(Table 2). The DS in all 6 patients in remission was 0,
indicating no disability.

One of 4 patients previously treated with intrave-
nous immunoglobulin dropped out of the study be-
because of adverse effects, but all of the others responded
to pulsed oral methylprednisolone treatment. At 3 months,
the NMS increased from 106, 100.5, and 93 to 111, 106.5,
and 118.5, respectively. Remission ultimately occurred
in 2 of these 3 patients.

Median weight increased from a baseline of 190 lb
(range, 153-264 lb) to 215 lb (range, 158-300 lb) (to con-
vert pounds into kilograms, multiply by 0.45) at 1 year
(P = .01); the range of weight change was −3 lb to 36 lb
(−2% to 14%). No further statistically significant weight
change was noted at 2 years. Median weight at 2 years
was 219 lb (range, 148-243 lb); range of weight change
compared with baseline was −31 lb to 29 lb (−12% to 15%)
(Table 3). There was no significant change in blood pres-
sure from a baseline of 130/77 mm Hg to 132/80 mm Hg
at 1 year and 129/75.5 mm Hg at 2 years (Table 3).

Glycated hemoglobin levels were available for 4
patients. One obese patient developed diabetes melli-
tus after 9 months of treatment. One patient with pre-
existing type 2 diabetes mellitus had a reduction in the
glycated hemoglobin level from 7.8% to 7.0% at 1
year, without additional treatments. In the remaining
2 patients, glycated hemoglobin levels were normal at
1 year.

Dual-energy x-ray absorptiometry revealed that bone
mineral density decreased significantly into the osteo-
porotic range in 5 of 9 patients across 3 years (1 point at
1 year, 2 points at 2 years, and 2 points at 3 years). The
median age of the 5 patients who developed osteoporosis
was 54 years (range, 41-84 years) and of the 4 pa-
tients who did not was 40 years (range, 22-49 years).

Most patients reported an unpleasant taste, insomnia,
mood change, and fatigue for 1 to 2 days after the
weekly treatment. No significant adverse effects were
noted during the remainder of the week. Moreover, the
adverse effects became milder with continued treat-
ment. Heartburn, blurred vision, ankle edema, skin thin-
ing, moon facies, and rash were seen in a few patients
(Table 4). The treatment was generally well tolerated,
and although some patients experienced adverse ef-
teffects, they were short-lived, and none of the patients dis-
continued treatment because of adverse effects.

The results of this study suggest that pulsed oral meth-
ylprednisolone is efficacious in the long-term treatment
of CIDP. Compared with daily steroid treatment, the ad-
verse effects seem to be more acceptable to the patients.
Steroid-related osteoporosis remains a problem, espe-
cially in older patients, but it may be prevented using vari-
ous strategies.

Chronic inflammatory demyelinating polyneuropa-
thy responds to immunosuppressive treatments, such as
prednisone, intravenous immunoglobulin, and Plex.2,7-10
Treatment with daily prednisone is inexpensive and ef-
fective but is associated with long-term adverse effects.
Intravenous immunoglobulin and Plex are also effective
but are expensive, are inconvenient, and have uncom-
bined but potentially serious adverse effects. It has been
suggested that pulsed intravenous methylprednisolone6
and oral dexamethasone are efficacious and better tol-
ertated than is daily steroid treatment.2 There is increas-
ing evidence that pulsed steroids have nongenomic ac-
tions, not seen with lower-dose steroids, and may be more
effective in treating immune-mediated conditions. These
nongenomic actions occur within seconds to minutes and
include nonspecific inhibition of arachidonic acid re-
lease and of cationic transport across plasma mem-
branes of immune cells and perhaps specific actions
mediated through a membrane receptor. We, therefore, sought to investigate the long-term efficacy, tolerability, and safety of pulsed oral methylprednisolone treatment in patients with CIDP.

Our data suggest that pulsed oral methylprednisolone may be an effective long-term treatment for CIDP. Of the 10 patients who participated in this study, 1 dropped out because of adverse effects, but the NMS and DS improved in all of the other patients at 1 year. In general, onset of improvement was at least as early as 3 months in most patients and by 6 months in all patients treated.

The median NMS increased by 14% and DS by 80% at 1 year. In the trial comparing intravenous immunoglobulin with Plex, Neurological Disability Score-Weakness (NDS-W) increased by almost 50%. Other studies have reported a 52% and a 32% improvement with Plex and intravenous immunoglobulin, respectively. The smaller improvement in the present study could be related to a lower mean NMS at baseline (NMS=106) compared with an NDS-W of 63 and 73.3 in the other studies. Another possibility is that we used a wider weakness rating scale (0-5 Medical Research Council scale), with 0.5-point increments/ decrements as against the 1-, 2-, 3-, 4-point scale in NDS.

Remission was induced in 6 patients, 2 continued receiving low-dose pulsed oral methylprednisolone, 1 dropped out of the study because of adverse effects, and 1 died of unrelated causes. Duration of disease was shorter in patients in whom remission was induced, suggesting that early treatment may be important. Improvement in the 6 patients in remission was striking, without residual weakness or disability. Moreover, remission was sustained for 17 to 39 months, and at the time of this study none of the patients had relapsed. We did not find a relationship between the occurrence of remission and the age of the patient, absence of axon loss, or median nerve conduction velocity. One of 2 patients with significant axon loss and 4 of 5 patients with severe median motor conduction slowing went into remission.

Remission rates reported in the literature range from 4% to 73%, but they are difficult to compare with the present data because of adverse effects, and 1 died of unrelated causes. Duration of disease was shorter in patients in whom remission was induced, suggesting that early treatment may be important. Improvement in the 6 patients in remission was striking, without residual weakness or disability. Moreover, remission was sustained for 17 to 39 months, and at the time of this study none of the patients had relapsed. We did not find a relationship between the occurrence of remission and the age of the patient, absence of axon loss, or median nerve conduction velocity. One of 2 patients with significant axon loss and 4 of 5 patients with severe median motor conduction slowing went into remission.

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Financial Disclosure: None reported.

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4. Dyck PJ, O'Brein PC, Oviatt KF, et al. Prednisone improves chronic inflamma-
5. Dyck PJ, Lais AC, Ohta M, Bastron JA, Okazaki H, Groover RV. Chronic inflamma-


**Announcement**

**Trials Registration Required.** In concert with the International Committee of Medical Journal Editors (ICMJE), *Archives of Neurology* will require, as a condition of consideration for publication, registration of all trials in a public trials registry (such as http://ClinicalTrials.gov). Trials must be registered at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005. For trials that began enrollment before this date, registration will be required by September 13, 2005, before considering the trial for publication. The trial registration number should be supplied at the time of submission.

For details about this new policy, and for information on how the ICMJE defines a clinical trial, see the editorial by DeAngelis et al in the January issue of *Archives of Dermatology* (2005;141:76-77). Also see the Instructions to Authors on our Web site: www.archneurol.com.