Methylprednisolone May Improve Lumbosacral Radiculoplexus Neuropathy

P. James B. Dyck, Jane E. Norell, and Peter James Dyck

ABSTRACT: Objective: To report on an open trial of intravenous methylprednisolone (IV MP) in nondiabetic lumbosacral radiculoplexus neuropathy (LSRPN). Background: Lumbosacral radiculoplexus neuropathy is a subacute, unilateral or asymmetric syndrome of pain, weakness, and paresthesia of the lower extremity, which is attributed to ischemic injury from microvasculitis in lumbosacral roots, plexus, and nerves. Methods: Eleven nondiabetic patients with worsening LSRPN were treated – ten with infusions of IV MP (1 gm/wk) for 8 to 16 weeks and one with an equivalent dosage of oral prednisone. The main endpoints evaluated were: 1) the Neuropathy Impairment Score (NIS), and 2) the Neuropathy Symptoms and Change (NSC) scores. Results: The median age of our patients was 67 years, range 49 to 86 years. Seven patients were women. All 11 patients reported improvement during treatment – nine reported marked improvement. The median NIS improved from 42 points (range 9 to 106 points) before treatment, to 20 points (range 5 to 57 points) (p = 0.005) after treatment. Pain was completely resolved in four patients and much improved in seven. The change subscore and the severity subscore of the NSC were statistically significantly improved after treatment. Prior to treatment, all patients had significant weakness with six confined to wheelchairs and four using mechanical devices to aid in ambulation. After treatment, the weakness was markedly improved in nine patients; only one still required a wheelchair and six walked independently (p = 0.03). Conclusions: 1) In LSRPN, pain and neurological deficits improved (often dramatically) with IVMP treatment. 2) Although our results should be interpreted with caution since this trial is uncontrolled, IV MP may favorably affect the natural history of LSRPN. 3) The results are sufficiently promising to provide a rationale for prospective, sham controlled, double blind trials.

Among neuropathies, inflammatory varieties are common and include such disorders as acute inflammatory demyelinating polyneuropathy, chronic inflammatory demyelinating polyneuropathy, vasculitic neuropathies, and granulomatous neuropathies among others. Some of these conditions have been shown to respond favorably to immune modulating therapy. Response to immunotherapy may be recognized by amelioration of symptoms and impairments which persists for a period of time thereafter, (perhaps the typical response in CIDP) or by lessening the severity and duration of the disease (as in AIDP and perhaps also in nondiabetic lumbosacral radiculoplexus neuropathy (LSRPN) as discussed here).
Non-diabetic lumbosacral radiculoplexus neuropathy, first recognized in 1981, is a syndrome of unilateral or asymmetric lower-limb pain, weakness and paresthesia which occurs in patients without diabetes mellitus. Since then, only a few reports have been published. Bradley et al. reported ischemic injury and perivascular inflammatory cell cuffing in biopsies from six cases with increased sedimentation rates, three with and three without diabetes mellitus. Recently, we studied biopsied distal nerves from 47 LSRPN cases (some included in this report) and found evidence of ischemic injury and microvasculitis. We also found that although the condition tends to be monophasic, there is pronounced long-term morbidity in almost all patients.

In spite of this long-term morbidity, there is no proven treatment for LSRPN. There are reports of improvement with prednisone and intravenous immunoglobulin in a small number of patients. Here, we report on an open trial of intravenous methylprednisolone (IV MP) in 10 patients with LSRPN and the treatment of one LSRPN patient with an equivalent dose of oral prednisone.

**Materials and Methods**

**Patient selection**

Our 11 cases had subacute onset of pain, weakness, or paresthesia of one or both lower extremities and clinical and electromyographic characteristics in keeping with localization of the disease process to lumbosacral roots, plexuses, or nerves. For inclusion, patients had to show electromyographic abnormalities attributable to lesions in at least two peripheral nerves and in the distribution of at least two nerve roots. Cases were not included if their neuropathic disorder was explained by such structural lesions as tumor or compression, if they were clinically improving, if they had a history of diabetes mellitus, or their fasting blood sugars were in the diabetic range by American Diabetes Association criteria (fasting plasma glucose ≥126 mg/dL) (7.0 mmol/L). Also excluded were patients with systemic vasculitis or connective tissue diseases, Lyme disease, sarcoidosis, inherited tendency to pressure palsies, radiation neuropathy or other diagnoses that could explain the neurological deficit. Patients were selected irrespective of whether the clinical involvement was localized primarily to the buttock, hip, thigh, or leg. Patients were not excluded if they also developed some upper extremity symptoms or signs, but the most severely involved segment had to be in the lower extremities and the pattern had to be that of an asymmetric disorder, not that of a length-dependent polyneuropathy.

**Neuropathic evaluations**

The characteristics and distribution of the neuropathy were quantitated using the Neuropathy Impairment Score (NIS), which provides a single score of neuropathic impairment summatting muscle weakness, decrease of muscle stretch reflexes, and decreased sensation based on a standard evaluation of a fixed group of tests and corrected for age, gender, anthropometric features, and physical fitness. The score is designed to give a higher score for weakness than for sensory loss or reflex change. Neuropathic symptoms were evaluated by the Neuropathy Symptoms and Change (NSC) score. Included in the NSC are number of neuropathic symptoms (from 38), summated severity (graded 1 to 3 for each item of NSC) and summated change (symptoms after treatment compared to symptoms at baseline or a defined date) and graded as unchanged [0], better [1 to 3], or worse [–1 to –3] for each item of NSC. Also assessed were activities of living outcomes.

**Analysis**

Descriptive statistics were used to express results and to compare attributes between groups. For continuous measurements, we expressed results as medians and ranges and compared groups using Wilcoxon Rank Sum Tests. For dichotomous variables, we used Fisher’s Exact Test.

**Results**

**Characterization of the neuropathy**

The median age of the eleven LSRPN patients was 67 years, range 49 to 86 years. Four were men and seven were women. The characteristic symptoms were asymmetric lower limb pain, weakness and atrophy, and paresthesia. The different types of pain included aching or hurting, stabbing or electrical shock-like sensations, and burning. Excessive tenderness to touch (allodynia) was a prominent feature in many patients. In general, the disorder began with pain followed by weakness and followed a subacute course that had been progressive over months.

Two patients had unilateral disease whereas nine patients had bilateral disease. All patients’ disease began unilaterally or asymmetrically. One patient had predominant involvement in L2, L3, L4 segments, one in L4, S1 segments and nine in both. Four patients had mild upper-limb involvement, which were probably due to compressive neuropathies (three ulnar neuropathies at the elbow and one median neuropathy at the wrist). At initiation of this open trial, the symptoms and impairments of all patients were moderate or severe and static or worsening.

**Therapeutic treatment trial**

Of the 11 patients, ten received weekly infusions (1 gram/week) of IV MP for eight to 16 weeks. The other patient received an equivalent dosage of oral prednisone therapy. Four patients received multiple infusions during the first week of treatment.

Before the initiation of therapy, the neuropathy had been present for a median of 5.0 months (range 1.0 to 48.0 months). The median time of follow-up after initial evaluation was 3.8 months (range 1.8 to 10.1 months). Usually, patients were evaluated shortly after the end of the infusions to grade their response to treatment. Some patients were seen multiple times in follow-up (see Figure).

All eleven patients improved, sometimes dramatically during the treatment period. Nine of the eleven judged their improvement as marked. The median NIS before treatment was 42 points (range 9 to 106 points), whereas after treatment, the median NIS was 20 points (range 5 to 57 points) (p = 0.005, paired t test). In assessing the change in NIS scores of individual patients, all improved during treatment and five of 11 improved by at least 50 percent (Figure). Most of the improvement reflected improved measured weakness of lower limb muscles. Consequently the NIS lower limb (NIS [LL]) also improved dramatically. Before treatment, the median NIS (LL) was 40
We found that both conditions tend to start unilaterally but become bilateral, have substantial weight loss and are monophasic disorders. Nevertheless, patients with both LSRPN and DLSRPN are left with long-term impairments and morbidity due to pain and weakness and only a small minority feel that they have recovered years later. The main difference is the occurrence of diabetes mellitus in DLSRPN.

Little attention has been given to finding effective treatments for either DLSRPN or LSRPN. It may be that investigators have not sought treatment since the disorders are reported to have a favorable outcome and because they are monophasic. However, both DLSRSN and LSRPN are debilitating, painful, paralytic and protracted conditions for which efficacious treatment is needed. Treatment that could reduce the severity and duration of the symptoms and impairments would undoubtedly decrease the disability, which is usually severe and prolonged. Although most patients improve over time, most do not return to their pre-morbid baseline. Also, in our referral practice, LSRPN is not an uncommon diagnosis and is probably under recognized by most neurologists.

The data on treatment response of LSRPN are limited and variable. Bradley et al. reported that four of their six patients improved with prednisone. Awerbuch et al. reported that their one patient treated with prednisone did not improve. Verma et al. reported that two patients responded to high dose intravenous immunoglobulin. Triggs et al. reported that five patients improved with intravenous immunoglobulin. Although these data are encouraging, they are conducted on small groups of patients, are uncontrolled and the treatment response is not quantitated.

Here, we report our experience of an open trial of IV MP in treating LSRPN patients. Our studies were also uncontrolled but...
they involved a somewhat larger group of patients than previously reported and stereotyped treatments and quantitative endpoints were used. All patients had marked improvement in pain and many had complete resolution of pain. All had some degree of improvement of weakness and most had major improvement in weakness. The NIS score, the change scale of the NSC, and the severity scale of the NSC were statistically significantly improved after the treatment trial. More specifically, the NIS score and the change scale of the NSC improved in every case, and in half of the patients the improvement in the NIS was marked (see Figure). Patients were significantly less dependent on wheelchairs and aids in ambulating after treatment than they were before treatment. All patients reported deterioration before treatment and felt their improvement started shortly after initiation of IV MP therapy.

Although we think these results of treatment with IV MP in LSRPN are strongly suggestive of efficacy, we do believe that they are preliminary and not definitive. This was an open trial with no control patients. Furthermore, as mentioned above, LSRPN may improve spontaneously and so it is difficult to know how much of the improvement can be attributed to the treatment. However, the information available about natural history suggests that spontaneous improvement is usually slow and incomplete. In our series of long-term follow-up of LSRPN patients, only three of 42 patients had recovered back to baseline at a median of 35.5 months (range 5.0 to 198.5 months). It seems likely that the degree of improvement seen in our treated LSRPN patients exceeded spontaneous improvement for the following reasons: 1) improvement in pain and weakness began with initiation of treatment in all cases; 2) the improvement was often of a large magnitude; 3) all patients reported that their symptoms had been worsening for the preceding months (in a few cases, years) before treatment; and 4) all patients had improvement of pain and weakness at follow-up (and none were worse). Nonetheless, placebo-controlled, double blind, prospective studies will be needed to answer definitively whether IV MP is efficacious or not. However, our results are sufficiently promising to provide a rationale for such trials in LSRPN as we are presently conducting in DLSRPN.

ACKNOWLEDGEMENTS

We thank Mary Lou Hunziker and Carol Overland in the preparation of the manuscript.

This work was supported in part from grants received from the National Institute of Neurologic Disorders and Stroke (NS36797).

REFERENCES