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Treatment of chronic inflammatory demyelinating polyneuropathy with high dose intravenous methylprednisolone monthly for five years: 10-Year follow up

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ABSTRACT

Objective: Although various modalities of treatment of chronic inflammatory demyelinating polyradiculopathy (CIDP) there are not any treatment protocol agreed.
Materials and methods: We retrospectively evaluated the 20 CIDP patients (14 male, 6 female). Five patients were excluded from the study because they could not continue their treatments due to various problems during the treatment. The remaining 15 patients treated with monthly high dose intravenous methyl prednisolone for five years (IVMP) and followed up for 10 years.
Results: The mean age of the patients was 48.1 ± 14.6 years. The mean duration of disease was 6.8 ± 3.1 years. We were found statistically significant difference between the pre-treatment and sixth month modified Rankin scores ($p < 0.001$). Similarly, significant improvement was observed at the end of first, fourth and fifth years of treatment. Statistically significant difference was found between baseline and tenth year modified Rankin scores of 12 patients who were treated with only IVMP during 10 years follow-up.
Conclusion: Long-term monthly IVMP pulse therapy seems to be very effective in the treatment of CIDP.

1. Introduction

Chronic inflammatory demyelinating polypadiculopathy (CIDP) is a chronic, acquired, immune mediated condition affecting the peripheral nervous system and its' pathogenesis is incompletely understood including several humoral and cell-mediated mechanisms [1,2].

Various modalities of treatment such as immunomodulating drugs, intravenous immunoglobulin (IVIG), steroids and plasmapheresis have been used for the treatment of this disease [2]. Additionally, cyclophosphamide is used in patients who did not respond to IVIG, steroids or plasmapheresis [3]. Oral steroids have been used for a long time. It has been shown that steroids are effective in both chronic progressive cases and those with attacks [4]. There are some, though not many, studies on oral steroids, but there is very few study on intravenous methyl prednisolone (IVMP) [5].

In this study, we retrospectively evaluated the CIDP patients who were treated with monthly high dose IVMP for five years and were followed up them for 10 years in the Neurology Clinic of Dr. Lütfi Kırdar Kartal Research and Training Hospital from 1998 January to 2013 January. We examined disease history, clinical findings, treatment outcomes, adverse effects and complications.

2. Materials and methods

We retrospectively evaluated the clinical and laboratory findings of all 20 adult patients with a diagnosis of CIDP. Five patients were excluded from the study because they could not continue their treatments because of various problems during the treatment. They were followed up and evaluated in the Neurology Clinic of Dr. Lütfi Kırdar Kartal Research and Training Hospital from January 1998 to 2013 January.

Patients, who were diagnosed as CIDP according to clinical, electrophysiologic and nerve biopsy findings, were included in study. We used the diagnostic criteria of American Academy of Neurology

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Table 1
The demographical characteristics of patients dropped out from the study.

Patient no.	Age	Sex	mRS at start	Treatment	Treatment duration (Mo)	Cause of drop out
1	62	F	4	IVIG	5	Intolerable side effect (hypertension, intractable nausea)
2	38	M	2	IVIG	3	Moved to an other city
3	26	M	2	IVMP	5	Moved to an other city
4	29	F	1	IVMP	2	Pregnancy
5	27	M	2	IVMP	2	No response to treatment

IVIG: intravenous immunoglobulin, IVMP: intravenous methylprednisolone, mRS: modified Rankin score.

[6]. The diagnosis was based on clinical examination, laboratory findings, electrophysiologic examination and nerve biopsy. Electrophysiologic studies were performed on all patients including median and ulnar nerve sensorial-motor conduction studies in upper extremity; peroneal and posterior tibial nerve motor and sural nerve sensorial conduction studies in lower extremity. All patients had electrophysiological evidence of demyelination that met at least one set of diagnostic criteria for CIDP as proposed by the American Academy of Neurology [6–8]. Fulfilling one set of criteria was considered evidence for the presence of demyelinating polyneuropathy. The other causes that contributes the cause of demyelinating polineuropathy are excluded for example; neuropathies from an endocrinologic causes, hypovitaminosis, vitamin B12 deficiency, monoclonal gammopathies, toxic neuropathies and clinical or laboratory evidence of a hereditary demyelinating neuropathies. Consequently, the alternative ethiologic factors that cause demyelinating polineuropathies are eliminated from the study.

Routine blood analyses (hemogram, liver functions, renal functions, serum glucose, ions, thyroid functions, vitamin B12 and folic acid levels and sedimentation rate) and urinalysis were performed before the treatment. There was no abnormality in routine blood analyses of the patients prior to treatment. Only hemogram, liver functions, renal functions, serum glucose, ions, and urinalysis were performed before the subsequent monthly therapies. Diagnostic lumbar puncture was done patients who did not reject it. There were not any cells in the CSF of the four patients who underwent lumbar puncture. Protein level was slightly high in only two patients. We did nerve biopsy in 14 patients (10 sural, 4 peroneal). One patient did not give consent for biopsy. Typical segmentary demyelinating–remyelinating zones were detected in all the biopsies. In addition, signs of mononuclear inflammation were found in biopsies in six patients. We started treatment just after the biopsy.

All participants gave informed written consent before treatment. In the beginning, we gave an intravenous bolus dose of 1000 mg/day methyl prednisolone for ten 10 days. Then, we gave 1000 mg/day intravenous pulse prednisolone once every 4 weeks. Patients were treated for 5 years and they were followed up for 10 years. We did not treated patients with an other immunomodulatory treatment during IVMP treatment.

Modified Rankin Scale was used to evaluate the functional status of the patients. The scale runs from 0 to 6, running from the perfect health without symptoms to death. All patients underwent clinical examination and modified Rankin score was assessed prior to treatment and monthly thereafter. One point reduction in modified Rankin score was assessed as response to treatment and 1 point increase in modified Rankin score was assessed as relapse.

The correlations of age and pre-treatment disease duration with response to treatment were analyzed with Spearman correlation test. Modified Rankin scores before treatment, and 2, 6, 12, 48, 60 and 120 months after the beginning of treatment were analyzed with Repeated Measures test. Response to treatment and the relation between response to treatment and axonal degeneration were assessed by chi-square test.

3. Results

We had 20 patients (14 males and 6 females) with the diagnosis of CIDP. Sixteen patients had typical CIDP, 2 patients had pure motor CIDP and 2 patients had pure sensory CIDP. Five patients were excluded from the study. Three of the patients (2 male, 1 female) were treated with IVMP and 2 (1 male, 1 female) of them were treated with IVIG. Two patients moved two other cities. Other patients gave up treatment due to side effects like hypertension and intractable nausea (1 patient), pregnancy (1 patient) and no response to treatment (1 patient). These patients could not complete the 5-year treatment. That's why we did not evaluate these patients' findings. Table 1 shows the demographical characteristics, treatments and drop out causes of the patients, who were excluded from the study. Remaining 15 patients' data were evaluated.

The mean age of the patients was 48.1 ± 14.6 (median age: 52) years (males: 51.2 ± 4.8; females: 42 ± 5.6), mean time from the emergence of first symptoms to treatment was 1.9 years and mean modified Rankin score was 2.7 ± 0.5 at the start of treatment. Table 2 shows the age, sex, duration of disease, clinical findings, CIDP phenotype and of 15 patients.

The mean modified Rankin scores at the baseline, second and sixth month, first, fourth and fifth year of treatment were respectively 2.7 ± 0.5, 2 ± 0.8, 1.5 ± 0.5, 1.3 ± 0.5, 1.1 ± 0.3 and 0.5 ± 0.5. Statistically significant difference was found between the pre-treatment and second month modified Rankin scores ($p = 0.004$). Similarly, significant improvements were observed between pre-treatment and sixth month ($p = 0.000$), first ($p = 0.000$), fourth ($p = 0.000$) and fifth ($p = 0.000$) years modified Rankin scores too. Statistically significant difference was found between the modified Rankin scores at the end of first and fifth years treatment ($p = 0.001$). All patients' modified Rankin scores were improved at first and fifth year compared with baseline. Table 3 shows the modified Rankin scores and of 15 patients.

We did not treated patients, who did not have relapse after 5-year treatment, with immunomodulatory drugs between fifth and tenth years. The disease relapsed in six patients (%40) 9.5 ± 2.3 months after the cessation of treatment. 1000 mg IVMP was given again to these patients once every 4 weeks for one year. Tree patients responded to treatment. Monthly IV 800 mg/m^2 cyclophosphamide (CYC) was administered to three non-responding patients for 6 months. Two of them responded to CYC treatment. One patient, 66 year-old male, did not respond to the IVMP and CYC treatment and he was treated with 0.4 g/kg intravenous immunoglobulin (IVIG) 5 consecutive days and 0.4 g/kg every 4 weeks. He responded to this treatment and his treatment still continues. Table 4 shows the relapse, time to relapse, relapse treatments and CIDP disease activity status scores (CDAS).

The modified Rankin score after 10 years in the 12 patients who only received steroids during 10 years follow-up period, were 2.7 ± 0.5 at baseline, 0.6 ± 0.5 at fifth year and 0.3 ± 0.4 at tenth year. Statistically significant differences were found between baseline and fifth ($p = 0.02$) and tenth year ($p = 0.02$) modified Rankin scores of these 12 patients. No significant difference was found between the fifth and tenth year modified Rankin scores ($p = 0.1$). We could