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SHORT COMMUNICATION

EFFECT OF INTRAVENOUS IMMUNOGLOBULIN IN PATIENTS WITH POST-POLIO SYNDROME – AN UNCONTROLLED PILOT STUDY

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Objective: **To analyse changes in muscle strength, physical performance and quality of life during intravenous immunoglobulin (IVIg) treatment in patients with post-polio syndrome.**
Design: **Open clinical trial.**
Patients: **A total of 14 patients (6 women, 8 men; mean age 57 years, range 43–67 years) were included in the study.**
Intervention: **Treatment with 90 g IVIg (30 g daily for 3 days).**
Main outcome: **Muscle strength, measured with dynamic dynamometry, muscle function, by means of performing the 6-minute walk test, and quality of life, analysed by means of the SF-36 questionnaire, were performed before and after treatment.**
Results: **For quality of life there was a statistically significant improvement for all but one of the 8 multi-item scales of SF-36 when comparing data before and after treatment with IVIg. The multi-item scale most improved was Vitality. There was no significant increase in muscle strength and physical performance.**
Conclusion: **Data indicate that IVIg may have a clinically relevant effect, with an improvement in quality of life. The effect may be due to a decrease in an inflammatory process in the central nervous system, which earlier has been reported in patients with post-polio syndrome after IVIg treatment. Since a possible placebo effect cannot be ruled out, a randomized controlled study is needed.**

Key words: post-polio syndrome, quality of life, SF-36, physical performance, intravenous immunoglobulin.

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INTRODUCTION

The appearance of new or increased neuromuscular symptoms decades after acute poliomyelitis constitutes post-polio syndrome (PPS) (1). Clinically, it is characterized by progressive muscular weakness, disabling fatigue and pain and the diagnosis is based on the criteria given by Halstead & Rossi (2). In a neurophysiological study, Grimby et al. (3) demonstrated that muscle strength decreased by 9–15% during an 8-year follow-up period in 21 patients with PPS and there was evidence of an ongoing denervation/reinnervation process. Failing capacity to maintain large motor units resulting in an uncompensated loss of motor units and decrease in strength has been suggested to be the background to the decrease in muscle strength in PPS (1, 3).

One hypothesis for the background of the denervation is that of a persistent spinal cord inflammation with subsequent degeneration of anterior horn cells in the central nervous system (CNS). An increase in markers of inflammation and antibody response in the cerebrospinal fluid (CSF) has been reported, and, recently, Gonzalez et al. (4) demonstrated the presence of cytokines in the CSF of patients with PPS, indicating an inflammation in the CNS. The cytokine levels were almost the same as in patients with multiple sclerosis (MS), a known neuroinflammatory disorder. It was also shown that the cytokines could be downmodulated with intravenous immunoglobulin (IVIg) to an almost normal level (5).

The aim of this study was to evaluate the clinical effect of IVIg treatment in patients with PPS. Muscle strength, physical performance and quality of life were evaluated in patients with PPS before and after IVIg treatment. The cytokine levels in CSF of the patients have been published earlier (5).

MATERIAL AND METHODS

Patients

Fourteen patients (6 women and 8 men, mean age 57 years, range 43–67 years) with established PPS diagnosis according to Halstead & Rossi (2) were included in the study. All patients performed the 6-minute walk test (6MWT) and SF-36 while 13 of the patients performed muscle strength measurement. For demographic data see Table I. All patients were ambulatory since motor function was to be assessed and all had a body-mass index (BMI) of less than 28.

General design

This pilot study was designed as an open label study, in which the subjects were evaluated before and after treatment with a total of 90 g of IVIg administered during 3 consecutive days (30 g/day).

The evaluation consisted of muscle strength measurement by means of dynamic dynamometry in 2 muscle groups (quadriceps femoris and hamstrings) and physical performance by means of the 6-minute walk

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Table I. *Demographic data of the 14 patients with post-polio syndrome (PPS)*

Gender	Age (years)	Age when affected by acute polio (years)	Time between acute polio and PPS (years)	Time with PPS before treatment (years)
M	67	15	48	4
F	50	1	44	5
M	55	12	42	1
F	58	8	47	3
F	57	4	46	7
F	50	3	41	6
M	43	3	34	6
M	58	10	39	9
M	59	2	51	6
F	66	10	50	6
F†	69	7	49	14
M*	56	9	40	7
M*	47	4	36	7
M	64	16	38	10
M/F	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
8/6	57 (8)	7 (5)	51 (7)	7 (3)

*Peak torque 120°/second, total work 180°/second.
†No SF36 after 2 months.
M = male; F = female.

test (6MWT) performed before and 2 months after completed treatment. Quality of life was evaluated by means of the SF-36 health survey questionnaire performed pre-treatment and 2 months and 6 months after treatment.

Muscle strength measurement

The Biodex System 2 Dynamometer (Biodex Medical Systems, Shirley, NY, USA) was used. All measurements were performed on both legs. The weakest leg was taken into analysis. The anatomical axis of the knee was aligned with the axis of the dynamometer, and the distal aspect of the arm of the dynamometer was placed 2 cm proximal to the medial malleolus. The dynamometer seat-back was placed at 97°. The ankle was fastened to the dynamometer arm, and the chest, thigh and waist were fastened to the dynamometer seat with hook-and-loop tape stabilization straps to minimize extraneous movements. The measurement was performed during 5 repetitions of a combined extension/flexion movement pattern in a concentric isokinetic mode. Torque, speed and position analogue data were collected from the Biodex during all muscle performance measurements and digitized for storage and later analysis. The 2 parameters used were the peak torque (PT) (60°/second, for 2 patients 120°/second) and total work (TW) (120°/second, for 2 patients 180°/second) for both quadriceps femoris/hamstrings.

Physical performance

Physical performance was assessed by the 6MWT. The patients were asked to walk at their own preferred speed as far as they could for 6 minutes without any help or encouragement. The total distance was then measured and the time was registered if the subjects failed to complete the test.

SF-36 questionnaire

The standard Swedish version of the SF-36 questionnaire (6) was used. The SF-36 is grouped in 8 multi-item scales: Physical functioning (PF), Role limitations due to physical problems (RP), Bodily pain (BP), General health perceptions (GH), Vitality (VT), Social functioning (SF), Role limitations due to emotional problems (RE) and Mental health (MH).

The SF-36 is scored from 0 to 100, 0 indicating extreme problems and 100 indicating no problems. The obtained values were compared with a corresponding Swedish normative population data for the age group 55–64 years (6).

Statistical methods

Differences between muscle strength and 6MWT data before and 2 months after IVIg treatment were tested for significance with paired *t*-test. The Friedman non-parametric test (SPSS software) was used in order to evaluate statistically significant differences of SF-36 data obtained before and 2 and 6 months after the treatment.

RESULTS

There was no significant increase in muscle strength for PT and TW in the patients with PPS when values were compared before and 2 months after IVIg treatment (Table II). The increase in 6MWT from 321 metres (SD 175 metres) before the treatment to 347 metres (171 metres) after the treatment was not statistically significant (Table II).

A statistically significant improvement was found for all SF-36 sub-scales, with the exception of RE, when comparing values before with values 2 and 6 months after treatment (Fig. 1). The sub-scale with the highest increase was Vitality. In half of the SF-36 sub-scales there was a decrease in the values between the analysis 2 and 6 months after treatment. However, there was no statistically significant difference between mean values obtained 2 and 6 months after IVIg treatment for any of the sub-scales.

DISCUSSION

In earlier studies a cytokine increase, indicating an inflammatory process in the CNS of patients with PPS, has been demonstrated (4). The inflammatory process was down-modulated by means of treatment with IVIg (5). The results of the present study indicate a positive effect for quality of life mainly for sub-scales concerning well-being.

Fatigue, physical as well as mental, is a common complaint of patients with PPS (7). It leads to decreased well-being and to

Table II. *Muscle strength (n = 13) and physical performance (n = 14) before and 2 months after intravenous immunoglobulin treatment. Peak torque (PT) 60°/second and total work (TW) 120°/second (n = 11) and peak torque (PT) 120°/second and total work (TW) 180°/second (n = 2, see Table I).*

Muscle strength			Before Mean (SD)	2 months after Mean (SD)	*P*
Quadriceps femoris	PT	(Nm)	61 (48)	65 (45)	0.424
	TW	(J)	445 (332)	463 (323)	0.509
Hamstrings	PT	(Nm)	32 (22)	33 (21)	0.599
	TW	(J)	214 (189)	230 (170)	0.399
Physical performance 6MWT ($n = 14$)		(m)	321 (175)	347 (171)	0.083

Nm = Newtonmetre; J = Joule; m = metre; 6MWT = 6-minute walk test.

decreased participation in society with a decreased ability to function in a social context with consequences for family life and the ability to work. Thus, a positive treatment effect within this area is of great importance for this patient group.

The background for the increased cytokine levels and the role of IVIg is at the moment unclear. In animal experiments cytokines, i.e. tumour necrosis factor (TNF)α and interferon (IFN)γ have been shown to have a negative effect on α-motoneurones (9). Thus, the increased cytokine levels in the patients with PPS may be a part of a pathophysiological event leading to denervation of the remaining motor-units. In this respect, IVIg may thus have a neuroprotective effect in PPS.

Farbu et al. (10) reported a patient with PPS who had an increase in muscle strength and experienced less fatigue after IVIg treatment. It was interpreted as a stabilization of an autoimmune dysfunction. Furthermore, Farbu and collaborators (11) reported an effect on pain in 20 patients with PPS receiving IVIg or placebo. The data of this study corroborates the observations of Farbu et al. (11) and they point to that the pathogenesis or a part of the pathogenesis of PPS may be of an immunological character.

However, the possibility of a "learning" and/or placebo effect leading to improved physical performance cannot be disclosed by this study. It is obvious that the design of the present study has its shortcomings; however, we believe that the findings open the way for a double-blinded and placebo-controlled study to be carried out in order to establish a possible effect of IVIg. If the results of the present study are confirmed there would be the possibility to develop new and effective treatment strategies for PPS.

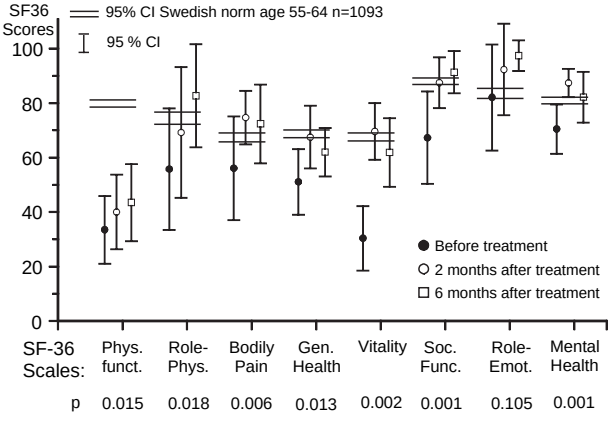

Fig. 1. Results of SF-36 before and after intravenous immunoglobulin treatment in the 14 subjects with PPS. *p*-values for statistically significant differences between values before and after (combined 2 and 6 months) treatment.

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