ORIGINAL REPORT

PATIENTS WITH NEUROMUSCULAR DISEASES BENEFIT FROM TREATMENT IN A WARM CLIMATE

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Objective: Several studies have shown positive effects of treatment of chronic diseases in a warm climate. The aim of this study was to evaluate the long-term effect of a 4-week rehabilitation programme in a warm climate for patients with neuromuscular diseases.

Design: A randomized controlled trial with a cross-over design. One period of intervention and one period of “life as usual”.

Patients: A total of 60 persons with a neuromuscular diagnosis.

Methods: Long-term effects were defined as changes in physical and psychological functions persisting after 3 months. Several scales were used according to the World Health Organization’s classification of functioning.

Results: A comparison of the changes in the 2 periods showed significantly better results for all primary outcome scales in favour of the intervention. Mean difference in changes in pain (VAS scale), 6-min walking test and “timed up and go” were 9.0 (SD 28.8) units, 52 (75) m and 1.0 (2.3) sec, *p* = 0.03, < 0.01 and 0.01, respectively. Median difference in changes in “Fatigue Severity Scale” and “Life Satisfaction Scale” were 0.4 (–0.5, 1.7) and 0.0 (0.0, 1.0), *p* = < 0.01 and 0.01, respectively.

Conclusion: This study shows positive long-term effects on different dimensions of health after a 4-week rehabilitation programme in a warm climate for patients with neuromuscular diseases. This effect might be due to the programme, the warm climate, or a combination of both.

Key words: neuromuscular disease, climate, rehabilitation, comparative study, treatment outcome.


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INTRODUCTION

The number of persons suffering from a neuromuscular disease in Norway is approximately 5000 (1–6). The heterogeneous group of neuromuscular diagnoses can be divided into 3 main groups; myopathies, where the disease is located in the muscle fibre or its energy metabolism, neuropathies (disease in the peripheral nerves), and neuromyopathies, where both the muscle fibres and the nerves are affected (1–6). There are hereditary, congenital neuromuscular diseases in all of these 3 main groups. The diagnoses are relatively slowly progressive (2, 3, 6). Even though neuromuscular disorders are a heterogenic group, both in terms of pathophysiology and clinical manifestations, it is possible to identify common impairments that influence quality of life and ability to cope with everyday living. Some of the common problems and complaints are muscle weakness of various severity, exercise intolerance, reduced endurance, fatigue, pain and problems with ambulation (1, 7, 8).

Many individuals with neuromuscular diseases have reported that staying in countries with a warm climate for a period, or following a rehabilitation programme in countries with a warm climate, has positive effects on their health. The reported effects have been on both a physical and a psychosocial level, including health-related quality of life and general well-being. In Norway there is a long tradition of sending patients to warmer climates for intensive physiotherapy. This health service was originally offered to patients with rheumatic diseases. A public report about this concept concludes that patients with other chronic, somatic diseases might also benefit from treatment in a warm climate (9).

Recommending treatment in a warm climate for various patient groups, especially persons with neuromuscular diseases, is controversial. Requests for such treatment from these patients themselves are increasing. This study was set up as a result of the claim that the effect of treatment in a warm climate should be evaluated thoroughly. The aim of this study was to evaluate whether treatment in a warmer climate had long-term effects on physical, psychological and social dimensions of health in persons with neuromuscular diseases. Long-term effects were defined as changes in physical and psychological functions persisting 3 months after intervention.

METHODS

This study was announced in 6 of Norway’s largest daily newspapers and in the Norwegian neuromuscular organization’s newsletter. Information about the study was also sent to the local groups of
the Norwegian neuromuscular organization and to the 2 university hospitals in Norway with special units for neuromuscular diseases (Rikshospitalet-Radiumhospital Medical Centre and University Hospital of North Norway).

The main inclusion criterion was a neuromuscular disease of hereditary, slowly progressive type, diagnosed by a neurologist. In addition, participants should be able to handle primary activities of daily living without assistance (10). Participants were recruited from persons who answered the announcement and met the inclusion criteria. Exclusion criteria were other medical conditions that could influence safe participation in the rehabilitation programme in a warm climate, such as serious cardiovascular disease, serious psychiatric conditions, and alcohol or drug addictions.

Use of a manual or powered wheelchair did not exclude persons from the study, but due to airline company restrictions the inclusion of persons with an absolute need for a powered wheelchair was limited.

A total of 99 persons applied to participate in the study. Of these, 67 met the inclusion criteria, and after a random draw 60 were invited to participate.

The study followed a cross-over design with 2 intervention periods (Fig. 1). The first period started (first baseline) in May 2003, with a 4-week intervention in June for half of the participants, and a re-test in October (3 months after intervention) for all participants. The second period started in May 2004 with a baseline test (second baseline), and intervention was offered to the other half of the patients. Again, all participants were re-tested in October. Participants selected for intervention in the first or second period were determined by randomization, after stratification on diagnosis and use of powered wheelchair. Randomization was performed after the first baseline examinations.

The intervention was performed at Reuma-Sol centre, a modern rehabilitation centre situated on the coast of Spain (Costa Blanca), with facilities such as gym and swimming pools. The climate in Spain during the intervention periods was mostly dry and sunny, with mean temperatures of 25°C. The rehabilitation programme at Reuma-Sol was specially organized for the intervention periods (2003 and 2004) of this study. The participants received a combination of individual and group therapy with low to moderate intensities regarding both strength and endurance training. Depending on the weather and temperature, the indoor or outdoor pools were used for daily training, both in groups and for individual self-training activities. Furthermore, the programme included classes in relaxation, group training in the gym and instruction in self-training. The participants were a heterogeneous group and, in order to be able to provide an adapted level of training, the group was divided into 3 training groups based on clinical evaluation of physical function by the physiotherapists. In addition, each person was prescribed an individually adapted training programme based on his or her functional level.

The participants attended daily training/treatment in the swimming pool (60 min) and daily group training in the gym (60 min). Individual physiotherapy was received on average 4 times a week. The organization of the daily programme gave the participants opportunity to recover, do exercise or take a walk on their own, according to their individual need. A physician and a physical therapist from Sunnaas Rehabilitation Hospital were responsible for a patient education programme.

The study period May to October includes the Norwegian summer. Norwegian climate during summer varies throughout the country. In northern Norway, the summer period is shorter and the temperature is lower than in the south, where the weather is more stable and dry. During this period in Norway the participants were told to “live as usual”, besides participating in the test procedures. Some of them had regular physiotherapy and/or pool training sessions or other physical activities, while others had no physical therapy or training.

The outcome measures were chosen due to the complexity of a clinical evaluation of patients with neuromuscular diseases, which requires that a large variety of physical and psychological symptoms and complaints are taken into consideration. They also aimed to cover the 3 levels of the World Health Organization (WHO)’s defined consequences of disease: body functions and structures, activities and participation (11). Based on the most common problems and previous findings during treatment in a warm climate for other patient groups, the following five primary outcome measures were chosen: for body functions and structures, pain registered on a visual analogue scale (VAS) (12) and Fatigue Severity Scale (13, 14); for activities, endurance (measured by a 6-minute walking test) (15, 16) and mobility/balance (measured by “timed up and go”) (17); and, for participation, Life Satisfaction Scale (18, 19), Secondary outcome measures were: Profile of Mood States (POMS) (20), Health-related problems (measured by Holger Ursin Inventorium) (21), Rivermead Mobility Index (15), and fast walking (measured by a 20-m walking test) (15, 16).

The participants were examined immediately before (week 0) and 3 months after ending the 4-week rehabilitation period (week 16). Long-term effects of intervention were defined as changes in physical and psychological function persisting 3 months after intervention.

Several of the outcome measure scales used in this study are based on numerical scales, and some are based on ordinal scales. Descriptive statistics for the ordinal scales are presented as median and quartiles, and the corresponding tests are non-parametric; Mann-Whitney U-test for unpaired data and Wilcoxon signed-rank test for paired data. Descriptive
the data from the cross-over study were analysed as described elsewhere (22: p. 467–471). No significant period or carry-over effects were found for the changes, and the analyses were therefore performed on the material as a whole, not regarding the order in which intervention was given. Paired t-tests and Wilcoxon test for paired samples were used to analyse the changes from baseline (May) to re-test (October), both for the intervention period and for the control period.

Paired t-tests and Wilcoxon test for paired samples were also used to compare the changes in the intervention period with the changes in the control period. The numbers reported in the results (p-values and confidence intervals (CI)) were not adjusted for multiple testing, as all tests represent comparisons of only 2 different settings (intervention and “life as usual”). However, the choice of 5 different primary measures still raises the question of adjustment due to multiple testing, and a Bonferroni-type approach was considered, with a correction factor of 5. Two-sample t-tests and Mann-Whitney U-tests were used to analyse gender differences. No other stratified analyses were performed. The computer program SPSS 12.0 was used for all analyses. A p-value less than 0.05 was considered statistically significant.

**Ethics**

The study was approved by the internal ethics committee at the Sunnaas Rehabilitation Hospital, University of Oslo, based on the fact that an all-identical study on patients with post-polio syndrome was approved by the Regional Ethics Committee of Eastern Norway the year before (23). All participants gave their written consent, and could withdraw by the Regional Ethics Committee of Eastern Norway the year before. The study was approved by the internal ethics committee at the Sunnaas Rehabilitation Hospital, University of Oslo, based on the fact that an all-identical study on patients with post-polio syndrome was approved by the Regional Ethics Committee of Eastern Norway the year before (23). All participants gave their written consent, and could withdraw by the Regional Ethics Committee of Eastern Norway the year before (23).

**RESULTS**

The study design, number of participants and drop-outs are shown in Fig. 1. There were some missing values because some participants only answered postal questionnaires and did not meet for physical testing. Due to drop-out and missing physical tests, the total numbers of measurements used in the analyses varied between 42 and 53. All participants followed the prescribed programme with only minor deviations, based on therapists’ statements.

Demographic factors and disease related factors, including diagnoses, are summarized in Table I. More women than men (38 vs 22) participated in the study. This does not reflect the gender distribution in the patient population. Although the participants were able to handle primary activities of daily living (ADL) without assistance, the median score on Sunnaas ADL Index (0–120) was 32.5. This indicates that the group had a considerable reduction in functional ability. Most of the participants were in need of orthopaedic devices and technical aids, and 20 persons had other diseases not related to their primary diagnosis. These were diseases that did not interfere substantially with the training, such as mild hypertension, allergy, asthma, diabetes mellitus and hyper/hypo-thyroidism. Hereditary motor and sensory neuropathy (HMSN) was the most frequent diagnosis among the participants (n = 3), twice as often as limb-girdle muscular dystrophy (n = 10) and myotonic dystrophy (n = 11). A small group of the participants were diagnosed with spinal muscular atrophy (n = 3).

Baseline data from the first test, before randomization, are shown in Table II. This table also gives descriptive statistics for changes in all outcome measures related to both intervention in Spain, and to a stay in Norway during summer. The effects of intervention, expressed as changes from baseline (week 0) to re-test 3 months after 1 month of intervention (week 16), showed improvement in all outcome measures, except for the

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<th>Table I. Patient characteristics. Mean and standard deviation (SD) are given for age, age at diagnosis and body mass index (BMI). Median and quartiles are given for activities of daily living (ADL) score</th>
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*BMI: weight / height².
status quo found in the Rivermead Mobility Index and life satisfaction. In contrast, long-term effects of being in Norway during the summer, expressed as changes in outcome measures from week 0 to week 16, showed mostly non-significant, but slightly negative, results. Life satisfaction represented the only significant outcome measure, with a negative change from week 0 to week 16.

Table II also shows differences between intervention and “life as usual” in Norway, expressed as changes from week 0 to week 16 in the 2 periods. The changes, summarized in means and medians are in favour of the intervention in warm climate for all outcome measures, except for the Rivermead Mobility Index, which did not show any significant change. No gender differences were found (data not shown).

All p-values and confidence intervals given in Table II are reported without adjustment for multiple testing. However, all significant p-values found in the primary measures in Table II, except for the overall difference in pain, would still have been significant if adjusted by a factor of 5.

DISCUSSION

This study shows positive long-term effects on physical function, health-related quality of life and general wellbeing following a 4-week rehabilitation programme in a warm climate for persons with neuromuscular diseases. Statistically significant improvements were found in the primary outcome measure for pain (VAS), endurance (6-min walking test (6MWT)), fatigue (Fatigue Severity Scale) and mobility (timed “up and go”) after a 4-week rehabilitation programme in a warm climate. Whether these improvements are clinically significant is debatable. In a study on acute pain in emergency medicine (24), the minimal clinically significant difference (MCSD) in VAS pain score is determined to be 12 mm (95% CI: 9–15 mm). This study concludes that the MCSD in VAS pain score does not differ with the severity of pain experienced. Another study of patients with both traumatic and non-traumatic pain found the MCSD in VAS pain score to be 9 mm (95% CI: 6–13 mm), and that the MCSD did not differ significant according to age, sex and cause of pain (25). Hence, our finding of a 9.0 mm (95% CI 0.9–17.1) mean difference between intervention (Spain) and Norway in change from baseline might be considered borderline clinically significant.

In the present study the mean baseline of the 6MWT was 387 m, and the mean difference for the intervention group was 38 m, which represents a 14% improvement. Other studies with 6MWT as the primary outcome measure differ in their definition of MCSD, from 30 and 56 m (26, 27). Enright (28) reports that a 12–40% mean improvement from baseline values has been published for various interventions.

In fact, some improvements attained in this study are on the border of clinical significance. Bearing in mind that these patients have neuromuscular diseases of a slowly progressive nature, this could be an interesting finding. If the improvements were artificially better results due only to the positive attention of being included in a study; the so-called Hawthorne effect (29), one should expect the same effect for both the Norway and Spain period.
Why should patients with neuromuscular diseases profit from treatment in a warm climate? It has been shown previously that persons with neuromuscular disorders may profit from regular physical training and treatment (30–33). However, when the physical training is carried out in a warm climate, a number of other factors are introduced that might also influence the result. Not only the higher temperature, but the contact with other people with the same problems, the change of environment, being far away from home and daily duties such as work and housework, and less limitations of physical activity might be of importance. This study did not control for these factors, thus one has to look upon the intervention as multifactorial. Two similar studies of training in a warm climate have shown a better effect of physiotherapy in a warm climate than in a cold climate for patients with neuromuscular diseases (34) and post-polio syndrome (23), respectively; although neither study was controlled for the additional factors related to a warm climate.

When isolating the different aspects of treatment in a warm climate is difficult, the interpretation of the mechanism of effect becomes complicated. The patients report that it is not only the structured training programme or the warm climate that is important, but the combination of these. Having time to recover after training/treatment was also thought to be important. Finally, the patients found it beneficial that the rehabilitation was provided for a group of patients with similar diagnosis. Many of the participants experience social isolation at home due to their physical limitations. To meet other people with the same types of diagnoses can be valuable in terms of handling the stress that may derive from loss of abilities regarded as valuable (35).

The questionnaire Life Satisfaction Scale did not show significantly improved quality of life 3 months after a 4-week rehabilitation period in Spain. This is in contrast to the impression based on the participants’ statements. A possible explanation may be that this questionnaire focuses on satisfaction with life in general and everyday life, and might not be sensitive to possible changes in aspects such as coping and self-esteem.

Many of the participants in the present study regularly followed physical training and treatment at home 1–2 times a week. Weekly training and treatment with a frequency of 1–2 times per week might have more effect on preserving functional level/maintaining function, while a continuous, co-ordinated training programme at an adapted level appears to be more useful for improving physical function.

In this study, long-term effect was defined as 3 months; after this no further follow-up was performed. Eleven months after intervention (second baseline) the gained effect was returned to the first baseline level. The fact that no carry-over effect was found is methodologically important when using cross-over design, and this indicates that the effect of the intervention vanishes before 11 months. Dahl et al. (34) reported an effect on the 6-min walking test 6 months after intervention for patients with neuromuscular disease. Strumse et al. (23) showed that effect on most outcomes persists 6 months after intervention in patients with post-polio syndrome.

When it comes to methodological considerations, there are some potential biases in our study: the fact that the participants self-selected into this study implicates a selected part of the total patient population. More women than men (38 vs 22) participated in the study, and since this does not reflect the gender distribution in this patient population, it might be a bias. Differences in the composition of the 2 groups comprise fewer problems in cross-over designs: all participants undergo the same intervention and it is the comparison between Norway and Spain that is interesting.

This study includes persons with different neuromuscular diseases. Ideally, one should study each diagnosis in isolation, but since each neuromuscular disease has a low prevalence, it is difficult to find enough patients for this purpose. However, as this study focuses on changes at the functional level, which is a common subject for these patients, it might be acceptable to merge different conditions.

A co-ordinated rehabilitation programme in a warm climate is considered a valuable complement to the existing programme for these patients. It is important that the basic medical and training services in national rehabilitation centres are available for all, and especially for those with contraindications to travelling abroad. Treatment in a warmer climate could be included in an individual rehabilitation plan, based on a recommendation from a specialist.

In conclusion, this study shows positive effects on different dimensions of health of at least 3 months’ duration following a 4-week rehabilitation programme in a warm climate for patients with neuromuscular diseases. However, the study does not show what part of the programme is the most effective. Treatment in a warm climate comprised 2 main aspects: intensive physical training/treatment and warm climate, but there were also a variety of confounding variables, such as being away from home, social contact, and being free from everyday duties, allowing the possibility of recovery after training. There is a need for future studies with a complementary design, such as a control group following an organized training/treatment programme in Norway and a group in a warm climate without intervention.

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