LONG-TERM PAIN, FATIGUE, AND IMPAIRMENT IN NEURALGIC AMYOTROPHY

Nens van Alfen, MD, PhD, Sieberen P. van der Werf, MSc, PhD, Baziel G. van Engelen, MD, PhD


OBJECTIVES: Recently, it has become clear that neuralgic amyotrophy (NA; idiopathic and hereditary brachial plexus neuropathy) has a less optimistic prognosis than usually assumed. To optimize treatment and management of these patients, one needs to know the residual symptoms and impairments they suffer. Therefore, the objective of this study was to describe the prevalence of pain, psychologic symptoms, fatigue, functional status, and quality of life in patients with NA.

SETTING: Neurology outpatient department of an academic teaching hospital.

PARTICIPANTS: NA patients (N=89) were studied, and clinical details were recorded. Self-report data were on average collected 2 years after the onset of the last NA episode.

MAIN OUTCOME MEASURES: Pain was assessed with the McGill Pain Questionnaire, fatigue with the Checklist Individual Strength, and psychologic distress with the Symptom Checklist 90. Functional status and handicap were assessed with the modified Rankin Scale and Medical Outcomes Study 36-Item Short-Form Health Survey.

RESULTS: Pain was usually localized in the right shoulder and upper arm, matching the clinical predilection site for paresis in NA. About a quarter to a third of the patients reported significant long-term pain and fatigue, and half to two thirds still experienced impairments in daily life. Over one third of the individual patients suffered from severe fatigue. The group did not fulfill the criteria of chronic fatigue or major psychologic distress. There was no correlation of pain or fatigue with the level of residual paresis on a Medical Research Council scale, but patients with a comorbid condition fared worse than patients without.

CONCLUSIONS: A significant number of NA patients suffer from persistent pain and fatigue, leading to impairment. Symptoms were not correlated with psychologic distress. This makes it likely that they are caused by residual shoulder or arm dysfunction but not as part of a chronic pain or fatigue syndrome in these patients.

KEY WORDS: Brachial plexus; Fatigue; Pain; Rehabilitation.

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From the Departments of Neurology (van Alfen, van Engelen), Medical Psychology (van der Werf), and Clinical Neurophysiology (van Alfen), Neuromuscular Centre Nijmegen, Donders Center for Neuroscience, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit on the authors or on any organization with which the authors are associated.

Reprint requests to Nens van Alfen, MD, PhD, Neuromuscular Centre Nijmegen, Dept of Neurology, 920 KNF, Donders Centre for Neuroscience, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands, e-mail: n.vanalfen@neuro.umcn.nl.

0003-9993/09/0003-0044$36.00/0
doi:10.1016/j.apmr.2008.08.216

List of Abbreviations

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<tr>
<td>CIS</td>
<td>Checklist Individual Strength</td>
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<td>HNA</td>
<td>hereditary neuralgic amyotrophy</td>
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<td>MPQ</td>
<td>McGill Pain Questionnaire</td>
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<td>NA</td>
<td>neuralgic amyotrophy</td>
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<td>PNS</td>
<td>peripheral nervous system</td>
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<td>QOL</td>
<td>quality of life</td>
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<td>RAND-36</td>
<td>RAND 36-Item Short-Form Health Survey</td>
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<td>SCL-90</td>
<td>Symptom Checklist-90</td>
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<td>VAS</td>
<td>visual analog scale</td>
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METHODS

Self-report data were collected from questionnaires in 87 patients (55 men) with idiopathic (n=65) or hereditary (n=22) neuralgic amyotrophy. Patients were consecutively recruited from our outpatient clinic during 2003 and had been diagnosed with NA if they met the criteria for the disorder or with high level of fatigue, a high level of concentration problems, low activity level, and some help with household activities. Costs were noted. The residual paresis or global strength on follow-up was defined as the mean of the Medical Research Council sum score of the affected muscles. Outcome variables of current physical and psychologic health status consisted of the following validated self-report questionnaires.

Pain

The MPQ was used for the assessment of the presence and distribution of pain. The main outcome measures were a VAS for the present pain intensity (VAS now) and one for the most (VAS max) pain experienced previously. In addition, the MPQ included a whole body outline to indicate the distribution of the patient’s pain.

Fatigue

The CIS is a 20-item questionnaire and measures the following 4 aspects of fatigue during the previous 2 weeks: fatigue severity (8 items; range, 8–56), concentration problems (5 items; range, 5–35), reduced motivation (4 items; range, 4–28), and reduced activity (3 items; range, 3–21). Each item was scored on a 7-point Likert scale. High scores indicate a high level of fatigue, a high level of concentration problems, low motivation, and low levels of physical activity. A CIS fatigue subscale score more than 35 indicates severe fatigue. The CIS questionnaire has good reliability and validity, including discriminative validity and has been used in studies with multiple sclerosis, stroke, and neuromuscular patients.

Psychologic Distress

The SCL-90 was used to measure psychologic distress. This scale is widely used, and the reliability and validity, including discriminative validity, are good. The scale consists of 90 items scored on a 5-point Likert scale and rates symptoms as anxiety, depression, sleeping problems, and somatization. The total score ranges from 90 to 450, with a mean SCL-90 total score ± SD of 118 ± 32 according to normative data for the general population in The Netherlands. Higher scores indicate more distress. To explore a relation between pain and fatigue with psychologic distress, we correlated the SCL-90 total score with both the CIS fatigue severity subscale and maximum VAS pain score in the week before evaluation.

Functional Status and Handicap

A modified Rankin score was obtained, which is a global functional index with an emphasis on physical disability. A Rankin score of 0 indicates no symptoms, 1 means no significant disability despite symptoms, 2 shows slight disability but still able to look after one’s own affairs without assistance, 3 indicates moderate disability and requiring some help, 4 indicates moderately severe disability requiring assistance when walking or attending to one’s own bodily needs, and 5 indicates severe disability requiring constant care. Patients were also asked to report any of the following 5 disabilities in daily life: difficulties writing, driving a car, personal hygiene, performing household activities, and sports.

Quality of Life

For assessment of the quality of life, the RAND-36 was used, which is a generic health status questionnaire with 36 items in the domains of physical functioning (10 items), role limitations due to physical dysfunction (4), role limitations due to emotional dysfunction (3), social functioning (2), body pain (2), mental health (5), vitality (4), general health perception (5), and change in health (scored separately). The score in each domain ranges from 0 to 100; a high score indicates better health or less bodily pain, and a score below 40 indicates a significant impairment.

Statistical Analysis

Data analyses were performed by using SPSS version 14. Numeric variables were compared with a Student t test or a nonparametric Mann-Whitney U test in case of a skewed distribution, and a chi-square test was used to compare categorical variables. Correlations for numeric variables were tested with a Pearson correlation test. P values less than .05 were regarded as statistically significant.

RESULTS

Clinical Data

Clinical variables were similar to those found earlier in the larger NA cohort, with a mean age at the time of evaluation of 44 years, a mean age of onset of 26 years in the HNA group, and a mean age of onset of 43 years in idiopathic neuralgic amyotrophy patients. The mean time between the onset of the last attack and the self-report evaluation was almost 2.5 years (135 weeks), with a median of 67 weeks (range, 1–1226 weeks). Ninety-one percent of the patients were right-handed, 6% left-handed, and 3% ambidextrous.

The mean number of attacks for the group as a whole was 2, and the median was 1 (range, 1–16); 8% of the patients had suffered more than 4 attacks at the time of evaluation. As could be expected, HNA patients had suffered more attacks on average (mean=3.7) than idiopathic neuralgic amyotrophy patients (mean=1.3). The residual paresis on follow-up and global strength on a Medical Research Council scale are shown in Table 1. In this study, no specific ascertainment of the amount of scapular instability was made.

<table>
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<tr>
<th>Mean Paresis/Strength From MRC Sum Score</th>
<th>Severe (≤3) (%)</th>
<th>Moderate (3 to ≤4) (%)</th>
<th>Mild (4 to ≤5) (%)</th>
<th>Full Recovery (5) (%)</th>
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</thead>
<tbody>
<tr>
<td>Overall</td>
<td>18</td>
<td>18</td>
<td>58</td>
<td>6</td>
</tr>
<tr>
<td>Idiopathic NA</td>
<td>17</td>
<td>16</td>
<td>59</td>
<td>8</td>
</tr>
<tr>
<td>Hereditary NA</td>
<td>21</td>
<td>26</td>
<td>53</td>
<td>0</td>
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Abbreviation: MRC, Medical Research Council.
Fifty percent of the patients had 1 or more comorbid conditions: 13% a previously lumbar herniated disk, 4% previous cervical degenerative pathology, 5% an allergic diathesis, 3% another autoimmune disorder, 4% diabetes mellitus, and 20% had other disorders (such as previous cerebrovascular disease, malignancy, rotator cuff pathology, alcohol abuse, Cushing disease; all isolated cases).

Twenty percent of the patients still used pain medication, 13% used a homoeopathic preparation, 9% acupuncture, and 4% some other form of alternative medicine. Physical therapy was given to 88% of the patients at the time of study, of whom 68% subjectively found it useful. Occupational therapy had been given to 28% of the patients, and 76% had found it useful. Thirty-two percent had been treated by a physiatrist, of whom 80% had found treatment useful.

Pain
Fifty-three patients completed the MPQ. Only 10% of the patients had no pain (VAS score 0) at all. For those who did have pain, the distribution in a body outline is shown in figure 1. The majority of patients reported pain in the right periscapular region. The mean present pain intensity on a VAS scale was 30mm (range, 0–95), with 13.2% having a score of 70mm or more (severe pain), 20.8% with a score of 4 or more but less than 7 (moderate pain), and 66% with a score of less than 4 (slight to no pain). The mean maximum VAS score in the week before the evaluation had been 56mm (median=71 mm; range, 0–100), with 52.8% of the patients scoring 70mm or more (severe pain), 13.2% scoring 4 or more but less than 7 (moderate pain), and 34% with scores less than 4 (slight to no pain). There was no statistically significant correlation of the maximum VAS pain score with the residual paresis or strength on follow-up defined in Medical Research Council categories, but patients with a comorbid condition were found to have a significantly higher mean maximum VAS score of 65 versus 43 in the group without comorbid disease ($P=.02$). A higher mean maximum VAS score was found in patients receiving physical therapy (61 in patients with vs 36 in patients without physical therapy), but this was not statistically significant ($P=.08$).

Fatigue
The CIS scores were available from all 89 patients. The mean overall CIS score was 66.9 (mean=69; range, 20–125), which is more than 1 SD above the mean score of healthy subjects (mean ± SD, 41.5±19.8) but well below the scores of patients with a chronic fatigue syndrome (mean ± SD, 113.1±14.6). The mean score on the CIS fatigue severity subscale for the group as a whole was 29.6 (median=32; range, 8–55), but 32 individual patients (37%) had a score greater than 35, indicating severe fatigue. There was no correlation between the CIS fatigue severity subscale and residual paresis or strength on follow-up, but again a significantly larger proportion of

Fig 1. The distribution of pain in a body outline.
patients with a score greater than 35 was found in the group suffering from a comorbid condition (21/42 vs 11/40 without a comorbid disease, P=.04).

**Psychologic Distress**

The mean SCL-90 total score of 53 patients was 127.2 (median=120; range, 90–241), which was within 1 SD of the mean SCL-90 total score (118.3±32.4) of the Dutch general population. There were 3 patients (6%) with a score exceeding more than 2 SDs of the population mean score. There was a relatively strong and significant positive correlation (r=.64, P<.001) between the SCL-90 total score and CIS fatigue score. Still, 11 (79%) of the 14 patients with severe fatigue fell within the normative population ranges of the SCL-90 total scores. No clinically meaningful correlation was found between the VAS pain score and the SCL-90 total score nor did we find higher SCL-90 total scores in the group with a comorbid condition. The same 3 patients with the SCL-90 total scores above 2 SDs also had the highest VAS scores and the highest CIS fatigue scores. This makes it likely that they are statistical outliers with unusually severe complaints that interacted on several symptom domains.

**Functional Status and Handicap**

From clinical history, the following disabilities were reported: 30 of 64 (47%) had difficulties with activities of daily life such as personal hygiene and grooming; 44 of 66 (67%) had difficulties in performing household tasks such as shopping, cooking, and cleaning; 27 of 63 (43%) had problems with writing; 23 of 48 (48%) had difficulty driving a car; and 39 of 64 (71%) had stopped their sports activities because of the symptoms after the NA attack(s). Women more often reported disabilities in activities of daily living (62.5% vs 37.5% of men, P=.05). Slightly more disabilities were found in the group with comorbid disorders, but the differences were not significant for any of the variables. A larger proportion of patients currently receiving physical therapy had more problems with writing than patients without (P=.02); no difference was found for the other abilities of daily life.

Forty percent of the patients in the productive age (18–65y) were unemployed because of their illness. More HNA (64%) than idiopathic neuralgic amyotrophy (31%) patients were unemployed (P=.04). Rankin scores of 82 HNA and idiopathic neuralgic amyotrophy patients can be found in table 2; there were no patients with a Rankin score of 4 or 5. There were more HNA patients (P=.03) and more women with a higher Rankin score (31% with Rankin 3 vs 19% of men, P=.001), but the Rankin score was similar for patients with or without a comorbid disorder. The Rankin score tended to be higher in patients currently receiving physical therapy (P=.07).

**Quality of Life**

RAND-36 mean subscale scores of the NA patients are displayed in figure 2. The mean scores of the subscales role limitations due to physical problems and health expectations exceeded the cutoff, whereas the other subscale scores fell within the normal range of the general population. The mean score on the role limitations due to physical problems subscale was lower in patients with a comorbid condition (21) than in patients without (37), but this difference was not statistically significant (P=.06). There was no difference in health expectations between these groups.

**DISCUSSION**

This study confirms that a significant proportion of neuralgic amyotrophy patients has persistent pain and fatigue in the first several years after their (last) attack. About a quarter to a third of the patients report significant persisting pain and fatigue, and half to two thirds still have disabilities in several personal grooming or household tasks and sports. A large proportion of the patients indicated some degree of working disability because of their NA-related problems. Patients suffering from comorbid conditions seem especially prone to developing persisting pain and fatigue and tended to have more disabilities and physical impairments in daily life. The percentage of patients with diabetes mellitus in our study population was equal to that in the general Dutch population (4%), which does not support a role for diabetes mellitus in triggering brachial plexus NA episodes even though diabetes is known to cause lumbosacral plexopathies in about 1% of the cases.

The majority of our patients did not fulfill the criteria of chronic fatigue or extreme levels of psychologic distress. Therefore, we hypothesize that the persistent pain and fatigue are caused by residual physical (ie, hardware) dysfunction and that even slight paresis and altered biomechanics of the shoulder girdle can lead to strain of the paretic and compensating muscles, in turn causing the persistent myalgia and fatigue.

Only recently, it has become clear that many neuromuscular disorders lead to pain and fatigue in a significant number of patients. In several studies of patients with muscular dystrophies, hereditary sensory motor neuropathies, and forms of motor neuron disease (with the noticeable exception of adult spinal muscular atrophy), pain was found to be present in around 60% to 80%. Severe fatigue was found on the CIS fatigue subscale in 61% to 74% of 598 patients with 3 different neuromuscular disorders and in 80% of the 113 patients with demyelinating immune-mediated neuropathies assessed with the Fatigue Severity Score. Many of these latter patients had normative severity or sensation. We also found no correlation between strength measured on a Medical Research Council scale and functional status, and this is corroborated by

![Fig 2. RAND-36 mean scores profile.](image)
the results of another study of 97 patients with hereditary and acquired polyneuropathies. These findings emphasize the fact that strength (or residual paresis) alone is not sufficient to estimate or predict the disability in patients with PNS disorders.

As for QOL, patients with a focal peripheral neuropathy caused by NA seem to fare better than patients with a generalized chronic polyneuropathy. In a QOL study among 90 patients with chronic idiopathic axonal polyneuropathy and hereditary sensory motor neuropathy, patients scored worse compared with the general population on 7 of the 8 domains of RAND-36. Our NA group did worse on only 2 of the RAND-36 subscales and turned out to be most impaired by the role limitations due to physical problems.

It is noteworthy that persisting pain in NA is mostly reported in the right shoulder and upper arm, which exactly matches the usual distribution of the initial paresis. This supports the hypothesized role of scapular and glenohumeral instability in maintaining these symptoms and might also explain the reported role limitations too. We hypothesize that pain itself is not the main impairment leading to physical disability but that pain is probably caused by physical strain to which the patients are more prone because of their persisting physical disabilities that are usually centered around the shoulder area. Further studies that include a measure of the amount of residual scapular instability in these patients are required to validate this hypothesis. In other neuromuscular disorders with clear prediction sites, a tendency has been found also for the persisting pain to be localized in areas that suffered the maximum paresis and strain during daily life, such as the legs and feet in hereditary sensory motor neuropathies and the shoulders, back, and buttocks in facioscapulohumeral dystrophy.

Many patients in this study still received physical therapy, and more pain, problems with writing, and a tendency for a higher Rankin score were found in this group. Unfortunately, our study does not allow for conclusions on whether physical therapy leads to more pain or whether patients who still have symptoms merely continue their physical therapy. Subjectively, the majority of patients found that they had profited from the therapies offered.

CONCLUSIONS

Most NA patients continue to have pain, disability, and reduced QOL 2 years after their acute illness, even though persistent pain and fatigue after NA do not deserve to be labeled as psychosomatic (ie, detached from a physical cause). Given the predominant location of pain and tenderness involving the scapular stabilizing muscles, they could potentially benefit from rehabilitation that addresses muscle weakness, imbalance, and adaptation to their disability, taking into account the patients’ limits of their residual physical impairments. This helps to prevent strain and minimizes the chance of excessive fatigue and musculoskeletal pain.

References