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Full Length Research Paper

Chronic idiopathic polyneuropathy: Patients' own perception of well-being in correlation to clinical condition

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Chronic idiopathic polyneuropathy (CIP) is a disease of the elderly where further follow-up is usually not indicated after diagnosis. The aim of the study was to evaluate the self-reported functioning and well-being in patients with CIP in correlation to clinical findings. We examined forty-eight patients with CIP. The Fatigue Severity Scale, Visual Analogue Scale for pain, Disability Rating Index, Berg Balance test and Medical Outcome Study 36-item short-form health status scale were correlated with clinical variables at long-term follow-up. Predominantly sensory symptoms and signs were found. Reduced balance and sensory function explained up to 31% of variance in self-reported physical impairment ($p < 0.0001$). Otherwise, self-reported functioning and well-being could not be explained by clinical symptoms. Sensory deficits and balance problems are typical in CIP, and reduced balance and sensory functioning partially explained impaired physical functioning and well-being. Further follow-up could be indicated to investigate the effect of specific training programs and whether other factors may contribute to impaired functioning and well-being as well.

Key words: Evaluation, functioning, polyneuropathy, well-being, outcome.

INTRODUCTION

Even after intensive investigation, the cause of peripheral neuropathy remains unclear in 10 to 40% (McLeod et al., 1984; Verghese et al., 2001). A slow axonal deterioration of sensory and motor or pure sensory function over years is typical for these patients. It is generally accepted to coin the disorder chronic idiopathic axonal polyneuropathy (Notermans et al., 1993; 1994; Wolfe et al., 1999; Vrancken et al., 2002; Hughes et al., 2004). The disease shows a male pre-dominance and seems to be a common hospital-referred polyneuropathy (McLeod et al., 1984; Wolfe et al., 1999; Vrancken et al., 2002; Teunissen et al., 2000; Mygland and Monstad, 2001; Rudolph and Farbu, 2007). Re-evaluation is often not recommended as no cause of the polyneuropathy is found after repeated follow-up investigation (Notermans et al., 1994; Jann et al., 2001).

As slow deterioration is typical, severe disability or ambulatory impairment are not common up to ten years after disease onset. Nevertheless, quality of life may be reduced at long-term follow-up (Notermans et al., 1994; Wolfe et al., 1999; Vrancken et al., 2002). It has been shown that physical, mental, emotional and social well-being seem to be impaired up to one decade after onset (Hughes et al., 2004; Teunissen et al., 2000; Erdmann et al., 2007; Rudolph et al., 2009).

Additionally, fatigue as an overwhelming sense of tiredness and lack of energy has recently been noticed in these patients, particularly in those with physical impairment (Erdmann et al., 2007; Rudolph et al., 2009).

CIP is a disease of the elderly, and the number of people affected is expected to increase in view of a growing aging population. As these patients usually do not undergo follow-up examinations it would be of interest, whether clinical symptoms, in particular sensory impairment, are indicative of the patients' own perception

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of daily function and health at long-term follow-up.

We therefore investigated CIP-patients' own perception of the disorder at long-term follow-up, by measuring the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) status, Fatigue Severity Score (FSS), Visual Analogue Scale (VAS) for pain and self reported disease progression in relationship to the clinical variables muscle strength, sensory dysfunction, disability and balance.

METHODS

Patients and controls

The patient records of the Stavanger University Hospital (SUH), South-Western Norway were screened for the diagnosis chronic idiopathic polyneuropathy (CIP) from January 2000 to July 2008. All patients were examined by a neurologist. Diagnostic guidelines were: (1) slowly progressive course of peripheral sensory and/or motor dysfunction over at least six months, (2) predominantly axonal pattern on neurophysiological studies and (3) etiology not found after investigation. In all, 84 patients with previously diagnosed CIP were identified. All patients were contacted by mail and asked for participation in the study. Sixty patients (response rate 71%) gave their signed informed consent to participate in a thorough follow-up investigation. Because three patients withdrew their consent shortly afterwards due to personal reasons, 57 patients underwent follow-up examination at the Outpatient Clinic of the Department of Neurology, SUH. A new evaluation of the polyneuropathy was performed in all 57 patients to exclude causes, which could have become apparent over time. The following investigations had to be normal: fasting serum glucose, HbA1C, full blood count, haemoglobin, liver-, kidney- and thyroid function tests, paraprotein screen, vitamin B12 and folic acid, alcohol abuse (no daily alcohol intake), family history of similar cases and exposure to toxins. None of the patients used medications contributing to polyneuropathy. If clinically indicated, CSF-examination, anti-GM1-, anti-MAG-antibodies, rheumatoid factor, anti-cyclic citrullinated peptide antibody, antinuclear antibodies, antineutrophil cytoplasmatic antibody, cryoglobulines, hepatitis C serology tests, erythrocyte sedimentation rate, anti-Hu-, anti-Yo-, anti-Ri-antibodies, x-ray of the lungs and abdominal ultrasound were performed to rule out possible underlying causes. After re-evaluation, patients with other diagnoses than CIP were excluded.

The study was approved by the Regional Norwegian Ethics Committee and was done in accordance with the Helsinki Declaration.

Evaluations of patients with previous CIP-diagnosis at follow-up

Clinical examination included manual muscle strength testing, tendon reflex testing, evaluation of light touch, pinprick, position sense, vibratory sensation, and balance testing. Medical Research Council (MRC) sum score, modified Inflammatory Cause and Treatment Group-sensory sum score (mISS) and Berg Balance Scale (BBS) were used. The MRC sum score is a generally accepted measurement of the Medical Research Council grades and ranges from 0 ("total paralysis") to 60 ("normal strength") (Kleyweg et al., 1991). The mISS summarizes light touch, pin prick, position sense and vibratory sensation in the arms and legs and ranges from 0 ("normal sensory deficit") to 64 ("maximum sensory deficit"). The BBS consists of 14 items in which the patients have to complete functional balance tasks, predominantly in standing position. Each item ranges from 0 ("most impaired balance") to 4 ("normal balance") with a total score ranging from 0-56 points. The BBS is a reliable and valid instrument (Berg et al., 1992). Good internal consistency has been described in patients with CIP (Erdmann et al., 2007). Additionally, we calculated disease related disability at first neurological presentation respectively by collecting previous information from the patient files, and at follow-up by using the Hughes Disability Grading Scale (0: no symptoms or signs; 1: minor symptoms or signs and capable of manual work; 2: walk without support but incapable of manual work; 3: walk with support; 4: bed bound; 5: ventilated). This scale has been used in patients with inflammatory polyneuropathies (Merkies et al., 2002).

After re-evaluation, patients with unchanged diagnosis of CIP received self-administered questionnaires for evaluation of self-reported fatigue, pain, functioning and well-being. The Fatigue Severity Scale (FSS) is a self-assessment nine-item questionnaire. The answers are ranging from `1` (no signs of fatigue) to `7` (disabling fatigue). Good internal consistency has been shown in CIP (Merkies et al., 1999). The Visual Analogue Scale (VAS) is a self-assessment linear scale to investigate pain. To allow assessment of pain, a 10 cm line was labelled at `0` (no pain) and `10` (worst pain). The VAS has been used in patients with immune-mediated polyneuropathies (Moulin et al., 1997). The Disability Rating Index (DRI) is an eleven-item questionnaire to evaluate self-reported functional status by performing complex tasks and tasks with the lower limbs. The answer to each question was marked on a visual analogue scale, ranging from `0` (no disabling) to `10` (worst disabling). A total mean score of all questions was calculated. The DRI has been described as an instrument of good responsiveness and acceptability for the assessment of disability caused by impairment of motor function in different populations (Salen et al., 1994). The Medical Outcome Study 36-item short-form health status scale (SF-36) is a self-administered questionnaire with 36 items, covering eight subscales of the health status. Four physical and four mental subscales are summarized in the dimensions physical (PCS) and mental compound summary score (MCS). A score between 0 and 100 is calculated. A higher score indicates a better state of health. The SF-36 has been used in CIP (Hughes et al., 2004). Self-reported disease progression was assessed by questioning the patients about deterioration (yes / no) of their condition after initial diagnosis prior to inclusion in the study. The clinical variables MRC, mISS, BBS and Hughes Disability Grading Scale were correlated with self-reported FSS, DRI, VAS and SF-36.

Statistics

The program SPSS 14.0 (SPSS Inc., Chicago, IL., USA) was used to statistical analyses. Descriptive statistics were used to describe the sample. For analysis of the explanatory variables strength (MRC sum score), sensory function (mISS), balance ability (BBS) and disability (Hughes score) on self reported well-being (SF-36), fatigue (FSS), Visual Analogue Scale (VAS) of pain, and self-reported disease progression we used univariate linear regression analysis; p-values ≤ 0.05 were considered statistically significant. The strength of the variables was shown as R^2, meaning the fraction of variance explained by the independent variable from the regression model.

RESULTS

Demographic and clinical characteristics at disease onset and follow-up in patients with confirmed CIP

In nine patients the possible causes were found after reinvestigation: probable hereditary origin (n=4),

Table 1. Demographic and clinical characteristics of patients with CIP after follow-up investigation. CIP = chronic idiopathic polyneuropathy.

Demographic variables and tests	CIP, n (%)
Total number	48
Gender	
Male	33 (69)
Female	15 (31)
Mean age at follow-up	
years ± SD	69.4 ± 8.9
Median disease duration at follow-up	
months ± SD	84.0 ± 59.5
Median disease duration after diagnosis	
Months ± SD	38.0 ± 44.3
Median Hughes disability grade at time of diagnosis ± SD	1.0 ± 0.3
Median Hughes disability grade at follow-up ± SD	1.0 ± 0.8
Self-reported disease progression after onset	
Yes	30 (63)
No	18 (37)
Self-reported pain at follow-up	
Yes	33 (69)
No	15 (31)
Neurophysiological pattern at time of diagnosis	
Sensory and motor axonal	32 (67)
Sensory and motor axonal > demyelinating	10 (21)
Sensory axonal	4 (8)
Sensory axonal > demyelinating	2 (4)
Median FSS-score + SD	4.7 + 1.6
Median DRI-score + SD	3.7 + 1.8
Median VAS-score + SD	4.0 + 2.3
Median MRC-score + SD	60.0 + 2.2
Median mISS-score + SD	11.0 + 7.3
Median BBS-score + SD	50.0 + 10.5

SD = standard deviation. FSS = Fatigue Severity Scale. DRI = Disability Rating Index. VAS = Visual Analogue Scale. MRC = Medical Research Council motor sum score. mISS = Inflammatory Cause and Treatment Group-sensory sum score. BBS = Berg Balance Scale.

increased fasting venous serum glucose levels (> 6.0 mmol/l < 7.5 mmol/l), and elevated HbA1C (> 6.0%) (n=3), indicating impaired glucose metabolism over time, monophasic chronic inflammatory demyelinating polyneuropathy (CIDP) with secondary axonal degeneration (n=1) and subacute combined degeneration due to alcohol abuse (n=1).

The basic characteristics of the 48 patients with confirmed CIP are shown in Table 1. Mean age at follow-up was 69.4 years (SD ± 8.9), and median disease duration at follow-up was 84 months (SD ± 59.5). Sixty nine percent were men. Median Hughes-score at first neurological presentation was 1.0 (SD ± 0.3) and axonal affection of both sensory and motor nerves was the most common neurophysiological finding (67%). Since the first neurological examination at median 38 months (SD ±

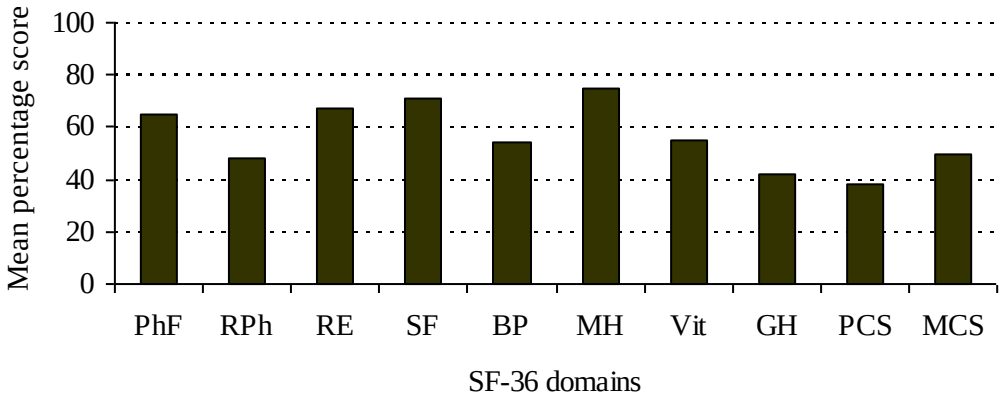

Figure 1. Short Form health survey 36 (SF-36) in patients with CIP (n = 42). Median SF-36 domains: PhF = physical functioning; RPh = role-physical; RE = role-emotional; SF = social functioning; BP = bodily pain; MH = mental health; Vit = vitality; GH = general health; PCS = physical component summary score; MCS = mental component summary score.

Table 2. Linear univariate regression analysis to show correlation between various clinical scales and patients self-reported variables.

Dependent variables	Independent variables			
	MRC	mISS	BBS	Hughes-score
Disability Rating Index (DRI)	0.11*	0.22**	0.31**	0.31**
Physical functioning	0.14*	0.17**	0.21**	0.17*
Physical compound summary score	ns	ns	0.11**	0.11**
Self-reported disease progression	ns	ns	ns	0.09*

MRC = Medical Research Council sum score. mISS = modified Inflammatory Cause and Treatment Group-sensory sum score. BBS = Berg Balance Scale. The strength of the variables was shown as R^2, meaning the fraction of variance explained by the independent variable from the regression model. All *p*-values are two-tailed; *$p < 0.05$; **$p < 0.01$.

44.3) previously, approximately two-thirds of the patients reported disease progression and pain at follow-up. Median MRC-score was 60.0 (SD ± 2.2), median mISS-score 11.0 (SD ± 7.3), median BBS-score 50.0 (SD ± 10.6), median FSS-score 4.7 (SD ± 1.6), median DRI-score 3.7 (SD ± 1.8) and median VAS-score 4.0 (SD ± 2.3). The median SF-36 scores are presented in Figure 1. The lowest scores were found in the physical compound summary score 37.6 (SD ± 10.5), general health 42.0 (SD ± 23.4) and role-physical 48.0 (SD ± 39.0). The highest score was found in the domain mental health 74.9 (SD ± 18.2).

Univariate regression analysis of impairment on functioning and well-being

In general, self-reported functioning and, to a lesser degree, physical well being correlated with the clinical scales, used in this study (Table 2). The strongest association was found for the BBS and Hughes-score, explaining 31% of the variance in self-reported functioning ($p < 0.0001$). The MRC was the weakest explanatory variable of self-reported functioning. The BBS was also the best explaining variable of the variance in physical well-being ($R^2 = 0.21$; $p < 0.0001$), followed by mISS, Hughes-score and MRC, explaining 14-17% of variance. The statistically strongest explanatory variables of the variance in the physical compound summary score were the BBS and Hughes-score ($R^2 = 0.11$; $p < 0.05$). The Hughes-score explained 9% of self reported disease progression, ($p < 0.01$). Variance in FSS, VAS, general health, social functioning, role-emotional, role-physical, vitality, bodily pain, mental health and self-reported pain could not be explained by the clinical scales.

DISCUSSION

The results of the current study indicate that CIP is a less disabling and predominantly sensory polyneuropathy seven years after onset. Clinical evaluation of disability, balance and sensory functions explained up to one-third of variance in self-reported functioning and to a lower degree in physical well-being. In line with previous results, we found that CIP seems to have a slowly

progressive course with predominantly sensory symptoms at long-term follow-up.

Impaired sensory functioning, particular vibration sense, is the most common finding at long-term follow-up and may lead to gait disturbances and functional disability (Notermans et al., 1993; Wolfe et al., 1999). In our study, only minor balance problems were typical, indicating that other factors e.g. pain and fatigue may contribute (Erdmann et al., 2007; Wolfe and Barohn, 1998). On the other side, our clinical experience is that CIP patients often complain about balance problems when walking. This raises the question whether we have used appropriate validated measurements for testing balance in patients with CIP. To our knowledge, there is no validated balance test specific for CIP. Validation of the BBS should therefore be investigated in patients with CIP. A more demanding balance test including dynamic motor tasks and balance training could maybe lead to better assessment and treatment of gait disturbances. The low frequency of disabling motor symptoms at long-term follow-up has also been reported from other studies (Notermans et al., 1993; Wolfe et al., 1999; Erdmann et al., 2007).

Our patients with CIP reported substantial fatigue, in line with other cohorts (Erdmann et al., 2007; Rudolph et al., 2009). As previously shown in Guillain Barré syndrome (GBS), our findings suggest, that fatigue is independent from muscle strength, sensory function and the Hughes score (Merkies et al., 1999; Rudolph et al., 2008). Axonal degeneration at long-term follow-up is typical in CIP and may also occur in GBS (Wolfe and Barohn, 1998; Dornonville and Jakobsen, 2005). Additionally, CIP-patients with higher physical impairment tend to be more fatigued (Erdmann et al., 2007; Rudolph et al., 2009). A hypothesis may therefore be that axonal degeneration leads to impaired physical activities, disability and decondition. It would be of interest to examine, whether fatigue in CIP can be counteracted by physical training as in inflammatory polyneuropathy (Erdmann et al., 2007; Garssen et al., 2004).

In our study, none of the variance in social functioning could be explained by clinical symptoms, which is in contrast to other studies, reporting that decreased social functioning could be explained by sensory functioning and fatigue (Hughes et al., 2004; Erdmann et al., 2007; Rudolph et al., 2009). Therefore, other factors related to decreased social functioning as for example anxiety and depression have to be considered.

About two-thirds of the patients reported disease progression after onset, whereas the Hughes-score tended to be unchanged at three and seven years follow-up. A reason may be that the Hughes-score is based on worsening of symptoms from minor to severe. Validation of a more sensitive instrument for measuring slight changes in disability could be recommended in this group of patients (Notermans et al., 1993; Wolfe et al., 1999).

Some limitations of the current study should be addressed. First, our patients were not compared to age-matched controls, raising the question whether our results are partially related to the ageing process. Sensory signs without clinical significant influence may be found in elderly healthy individuals (Vrancken et al., 2002). Hence, our sensory findings at follow-up have to be considered with some caution, in spite of the fact that all patients had clinical symptoms and Neurophysiological evidence of a polyneuropathy. When comparing our patients with a large Norwegian reference population with similar age, our patients were more fatigued and reported lower wellbeing on all SF-36 scales, indicating that age did not influenced our results to a considerable degree (Loge and Kaasa, 1998; Lerdal et al., 2005). Additionally, age did not seem to affect the course of CIP and we do not think that age significantly influenced symptoms, signs, and general health status at follow-up (Vrancken et al., 2002). Furthermore, results of self-reported measurements need to be interpreted cautiously, as patients self reports may be unreliable (Wechsler et al., 2011).

Conclusion

Despite a less disabling course of CIP, disability, balance and, particular, sensory function have a significant long-term impact on physical functioning and well-being. Further follow-up could be indicated to investigate the effect of specific training programs and whether other factors contribute to impaired functioning and well-being as well. Additionally, validation of scales to assess clinical symptoms and self-reported function will be helpful to give an appropriate description of patients` status.

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