



Health-related quality of life in patients with myotonic dystrophy type 1 and amyotrophic lateral sclerosis

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Abstract

The aim was to assess factors that might influence health-related quality of life (HRQoL) in patients with two different neuromuscular disorders – myotonic dystrophy type 1 (DM1) and amyotrophic lateral sclerosis (ALS).

A cross-sectional study was performed on 79 patients with DM1 and 74 with ALS. The HRQoL was evaluated by SF-36, Serbian version. Depressive and anxiety symptoms were assessed using the Hamilton rating scale for depression and the Hamilton rating scale for anxiety respectively. Severity of muscular involvement in DM1 was measured with MRC scale and severity of ALS with ALSFRS_r score.

The mean total score as well as all domain scores of SF-36 were similar in DM1 and ALS patients ($p > 0.05$), except that ALS patients experienced less bodily pain ($p < 0.05$). Depressiveness was found in 51% and marked anxiety in 38% of DM1 patients. Emotional status and severity of muscular involvement emerged as significant independent contributing factors to the total SF-36 in DM1 patients ($p < 0.05$). Only 3% of ALS patients showed depressiveness and 4% anxiety symptoms. The factors found to contribute to HRQoL in ALS patients were severity of disease and educational level of patients ($p < 0.05$).

We found significant percentage of potentially treatable emotional disturbances which together with severity of disease significantly contributed to HRQoL in DM1 patients. On the other hand, in ALS patients depressiveness and anxious symptoms were uncommon and the factors found to contribute to HRQoL were severity of disease and educational level.

Key words: Myotonic dystrophy type 1; amyotrophic lateral sclerosis; health-related quality of life.

Introduction

Health-related quality of life (HRQoL) measures obtained through patient-oriented tools are now con-

sidered essential in the evaluation of neurological diseases, especially in those that may affect the general health status of patients (1). Quality of life assessments contribute to a greater understanding of disease's consequences, the effects of its treatment and palliative care of patients (2). Despite these facts, it is striking that there is a relative paucity of work assessing quality of life in two or more different neurological disorders, comparatively. Identification of potentially treatable factors that might influence HRQoL in incurable neurological diseases is of major significance in palliative care.

DM1 is a hereditary, autosomal dominant disorder (3). It is a slowly progressive, but disabling and incurable multisystemic disease (3). Amyotrophic lateral sclerosis (ALS) is a fatal, neurodegenerative disorder of unknown etiology characterized by rapidly progressive loss of motor neurons (4). It is a fatal and incurable disease with a survival time less than 5 years (4).

Emotional disturbances might be expected in both these disorders either as an adaptive reaction to the threatening implications of the disease or as an effect of central nervous system lesions which have been reported in both disorders (5, 6).

The aim of this study was to assess factors that might influence self-reported HRQoL in patients with two different neuromuscular disorders - DM1 and ALS.

Patients and methods

A cross-sectional study was used to assess HRQoL in 153 patients consecutively recruited from the outpatient unit Department of Neuromuscular Disorders of The Institute of Neurology, Clinical Centre of Serbia in Belgrade in the period from September 2008 until May 2009 (Table 1). Patients

Table 1

Demographic, clinical and emotional characteristics of patient groups

	DM1 (n = 79)	ALS (n = 74)
sex (%) ^a		
male	52	61
female	48	39
age ^a (mean years $\pm$ SD)	45 $\pm$ 11	57 $\pm$ 11
marital status (%) ^a		
living together	54	81
single	46	19
education level (%) ^b		
without school	5	12
primary and craft school	35	26
high school	52	50
university degree	8	12
duration of disease ^a (mean months $\pm$ SD)	228 $\pm$ 108	29 $\pm$ 27
severity of disease	MRC score	ALSFRS _r
	15 $\pm$ 3	34 $\pm$ 8
Ham-D score ^a (mean $\pm$ SD)	16 $\pm$ 10	5 $\pm$ 4
Ham-A score ^a (mean $\pm$ SD)	15 $\pm$ 8	5 $\pm$ 3

^a $p < 0.05$

^b $p > 0.05$

with cognitive deficits or any other associated severe disease were excluded from the study. All patients gave their informed consent to participate in the study and the study was approved by the Ethical Board of The Institute of Neurology.

The first group was composed of 79 of 93 patients with adult onset DM1 originally admitted to our Institute during this period. In all patients the diagnosis was confirmed by gene analysis. Exclusion criterion was congenital or infantile form of DM1. The severity of muscular involvement in DM1 was measured by Medical Research Council (MRC) scale (7). In accordance to this scale, the strength of the most affected proximal and distal muscles of upper and lower limbs was scored on a 0-5 point scale. In addition, strength of facial muscles was scored on a 0-3 point scale (0 meaning Bell's phenomenon, 3 meaning full strength). The overall MRC score of 5 investigated regions reflected muscle strength in general (0 - 23 point scale). The mean MRC score in our group of DM1 patients was 15 $\pm$ 3 (Table 1).

The second group of analyzed patients was composed of 74 of 88 patients with probable or definite ALS (according to El-Escorial criteria) (8) originally admitted to our Institute during this period.

Exclusion criteria included diagnosis of ALS plus syndrome, inability of communication and usage of mechanic ventilation or gastrostomy tube. Functional impairment of ALS patients was measured by ALSFRS_r which is the most widely used functional rating scale in ALS with proven reliability and validity (9). The ALSFRS_r assesses limb, bulbar and respiratory function of patients with ALS. Maximum of 48 points on this scale reflects no functional impairment. In our series of ALS patients ALSFRS_r score was 34 $\pm$ 8 (Table 1).

The cross-sectional study was used to assess HRQoL in patients with DM1 and ALS. The HRQoL was evaluated by MOS 36-item short form health survey (SF-36), Serbian version (10), which is the most widely used patient-based health-related generic questionnaire (11). It is short and easy to complete. The SF-36 is a multi-item scale that assesses eight health concepts - limitations in physical activities (PF), limitations in usual role activities due to physical problems (RP), bodily pain (BP), general health perception (GH), vitality (VT), limitations in social activities (SF), limitations in usual role activities due to emotional problems (RE) and general mental health (MH). Each of eight domains is scored on a 0-100 scale, with a higher score indicating a better HRQoL. In addition, it is possible to calculate physical composite score (PCS) consisting of PF, RP, BP and GH domains, mental composite score (MCS) consisting of VT, SF, RE and MH domains, as well as total SF-36 score. All scores are given in a 0-100 point scale.

Depressive and anxious symptoms were assessed using the Hamilton rating scale for depression (Ham-D) 21-item version (12) and the Hamilton rating scale for anxiety (Ham-A) (13) respectively. Both rating scales were administered by a psychiatrist. For both scales, higher score indicated worse emotional functioning. Ham-D score above 17 indicated depressiveness (12) while Ham-A score above 18 indicated marked anxiety symptoms (13).

Normality was tested by the Kolmogorov-Smirnov test. To compare the two patients groups, Mann-Whitney U test, Student's t-test and chi square test were used, as appropriate. Correlations were calculated using Spearman's coefficient. Factors found to correlate with total SF-36 score were further analyzed by linear regression analysis (enter method) which assessed their contribution to the HRQoL. Significant testing was two-sided, with α set at 0.05.

Results

Demographic, clinical and emotional features of investigated patients are listed in Table 1. Significant

Table 2
Comparison of SF-36 mean score profiles in patients with DM1 and ALS

	DM1 (n = 79)	ALS (n = 74)	p value
PF	38 ± 29	32 ± 30	0.103
RP	22 ± 31	20 ± 32	0.551
BP	58 ± 29	67 ± 31	0.048
GH	34 ± 22	32 ± 18	0.975
VT	38 ± 25	38 ± 19	0.670
SF	56 ± 31	46 ± 29	0.069
RE	28 ± 40	23 ± 26	0.616
MH	53 ± 21	52 ± 20	0.917
PCS	38 ± 22	38 ± 19	0.660
MCS	41 ± 22	38 ± 18	0.695
total SF-36	41 ± 22	39 ± 19	0.888

difference in gender was observed between the two groups ($p < 0.05$), but no significant difference was found in educational level ($p > 0.05$). DM1 patients were significantly younger, more often single and with longer duration of disease in comparison to ALS patients ($p < 0.05$) (Table 1).

The two patient groups differed in both Ham-D and Ham-A scores (16 ± 10 and 15 ± 8 in DM1 patients vs. 5 ± 4 and 5 ± 3 in ALS patients, respectively) (Table 1). Significant depressiveness on Ham-D scale was observed in 51% of DM1 and just 3% of ALS patients. Marked anxiety symptoms were found in 38% of DM1 and 4% of ALS patients.

The mean total score as well as all domain scores of SF-36 were similar in DM1 and ALS patients ($p > 0.05$), except that ALS patients experienced less bodily pain than DM1 patients ($p < 0.05$) (Table 2).

The best subscores of SF-36 in both groups of patients were observed for BP, SF and MH, while the worst subscores were observed for RP and RE (Table 2). Furthermore, PCS did not differ from MCS in any of the groups ($p > 0.05$).

In DM1 patients all eight domains of SF-36 were inversely associated with age ($p < 0.05$), while gender and marital status were not in association with any of the scores ($p > 0.05$). Higher level of education was in association with better scores on all subscales of SF-36 in DM1 subjects ($p < 0.05$), except BP and MH ($p > 0.05$). Longer duration of DM1 and more severe muscular impairment (lower MRC score) were in correlation with worse results in SF-36 domains ($p < 0.05$). Both Ham-D and Ham-A scores correlated to all SF-36 domains ($p < 0.05$) (Table 3). We performed regression analysis for factors which significantly correlated with total SF-36 score. Because of the strong correlation between Ham-D and Ham-A scores ($r = 0.895$, $p < 0.05$), we formed new variable named emotional status by

adding these two values. In this way we avoided collinearity of independent variables. Emotional status was in significant correlation with total SF-36 score ($r = -0.732$, $p < 0.05$). Regression analysis showed that investigated factors (namely, age and educational level of patients, duration and severity of disease and emotional status) contributed to a significant percentage of variation of total SF-36 score (adjusted total $R^2 = 0.640$). Emotional status and severity of muscular involvement measured by MRC score emerged as significant independent contributing factors to the total SF-36 in DM1 patients ($\beta = -0.448$ and $\beta = +0.343$, respectively; $p < 0.05$) (Table 5).

Gender and marital status of ALS patients were not associated with scores on SF-36 ($p > 0.05$). Age of patients inversely correlated only with RP and BP ($p < 0.05$), while better level of education in ALS patients was in association with better BP, GH, SF, MH, PCS and total SF-36 scores ($p < 0.05$). Duration of disease did not correlate with HRQoL ($p > 0.05$), but ALSFRSr score was in a positive correlation with all domains of SF-36 ($p < 0.05$), except VT and RE ($p > 0.05$). Neither Ham-D nor Ham-A scores were in correlation with SF-36 domains ($p > 0.05$) (Table 4). We performed regression analysis for factors which significantly correlated with total SF-36 score (namely, severity of disease measured by ALS-FRSr score and level of education). This analysis showed that only 24% of variation of total SF-36 score was due to investigated factors and these two factors significantly contributed to HRQoL ($\beta = +0.405$ and $\beta = +0.237$, respectively; $p < 0.05$) (Table 5).

Discussion

Our findings that 51% of DM1 patients had depressiveness and 38% had marked anxiety symptoms are in accordance with a previous study (14). However, some authors stated that patients with DM1 rather present significant depressive or anxious symptoms than real emotional deficit (15). It still remains unclear if emotional disturbances found in DM1 patients reflect an adjustment to this progressively disabling condition (16) or represent consequences of well-known brain involvement in DM1 patients (5, 17).

In contrast, the presence of emotional dysfunction measured by Ham-D and Ham-A scales in our group of ALS patients was surprisingly rare, in spite of the devastating nature of the disease. We found that only 3% of ALS patients had significant depressiveness, similarly to one recent study which found depressed mood in 8.2% of examined ALS patients (18). Other

Table 3

Correlations between HRQoL and demographic, clinical and emotional characteristics of 79 patients with DM1 (q of Spearman)

	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS	total score
sex	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
age	-0.55*	-0.40*	-0.55*	-0.40*	-0.40*	-0.49*	-0.23*	-0.28*	-0.60*	-0.45*	-0.55*
marital status	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
education level	+0.23*	+0.32*	ns	+0.30*	+0.31*	+0.26*	+0.32*	ns	+0.29*	+0.36*	+0.33*
duration of disease	-0.38*	-0.30*	-0.34*	-0.37*	-0.36*	-0.41*	-0.39*	-0.24*	-0.44*	-0.46*	-0.46*
MRC score	+0.70*	+0.45*	+0.30*	+0.46*	+0.47*	+0.43*	+0.48*	+0.23*	+0.61*	+0.52*	+0.57*
Ham-D score	-0.49*	-0.42*	-0.55*	-0.61*	-0.58*	-0.62*	-0.38*	-0.72*	-0.65*	-0.71*	-0.69*
Ham-A score	-0.58*	-0.46*	-0.61*	-0.63*	-0.63*	-0.67*	-0.41*	-0.71*	-0.72*	-0.74*	-0.74*

* $p < 0.05$

ns = non significant.

Table 4

Correlations between HRQoL and demographic, clinical and emotional characteristics of 74 patients with ALS (q of Spearman)

	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS	total score
sex	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
age	ns	-0.24*	-0.26*	ns	ns	ns	ns	ns	ns	ns	ns
marital status	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
education level	ns	ns	+0.32*	+0.26*	ns	+0.23*	ns	+0.30*	+0.30*	ns	+0.30*
duration of disease	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
ALSFRS _r score	+0.49*	+0.31*	+0.31*	+0.26*	ns	+0.33*	ns	+0.23*	+0.46*	+0.35	+0.44*
Ham-D score	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
Ham-A score	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns

* $p < 0.05$

ns = non significant.

studies suggested that significant depressive symptoms were not inevitable or common in ALS patients and that most patients adjust to the stress associated with the illness at any stage (19). ALS patients earned the reputation of being bravely stoic because they focus on the psychosocial and spiritual domains instead on life areas dependent on physical functioning (20). There is little evidence that depressive symptoms increase in ALS as physical disability worsens, even during the terminal phase of the disease (21). Furthermore, one study showed the same level of depression in 20% of ALS patients expressing a wish to die as in the remaining 80% of patients (22). We speculate that the desire to hasten dying in the end-stage of the disease gives the patients a perception of better control of their disease thus improving their emotional functioning.

Our results showed that HRQoL was equally impaired in DM1 and ALS patients in all SF-36

domains, except BP. Data from literature revealed that all SF-36 scores of DM1 patients were lower than those of controls (14, 23), and that generic measures (SIP and SF-36) showed constant decrease in HRQoL of ALS patients over time (24). This is usually referred to the fact that SF-36 total score involves questions about functional activities which decline in ALS with the progression of disease, influencing total score (24). In accordance to this finding, other authors found impairment of HRQoL in ALS patients as well as decrease in time in physical but not in mental domains of SF-36 (24). Our study did not confirm this fact, but found an obvious decline in both PCS and MCS in ALS patients. Consistent to our findings, a recent study demonstrated that quality of life measured by Single Item McGill Quality of Life Scale does decline with advancing ALS (26).

The worst scores in both groups, as expected, were found for the roles domains (RP and RE).

Table 5

Contribution of investigated factors to the total SF-36 score in DM1 and ALS patients – linear regression analysis

independent variables:	dependent variable - total SF-36 score			
	DM1 (n = 79)		ALS (n = 74)	
	β	p value	β	p value
age	-0.163	0.068	/	/
education level	+0.133	0.082	+0.224	0.040
duration of disease	-0.044	0.603	/	/
severity of disease (MRC/ALSFRS _r)	+0.334	0.000	+0.437	0.000
emotional status	-0.448	0.000	/	/
Total R ² (adjusted)	0.640		0.244	

Significant difference between SF-36 subscores was found only for BP which is in accordance to the fact that pain is often cited as a problem in DM1 patients (3), but is not a common feature of ALS (27). However, BP was the domain with the best score in ALS as well as in DM1 patients. This finding indicates that the role of palliative care in pain relief is probably overestimated in DM1 patients.

Although social support is a factor that improves an individual's quality of life (28), our study did not find correlation between HRQoL and marital status of DM1 patients. We assume that they had adequate support from individuals other than spouse including family members (usually parents) and friends who compensate for the absence of spouse. This study showed that HRQoL of DM1 patients was associated with many factors, including educational level of patients, characteristics of the disease itself (duration and severity), and emotional functioning. These findings are in accordance to a previous study on a smaller number of patients (14). We further performed regression analysis which revealed that emotional status and severity of disease were factors that significantly contributed to HRQoL in DM1 patients. This finding suggests that treatment of emotional disturbances might improve quality of life in DM1 patients. It is of major importance for health care of DM1 patients because muscular impairment is still incurable.

In our ALS patients, the only demographic factor, contributing significantly to the better HRQoL was better education. This is not in accordance to the findings of a previous study (29) in which this association was not found. Moreover, severity of disease measured by ALSFRS_r was the most important factor that contributed to HRQoL in ALS patients. Some previous studies showed lack of correlation between quality of life and disease severity (30, 31), while other found significant association (32) or dif-

ferent results with different measures (24, 33). Other factors affecting quality of life of ALS patients have been identified, but only a few studies considered emotional disturbances (particularly depression) to be one of them (31). Our study found no correlation of Ham-D and Ham-A scores with HRQoL in ALS patients. Only 24% of variation of total SF-36 score in ALS patients could be accounted for with investigated factors. Therefore we should measure other factors that may contribute significantly to HRQoL in ALS such as religious and spiritual beliefs, cognitive impairment, social support (other than marital status), resilience, health locus of control, purpose in life etc. (2, 25, 26, 28). We also suggest that semi-structured questionnaires probably describe quality of life of ALS patients better than generic questionnaires. It is because of the frame-shift phenomenon, i.e. expectations and goals of patient change in association with the experienced reality (25). Thus, usage of semi-structured questionnaire probably will show correlation between emotional status and quality of life in ALS patients.

The main limitation in this study is its cross-sectional design. Long term follow-up of individuals affected with these two disorders will hopefully bring up more knowledge about HRQoL. We also could not guarantee the avoidance of selection bias.

Conclusions

The mean total score as well as all domain scores of SF-36 were similar in DM1 and ALS patients ($p > 0.05$), except that ALS patients experienced less bodily pain than DM1 patients.

We found significant percentage of potentially treatable emotional disturbances which together with severity of disease significantly contributed to HRQoL in DM1 patients. On the other hand, in ALS patients depressiveness and anxious symptoms were

uncommon and the factors found to contribute to HRQoL were severity of disease and educational level.

Further investigations should be undertaken in order to identify new possibly treatable factors that contribute to HRQoL in DM1 and especially ALS patients.

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