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Characteristics of Long-time Patients with Myasthenia Gravis in a Danish Population

The National Rehabilitation Centre for Neuromuscular Diseases, Denmark

Asger Frost: asfr@rcfm.dk

BACKGROUND

Thanks to advances in medical treatment, MG is no longer a life threatening disease but rather a chronic condition with almost normal life expectancy. About 2-3 years after onset of symptoms, the disease stabilizes with regard to progression and control of neurological symptoms (Grob 2008).

However, MG Patients in their active working age have an increased risk (> factor 5 compared to healthy controls) of losing their attachment to the labour market (LMA) two years after diagnosis (Frost 2016). Whether this is a permanent situation and whether other factors such as fatigue have a permanent impact on the patients daily life has not yet been answered.

AIM

The aim of this study was to gain information on long-term effects of MG from patients who have lived with MG for at least 24 month after time of diagnosis.

METHODS:

Patients diagnosed between 1997 and 2012 and in active working age (18-65 y) were invited to the study. Patients were excluded if they had not had a diagnosis of MG for at least 24 month.

A comprehensive questionnaire covering a variety of rehabilitation themes and factors was constructed. The themes were:

- Baseline characteristics: age at diagnosis, gender, sero logical profile,need of treatment with immunosuppressive agents, status on thymectomy, comorbidity, and status on attendance at MG specialized outpatient clinic
- Neurological characteristics: course of progression and remission, current treatment and refractory to treatment
- Impact on daily life: quality of life (WHOQOL-BREF), need for assistance and/or assistive devices, fatigue (Fatigue Severity Scale), labour market attachment (LMA) 12 month prior to diagnosis and at time of reply

The questionnaire was mailed to 143 RCFM-registered patients; 124 (86%) responded and returned the questionnaire. 93/124 respondents met the inclusion criteria and were eligible for analysis.

The respondents were divided into three groups according to how long the patients had lived with MG: Group I: > 24 and < 76 months (N=39); group II: ≥ 76 and < 126 months (N=35); group III: ≥ 128 and < 180 months (N= 19).

Based on register data from the Danish population of patients with MG in active working age, the MG population at RCFM is characterized by younger age (35.8Y vs 42.7 Y) fewer male patients (19.3% vs 39.4%) and *more patients treated with immunosuppressive agents* (65.9% vs 52.1%)) (not published data).

RESULTS

Baseline characteristics

The study population included 72 women and 21 men. Mean age at diagnosis was 36 years (15-61 y). The serological profile resembles populations in other studies with 78% of ARaB positive blood tests. Baseline data are illustrated in Table 1.

This MG population displayed a similar pattern of baseline characteristics across the three groups except for group no. III who had lived longest with MG, where more patients had been thymectomized and fewer had immunosuppressing medicine compared to the population as a whole.

30% of the respondents reported impact from comorbidity at the level of physical functioning in daily activity. For unknown reasons the comorbidity rate was higher in group II.

94% attended a specialized MG outpatient clinic.

Table 1: Baseline characteristics:	Grp. I >24<76 months with MG≥ year of diagnosis:2006-2012 N=39	Grp. II 77<128 months with MG≥128 year of diagnosis:2002-2006 N=35	Grp. III < 180 months with MG year of diagnosis: 1997-2002 N=19	Total n=93
Age at diagnosis - (SD)	16-61 y (13.8)	16-54 y (9.9)	15-52 y (11.5)	15-61 y (12.1)
Age at diagnosis - average	38,9 y	34,3 y	32,9 y	36,0 y
Age at diagnosis - median	34 y	35 y	29 y	35 y
Gender (male) no. (%)	12 (31)	6 (17)	3 (16)	21 (23)
Serologi: ARAb-positive no. (%)	30 (77)	28 (80)	15 (79)	73 (78)
Treatment with immunosuppressive agents no. (%)	27 (69)	22 (63)	8 (42)	57 (61)
Thymectomy surgery no. (%)	12 (31)	11 (31)	13 (68)	36 (39)
Comorbidity, affecting level of daily functioning no. (%)	14 (36)	19 (54)	7 (37)	40 (43)
Treatment with immunosuppressive agents no. (%)	27 (69)	22 (63)	8 (42)	57 (61)
Attachment to specialized outpatient clinics	39 (100)	31 (89)	17 (89)	87 (94)

Impact on daily life

Quality of life scored by WHOQOL-BREF are homogeneous on all 4 domains across the three groups. This may indicate that the course of disease is stable two years after diagnosis.

63% of the participants did not need assistance or assistive devices in their daily life e.g. for transportation.

Fatigue seemed to play at major role. 78 % of the study population had a score ≥ 4 on the FSS meaning that fatigue affects daily living, and 44% had scores ≥6 indicating they are severely affected by fatigue. Problems with fatigue do not seem to be improved related to length of time with MG. Table 2

Table 2: Impact on daily life	Grp. I	Grp. II	Grp. III	Total
Quality of life:				
QOL BREF - dom. 1 physical health	14.2	14.1	13.3	13.9
QOL BREF - dom. 2 psychological healt	14.2	14,0	13.4	13.8
QOL BREF - dom. 3 sociale relationships	14.7	14.8	13.5	14.5
QOL BREF - dom. 4 environtmental	13.8	13.6	13.6	13.7
Need of assistance, assistive devices				
Need of assistive devices or assistance: no. (%)	30 (77)	17 (49)	12 (63)	59 (63)
Need of assistive devices including transportation: no. (%)	9 (23)	12 (34)	7 (37)	28 (30)
Need of assistance: no. (%)	0 (0)	0 (0)	0 (0)	0 (0)
Combination of assistive divices and assistance: no. (%)	0 (0)	0 (0)	6 (32)	6 (7)
Fatigue:				
>5 and < 6 on the FSS: no. (%)	13 (33)	6 (17)	2 (11)	21 (23)
≥ 6 on the FSS: no. (%)	16 (41)	15 (43)	10 (53)	41 (44)
Not affected by fatigue: FSS < 4: no. (%)	10 (26)	7 (20)	3 (16)	20 (22)

Impact on labour market attachment

56 (60%) of 85 (91%) of the study population, who 12 months before diagnosis had a positive LMA cannot maintain this at time of reply. This is a similar tendency across the three groups.

Of the whose who were not able to maintain a positive LMA, 46% had part time jobs with payment supplements from the state, 33% had a full time disability pension, 20% were on sick leave etc. the majority of which was in group I. Table 3.

Table 3: Impact on labour market attachment	Grp. I 12 months before diagnosis	time at reply	Grp. II 12 months before diagnosis	time at reply	Grp. III 12 months before diagnosis	time at reply	Total 12 months before diagnosis	time at reply
Positive LMA:								
Employed/selfsupporting: no. (%)	28 (72)	8 (13)	20 (57)	10 (29)	13 (68)	5 (26)	61 (66)	23 (25)
Being educated: no. (%)	6 (15)	4 (10)	9 (26)	1 (3)	4 (21)	0 (0)	19 (20)	5 (5)
Unemployed: no. (%)	2 (5)	5 (13)	2 (6)	1 (3)	1 (5)	3 (16)	5 (5)	9 (10)
Negative LMA:								
Supplemented part time job: no. (%)	0 (0)	7 (18)	1 (3)	13 (37)	0 (0)	5 (26)	1 (1)	25 (27)
Disability pension: no. (%)	2 (5)	7 (18)	1 (3)	8 (23)	1 (5)	4 (21)	4 (4)	19 (20)
Early retirement: no. (%)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	3 (3)
Undecided/sick leave: no. (%)	0 (0)	6 (15)	1 (3)	2 (6)	0 (0)	1 (5)	1 (1)	9 (10)
At home with no income: no. (%)	1 (3)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	2 (2)	0 (0)

CONCLUSION

In this population of MG patients, neurological symptoms stabilize two years after time of diagnosis. Even though these MG patients attend a specialized MG outpatient clinics, rates of remission are favourable and only a few are in need of assistance or assistive devices, fatigue continues to affect daily life, and a large group of patients cannot maintain their labour market attachment after this period at neither short or long term.

This raises some central questions:

- Is this pattern of disease known in other MG populations or in other autoimmune diseases?
- How can symptoms of fatigue be addressed in settings of neurological outpatient clinics and perhaps diminished through possible treatment or rehabilitation services?

Neurological evaluation

58% of the respondents had no progression of neurological symptoms compared to the time of diagnosis; 30% had experienced a progression that included more than to muscle-groups.

69% had had remission within more than 2 affected muscles groups, and 10 % were in full remission of the neurological symptoms at the time of reply. The data indicates that neurological symptoms slightly deteriorates in relation to the time living with MG.

30% had remained on AchR esteraseinhibitor (AchREI) in mono therapy at an average dose of 252 mg/day, 45% receive a combination of AchREI and immunosuppressives agents with an average AchREI dosis of 571 mg/day.

39% were treated with azathioprine at an average dose of 140 mg/day; 20% were treated with corticosteroids at an average dose of 11mg/day.

32% of the study population is resistant to the general treatment regimen (AcHREI+Azathioprine+Corticosteroids) and are in need of other immunosuppressive agents or immunomodulating treatment (refractory group).

WHOQOL-BREF (The WHOQOL Group 1998)

- Has 26 items covering four domains: physical health (7 items), psychological health (6 items), social relationships (3 items) and environment (8 items). Two other items measure overall QoL and general health.
- Items are rated on a 5-point Likert scale.
- Mean score for each domain is calculated (min 4 – max 20)
- The higher score the higher perceived quality of life

Fatigue Severity Scale (Krupp 1989):

- Assesses the self-reported impact on fatigue on daily functioning
- Has nine items, each rated on a 7-point scale ranking from 1 = “strongly disagree” to 7 = “strongly agree”
- The FSS score is calculated as the mean of all item scores
- An FSS score ≥ 4 indicates that fatigue is a problem in daily life, a score of ≥ 5 indicates severe fatigue

REFERENCES: Grob D. et al. Lifetime course of Myasthenia Gravis. Muscle & Nerve 2008 (pp.141-149) Frost A. et al. Labour Market Participation and Sick leave among Patients diagnosed with Myasthenia Gravis in Denmark 1997-2011. BMC Neurology 2016 (16:224)