Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/pjnns

Original research article

The Myasthenia Gravis-specific Activities of Daily Living scale as a useful outcome measure and in routine clinical management in Polish patients

Izabela Monika Rozmilowska [a,*], *Monika Helena Adamczyk-Sowa* [a], *Damian Czyzewski* [b]

[a] *Department of Neurology in Zabrze, Medical University of Silesia, ul. 3-go Maja 13-15, Zabrze 41-800, Poland*
[b] *Department of Thoracic Surgery, Medical University of Silesia, ul. 3-go Maja 13-15, Zabrze 41-800, Poland*

ARTICLE INFO

Article history:
Received 14 June 2017
Accepted 28 December 2017
Available online 11 January 2018

Keywords:
Quality of life
MG-ADL
Myasthenia gravis
Polish population

ABSTRACT

Introduction: The Myasthenia Gravis-Activities of Daily Living scale (MG-ADL) is a short, and easy to use disease-specific quality of life during daily routine tool in myasthenia gravis.
Objectives: The purpose of our work was to evaluate neurological condition patients with myasthenia gravis using the form MG-ADL in order to enable the introduction in common use of an instrument which allows for the assessment of patients with myasthenia gravis.
Patients and Methods: The total number of 50 patients with MG were qualified for the examination. Each patient underwent neurological examination and completed the quality of life evaluation questionnaire MQ-ADL. Additionally, each patient was asked to evaluate the quality of his/her life by means of questionnaire MG-QOL 15 and MG Composite in Polish language version.
Results: Our analysis showed a positive correlation with other scales used - MG-QOL 15, MGFA, MG Composite. The intensification of neurological symptoms showed significant relation with obtained higher number of points in MG-ADL questionnaire. The MG-ADL was found to have high internal consistency, test–retest reliability, and concurrent validity.
Conclusion: We confirmed reliability and dependability of the questionnaire in the the test-retest assessment. The MG-ADL is accepted to be a reliable and valuable tool for measuring disease-specific QOL in Polish patients with MG.

1. Introduction

Myasthenia gravis (MG) is a complex nervous system disease; more precisely, it concerns the neuromuscular junction, and its pathomechanism has auto-immunological background. It is characterized by extensive muscular fatigue. The unnatural weakness of muscle strength occurring in myasthenia presents variable intensification [1]. The epidemiological examinations showed that the disease occurs with frequency of 10–15 persons

* *Corresponding author at*: Department of Neurology, Medical University of Silesia, ul. 3-go Maja 13-15, 41-800 Zabrze, Poland.
E-mail address: irozmilowska@gmail.com (I.M. Rozmilowska).
https://doi.org/10.1016/j.pjnns.2017.12.012
0028-3843/

per 100,000 population. The diagnostics of myasthenia is based on marking the level of antibodies anti-AChR, which occur at 85% patients. The remaining 15% described as seronegative may have other types of antibodies, such as against muscle-specific tyrosine kinase (anti-MuSK) or anti-titin antibodies. The patients with diagnosed myasthenia are characterized by a significant variability of the course of their disease [2,3].

For doctors, the grounds for assessment of the patient's clinical condition are the occurring neurological symptoms and their evolution observed by the patient himself. The treatment process is difficult and the therapy should be precisely adjusted to the existing symptoms. Thus, the point of reference in the assessment of patients are observations performed during the patient's successive appointments. One of the instruments used to assess patients with myasthenia gravis is the Myasthenia Gravis-specific Activities of Daily Living scale (MG-ADL). This scale was developed in the 1990s by Wolfe Gil. It is an easy to use, 8-item questionnaire, which may be completed both by the doctor and the patient himself [4].

The purpose of our work was to evaluate neurological condition of myasthenia gravis patients using the MG-ADL form, in order to validate the tool and enable its introduction for daily use in the assessment of patients suffering from myasthenia gravis.

2. Materials and methods

2.1. *Patients and material*

The examination was carried out in the Department of Neurology at Medical University in years 2015–2016. The uniform criteria of inclusion in the examination covered: (1) patients with ocular or generalized form of myasthenia on the grounds of clinical criteria, serological and electro-stimulating tests, (2) over 18 years of age, (3) the minimum duration of the disease 6 months. The patients were subjected to neurological examination, they underwent detailed interviews and on the grounds of the obtained information, a doctor completed an MG-ADL questionnaire. Relatively small study sample was the limitation of the study.

2.2. *The Myasthenia Gravis-specific Activities of Daily Living questionnaire*

The Myasthenia Gravis-specific Activities of Daily Living scale consists of the assessment of 8 parameters: speaking, chewing, swallowing, breathing, self-care activities (brushing the teeth or combing the hair), simple physical activities (getting up from a chair), double vision and eye lid dropping. Each parameter is subjected to assessment depending on the degree of symptoms intensification, awarding points from 0 to 3 points. The maximum number a patient may receive is 24 points. The higher the score of points, the bigger limitations of the patient in everyday life activities caused by intensification of myasthenia gravis [4,5]. Table 1 presents the Polish version of the questionnaire The Myasthenia Gravis-specific Activities of Daily Living.

Each patient was assessed twice to confirm the scale reliability (test–retest) – the second assessment was conducted during the follow-up after 4 weeks from the first meeting. Additionally, the classification of patients into adequate MGFA classes (Myasthenia Gravis Foundation of America clinical classification) was made on the grounds of their neurological examination and in conformity with MG Composite scale (Myasthenia Gravis Composite) [6,7]. The above scales were

Table 1 – MG-ADL questionnaire in the Polish language version. MG-ADL (Ocena czynności dnia codziennego w miastenii gravis).

Klasyfikacja	0	1	2	3	Wynik punktowy
1. Mówienie	prawidłowe	mowa okresowo bełkotliwa lub nosowa	mowa stale bełkotliwa lub nosowa, jednak zrozumiała	mowa trudna do zrozumienia	
2. Żucie	prawidłowe	utrudnione połykanie produktów stałych związane z nużliwością	utrudnione połykanie produktów płynnych związane z nużliwością	odżywianie możliwe wyłącznie przez sondę żołądkową	
3. Połykanie	prawidłowe	sporadyczne krztuszenie się	częste krztuszenie się, wymagające modyfikacji diety	odżywianie możliwe wyłącznie przez sondę żołądkową	
4. Oddychanie	prawidłowe	duszność wysiłkowa	duszność spoczynkowa	wentylacja mechaniczna	
5. Utrudnione mycie zębów lub czesanie włosów	brak	Wzmożony wysiłek, jednak bez konieczności odpoczynku	odpoczynek jest niezbędny	niemożność wykonania jednej z wymienionych czynności	
6. Utrudnione wstawanie z krzesła	brak	łagodne, czasami wymaga podparcia rękami	umiarkowane, zawsze wymaga podparcia rękami	ciężkie, wymaga asekuracji	
7. Podwójne widzenie	brak	obecne, jednak nie każdego dnia	codziennie, ale niestale	stałe	
8. Opadnie powiek	brak	obecne, jednak nie każdego dnia	codziennie, ale niestale	stałe	
				Wynik całkowity:	

used both for patient classification and for the assessment of ''severity'' of the disease. Each patient also filled in the MG-QOL 15 (Myasthenia Gravis – quality of life 15) form [8].

2.3. Ethics

The work described in this article has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans Nr KNW/0022/KB1/68/15; uniform requirements for manuscripts submitted to biomedical journals. Each patient expressed a written consent for participation in the test. Before starting the study, we had received a written consent from the author of the scale regarding the performance of the test.

2.4. Statistical analysis

The basic statistical analysis included elements of descriptive statistics such as average, median, standard deviation, percentage distribution and variance. The analysis of correlation between MG-ADL, MG-QOL 15 and MG Composite was performed. For this purpose, both Pearson's coefficient and Spearman's coefficient were used. Receiver operating characteristic (ROC) curve and sensitivity/specificity analyses were conducted based on the physician's impression of change according to cutoffs. The reliability of this method was confirmed in the test–retest reliability. The correlations obtained in all cases were almost equal. The study of results was conducted on the grounds of statistical analysis using STATISTICA v 12 PL and EXCEL programmes.

3. Results

50 patients were qualified for the test. The patients with ocular myasthenia gravis constituted 48%, and generalized MG – 52%. The average age of the patients was 60.6 years, the average duration of the disease was 9.5 years, and 56% of patients were women. A total of 86% of patients were acetylcholine receptor antibody positive (AChR+) – with 8.93 nmo/l on average; at 56% of patients persistent thymus was diagnosed during the diagnosis, and thymoma at 10%. The division of patients according to MGFA classification was distributed in the following way: 38% class I, 16% class II a, class II b 4%, in class III a 12% and III b 2%, class IV a and 4, whereas class IV b 2%. There were 22% in the remission state, i.e. class 0 none of the examined persons was intubated and (class V). Analysing the applied treatment, 98% of patients took acetylcholinesterase inhibitors, 16% additionally used steroid therapy, and 6% – azathioprine.

The results of analysis of basic descriptive statistic, taking into account the division of patients according to selected criteria, are presented in Table 2.

Pearson's and Sperman's correlation between MG-ADL, MG-QOL 15, MG Composite and MGFA was conducted. The comparison of results of MG-ADL questionnaire showed a positive correlation with all results of questionnaires, respectively MG-ADL vs MG-QOL 15 $r = 0.85$ points, MG-ADL vs MGFA $r = 0.80$ points and MG-ADL vs MG Composite $r = 0.96$ point.

Table 2 – Demographic and clinical characteristics of patients enrolled into the study.

Patients (*n*)	50
Myasthenia character	
Ocular (%)	48
Generalized (%)	52
Mean age of patients (years)	60.66
Range age (years)	30–81
Mean duration of disease (years)	9.48
Range of disease (years)	0.5–34
Gender	
Female (%)	56
Male (%)	44
Mean antibodies against rec. Ach (nmol/l)	8.93
Range antibodies against rec. Ach (nmol/l)	0.1–85
Treatment (%)	
Anticholinesterase drugs	98
Steroids	16
Azathioprine	6
Classification of MGFA (%)	
MGFA 0	22
MGFA I	38
MGFA II a	16
MGFA II b	4
MGFA III a	12
MGFA III b	2
MGFA IV a	4
MGFA IV b	2
MGFA V	0

These are statistically significant results at the level of $p < 0.001$, showing large correlation of coefficients, remarkably marked with reference to MG Composite scale. The presented correlations are shown in Figs. 1–3.

For the purpose of the study, the assessment of patients' clinical condition using MGFA classification was assumed as the so-called ''golden standard''. The patients qualified in neurological assessment for MGFA 0 – MGFA IIb groups were in the state of remission or they had intensified symptoms poorly diagnosed. The patients qualified for MGFA IIIa – MGFA V classes were those who revealed moderate or intensified image of symptoms in clinical examination. Sensitivity and specificity of MG-ADL classification were assessed. In our study, a few points of MG-ADL cutoff points were determined, which were later compared with the patients' neurological condition. The result of 10 points enabled the qualification of 90% of patients, according to a determined scheme, and the assessment according to MG-ADL scale was adequate to patients' neurological condition in conformity with MGFA classification. ROC curve analysis confirmed very good differentiating properties of MG-ADL (field below the curve pod 0.91; $p < 0.001$). Fig. 4 shows ROC curve for MG-ADL.

Another assessment of all patients was performed according to MG-ADL questionnaire after 4 weeks from the first visit. The average MG-ADL score at the first visit was 4.02, the median was 3.0, min. value 0.0, max value 17.0, the lower quartile equalled 1.0, the upper quartile – 5.0, and the standard deviation was 3.97. The MG-ADL results did not differ by more than 2 points between the assessments. The test–retest reliability coefficient was 92%, with a lower 94% confidence interval [CI] of 88%, indicating excellent test–retest reliability. The differences in assessment of particular test elements were

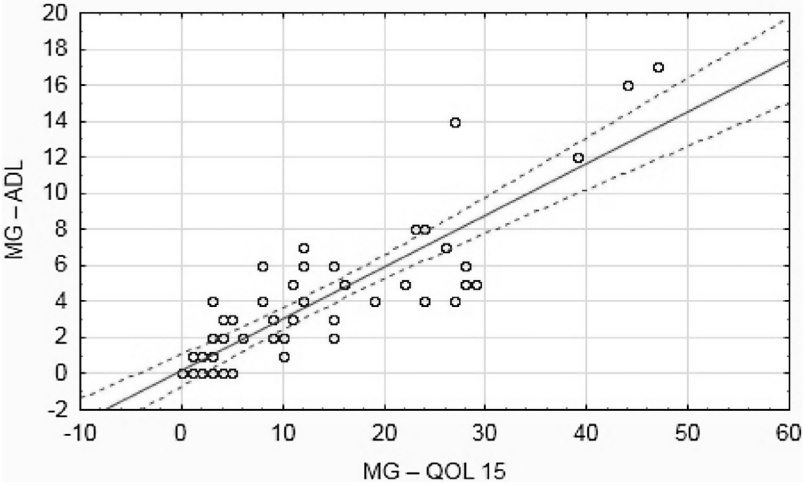

Fig. 1 – Correlation diagram questionnaire MG-ADL with MG-QOL 15 scale. (MG-ADL – Myasthenia Gravis-specific Activities of Daily Living scale; MG-QOL 15 – Myasthenia Gravis – quality of life 15).

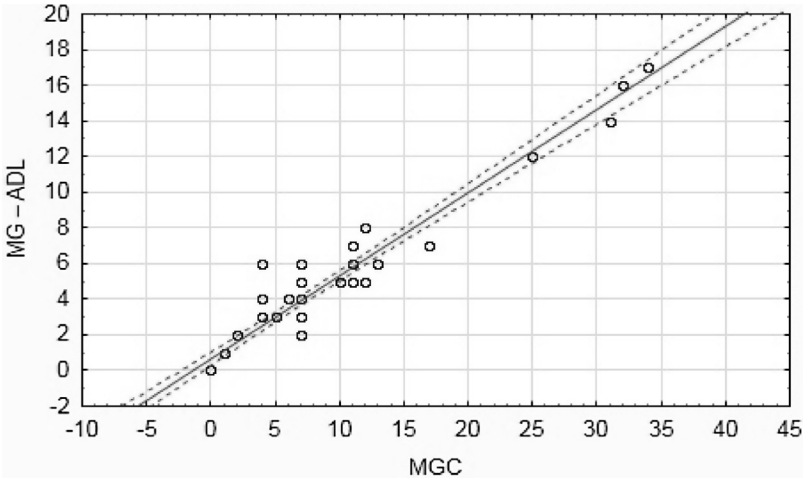

Fig. 2 – Correlation diagram questionnaire MG-ADL with MG Composite scale. (MG-ADL – Myasthenia Gravis-specific Activities of Daily Living scale; MGC – Myasthenia Gravis Composite).

most frequent in the eye lid dropping assessment (8/50) and double vision (7/50).

4. Discussion

Our observations confirmed MG-ADL questionnaire as a useful tool for assessment of everyday life functioning of Polish population patients with diagnosed myasthenia gravis taking neurological symptoms of the disease into consideration. Analysis showed a positive correlation with other scales used – MG-QOL 15, MGFA, MG Composite. The intensification of neurological symptoms (MGFA II b, MGFA III b and MGFA IV b), and in particular the presence of symptoms other than eye symptoms, showed significant relation with obtained higher number of points in MG-ADL questionnaire. The test–retest assessment confirmed reliability and dependability of the questionnaire, no statistically significant differences were determined for measurements conducted twice in a specific time interval. The obtained variability by over 2 points in two examined aspects (eye lid dropping and double vision) may be explained with significant fluctuation of apocamnosis symptoms over a short period of time (e.g. during a day). The confirmation of good sensitivity and specificity is ROC curve, and the differentiating properties of MG-ADL questionnaire were confirmed in other previous studies.

There are certain limitations in our research. Firstly, the most important is the number of persons included in the research. We are aware that the reliability of research is connected with the number of patients subject to assessment, and thus, we are continuously expanding our group by examining new patients with diagnosed MG. The second important matter is the difficulty in determining correct points of reference. The MG-ADL scale is also the scale in which a

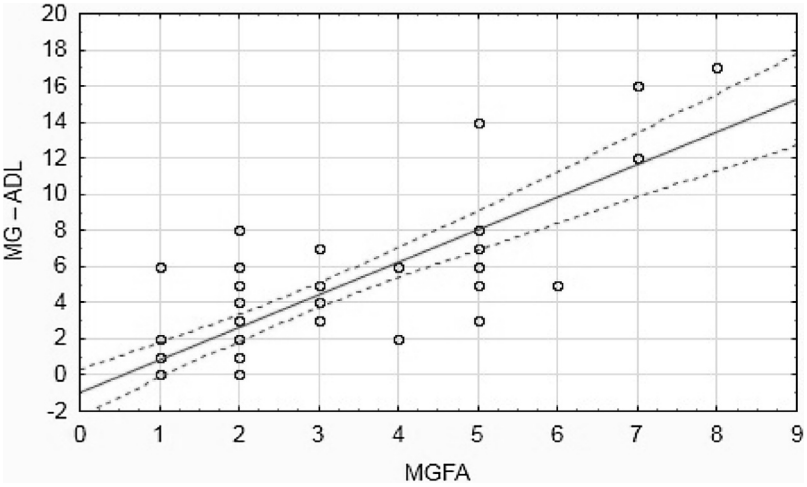

Fig. 3 – Correlation diagram questionnaire MG-ADL with neurological scale MGFA. (MG-ADL – Myasthenia Gravis-specific Activities of Daily Living scale; MGFA – Myasthenia Gravis Foundation of America clinical classification remission – 1; MGFA I – 2; MGFA IIa – 3; MGFA IIb – 4; MGFA IIIa – 5; MGFA IIIb – 6; MGFA IVa – 7; MGFA IVb – 8; MGFA V – 9).

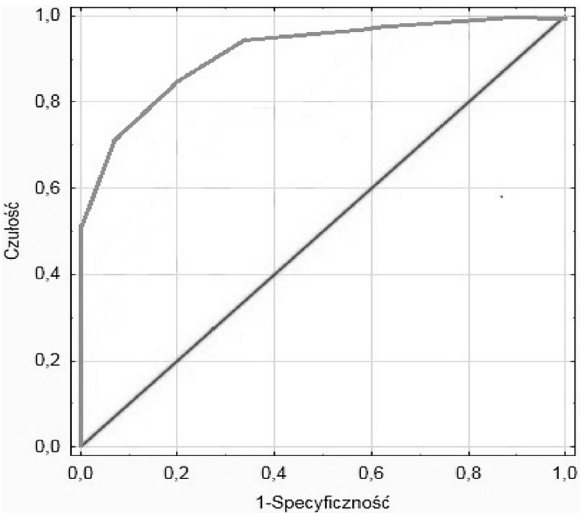

Fig. 4 – Receiver operating characteristic (ROC) curve of MG-ADL. (MG-ADL – Myasthenia Gravis-specific Activities of Daily Living scale).

patient subjectively assesses his/her health condition and its influence on everyday life, at the same time referring to existing clinical symptoms. It is difficult to clearly indicate which point value may indicate remission. Some patients in our study had a value of 0.0, which corresponded to an MGFA score. Patients who received 1.0 pts complained of occasional discomfort, which may also occur in patients with remission. Scores 2 and above in our opinion appear to be found in patients who, according to the MGFA classification, presented signs of myasthenia gravis. We used three other scales for our analysis, which reflected both the aspect of the patient's subjective feelings as well as objective neurological examination. The third important issue is, regardless of our analysis, but concerning the questionnaire itself, particular examined aspects – they are not equivalent. In the case where a patient receives the highest number of points (3 points) regarding respiratory disorders, it is the patient who needs mechanical ventilation. However, if he/she receives 3 points for permanent double vision or diplopia, his/her clinical condition may significantly differ from another patient with a similar total number of points. Thus, from a doctor's point of view, it is important and expedient to use MG-ADL scale as one of the parameters for assessment of a patient with myasthenia gravis.

Previous research suggests that assessment according to MG-ADL questionnaire may be the final stage of conducted observations in clinical examinations. A significant advantage of the questionnaire is its simplicity and the fact that it can be completed by a patient alone, without the doctor's participation.

MG-ADL scale was used as the final stage in recently completed research by Bourgue et al. it was a retrospective cohort study conducted in a hospital in Canada, the purpose of which was the assessment of efficiency of subcutaneous application of immunoglobulin in the course of myasthenia gravis. Statistically significant improvements were documented in the MG-ADL, MG-QOL and VAS scales [9]. Other pilot study assessing the influence of leflunomide treatment on the course of myasthenia gravis was conducted by Chen et al. In that project, MG-ADL questionnaire was also used as one of the final points, presenting a reliable insight into improvement or lack of improvement in case of the applied procedures [10]. Analysing other clinical research, it can be noted that MG-ADL questionnaire is used in the majority of studies concerning new forms of myasthenia gravis treatment, similarly to other projects concerning, among others, a therapy with methotrexate or tacrolimus. The study conducted by Zhao et al. showed the decrease of neurological symptoms, especially in patients with generalized form. The following scales were used as final points: MG-ADL, MMT (manual muscle testing), MGFA, which in joint analysis demonstrated large precision of measurements [11].

Other interesting observations were made by Gratton et al. In his research, he analyzed the influence of smoking cigarettes on the quality of life of patients with the ocular form of myasthenia gravis. The basic tool used to conduct the observations was the MG-ADL form, application of which enabled the patient to assess the occurring changes. The research results suggest that quitting smoking may have beneficial influence on symptoms reduction [12].

The course of myasthenia gravis is very variable in many patients. Clinical assessment of the treatment's effectiveness may be easier using scales specially designed for this purpose. In addition to the MG-ADL scale, it is worth noting the MG-Composite and MG-QOL 15 scale. The first one allows for relative objectivity of the patient's condition based on neurological examination. The second is an exponent of the functioning of patients and the assessment of psychosocial aspects. These observations have been included in many studies.

In recent years, the authors of the scale Wolfe G. together with Muppidi et al. conducted a multi-centre analysis of MG-ADL scale use with its validation. In their assessment, the reference point were scales MG-QOL 15 and MG-Composite. 87 patients were examined and the obtained results confirmed a high level of correlation between the instruments used. The test confirmed that the MG-ADL is useful as a research tool as well as in routine clinical management [5].

5. Conclusion

To sum up the above considerations, it is worth remembering the holistic assessment of patients. Myasthenia gravis with its specific symptoms often demonstrates significant influence on everyday life activities of the patients. Frequently, they cannot perform basic tasks such as washing themselves, driving a car or eating. Thus, therapeutic actions should aim at possibly significant reduction of symptoms visible in the patients' neurological condition improvement, but, at the same time, it should lead to improving the quality of life, which is evaluated by the patient himself.

Conflict of interest

None declared.

Acknowledgement and financial support

None declared.

REFERENCES

[1] Berrih-Aknin S, Frenkian-Cuvelier M, Eymard B. Diagnostic and clinical classification of autoimmune myasthenia gravis. J Autoimmun 2014;(48–49):143–8.
[2] Conti-Fine B, Milani M, Kaminski H. Myasthenia gravis: past, present, and future. J Clin Invest 2006;(116):2843–54.
[3] Szczudlik P, Szyluk B, Lipowska M, Ryniewicz B, Kubiszewska J, Dutkiewicz M, et al. Antititin antibody in early- and late-onset myasthenia gravis. Acta Neurol Scand 2014;130(4):229–33.
[4] Wolfe G, Herbelin L, Nations S, Foster B, Bryan W, Barohn R. Myasthenia gravis activities of daily living profile. Neurology 1999;52(7):1487–9.
[5] Muppidi S, Wolfe G, Conaway M, Burns T, MG Composite and MG-QOL15 Study Group. MG-ADL: still a relevant outcome measure. Muscle Nerve 2011;44(5):727–31.
[6] Jaretzki A, Barohn R, Ernstoff R, Kaminski H, Keesey J, Penn A, et al. Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. Neurology 2000;(55):16–23.
[7] Burns T, Conaway M, Cutter G, Sanders D. Construction of an efficient evaluative instrument of myasthenia gravis: the MG Composite. Muscle Nerve 2008;38:1553–62.
[8] Burns T, Conaway M, Cutter G, Sanders D, Muscle Study Group. Less is more, or almost as much: a 15-item quality-of-life instrument for myasthenia gravis. Muscle Nerve 2008;38(2):957–63.
[9] Bourque P, Piringle C, Cameron W, Cowan J, Chardon J. Subcutaneous immunoglobulin therapy in the chronic management of myasthenia gravis: a retrospective cohort study. PLOS ONE 2016;11(8):e0159993. http://dx.doi.org/10.1371/journal.pone.9930159
[10] Chen P, Feng H, Deng J, Lou Y, Qiu L, Ou C, et al. Leflunimide treatment in corticosteroid-dependent myasthenia gravis: an open-label pilot study. J Neurol 2016;263(1):83–8.
[11] Zhao C, Zhang X, Zhang H, Hu X, Lu J, Lu C, et al. Clinical efficacy and immunological impact of tacrolimus in Chinese patients with generalized myasthenia gravis. Int Immunopharmacol 2011;11(4):519–24.
[12] Gratton S, Herro A, Feuer W, Lam B. Cigarette smoking and activities of daily living in ocular myasthenia gravis. J Neuroopthalmol 2016;36(1):37–40.