Quality of Life of Myasthenia Gravis Patients

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Objective: *To investigate the impact of myasthenia gravis (MG) on the quality of life (QOL) of MG patients.*
Material and Method: *QOL was assessed with SF-36 questionnaire.*
Results: *Thirty-one patients participating in the present study, 74.2% female, with an average age of 44.9 years old. From the SF-36 questionnaire, emotional well being had the lowest score while other components were in average or high range. Ocular and mild generalized MG had better physical functioning than moderate generalized MG. With treatment, those who had no or minimal symptoms had better QOL in both physical and mental aspects. Immunosuppressant was not associated with poor QOL.*
Conclusion: *QOL of Thai MG patients is better than Westerners. However, MG still has significant impact to both physical and mental aspects. More emphasis is needed for mental aspects. The degree of disease control is very important in QOL and the use of immunosuppressant does not impair QOL.*

Keywords: *Quality of life, Myasthenia gravis, Thai, Disease control, SF-36*

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Myasthenia gravis (MG) is an autoimmune neuromuscular disease that can cause ocular or generalized weakness or even respiratory failure. The weakness directly affects the patient's daily activities and ability to work. Despite treatment with acetylcholinesterase inhibitors and immunosuppressive drugs or thymectomy, many patients still experience its symptoms, which may affect their quality of life (QOL). Previous reports about QOL in MG patients showed deficit in both physical and mental aspects[1,2]. Thymectomy has positive effects on QOL in only moderate to severe MG, but patients still have emotional deficit after long term follow-up[3]. Disease severity and regional myasthenic weakness also have an impact on both mental and physical aspects of quality of life, assessed by a standardized QOL questionnaires, Short-Form 36-item questionnaire for health survey (SF-36)[4]. However, most previous reports were from Western countries, which may be different from Asian countries due to the nature of disease, pattern of treatment, and culture and socioeconomic factors.

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Asian MG patients are quite different from Western MG patients in many aspects. The disease severity is milder, probably due to lower prevalence of MuSK antibody in sero-negative MG patients[5]. In Thai patients, the concomitant disease of hyperthyroidism is higher (17.5%)[6] with slightly lower prevalence of AchR Antibody positivity (60.3%) in generalized MG patients[7]. The association between autoimmune thyroid disease and DRB1*0803 were reported in Japanese which indicates the heterogeneity and different immunogenetic backgrounds from Westerners[8].

Therefore, the authors conducted the present study to assess QOL of MG patients with SF-36 in an outpatient neurology clinic and examined the relationship of many aspects of QOL that may be influenced by other factors.

Material and Method

The present study was conducted between December 1, 2006 and May 31, 2007 at Thammasat University Hospital, Pathumtani, Thailand, which serves inhabitants in the lower central region of Thailand and northern suburban area of Bangkok, as both primary care and tertiary care medical center. The study protocol was approved by the Faculty of Medicine's Ethics Committee. Written informed

consent was obtained from all patients. The patients were recruited from the out-patient neurology clinic of the hospital.

Myasthenia gravis was diagnosed by the neurologist, KK, based on the patients' clinical characteristics, positive result on prostigmine test or repetitive nerve stimulation test. The disease severity was classified according to Myasthenia Gravis Foundation of America (MGFA) classification. The patients were at least 15 years old and mentally competent to provide consent and data. They were excluded if they have significant co-existing diseases that may affect QOL, such as poorly controlled diabetes mellitus, stroke, renal failure, asthma, etc. The patients were screened by the neurologist for the eligibility to the present study, and then the experienced and trained physician (WJ) conducted the face-to-face interviews. SF-36 (version 1) was employed to inquire about the general health status of patients. It consists of 36 questions that provide eight specific categories of physical and emotional scores (physical functioning (PF), role, physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role, emotional (RE), and mental health (MH)). This version has been validated in both clinical and non-clinical conditions[9]. Frequency of symptoms was defined by re-appearance or exacerbation of patient's previous symptoms.

Statistical analyses were performed using SPSS version 10.0. Descriptive statistics were used to summarize the data. Nonparametric Kruskal-Wallis H test was used to compare data between groups. Non-parametric analysis of correlation was analyzed by Spearmann's rank correlation coefficient technique. For all analyses, the level of statistical significance was defined as a p-value < 0.05.

Results

All eligible patients were approached and all gave informed consent. Baseline demographic information and clinical characteristics were summarized in Table 1. SF-36 scores were summarized in Table 2. In general, the quality of life was in average range. Physical functioning (PF), social functioning (SF) and bodily pain (BP) were very good, while vitality/energy & fatigue (VT) and emotional well-being (EW) were below average to poor. Moreover, the role limitation due to emotional problem (RE) was significantly lower in the lower income group ($p < 0.05$), but it was not significant in other categories of QOL. Regarding gender difference, physical function (PF) was higher in female patients ($p < 0.05$) but there was no significant difference in other categories of QOL.

For disease severity, ocular MG and mild generalized MG patients had significantly higher QOL than moderate generalized MG patients in role limitation due to physical health (RP), role limitation due to emotional problem (RE), and bodily pain (BP), $p < 0.05$. There was a significant correlation between SF-36 score and frequency of muscle weakness, diplopia, respiratory or bulbar symptoms during the past year, medication side effect affecting work and medication side effect impacting activities of daily livings (correlation coefficient at 0.66, 0.582, and 0.631 respectively, all $p < 0.01$).

However, there was no significant correlation between immunosuppressive therapy and QOL. Immunosuppressive therapy, either steroid or other immunosuppressive drugs ($p = 0.182$, $p = 0.685$ respectively), did not significantly worsen QOL with similar degree of disease control. Thymectomy did not have an impact on QOL in all patient disease severity groups ($p > 0.05$). Therefore, good control of MG with minimizing medication side effect was significantly correlated with better QOL.

Table 1. Baseline demographic information and clinical characteristic of patients (n = 31)

	Number (%)
Demographic information	
Female	23 (74.2)
Married	18 (58.1)
Education below Bachelor degree	21 (67.7)
Unemployed status	11 (35.5)
Monthly income less than 300 USD/month	15 (48.4)
Clinical characteristics	
Ocular type	11 (35.5)
Mild generalized MG (IIA / IIB)	15 (48.4)
Moderate generalized MG	5 (16.1)
History of MG crisis or respiratory failure	2 (6.5)
Symptom improvement at last follow-up	29 (93.5)
Coexisting hyperthyroidism	5 (16.1)
Frequency of MG symptoms	
Asymptomatic	11 (35.5)
Less than 12 times per year	11 (35.5)
More than 12 times per year	9 (29)
Treatment	
Pyridostigmine	31 (100)
Steroid	24 (77.4)
Other immunosuppressive drugs	9 (29)
Thymectomy	13 (41.9)

Table 2. SF-36 score in 31 patients

SF-36 domains	Minimum	Maximum	Mean	SD
Physical function (PF)	25	100	72.9	21.5
Role limitation due to physical health (RP)	0	100	63.7	35.3
Role limitation due to emotional problem (RE)	0	100	59.1	40.1
Vitality/Energy & fatigue (VT)	40	100	54.4	8.4
Emotional well being (EW)	20	75	40.1	10.8
Social function (SF)	55	100	80.1	15.5
Bodily pain (BP)	32.5	100	76.4	21.4
General health perception (GH)	10	100	61.9	19.9

Table 3. Comparison of SF-36 mean score in diabetes, multiple sclerosis, epilepsy and myasthenia gravis

Domains	Diabetes[13] (n = 555)	Multiple sclerosis[13] (n = 85)	Epilepsy[13] (n = 271)	MG Padua et al[1] (n = 46)	MG Current study (n = 31)
Physical function (PF)	74.2	33.5	78.9	48.5	72.9
Role limitation due to physical problem (RP)	55.1	32.7	60.0	13.0	63.7
Bodily pain (BP)	71.7	72.2	72.8	54.2	76.4
General health (GH)	52.6	53.7	68.7	25.6	61.9
Vitality (VT)	54.3	41.9	55.4	36.5	54.4
Social functioning (SF)	81.2	60.2	77.3	41.8	80.1
Role limitation due to emotional problem (RE)	70.2	59.6	66.3	32.0	59.1
Emotional well being (EW)	73.0	67.8	68.4	45.6	40.1

Discussion

From the present data, MG patients were predominantly married females and in the lower to middle socioeconomic status. Most were in ocular and mild generalized MG groups whose diseases were under control. Hyperthyroidism coexisted in 16.1%, which was in line with a previous report[6]. The disease had significant impact on self-dependency, confidence, and some impact upon work. Regarding the medication effect, most did not have significant impact on activities of daily livings. Some who experienced side effects might have body discomfort and lack of self-confidence.

Though the mean score of QOL were in middle range, the mental aspect (emotional well-being) was still lower than other categories, despite good disease control. This finding was also in line with previous reports about mental aspects of MG[9,10]. Magni G et al[10] reported that psychiatric disturbances were observed in 51% of their patients in particular, adjustment disorders with depressed mood and mixed emotional features, affective disorders and personality disorders. Paradis CM et al[11] also suggested that the symptoms of myasthenia gravis might predispose vulnerable individuals to panic disorder/agoraphobia. Additionally, bulbar and generalized involvement resulted in impairment of mental aspects of quality of life, whereas ocular involvement did not[4].

Because of the overlapping symptoms of MG and psychiatric disorders, this intricate relationship of psychiatric disorders and myasthenia gravis needs to be explored further. Due to limited data and lack of clinical trials about treatment of this specific group of patient, therefore, psychiatric treatments must be carefully planned because of the risk of aggravating the underlying neurological disease[12]. Therefore, clinicians should pay more interest to the psychiatric aspects of this disease and actively manage them to improve QOL of MG patients.

When comparing the present data with previously published data in other chronic diseases[13] (Table 3), this data was better than that of Padua et al, especially in physical aspects but not in mental aspects. This is probably due to lesser severity of disease and symptoms, lower exacerbation and less medication side effect. In other chronic CNS diseases, such as

epilepsy and multiple sclerosis, physical aspects seem to be correlated with degree of neurological deficit but similar to MG in mental aspects.

In the present study, the correlation between SF-36 mean score and the degree of disease control was confirmed. Regarding thymectomy, there was no significant correlation between thymectomy and QOL in the present study. This may be due to less severity of disease and small number of patients. There is some evidence to suggest improvement in long-term outcome and QOL[3,14]. Witoonpanich et al advocated early thymectomy because the duration of the symptoms appeared to be the main determinant of the outcome[15]. Rostedt et al[16] also demonstrated the correlation between a patient-derived functional questionnaire, physical composite scores of SF-36 and abnormal neuromuscular transmission in SFEMG of MG patients.

Regarding the treatment pattern, most Thai MG patients were treated with pyridostigmine and prednisolone. Immunosuppressive drugs, other than azathioprine, were rarely used. From the present data, patients who experienced side effects from medication, which could be due to either pyridostigmine or immunosuppressive agents, also had significantly lower SF-36 score. However, there was no correlation between the usage of immunosuppressive medications, both steroid or other agents, and SF-36 score. Because most of the presented patients had minimal side effects from these medications, these findings could be interpreted as the degree of disease control and medication side effect both played an important role in QOL of MG patients.

The limitations of the present study were the small sample size and the specialist clinic setting which may have different treatment pattern and outcome from general neurology clinic in a community setting. Recently, the muscle study group has developed a QOL questionnaire specific to MG (MG-QOL) that assessed both physical and psychological aspects of function. This had been used in their mycophenolate clinical trial. The MG-QOL correlated highly with the SF-36, and demonstrated stronger associations with independent physical ability ratings[17]. They also reduced the questionnaire from 60 items to 15 items and it was found to be similar in sensitivity and correlated to the original 60 items, Quantitative Myasthenia Gravis (QMG), MG-specific Manual Muscle Testing (MG-MMT), and MG-specific Activities of Daily Living (MG-ADL)[18]. This tool will be helpful in future MG research.

In summary, with difference in clinical characteristics in Thai patients, QOL of these patients were better when compared to previous reports. However, MG still had significant impact to both physical and mental aspects. Mental aspect of this disease should be more emphasized. The degree of disease control played a significant role in QOL and the use of immunosuppressive drug did not impair QOL. Attempts should be made to completely control MG symptoms in order to maximize patient's QOL while being vigilant to and proactively manage treatment's side effects. The previous belief about adverse effect of immunosuppressive medication toward patient's QOL should also be reconsidered. Future studies in comparing QOL of MG patients among various clinical settings and treatment pattern will be helpful to confirm this finding.

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References

1. Padua L, Evoli A, Aprile I, Caliandro P, Mazza S, Padua R, et al. Health-related quality of life in patients with myasthenia gravis and the relationship between patient-oriented assessment and conventional measurements. Neurol Sci 2001; 22: 363-9.
2. Paul RH, Nash JM, Cohen RA, Gilchrist JM, Goldstein JM. Quality of life and well-being of patients with myasthenia gravis. Muscle Nerve 2001; 24: 512-6.
3. Busch C, Machens A, Pichlmeier U, Emskotter T, Izbicki JR. Long-term outcome and quality of life after thymectomy for myasthenia gravis. Ann Surg 1996; 224: 225-32.
4. Rostedt A, Padua L, Stalberg EV. Correlation between regional myasthenic weakness and mental aspects of quality of life. Eur J Neurol 2006; 13: 191-3.
5. Huang YC, Yeh JH, Chiu HC, Chen WH. Clinical characteristics of MuSK antibody-positive myasthenia gravis in Taiwan. J Formos Med Assoc 2008; 107: 572-5.
6. Ratanakorn D, Vejjajiva A. Long-term follow-up of myasthenia gravis patients with hyperthyroidism.

Acta Neurol Scand 2002; 106: 93-8.
7. Jitpimolmard S, Taimkao S, Chotmongkol V, Sawanyawisuth K, Vincent A, Newsom-Davis J. Acetylcholine receptor antibody in Thai generalized myasthenia gravis patients. J Med Assoc Thai 2006; 89: 68-71.
8. Suzuki S, Kuwana M, Yasuoka H, Tanaka K, Fukuuchi Y, Kawakami Y. Heterogeneous immunogenetic background in Japanese adults with myasthenia gravis. J Neurol Sci 2001; 189: 59-64.
9. Lim LL, Seubsman SA, Sleigh A. Thai SF-36 health survey: tests of data quality, scaling assumptions, reliability and validity in healthy men and women. Health Qual Life Outcomes 2008; 6: 52.
10. Magni G, Micaglio GF, Lalli R, Bejato L, Candeago MR, Merskey H, et al. Psychiatric disturbances associated with myasthenia gravis. Acta Psychiatr Scand 1988; 77: 443-5.
11. Paradis CM, Friedman S, Lazar RM, Kula RW. Anxiety disorders in a neuromuscular clinic. Am J Psychiatry 1993; 150: 1102-4.
12. Kulaksizoglu IB. Mood and anxiety disorders in patients with myasthenia gravis: aetiology, diagnosis and treatment. CNS Drugs 2007; 21: 473-81.
13. Hermann BP, Vickrey B, Hays RD, Cramer J, Devinsky O, Meador K, et al. A comparison of health-related quality of life in patients with epilepsy, diabetes and multiple sclerosis. Epilepsy Res 1996; 25: 113-8.
14. Bachmann K, Burkhardt D, Schreiter I, Kaifi J, Busch C, Thayssen G, et al. Long-term outcome and quality of life after open and thoracoscopic thymectomy for myasthenia gravis: analysis of 131 patients. Surg Endosc 2008; 22: 2470-7.
15. Witoonpanich R, Dejthevaporn C, Srisinroongruang T, Subhannachart W, Attanavanich S, Boonkasem S, et al. Long-term outcome and factors influencing the outcome of thymectomy for myasthenia gravis. J Med Assoc Thai 2004; 87: 1172-5.
16. Rostedt A, Padua L, Stalberg EV. Correlation between a patient-derived functional questionnaire and abnormal neuromuscular transmission in myasthenia gravis patients. Clin Neurophysiol 2005; 116: 2058-64.
17. Mullins LL, Carpentier MY, Paul RH, Sanders DB. Disease-specific measure of quality of life for myasthenia gravis. Muscle Nerve 2008; 38: 947-56.
18. Burns TM, Conaway MR, Cutter GR, Sanders DB. Less is more, or almost as much: a 15-item quality-of-life instrument for myasthenia gravis. Muscle Nerve 2008; 38: 957-63.

คุณภาพชีวิตของผู้ป่วย myasthenia gravis

ก้องเกียรติ กูณฑ์กันทรากร, วิวัฒน์ จรุงเกียรติกุล

วัตถุประสงค์: *เพื่อประเมินคุณภาพชีวิตของผู้ป่วย myasthenia gravis*

วัสดุและวิธีการ: *การศึกษาเชิงพรรณนาโดยทำการสัมภาษณ์ผู้ป่วย ซึ่งประกอบด้วย ข้อมูลทั่วไป ข้อมูลโรค และแบบสัมภาษณ์ SF-36 แล้วนำข้อมูลมาประมวลผลทางสถิติ*

ผลการศึกษา: *มีผู้ป่วยโรค MG จำนวน 31 คน เป็นหญิงร้อยละ 74.2 อายุเฉลี่ย 44.9 ปี จากแบบสำรวจสุขภาพ SF-36 พบว่า คะแนนสภาวะทางอารมณ์มีค่าต่ำที่สุด ส่วนคุณภาพชีวิตในด้านอื่นๆพบว่าอยู่ในระดับปานกลางถึงดี กลุ่ม MG ที่มีอาการน้อยหรือเฉพาะตามีคะแนนสมรรถภาพทางร่างกายดีกว่ากลุ่มที่มีอาการปานกลาง ผู้ที่มีอาการของโรคน้อยหรือเป็นปกติหลังรักษาจะมีคุณภาพชีวิตดีกว่าทั้งทางด้านร่างกายและจิตใจ การใช้ยากดภูมิคุ้มกันไม่ทำให้คุณภาพชีวิตลดลง*

สรุป: *คุณภาพชีวิตโดยรวมของผู้ป่วย myasthenia gravis ชาวไทยดีกว่าชาวตะวันตก อย่างไรก็ตาม โรคนี้มีผลต่อคุณภาพชีวิตทั้งทางร่างกายและจิตใจ การควบคุมโรคให้ดีจึงมีความสำคัญมาก ซึ่งการใช้ยากดภูมิคุ้มกันไม่ทำให้คุณภาพชีวิตลดลง*