Original Article
Yonsei Med J 2025 Apr;66(4):218-225
https://doi.org/10.3349/ymj.2024.0017
Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

Effect of the Administration of Cautionary Drugs on the Risk of Worsening Myasthenia Gravis: A Retrospective Matched Case-Control Study

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Purpose: Although some medications trigger the worsening of myasthenia gravis (MG), their clinical influence on patients with MG has not been significantly evaluated. We aimed to investigate whether the risk of clinical worsening of MG increases after administering cautionary drugs in patients with MG.

Materials and Methods: This retrospective case-control study was based on the medical records of patients diagnosed with MG between 2007 and 2020. We analyzed the risk of MG worsening in patients exposed to cautionary drugs during the risk period, defined as 6 months from the first exposure to cautionary drugs. The risk of MG worsening in the exposed patients was compared to that in the non-exposed patients, who were individually matched in a 1:1 ratio with exposed cases for sex, age, thymoma, and autoantibodies.

Results: Of the 2002 patients diagnosed with MG, 552 (27.6%) were exposed to cautionary drugs. Neuromuscular blocking agents (320 patients) and beta blockers (66123 person-days) were the most frequently prescribed medications. After exact matching, 220 exposed and 220 non-exposed patients were enrolled. The incidence rate of clinical worsening during the risk period was significantly higher in the exposed patients than in the non-exposed patients (odds ratio=4.09; 95% confidence interval, 1.88–8.90; $p<0.001$). Clinical worsening was observed in 31 (14.1%) of the exposed patients and in 8 (3.6%) of the non-exposed patients.

Conclusion: The administration of cautionary drugs increased the risk of clinical worsening in patients with MG. Clinicians should be aware of this risk when cautionary drugs need to be administered.

Key Words: Myasthenia gravis, myasthenic crisis, adverse drug reaction, autoimmune disease

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder of the neuromuscular junction characterized by muscle weakness and fatigue. Fluctuation of symptoms is a common clinical feature of MG, and patients with MG tend to experience recurrent worsening of their disease. Development of disease-modifying treatments, including thymectomy, corticosteroids, immunosuppressive agents, intravenous immunoglobulins, and plasmapheresis, has allowed a substantial number of patients with MG to stably maintain their daily activities without fluctuations. However, some patients still have wild fluctuations and recurrent worsening, which are sometimes sufficiently severe to be life-threatening. Up to 20% of patients with MG still experience at least one episode of myasthenic crisis, and a recent report on generalized MG estimated the incidence of MG exacerbation as 24.4 per 100 person-years.[1-3] Poorly controlled MG is associated with depression and low quality of life.[4,5] In addition, the worsening of MG often leads to hospitalization or visit to the emergency department, which imposes significant economic burden on the patients.[6-8]

Received: March 11, 2024 **Revised:** August 6, 2024
Accepted: August 18, 2024 **Published online:** December 3, 2024
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•The authors have no potential conflicts of interest to disclose.

Certain drugs may trigger MG worsening. The 2020 updated international consensus guidance for the management of MG provided a list of medications to avoid or use with caution in patients with MG.[9] Besides the international consensus guidance, various reports have suggested the list of medications that should be used with caution in patients with MG.[10-12] These commonly include antibiotics, beta blockers, calcium channel blockers, magnesium salts, botulinum toxins, desferrioxamine, D-penicillamine, quinine, and procainamides. However, the association between cautionary drugs and MG worsening is supported mostly based on case reports or case series.[13-22] Only few studies have evaluated the risk of MG worsening after the administration of such cautionary drugs.[10,17] To the best of our knowledge, no study has verified an increased risk of MG worsening in patients who were exposed to cautionary drugs compared to those who were not exposed.

The present study aimed to investigate the risk of clinical worsening of MG after the administration of cautionary drugs by comparing the incidence of worsening between patients with and without exposure to cautionary drugs.

MATERIALS AND METHODS

Study population

This retrospective, matched case-control study was conducted by reviewing the electronic medical records of patients diagnosed with MG in Severance Hospital between 2007 and 2020. The diagnosis of MG was established based on clinical symptoms and signs of muscle fatigability; presence of autoantibodies, including anti-acetylcholine receptor-binding antibody (AChR Ab) and anti-muscle-specific tyrosine kinase antibody (MuSK Ab); and results of low-frequency repetitive nerve stimulation and neostigmine challenge tests. Patients were classified into the exposed and non-exposed groups based on their history of exposure to cautionary drugs. The patients with MG who had been exposed to cautionary drugs after the diagnosis of MG were classified into the exposed group, whereas the patients who had never been exposed to cautionary drugs were classified into the non-exposed group. Cautionary drugs were defined as medications known to be avoided or be used with caution in patients with preexisting MG. These included neuromuscular blocking agents, fluoroquinolones, macrolides, aminoglycosides, beta blockers, calcium channel blockers, magnesium salts, botulinum toxins, D-penicillamine, desferrioxamine, and quinidine.[9,11] The list of cautionary drugs used in the current analysis is shown in Supplementary Table 1 (only online).

Data collection and definition

Basic demographics and clinical features, including sex, age, status of AChR Ab and MuSK Ab, presence of thymoma, severity of MG [assessed based on the Myasthenia Gravis Foundation of America (MGFA) clinical classification and MG Activities of Daily Living (MG-ADL) scores], and treatment for MG were obtained by reviewing medical records. Based on the status of AChR Ab and MuSK Ab, the patients with MG were classified into those with AChR Ab-positive, MuSK Ab-positive, and double seronegative MG. Patients with AChR Ab-negative MG not tested for MuSK Ab were excluded from this analysis. The history of overall prescriptions in our institution from the time MG was diagnosed was obtained through an electronic search of the medical record database. Based on this data, we analyzed the number of patients exposed to cautionary drugs and the number of prescriptions made to each patient. This study was approved by the Severance Hospital Institutional Review Board (Approval No. 4-2022-0571). Informed consent was waived for this retrospective study.

Matching

Worsening of MG can be influenced by sex, age, disease duration, presence of thymoma, and status of MG-associated antibodies.[1] Thus, the patients in the exposed group were individually matched in a 1:1 ratio with each non-exposed patient for sex, age stratified by 20-year intervals, presence of histologically confirmed thymoma, and status of MG-associated autoantibodies. The exposed patients who could not be matched with appropriate non-exposed controls were excluded.

Definition of risk period

The definition of risk period is illustrated in Fig. 1. In the exposed patients, a risk period was defined as 6 months from the time of the first prescription of the cautionary drugs. As disease duration is one of the factors that affects MG worsening (or exacerbation),[22] a hypothetical risk period of the non-exposed patient was set to minimize the effect of the disease duration

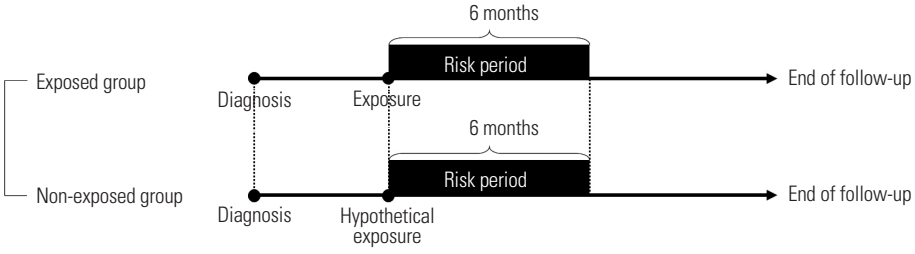

Fig. 1. A schematic illustration of exposure, hypothetical exposure, and risk period.

in the analysis of the occurrence of MG worsening. The hypothetical risk period was defined as 6 months from hypothetical exposure time point, which determined that the disease duration until the hypothetical exposure in non-exposed patients and that until cautionary drug prescription in their matched patients exposed to cautionary drugs would be the same. Hypothetical exposure was calculated by adding the time point of MG diagnosis in each non-exposed patient to the duration from MG diagnosis to the first cautionary drug prescription in the matched patient exposed to cautionary drugs: [hypothetical exposure=time of MG diagnosis of each non-exposed patient+(duration from MG diagnosis to the first cautionary drug prescription of the matched exposed patient)]. If the follow-up duration from cautionary drug exposure or hypothetical exposure was less than 6 months, the corresponding matched pair was excluded.

Exclusion after matching

As the severity of MG at certain time point is associated with the future risk of worsening,[3,23] we re-reviewed the records after matching to investigate the disease severity at the point of exposure and hypothetical exposure. Disease severity was classified into minimal (no symptoms or MGFA classification I), mild to moderate (MGFA classification II or III), and severe (MGFA classification IV or V). If there was a discrepancy in disease severity between the participants in a matched exposure and non-exposure pair, the pair was excluded from the analysis.

Clinical worsening

Clinical worsening was defined as the deterioration of MG-related symptoms over a period of days to weeks, reported by the patient and confirmed by the increase of MG-ADL score by 2 or more from the baseline score measured at the time of exposure or hypothetical exposure. The time point of clinical worsening was defined as the point at which the patient first experienced the worsening of MG-related symptoms.

Statistical analyses

Data are represented as median (Q1–Q3) for continuous variables or as numbers (percentages) for categorical variables. A Wilcoxon signed-rank or McNemar's test was used to compare the baseline characteristics between the exposed and matched non-exposed groups. The odds ratio estimated from generalized estimating equation was used for comparing the incidence of clinical worsening between the exposed and non-exposed groups. A p-value <0.05 was considered significant. The Statistical Package for the Social Sciences Statistics software (version 26, IBM Corporation, Armonk, NY, USA) was used for statistical analyses.

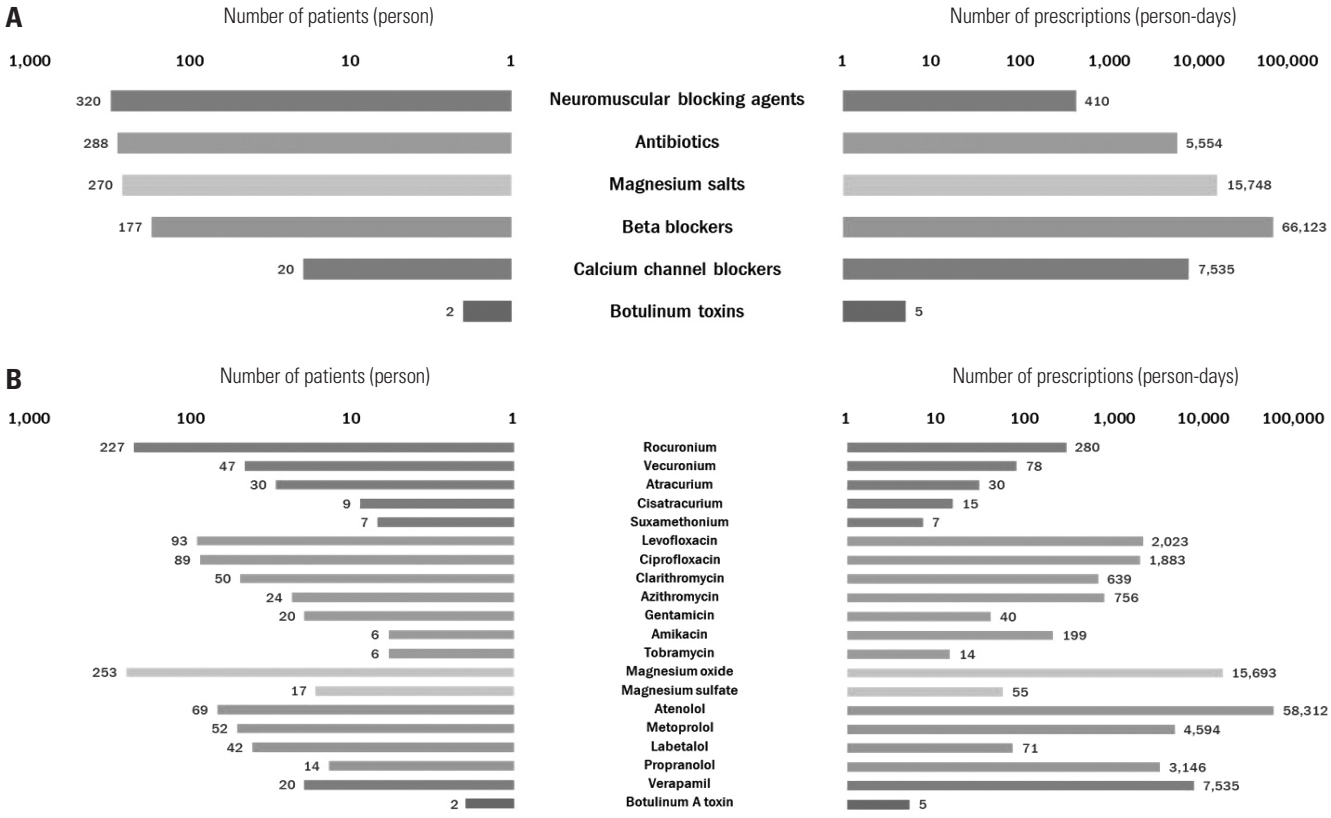

Fig. 2. Number of patients prescribed with cautionary drugs and number of prescriptions for cautionary drugs. Data are shown based on the class of drugs (A) or each agent (B).

https://doi.org/10.3349/ymj.2024.0017

RESULTS

Patients

Of the 2002 patients diagnosed with MG during the study period, 552 (27.6%) had been exposed to cautionary drugs. The number of patients exposed to cautionary drugs and the number of prescriptions for cautionary drugs (person-days) are presented in Fig. 2A. Of the cautionary drugs, neuromuscular blocking agents [320 (58.0%) patients] were prescribed to the largest number of patients, followed by antibiotics [288 (52.2%) patients], magnesium salts [270 (49.0%) patients], and beta blockers [177 (32.0%) patients]. In terms of the number of prescriptions, beta blockers (66123 person-days) were the most frequently prescribed, followed by magnesium salts (15748 person-days), calcium channel blockers (7535 person-days), and antibiotics (5554 person-days). The number of patients exposed to each specific agent and the number of prescriptions are presented in Fig. 2B. Magnesium oxide [253 (45.8%) patients] was the medication prescribed to the largest number of patients, followed by rocuronium [227 (41.1%) patients] and levofloxacin [93 (16.8%) patients]. In the number of prescriptions, atenolol (58312 person-days) was the most largely prescribed, followed by magnesium oxide (15693 person-days) and verapamil (7535 person-days). The medical situations for administering the cautionary drugs in patients with MG are shown in Supplementary Fig. 1 (only online).

Matching

After matching for age, sex, presence of thymoma, and status of autoantibodies between 552 exposed and 1450 non-exposed patients, 486 pairs of case-controls were matched. Of these, 40 pairs of patients whose follow-up ended before 6 months and 226 pairs of patients who had a discrepancy in severity of MG were excluded. Finally, 220 exposed patients and their 220 individually matched non-exposed patients were enrolled (Fig. 3). The clinical features, including age, sex, thymoma, autoantibody profile, disease severity, and immunosuppressive treatments, were not significantly different between groups (Table 1). The number of patients exposed to each cautionary drug and the number of prescriptions made in the exposed group after matching (n=220) are presented in Supplementary Fig. 2 (only online).

Worsening in the exposed and non-exposed groups

Clinical worsening of MG was observed in 31 (14.1%) of the 220 exposed patients during the risk period, whereas worsening was observed in 8 (3.6%) patients in the non-exposed group. The risk of worsening was significantly higher in the exposed group than in the non-exposed group (odds ratio=4.09; 95% confidence interval, 1.88–8.90; $p<0.001$). Among the 31 exposed patients who experienced worsening during the risk period, neuromuscular blocking agents [15 (48.4%) patients] were the medications most frequently prescribed prior to MG worsening, followed by magnesium salts [8 (25.8%) patients].

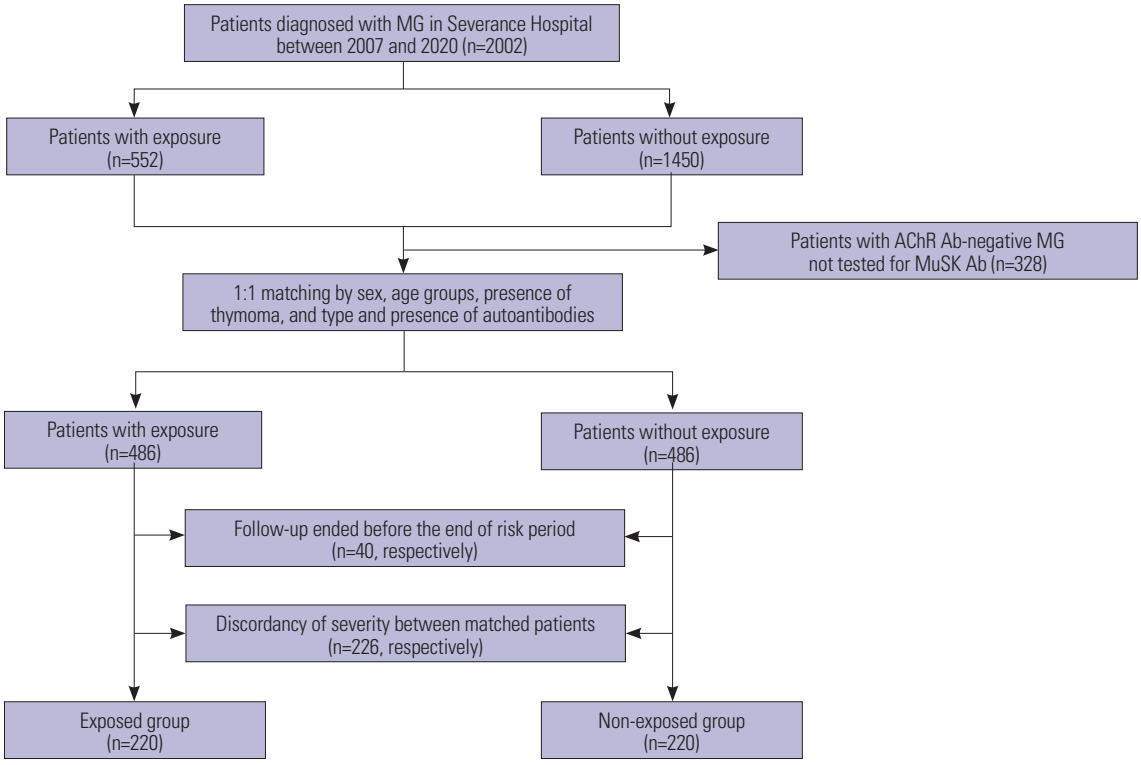

Fig. 3. A flowchart for the process of matching the exposed patients and non-exposed controls. MG, myasthenia gravis; AChR Ab, anti-acetylcholine receptor-binding antibody ; MuSK Ab, anti-muscle-specific tyrosine kinase antibody.

Table 1. Baseline Characteristics of the Exposed and Non-Exposed Patients after Matching

Variables	Exposed (n=220)	Non-exposed (n=220)	*p* value
Sex, male	74 (33.6)	74 (33.6)	>0.999
Age, years (stratified)			>0.999
≤20	11 (4.6)	11 (4.6)	
21–40	87 (36.1)	87 (36.1)	
41–60	106 (44.0)	106 (44.0)	
61–80	37 (15.4)	37 (15.4)	
>80	0	0	
Autoantibody			>0.999
AChR Ab-positive	197 (89.5)	197 (89.5)	
MuSK Ab-positive	4 (1.8)	4 (1.8)	
Double seronegative	19 (8.6)	19 (8.6)	
Thymus			>0.999
Thymomatous	72 (32.7)	72 (32.7)	
Non-thymomatous	148 (67.3)	148 (67.3)	
MGFA classification at exposure or hypothetical exposure			0.617
No symptoms	27 (12.3)	31 (14.1)	
Class I	88 (40.0)	84 (38.2)	
Class II	90 (40.9)	90 (40.9)	
Class III	15 (6.8)	15 (6.8)	
Class IV	0	0	
Class V	0	0	
Treatment			
Prednisolone	126 (57.3)	141 (64.1)	0.172
Azathioprine	45 (20.5)	45 (20.5)	>0.999
Cyclosporine	28 (12.7)	20 (9.1)	0.280
Tacrolimus	27 (12.3)	21 (9.5)	0.440
Mycophenolate mofetil	5 (2.3)	2 (0.9)	0.453
Maximum prednisolone dose, mg	20 [0–50]	25 [0–60]	0.093

AChR Ab, anti-acetylcholine receptor-binding antibody; MuSK Ab, anti-muscle-specific tyrosine kinase antibody; MGFA, Myasthenia Gravis Foundation of America.
Data are presented as n (%) or median [Q1–Q3].

Four (12.9%) patients were exposed to more than two types of cautionary drugs simultaneously: neuromuscular blocking agents and magnesium salts for three patients and antibiotics and beta blockers for one patient. Among 31 patients who experienced worsening after the exposure to cautionary drugs, 24 (77.4%) were prescribed cautionary drugs by non-MG experts. The change in the MG-ADL score and MGFA classification from the point of exposure or hypothetical exposure to the point of worsening is shown in Fig. 4. Change in MG-ADL score had no significant difference between the exposed group [3.0 (2.0–5.0)] and the non-exposed group [3.0 (3.0–4.0), p=0.929]. Among the patients in the exposed group, there were no significant differences in baseline characteristics between the patients who experienced worsening and those who did not (Supplementary Table 2, only online).

Duration from exposure to worsening

Fig. 5 demonstrates a distribution of clinical worsening during the risk period in the exposed group and from the hypothetical exposure to worsening in the non-exposed group. Of the 39 patients who experienced worsening during the risk period, the median duration from the exposure (or hypothetical exposure) to worsening was shorter in the exposed group [35.0 (11.0–107.0) days] than in the non-exposed group [84.0 (23.8–127.5) days, p=0.401], although not statistically significant. Of the 31 patients in the exposed group who experienced worsening, 14 (45.2%) experienced MG worsening within 30 days from the exposure. There was no difference in baseline characteristics between the patients who experiences early (within 30 days from the exposure) and late (after 30 days from the exposure) worsening among the patients in exposed group (Supplementary Table 3, only online).

DISCUSSION

In the present study, 27.6% of patients with MG had been exposed to cautionary drugs. MG worsening was observed in 14.1% of the patients exposed to cautionary drugs, within 6 months from the exposure. The exposed patients had 4.09-fold higher risk of MG worsening than the non-exposed patients.

Although avoiding the use of certain cautionary drugs for patients with MG has been consistently recommended, these medications are frequently prescribed to patients with MG in real practice. In the present study, 27.6% of patients with MG had been exposed to cautionary drugs. A previous retrospective observational study conducted in a single academic medical center reported that 84 out of 127 (66.1%) patients with MG had been exposed to cautionary drugs at least once, with beta blockers being the most frequently prescribed medication.[10] Another retrospective study conducted in a tertiary care hospital reported that 56.0% of patients had been prescribed a drug contraindicated in MG at least once during the 7-year study period.[24]

In the present study, clinical worsening was observed in 3.6% of the non-exposed patients during the hypothetical 6-month risk period. The distribution of worsening was remained relatively even throughout the hypothetical risk period. This pattern of worsening in the non-exposed group may represent MG worsening occurring in common clinical practice. A recent study demonstrated that the incidence rate of moderate to severe exacerbation was 12.2 per 100 person-years in patients with MG.[3] This exacerbation rate was similar to that of the non-exposed patients in the present study (7.2 per 100 person-years). In contrast, the worsening rate of the exposed patients was significantly higher (28.2 per 100 person-years) than that of the non-exposed patients. In addition, approximately half of the worsening was observed within 30 days from exposure to cautionary drugs. This result may provide additional evidence

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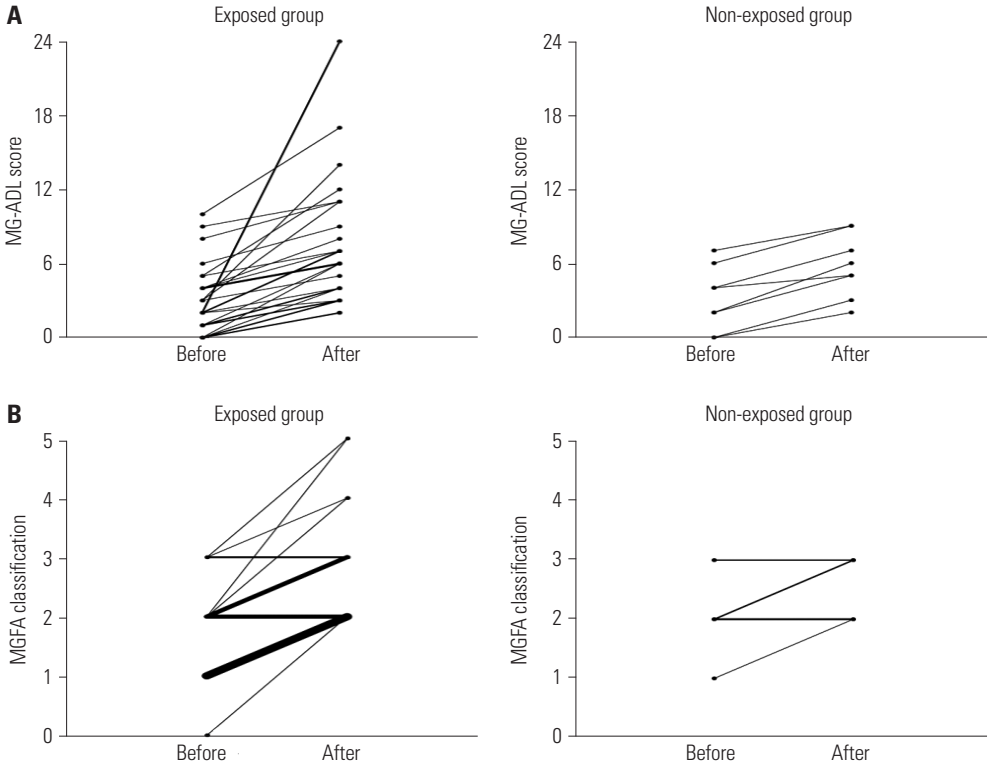

Fig. 4. Disease severity before and after worsening in the exposed and non-exposed patients. (A) Myasthenia Gravis Activities of Daily Living (MG-ADL) scores and (B) Myasthenia Gravis Foundation of America (MGFA) clinical classification.

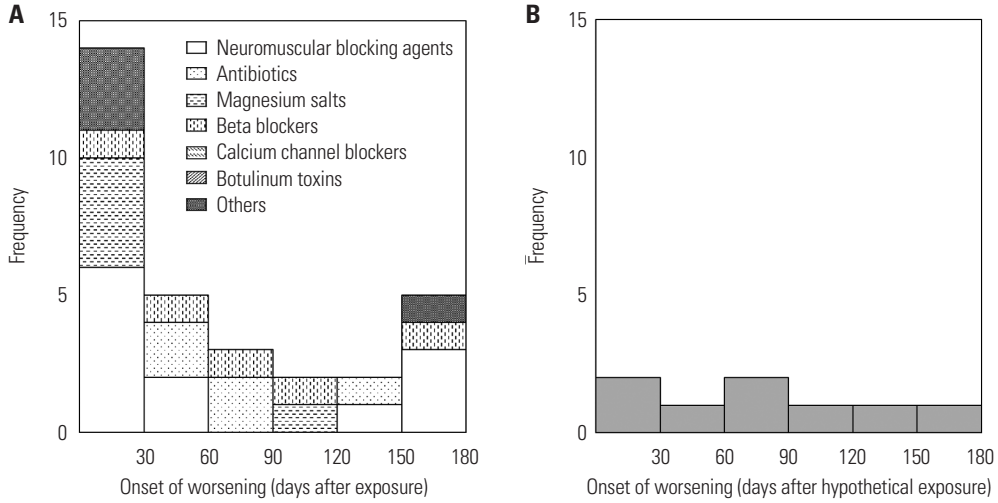

Fig. 5. Distribution of clinical worsening during the risk period in the exposed (A) and non-exposed groups (B).

for the increased risk of MG worsening after administering cautionary drugs. This result was also consistent with that of another study, which demonstrated that 22% of the patients with MG experienced exacerbation within 30 days after the prescription of cautionary drugs.[10] The frequency distribution of exacerbation was similar to the pattern observed in the present study, with most exacerbations occurring shortly after the exposure.

Although certain medications can cause worsening of MG, only a few studies have systematically assessed the risk of MG worsening after the administration of these drugs. Few studies have statistically analyzed the association between certain medications and the risk of MG worsening. A black box warning was designated for fluoroquinolones in patients with MG based on the post-marketing reports from the US FDA Adverse Event Reporting System.[16] Some retrospective cohort studies have demonstrated that beta blockers and calcium antagonists can increase the risk of MG worsening.[10,25] Otherwise, the medications listed in various guidelines to be used with caution in patients with MG are mostly based on an in vitro electrophysiological study or several case reports.[13-16,18-22] Although prospective

studies would be useful to demonstrate the clinical causality, ethical limitations exist in conducting a prospective study comparing the rate of exacerbation between exposed and non-exposed patients. Consequently, previous studies have attempted to assess the risk of MG worsening after the administration of cautionary drugs by performing a retrospective analysis of adverse drug reaction reports without adjustment for confounding factors.[25,26] The present study retrospectively compared the incidence of MG worsening between the exposed and non-exposed groups matched for age, sex, presence of thymoma, and type of autoantibodies. The result of our study may provide higher level of evidence regarding the risk of cautionary drugs in patients with MG.

It is important for clinicians to properly recognize the type of cautionary drugs to prevent MG worsening. However, in the present study, the cautionary drugs were prescribed to more than a quarter of patients with MG. The lack of awareness was especially pronounced among clinicians who are not MG experts. In the present analysis, 77.4% of prescriptions for cautionary drugs were made by clinicians who do not specialize in MG. Establishing a drug alert system for patients with MG might help clinicians to avoid inappropriate prescriptions. Drug alert systems have already been introduced in patients with renal disease or older patients to reduce inappropriate drug prescriptions.[27,28]

This study had some limitations. First, we only analyzed the drugs prescribed in our institute. Due to the retrospective study design based on a single center, we were unable to obtain the list of medications prescribed at other institutes. Further population-based study utilizing the National Health Insurance Database can be considered to overcome this limitation. Second, potential confounding factors, including infection, surgery, social stress, or drug compliance, were not considered in the present analysis. In addition, some of these factors are closely associated with certain types of cautionary drugs. For instance, antibiotics might have been used to treat infections, which can also cause MG worsening. Similarly, surgery or procedures requiring the use of neuromuscular blocking agents may have contributed to the worsening of the condition. Third, the course of the disease at a certain point, whether improving or deteriorating, can impact the prognosis. Although the severity of the disease at the time of exposure was matched in the present study, changes in disease severity before and after the exposure time point were not considered. Lastly, the effect of individual medications was not separately analyzed. The degree of the drug–disease relationship may differ between each medication included in the list of cautionary drugs. However, an analysis of this association was not possible due to the insufficient number of patients to perform a statistical analysis with adequate power.

In conclusion, cautionary drugs are prescribed to a substantial number of patients with MG. These cautionary drugs increase the risk of MG worsening. Establishing an alert system for the prescription of cautionary drugs to patients with MG will help prevent MG worsening caused by these drugs.

DATA AVAILABILITY

Anonymized data not published within this article will be made available upon request from any qualified investigator.

ACKNOWLEDGEMENTS

We thank our colleagues and patients from Severance Hospital for making this study possible.

AUTHOR CONTRIBUTIONS

Conceptualization: Ha Young Shin. Data curation: Seung Woo Kim and Hee Jo Han. Formal analysis: Myeongjee Lee, Hye Rim Kim, and Yun Ho Roh. Funding acquisition: Ha Young Shin. Investigation: Seung Woo Kim and Hee Jo Han. Methodology: Seung Woo Kim, Myeongjee Lee, Hye Rim Kim, and Yun Ho Roh. Project administration: Seung Woo Kim and Ha Young Shin. Resources: Ha Young Shin. Software: Ha Young Shin and Myeongjee Lee. Supervision: Seung Woo Kim and Ha Young Shin. Validation: Ha Young Shin. Visualization: Hee Jo Han. Writing—original draft: Seung Woo Kim and Hee Jo Han. Writing—review & editing: Ha Young Shin. Approval of final manuscript: all authors.

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REFERENCES

1. Grob D, Brunner N, Namba T, Pagala M. Lifetime course of myasthenia gravis. Muscle Nerve 2008;37:141-9.
2. Wendell LC, Levine JM. Myasthenic crisis. Neurohospitalist 2011;1:16-22.
3. Abuzinadah AR, Alanazy MH, Butt NS, Barohn RJ, Dimachkie MM. Exacerbation rate in generalized myasthenia gravis and its predictors. Eur Neurol 2021;84:43-8.
4. Bogdan A, Barnett C, Ali A, AlQwaifly M, Abraham A, Mannan S, et al. Prospective study of stress, depression and personality in myasthenia gravis relapses. BMC Neurol 2020;20:261.
5. Szczudlik P, Sobieszczuk E, Szyluk B, Lipowska M, Kubiszewska J, Kostera-Pruszczyk A. Determinants of quality of life in myasthenia gravis patients. Front Neurol 2020;11:553626.
6. Ignatova V, Kostadinov K, Vassileva E, Muradyan N, Stefanov G, Iskrov G, et al. Socio-economic burden of myasthenia gravis: a cost-of-illness study in Bulgaria. Front Public Health 2022;10:822909.
7. Landfeldt E, Pogoryelova O, Sejersen T, Zethraeus N, Breiner A, Lochmüller H. Economic costs of myasthenia gravis: a systematic review. Pharmacoeconomics 2020;38:715-28.
8. Sharma N, Bisen R, Rawat NS, Afaque A, Gupta S. Economic burden of myasthenia gravis in the US: a literature review. Value Health

https://doi.org/10.3349/ymj.2024.0017

2018;21(Supplement 1):S252.
9. Narayanaswami P, Sanders DB, Wolfe G, Benatar M, Cea G, Evoli A, et al. International consensus guidance for management of myasthenia gravis: 2020 update. Neurology 2021;96:114-22.
10. Gummi RR, Kukulka NA, Deroche CB, Govindarajan R. Factors associated with acute exacerbations of myasthenia gravis. Muscle Nerve 2019;60:693-9.
11. Krenn M, Grisold A, Wohlfarth P, Rath J, Cetin H, Koneczny I, et al. Pathomechanisms and clinical implications of myasthenic syndromes exacerbated and induced by medical treatments. Front Mol Neurosci 2020;13:156.
12. Sheikh S, Alvi U, Soliven B, Rezania K. Drugs that induce or cause deterioration of myasthenia gravis: an update. J Clin Med 2021;10:1537.
13. May EF, Calvert PC. Aggravation of myasthenia gravis by erythromycin. Ann Neurol 1990;28:577-9.
14. Bashuk RG, Krendel DA. Myasthenia gravis presenting as weakness after magnesium administration. Muscle Nerve 1990;13:708-12.
15. Hall DR, McGibbon DH, Evans CC, Meadows GA. Gentamicin, tubocurarine, lignocaine and neuromuscular blockade. A case report. Br J Anaesth 1972;44:1329-32.
16. Jones SC, Sorbello A, Boucher RM. Fluoroquinolone-associated myasthenia gravis exacerbation: evaluation of postmarketing reports from the US FDA adverse event reporting system and a literature review. Drug Saf 2011;34:839-47.
17. Pham Nguyen TP, Leonard CE, Bird SJ, Willis AW, Hamedani AG. Pharmacosafety of fluoroquinolone and macrolide antibiotics in the clinical care of patients with myasthenia gravis. Muscle Nerve 2021;64:156-62.
18. Pina Latorre MA, Cobeta JC, Rodilla F, Navarro N, Zabala S. Influence of calcium antagonist drugs in myasthenia gravis in the elderly. J Clin Pharm Ther 1998;23:399-401.
19. Singh P, Idowu O, Malik I, Nates JL. Acute respiratory failure induced by magnesium replacement in a 62-year-old woman with myasthenia gravis. Tex Heart Inst J 2015;42:495-7.
20. Singh YN, Marshall IG, Harvey AL. Some effects of the aminoglycoside antibiotic amikacin on neuromuscular and autonomic transmission. Br J Anaesth 1978;50:109-17.
21. Timmermans G, Depierreux F, Wang F, Hansen I, Maquet P. Cosmetic injection of botulinum toxin unmasking subclinical myasthenia gravis: a case report and literature review. Case Rep Neurol 2019;11:244-51.
22. Watts J, Brew B, Tisch S. Myasthenia gravis exacerbation with low dose ocular botulinum toxin for epiphoria. J Clin Neurosci 2015;22:1979-81.
23. Nelke C, Stascheit F, Eckert C, Pawlitzki M, Schroeter CB, Huntemann N, et al. Independent risk factors for myasthenic crisis and disease exacerbation in a retrospective cohort of myasthenia gravis patients. J Neuroinflammation 2022;19:89.
24. Such-Díaz A, Díaz-Marín C, Sánchez-Pérez R, Iglesias-Peinado I. [Drug exposure associated with exacerbation of symptoms in patients with myasthenia gravis]. Rev Neurol 2020;71:143-50. Spanish
25. Trillenberg P, Katalinic A, Thern J, Graf T. The risk of worsening of myasthenia by cardiovascular medication as reflected by reporting frequency. Eur J Neurol 2021;28:2965-70.
26. Trillenberg P, Katalinic A, Junghanns K, Thern J. Worsening of myasthenia due to antiepileptic, antipsychotic, antidepressant, and sedative medication: an estimation of risk based on reporting frequency. Eur J Neurol 2021;28:2349-56.
27. Arias Pou P, Aquerreta Gonzalez I, Idoate García A, Garcia-Fernandez N. Improvement of drug prescribing in acute kidney injury with a nephrotoxic drug alert system. Eur J Hosp Pharm 2019;26:33-8.
28. Lavan AH, Gallagher PF, O'Mahony D. Methods to reduce prescribing errors in elderly patients with multimorbidity. Clin Interv Aging 2016;11:857-66.