Poster 272

Autonomic Symptoms Differentiate Lambert–Eaton Myasthenic Syndrome from Myasthenia Gravis among Patients with Certain Ocular Signs

Andrew G. Lee[1], Guy Shechter[2], Luis Lay[3], Regina Grebla[4]

[1]Blanton Eye Institute, Houston Methodist Hospital, Houston, TX; [2]MedTech Analytics, LLC, Lexington, MA; [3]Catalyst Pharmaceuticals, Coral Gables, FL; [4]Northeast Epi, LLC, Bradford, NH

Conclusions

In a real-world cohort of MG and LEMS patients with ocular signs, autonomic signs predicted LEMS

Background

- Ocular findings are common in both myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS), however patients with LEMS may be distinguished by the presence of autonomic symptoms.
- Initial presenting symptoms of MG include ptosis and diplopia, whereas LEMS most often starts with mild upper leg weakness.[1]
- LEMS may be excluded among patients initially presenting with ocular findings which may ultimately delay the diagnosis of LEMS.[2]

Objective

- The objective of this study was to assess how autonomic signs can be used to distinguish LEMS from MG in a real-world cohort.

Methods

Data source and study design

- This retrospective cohort study used healthcare administrative claims (Symphony Health's PatientSource®) to identify patients with LEMS and MG.
  - PatientSource data include de-identified longitudinal medical and pharmacy healthcare claims for over 300 million US-based commercial and Medicare Advantage enrollees.
  - Eligible patients had ≥2 MG (ICD-9: 358.00, 358.01; ICD-10: G70.00, G70.01) or LEMS (ICD-9: 358.3, 358.30, 358.31, 358.39; ICD-10: G70.80, G70.81, G73.1) claims ≥30 days apart between 3/1/2014 - 4/30/2022.[3]
- Ocular or autonomic signs and symptoms were identified based on the presence of ≥1 claim(s) for:
  - **Ocular signs:** diplopia, ptosis, or abnormal saccades
  - **Autonomic findings:** anhidrosis, anisocoria, dry eyes, dry mouth, dry skin, constipation, urinary retention, erectile dysfunction, orthostatic hypotension, tonic pupil, Horner's syndrome, or other autonomic disorders
  - Claims for autonomic findings following pyridostigmine therapy were excluded.

Analysis

- Patients with ocular signs with LEMS and MG were descriptively compared using chi-square tests and two-sample t-tests. P values <.05 were considered statistically significant.
  - Firth logistic regression used to model the odds of LEMS relative to MG given the rarity of some events.[4]
- As some patients had claims for both LEMS and MG, a sensitivity analysis was performed modeling LEMS and LEMS+MG as separate outcomes relative to MG.
  - This analysis did not include dry eyes as a predictor, which was highly prevalent in the study population.

Results

- A total of 130,362 patients with MG and 2,013 patients with LEMS were identified. Among them, 42,702 (32.8%) patients with MG and 311 (15.5%) patients with LEMS had claims for ocular signs. Characteristics of these patients are presented in **Table 1**.
  - In patients with any ocular sign, ptosis was less frequent in LEMS than in MG (48.2% vs 58.5%, p=0.0003), while constipation (24.1% vs 12.3%, p<0.0001), dry eyes (16.4% vs 12.4%, p=0.0327), urinary retention (10.9% vs 4.7%, p<0.0001), other autonomic disorders (8.0% vs 2.1%, p<0.0001), orthostatic hypotension (7.7% vs 2.6%, p<0.0001), and dry mouth (3.2% vs 0.8%, p<0.0001) were more frequent among patients with LEMS.
- In multivariate analysis, autonomic signs predictive of LEMS relative to MG included dry mouth (OR: 2.74; 95% CI: 1.44-5.19, p=0.002), other autonomic disorders (OR: 2.57; 95% CI: 1.65, 3.99, p<0.0001), urinary retention (OR: 1.89; 95% CI: 1.29-2.75, p= 0.001), orthostatic hypotension (OR: 1.79; 95% CI: 1.14-2.80, p= 0.0112), and constipation (OR: 1.66; 95% CI: 1.25, 2.19, p= 0.0005). (**Table 2, Figure 1**).
- 1,613 patients with claims for LEMS and 400 patients with claims for both LEMS and MG were analyzed in the sensitivity analysis. Among them, 187 (11.6%) and 124 (31.0%) had claims for ocular signs.
  - In the multivariate sensitivity analyses (**Figure 2A**), Horner's Syndrome predicted LEMS vs MG (OR: 3.74; 95% CI: 1.43, 11.96, p= 0.009) in addition to the predictors observed in the main analysis.
  - In contrast, autonomic signs predictive of both LEMS and MG relative to MG were limited to other autonomic disorders and urinary retention (**Figure 2B**).

Table 1. Characteristics of patients with MG or LEMS* with ocular signs and symptoms (N= 43,013)

	LEMS* N=311	MG N=42,702	*P*
Age, years, mean (SD)	67.1 (12.5)	67.4 (15.7)	0.5785
Female, N (%)	186 (59.8)	21,163 (49.6)	0.0003
Ocular signs and symptoms, N (%)	311 (100.0)	42,702 (100.0)	
Diplopia	221 (71.1)	28,596 (67.0)	0.126
Ptosis	150 (48.2)	24,963 (58.5)	0.0003
Saccade	1 (0.32)	53 (0.12)	0.3244
*Autonomic ocular signs and symptoms, N (%)***	3 (0.96)	434 (1.0)	1.0
Adie syndrome	0 (0.0)	14 (0.03)	1.0
Anisocoria	0 (0.0)	221 (0.52)	0.4158
Horner syndrome	3 (0.96)	234 (0.55)	0.2459
*Other autonomic signs and symptoms, N (%)***	149 (47.9)	12,596 (29.5)	<0.0001
Anhidrosis	0 (0.0)	4 (0.01)	1.0
Other disorders of autonomic nervous system	25 (8.0)	876 (2.1)	<0.0001
Constipation	75 (24.1)	5,255 (12.3)	<0.0001
Dry eyes	51 (16.4)	5,291 (12.4)	0.0327
Dry mouth	10 (3.2)	341 (0.80)	<0.0001
Dry skin	18 (5.8)	1,620 (3.8)	0.0671
Erectile dysfunction	8 (2.6)	927 (2.2)	0.6285
Orthostatic hypotension	24 (7.7)	1,122 (2.6)	<0.0001
Urinary retention	34 (10.9)	2,007 (4.7)	<0.0001
*Autonomic (ocular or other) signs and symptoms***	151 (48.6)	12,847 (30.1)	<0.0001

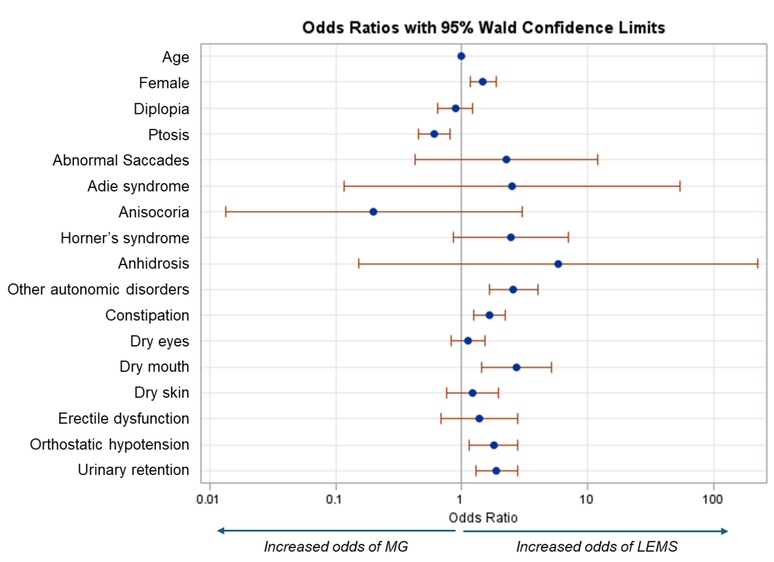
*Includes patients with claims for both LEMS and MG; **Autonomic signs and symptoms excluded claims that occurred after initiation of pyridostigmine. Fisher's Exact Test 2-sided *P* used for analyses with cell values ≤5. Abbreviations: LEMS, Lambert-Eaton Myasthenic Syndrome; MG, Myasthenia Gravis.

Table 2. Associations between ocular and autonomic signs and symptoms and claims for LEMS* vs MG (reference), among patients with ocular signs and symptoms (N= 43,013)

	Univariable Analysis			Multivariable Analysis		
Patient characteristic	**OR**	**95% CI**	**P**	**OR**	**95% CI**	***P***
Age	1.00	(0.99, 1.01)	0.658	1.00	(0.99, 1.01)	0.582
Female	1.51	(1.21, 1.90)	<.001	1.48	(1.17, 1.87)	0.001
Ocular signs and symptoms						
Diplopia	1.21	(0.95, 1.55)	0.127	0.89	(0.65, 1.23)	0.479
Ptosis	0.66	(0.53, 0.83)	<.001	0.61	(0.45, 0.81)	0.001
Saccade	2.60	(0.36, 18.83)	0.345	2.26	(0.42, 12.11)	0.340
*Autonomic ocular signs and symptoms***						
Adie syndrome	4.72	(0.25, 87.66)	0.298	2.51	(0.12, 54.02)	0.556
Anisocoria	0.31	(0.02, 4.97)	0.407	0.20	(0.01, 3.02)	0.245
Horner syndrome	1.77	(0.56, 5.55)	0.329	2.44	(0.86, 6.96)	0.094
*Other autonomic signs and symptoms***						
Anhidrosis	15.20	(0.58, 400.41)	0.103	5.85	(0.15, 223.27)	0.342
Other disorders of autonomic nervous system	4.17	(2.76, 6.32)	<.001	2.57	(1.65, 3.99)	<.001
Constipation	2.27	(1.74, 2.94)	<.001	1.66	(1.25, 2.19)	0.001
Dry eyes	1.39	(1.03, 1.88)	0.034	1.11	(0.82, 1.52)	0.498
Dry mouth	4.13	(2.18, 7.82)	<.001	2.74	(1.44, 5.19)	0.002
Dry skin	1.56	(0.97, 2.51)	0.069	1.23	(0.76, 1.97)	0.400
Erectile dysfunction	1.19	(0.59, 2.41)	0.629	1.38	(0.69, 2.77)	0.367
Orthostatic hypotension	3.10	(2.04, 4.72)	<.001	1.79	(1.14, 2.80)	0.011
Urinary retention	2.49	(1.74, 3.56)	<.001	1.89	(1.29, 2.75)	0.001

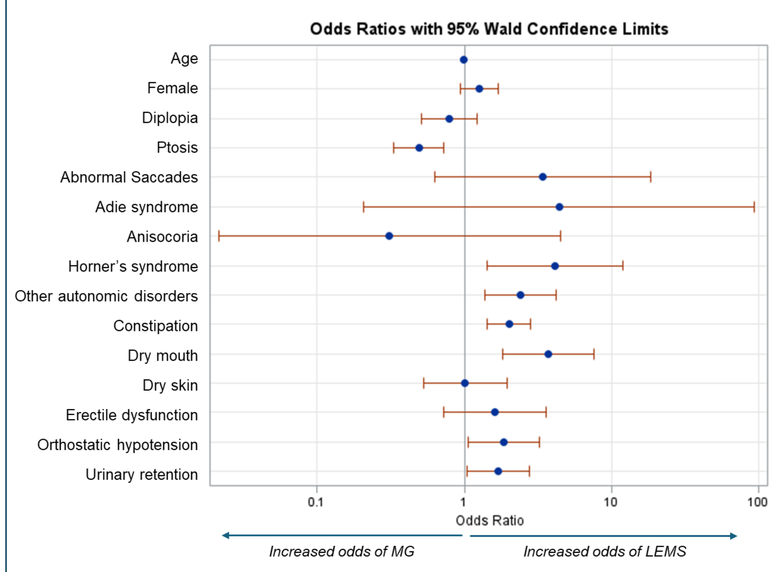
*Includes patients with claims for both LEMS and MG; **Autonomic signs and symptoms excluded claims that occurred after initiation of pyridostigmine. Abbreviations: CI, confidence interval; LEMS, Lambert-Eaton Myasthenic Syndrome; MG, Myasthenia Gravis; OR, odds ratio.

Figure 1. Adjusted odds ratios (95% CIs) of LEMS vs MG (reference), among patients with ocular signs and symptoms in the primary analysis (N= 43,013)



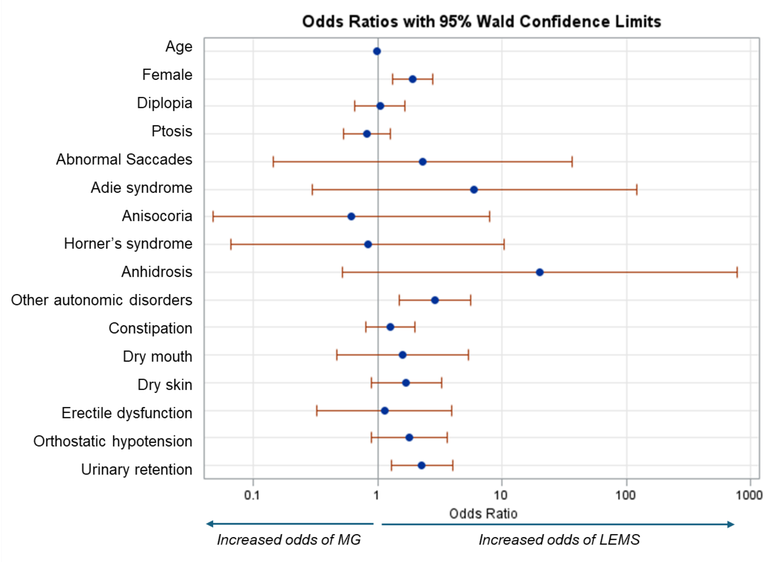
*Includes patients with claims for both LEMS and MG. Abbreviations: LEMS, Lambert-Eaton Myasthenic Syndrome; MG, Myasthenia Gravis.

Figure 2A. Adjusted odds ratios (95% Cis) of LEMS vs MG (reference), among patients with ocular signs and symptoms in the sensitivity analysis (N=42,889)



*Includes patients with claims for both LEMS and MG. Abbreviations: LEMS, Lambert-Eaton Myasthenic Syndrome; MG, Myasthenia Gravis. Note: anhidrosis in one LEMS patient was not included due to model non-convergence.

Figure 2B. Adjusted odds ratios (95% Cis) of LEMS+MG vs MG (reference), among patients with ocular signs and symptoms in the sensitivity analysis (N=42,826)



*Includes patients with claims for both LEMS and MG. Abbreviations: LEMS, Lambert-Eaton Myasthenic Syndrome; MG, Myasthenia Gravis.

Limitations

- The claims data used in this analysis relies upon ICD coding and may not capture all diagnoses or symptoms.
- The rarity of some events in our analysis may limit interpretability and generalizability of some findings.

References

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