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Oral medication treatment patterns in blepharospasm and Meige syndrome: a multi-institutional TriNetX study

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Background: Blepharospasm (BSP) and Meige Syndrome (MeS) are focal dystonias frequently associated with disability and reduced quality of life. While botulinum neurotoxin is the standard of care treatment for these conditions, they only partially and transiently relieve symptoms and can be painful. A variety of off-label oral medications may be tried to mitigate motor symptoms in BSP and MeS, but current treatment patterns have not been assessed. We explored real-world oral medication prescription patterns in individuals with BSP and MeS and identified predictors that influence prescriptions.

Methods: We used TriNetX, a database of deidentified medical data from healthcare organizations around the world, to conduct a retrospective cohort study of oral medication prescription patterns of BSP and MeS. Patient demographics, diagnoses, and medication history were extracted. Medications of interest were grouped into nine classes and analyzed for prescription prevalence, documented prescription interval (first to last record), and prescription of multiple classes of medication. Prescription data and patterns for all medications were analyzed, and multivariate logistic regression models were used to assess the odds of oral medical treatments based on demographic factors.

Results: A total of 20,485 cases of BSP and 6,854 cases of MeS were identified across a 20-year index period. We found 46.7% of patients were treated with at least one class of medication, and that benzodiazepines were the most prescribed class followed by muscle relaxers and gabapentinoids. Lower odds of receiving any oral medication prescriptions were associated with being male, Asian, and in the Southern U.S. while higher odds were associated with being Black. Of those prescribed medications, 35.0% of patients were only prescribed a medication from one class while another 38.3% were prescribed medications from three or more classes.

Conclusion: In a large database cohort, almost half of BSP and MeS patients were prescribed an oral medication that can lessen dystonia severity and the prescription patterns varied across sex, race, and region. In those patients

prescribed an oral medication, more than a third are being prescribed medications from three or more different classes suggesting current oral medication treatment options for BSP and MeS may be inadequate.

KEYWORDS

blepharospasm, meige syndrome, isolated dystonia, oral medication, treatment patterns

Introduction

Blepharospasm (BSP) is an isolated focal dystonia characterized by excessive orbicularis oculi muscle activity leading to abnormal blinking, involuntary eyelid closure, and difficulty with eye opening [1]. Those with BSP frequently experience spread of dystonia to muscles beyond the orbicularis oculi with approximately half of affected individuals experiencing spread to other muscles such as the lower face, mouth and jaw (oromandibular dystonia) [2–4]. A diagnosis of Meige Syndrome (MeS) is often given when an individual has both BSP and oromandibular dystonia [5, 6].

Intramuscular injection of botulinum neurotoxin (BoNT) into the orbicularis oculi and other affected muscles remains the treatment of choice for both BSP and MeS [7]. While BoNT therapy can effectively relieve symptoms in many patients, it requires chronically repeated intramuscular injections that often only partially relieve symptoms, can be painful, and can induce intolerable weakness or other adverse effects. Additionally, for many patients with BSP, the effects of BoNT injections wear off weeks prior to their next injection. In a study of patients with cervical dystonia, up to third of may discontinue BoNT treatment due to these limitations [8].

Many oral medications have been tried for BSP and MeS given the limitations of BoNT therapy and the significant negative impact these disorders can have on daily functions and quality of life [9]. No current oral medication, however, provides adequate relief. Muscle relaxants including anticholinergics, benzodiazepines and other medications targeting gamma-aminobutyric acid receptors (GABA agonists) are frequently tried based on their history of use in and treatment reviews for dystonia [10–13]. Dopaminergic and antidopaminergic medications (including dopamine depleters) are often tried as they can be effective for a variety of forms of dystonia [14]. Antiepileptic medications are occasionally given to BSP and patients as they may provide some symptomatic relief in dystonias [15]. For example, the sodium (Na) channel blocker, carbamazepine, has shown some potential benefit as an adjunct therapy to BoNT in BSP [16]. Also, the stimulant methylphenidate has also been reported to provide relief in individuals with BSP and MeS [17].

Although treatment patterns of medication use in isolated dystonia have been previously reported using data collected by the international multicenter Dystonia Coalition [18], this study involved a relatively small number individuals with BSP, did not include an analysis of individuals identified as having MeS, and most of the patient data analyzed had been collected at tertiary care medical centers possibly leading to a bias of greater medication use. In the present study we sought to use TriNetX, a federated network of Health Insurance Portability and Accountability Act (HIPAA)–compliant data from a large number of healthcare organizations predominantly across the U.S.[1], to assess general patterns of oral medication prescribing in patients with BSP and MeS.

Methods

Study design and data source

We conducted a retrospective cohort study using the TriNetX database platform and methodology similar to what we have recently reported [19]. At the time of our inquiry, November 11, 2024, TriNetX provided access to electronic health records (EHR) for approximately 86,324,341 patients from 91 healthcare organizations and aggregates outpatient and inpatient data from health systems from the US and 18 other countries in the TriNetX Research Network.

Informed consent and ethics

Data from TriNetX does not involve intervention or interaction with human subjects and is de-identified following the HIPAA Privacy rule. Therefore, it is exempt from IRB approval, which was confirmed by the Virginia Commonwealth University Institutional Review Board.

Study eligibility

Our data query included patients who were 30–80 years old with a diagnosis of BSP and/or MeS using the International Classification of Diseases 10 (ICD-10) codes of G24.4 and G24.5 and ICD-9 codes 333.81 and 333.82, respectively. The age range was chosen because the average of diagnosis of BSP and MeS is between ages of 50 and 60 years old, with most diagnoses occurring between the ages of 30 and 80 [20]. By limiting our inquiry

1 www.trinetx.com

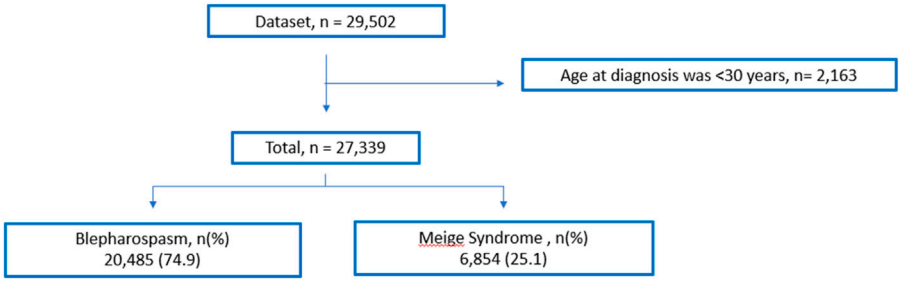

FIGURE 1
Patient cohort flow diagram.

age range we are able to capture most cases of isolated idiopathic BSP and MeS while limiting the possibility of potential confounders such as genetic forms of dystonia that can develop in early ages and acquired causes that affect older populations such as brain lesions and neurodegenerative disease [21, 22]. Exclusion criteria applied included and are not limited to diagnoses of hemifacial spasm, cervical dystonia, laryngeal dystonia, tardive dystonia, drug-induced dystonia, Parkinson disease, and atypical parkinsonian disorders (Supplementary Table 1).

The study period was from 1 July 2004, to 4 November 2024. A total of 29,551 unique patients met our eligibility criteria. The complete dataset was downloaded on 11 November 2024. We reviewed the provided data locally to confirm that all the patients had diagnostic codes consistent with BSP and/or MeS, that they were not diagnosed prior to age 30, and did not include exclusionary diagnoses. Our final cohort consisted of 27,339 eligible patients as seen in Figure 1.

Study variables

Available demographic data included year of birth, sex, race, ethnicity, and geographical region location in the US (Midwest, Northeast, South, or West). For privacy, TriNetX does not provide the exact date of birth for patients. Instead, the year of birth is available. Age for patients was estimated as the time between July 1 of the birth year and the date of the first documented diagnosis. The documented diagnosis interval was calculated as the time between the first date of diagnosis and the last date of diagnosis.

As psychiatric disorders are frequently associated with BSP and MeS [23, 24], and because these disorders may be treated with medications of interest for dystonia, a wide range of psychiatric comorbidities were assessed in the BSP and MeS patient cohorts. These included anxiety, depression, bipolar disorder, attention deficit/hyperactivity disorder, insomnia, and obsessive-compulsive disorder among others (Supplementary Table 2).

A list of 42 medications was generated using recent reviews of dystonia treatment options and published reports of potential benefit in BSP, MeS or more broadly in dystonia. Medication codes for each drug were searched in the TriNetX data query by using the RxNorm codes from the NIH database RxNav[2] and National Drug Codes (NDC) codes from the FDA National Drug Code Directory[3]. Medications were categorized by medication class in a manner analogous to what has been reported previously [12, 18], with some differences including the addition of zolpidem and sodium oxybate to baclofen as GABA agonists, an additional category for gabapentinoid medications, and a separate category for the stimulant methylphenidate (Table 1).

TABLE 1 List of oral medications used in dystonia searched by class.

Anticholinergics	GABA Agonists	Antidopaminergics
Trihexyphenidyl Diphenhydramine Benztropine	Baclofen Zolpidem Sodium oxybate	Quetiapine Clozapine Tetrabenazine Valbenazine Deutetrabenazine
Muscle relaxants	**Benzodiazepine**	**Dopaminergics**
Cyclobenzaprine Methocarbamol Tizanidine Metaxalone Orphenadrine Carisoprodol Chlorzoxazone Dantrolene Mexiletine	Clonazepam Lorazepam Diazepam Alprazolam Temazepam Triazolam Chlordiazepoxide Oxazepam Clorazepate Clobazam Estazolam Bromazepam	Levodopa Amantadine Pramipexole Ropinirole Bromocriptine
Gabapentinoids	**Na channel blockers**	**Stimulants**
Gabapentin Pregabalin	Carbamazepine Oxcarbazepine	Methylphenidate

Abbreviations: GABA, gamma-aminobutyric acid; Na = Sodium.

2 https://mor.nlm.nih.gov/RxNav/
3 https://dps.fda.gov/ndc

TABLE 2 Patient demographics.

Characteristic	BSP (n = 20,485)	MeS (n = 6,854)	Total (n = 27,339)
Age at diagnosis, median years (IQR)	52.4 (41.8, 62.7)	56.8 (46.7, 65.0)	53.7 (42.8, 63 0.3)
Sex (female), n (%)	13,911 (69.7)	4,652 (69.1)	18,563 (69.5)
Race, n (%)			
White	12,541 (61.2)	4,483 (65.4)	17,024 (62.3)
American indian or Alaska native	80 (0.4)	23 (0.3)	103 (0.4)
Asian	1,294 (6.3)	227 (3.3)	1,521 (5.6)
Black or African American	1,970 (9.6)	630 (9.2)	2,600 (9.5)
Native Hawaiian or Pacific islander	142 (0.7)	48 (0.7)	190 (0.7)
Other race	1,003 (4.9)	241 (3.5)	1,244 (4.6)
Unknown	3,455 (16.9)	1,202 (17.5)	4,657 (17.0)
Ethnicity, n (%)			
Hispanic or Latino	1,877 (9.2)	357 (5.2)	2,234 (8.2)
Non-Hispanic or Latino	13,480 (65.8)	4,481 (65.4)	17,961 (65.7)
Unknown	5,128 (25.0)	2,016 (29.4)	7,144 (26.1)
U.S. Region, n (%)			
Midwest	4,331 (21.1)	1,319 (19.3)	5,650 (20.7)
Northeast	5,582 (27.1)	1,828 (26.9)	7,398 (27.1)
South	6,112 (29.9)	2,241 (32.5)	8,353 (30.6)
West	2,927 (14.3)	890 (12.9)	3,817 (14.0)
Depression, n (%)	1,767 (8.6)	771 (11.3)	2,538 (9.3)
Anxiety, n (%)	4,611 (22.5)	1,387 (20.2)	5,998 (21.9)
Insomnia, n (%)	1,571 (7.7)	502 (7.3)	2,073 (7.6)
Narcolepsy, n (%)	200 (1.0)	56 (0.8)	256 (1.0)
ADHD, n (%)	198 (1.0)	89 (1.3)	287 (1.1)
OCD, n (%)	27 (0.1)	48 (0.7)	75 (0.3)

Abbreviations: BSP, blepharospasm; MeS, meige syndrome; ADHD, Attention-Deficit Hyperactivity Disorder; OCD, obsessive compulsive disorder; IQR, interquartile range.

Unfortunately, the TriNetX database does not contain usable BoNT treatment data. While some data do exist before BoNT data were deprecated in 2016, the number of patients treated were well under 10%, which is inconsistent with published data showing most of these patients have tried BoNT injections and that a majority (~60-75%) continue to receive these injections with good response out to 15-20 years [25–28].

For each medication we extracted prescription data, including the presence and date of prescription occurrence for each medication. As we cannot verify the actual duration of medication adherence, we calculated the documented prescription interval as the time between the first and last recording of medication prescription.

Statistical analysis

Data are reported descriptively as means with standard deviations or medians with interquartile ranges (IQR) or counts with percentages as appropriate. We performed multivariate logistic regression analysis with receipt of oral medication being the outcome to estimate the odds based on demographic factors such as age, documented diagnosis interval, sex, race, ethnicity and US region. To account for missing data (patients for whom race and ethnicity were unknown), we compared our full model results to a constructed secondary model where those patient cases with unknown race and/or ethnicity were removed. Statistical significance level for these analyses was set at p-value of <0.05. Statistical analysis was conducted using STATA MP 17.0.

Results

Patient demographics

Our data query resulted in a total cohort size of 27,339 patients in which 74.9% of patients had a diagnosis of BSP and 25.1% had MeS. Patient demographics are provided in Table 2. Median onset age was lower for BSP than for MeS. Both

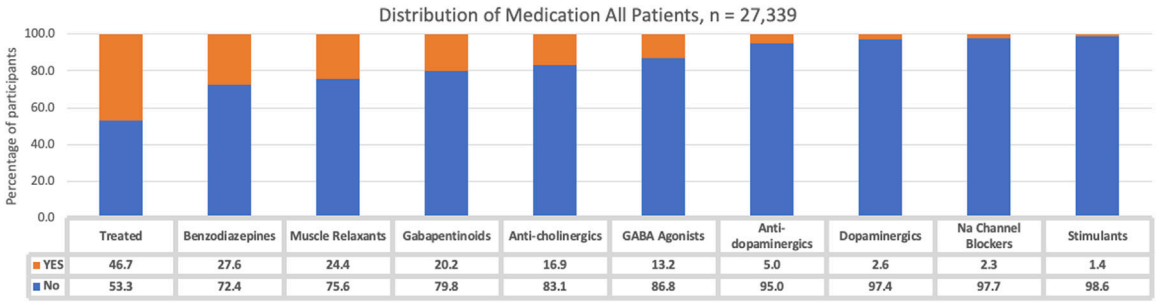

FIGURE 2
Distribution of medications for all patients, n = 27,339.

TABLE 3 Prescription prevalence and average duration of prescription.

Medication class	Total (n = 27,339)	BSP (n = 20,485)	MeS (n = 6,854)	Documented prescription duration, class Specific (Months), median (IQR)
Benzodiazepines, n (%)	7,556 (27.6)	5,155 (25.2)	2,401 (35)	15.8 (0, 70.3)
Muscle relaxants, n (%)	6,681 (24.4)	5,012 (24.5)	1,669 (24.4)	7.2 (0, 55.9)
Gabapentinoids, n (%)	5,511 (20.2)	3,889 (19.0)	1,622 (23.7)	9.1 (0, 50.5)
Anticholinergics, n (%)	4,618 (16.9)	3,137 (15.3)	1,481 (21.6)	0.1 (0, 31.4)
GABA agonists, n (%)	3,599 (13.2)	2,408 (11.8)	1,191 (17.4)	3.2 (0, 41.2)
Antidopaminergics, n (%)	1,377 (5.0)	497 (2.4)	880 (12.8)	6.4 (0, 38.6)
Dopaminergics, n (%)	710 (2.6)	303 (1.5)	407 (5.9)	0.5 (0, 12.6)
Na channel blockers, n (%)	6,681 (24.4)	346 (1.7)	283 (4.1)	3.8 (0, 32.1)
Stimulants, n (%)	5,511 (20.2)	252 (1.2)	127 (1.9)	4.8 (0, 41.9)

Abbreviations: BSP, blepharospasm; MeS = meige syndrome; IQR, interquartile range.

BSP and MeS patients were predominantly females (69.7% and 69.1%, respectively). Most patients were from U.S. centers (2,121 or 7.8% were from an unknown region or outside the U.S.).

Prevalence of prescriptions

In our sample, 46.7% of all patients were treated with at least one medication from Table 1 (Figure 2) with higher treatment rates in the MeS group (52.7%) than in the BSP group (46.8%) (Supplementary Figure 1). When considering all patients, the most prescribed medication class was benzodiazepines followed by muscle relaxants (Table 3). The longest median documented prescription duration was for benzodiazepines at 15.8 months (IQR: 0, 70.3, Table 3), while the shortest median documented prescription duration was for anticholinergic medications at 0.1 months (IQR: 0, 31.4, Table 3).

The relative frequencies of each medication within a class are shown in Figure 3. The most common benzodiazepine prescribed was clonazepam (30%) and the most common muscle relaxer prescribed was cyclobenzaprine (44%). More zolpidem was prescribed in the GABA agonists class (61% vs. 39%) and more diphenhydramine (66%) and benztropine (23%) were prescribed than trihexyphenidyl (11%).

Prescription predictors

A logistics regression model was created to explore the odds of receiving any oral medication used to treat dystonia within our cohort. As reported in Table 2, 17% of patients had unknown race and 26.1% had unknown ethnicities. As a result, two models were created: 1) a full model with all variables included (Table 4), and 2) a limited model without race and ethnicity (Supplementary Table 3). In the full model, statistically significant predictors of treatment included age at diagnosis, documented diagnosis interval, sex, and regional location. Male patients have lower odds of receiving treatment with oral medications, while patients who lived in any region other than the South were more likely to receive treatment. When including races and

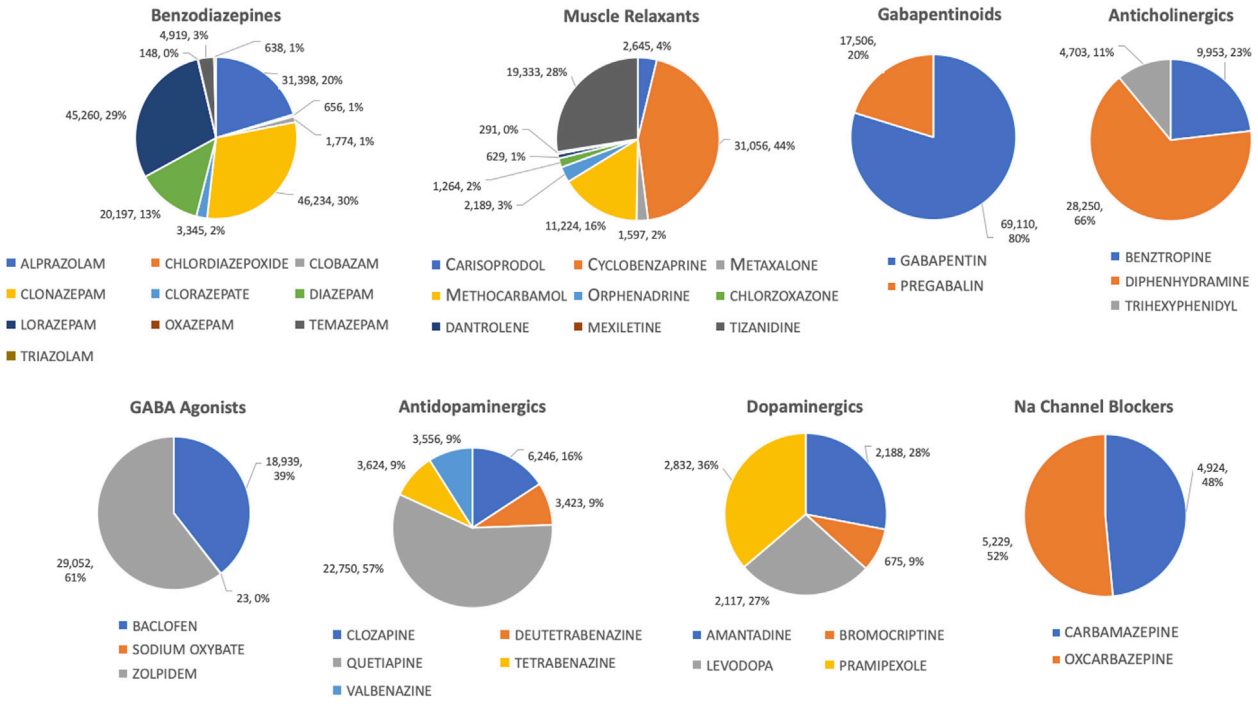

FIGURE 3
Distribution of prescribed medications by medication class.

ethnicities, Asian patients were less likely to receive treatment while Black patients were more likely.

Polypharmacy

Table 5 shows the number of patients prescribed one or more oral medications from each medication class as outlined in Table 1. A total of 35.0%% of patients were only prescribed a treatment from one medication class, and an additional 38.3% of patients were prescribed medications from 3 or more classes and 9.2% of patients were treated with 5 or more different classes of medications.

Comorbid conditions

Since the classes of medication used to treat BSP and MeS might also be used to treat other neurologic and psychiatric disorders, we assessed for the presence of numerous potential co-morbidities (Supplementary Table 2). In our total cohort, 21.9% had diagnosis of anxiety and 9.3% had a diagnosis of depression (Table 2). Rates of comorbid conditions were similar between those with BSP and those with MeS. Of the patients with benzodiazepine prescriptions 13.8% had a diagnosis of depression and 34.3% had a diagnosis of anxiety (Table 6). Benzodiazepines and muscle relaxants were also common in patients who carried a diagnosis of insomnia (10.4% and 11.6%, respectively) and narcolepsy (1.1% and 1.5%, respectively). In patients whose diagnosis list included attention deficit/hyperactivity disorder (n = 5,998), only 1.9% had been prescribed methylphenidate.

Discussion

In a cohort of 27,339 BSP and MeS patients identified using the TriNetX database platform, we found that approximately half were treated with at least one medication across nine different classes of medications that are often used to treat dystonia. The most prescribed medication class was benzodiazepines followed by muscle relaxants, gabapentinoids, and anticholinergic medications. This order of medications is consistent with the findings of a prior study of Dystonia Coalition patients [18]. The documented prescription duration of benzodiazepines was the longest in our cohort with a median of 15.8 months. While the prescription patterns were largely consistent between BSP and MeS patients, the frequency of benzodiazepine use was higher in MeS compared to BSP (35.0% vs. 25.2%, respectively), despite the levels of anxiety being similar between these dystonia subtypes (22.5% vs. 20.2, respectively). The reason for this difference is unclear. The use of benzodiazepines in dystonia disorders including BSP and MeS has been well-documented [29–31], but their effectiveness in each disorder has not been

TABLE 4 Odds of treatment based on patient characteristics in full model.

Characteristic	n (N = 18,544)	OR	95% CI	p-value
Age at diagnosis		1.000	1.000, 1.004	0.125
Documented diagnosis interval		0.948	0.936, 0.959	**<0.001**
Sex				
Female (reference)	12,862	—	—	—
Male	5,682	0.788	0.740, 0.840	**<0.001**
Race				
White (reference)	14,351	—	—	—
American indian or Alaskan native	84	0.700	0.453, 1.081	0.107
Black or African American	2,142	1.103	1.006, 1.211	**0.038**
Asian	967	0.687	0.602, 0.786	**<0.001**
Native American/Pacific islander	66	1.428	0.857, 2.380	0.172
Other	934	0.873	0.757, 1.007	0.063
Ethnicity				
Non-Hispanic or Latino (reference)	16,747	—	—	—
Hispanic or Latino	1,797	1.075	0.967, 1.195	0.180
U.S. Region				
Midwest	5,091	1.525	1.414, 1.645	**<0.001**
Northeast	3,526	1.262	1.161, 1.371	**<0.001**
South (reference)	6,411	—	—	—
West	3,516	1.535	1.408, 1.673	**<0.001**

Abbreviations: OR, odds ratio; CI, confidence interval. Bold p-values considered significant as $p < 0.05$.

thoroughly evaluated in large, controlled studies [14]. Nevertheless, it is possible that the more frequent use in MeS stems from differences in effectiveness or from greater number of cranial regions being affected by dystonia [32].

Anticholinergic medications have good evidence to relieve motor symptoms in dystonia, but their side effect profile likely makes them an infrequently applied treatment option, especially in older populations that tend to develop BSP and MeS [33]. Further supporting poor tolerance of anticholinergics in BSP and MeS patients is the very short median prescription duration, 0.1 months, seen in our study cohort (Table 3). The least commonly prescribed medication classes included dopaminergic and antidopaminergic medications, which have scant evidence in BSP and MeS, and methylphenidate, for which there is some limited evidence reported [17, 34, 35].

The finding that half of patients were not actively receiving any of the oral medications for dystonia could be attributed to low efficacy and the lack of oral treatment options for BSP and MeS patients [36]. While benzodiazepines are the most commonly prescribed medication class, the magnitude of improvements from this drug class have been described as modest [5]. Muscle relaxants and gabapentinoids were also commonly prescribed to patients with BSP and MeS, and the most common medications from those classes were cyclobenzaprine and gabapentin, respectively (Figure 3). Cyclobenzaprine is widely used for muscle spasms and though not an effective agent to lessen dystonic spasms it has been found to reduce pain in dystonia [12, 37, 38]. Studies of its effectiveness in BSP and MeS, however, have not been reported. Gabapentin has not been studied in isolated idiopathic BSP and MeS, but there is some evidence it can be helpful in drug-induced BSP [39, 40]. Another reason for the prescription of muscle relaxants and gabapentinoids for these patients may be to relieve pain that is associated with BSP and MeS [5, 41].

TABLE 5 Rates prescribing across multiple medication classes.

Number of classes	n (%)
1	4,470 (35.0)
2	3,408 (26.7)
3	2,279 (17.9)
4	1,432 (11.2)
5	783 (6.1)
6	306 (2.4)
7	76 (0.6)
8	14 (0.1)
9	0 (0.0)

Our regression analysis revealed some significant predictors of oral medication treatment in BSP and MeS. We found that

TABLE 6 Prescriptions per medication class by patient comorbidity.

Medication class	n	Depression	Anxiety	Insomnia	Narcolepsy	ADHD	OCD
Anticholinergics	4,618	698 (15.1)	1,273 (27.8)	500 (10.8)	69 (1.5)	52 (1.1)	26 (0.6)
Benzodiazepines	7,556	1,042 (13.8)	2,592 (34.3)	783 (10.4)	82 (1.1)	95 (1.3)	39 (0.5)
Muscle relaxants	6,681	979 (14.7)	2005 (30.0)	775 (11.6)	101 (1.5)	94 (1.4)	15 (0.2)
Gabapentinoids	5,511	870 (15.8)	1,534 (27.8)	676 (12.3)	86 (1.6)	85 (1.5)	14 (0.3)
GABA agonists	3,599	559 (15.5)	943 (26.2)	615 (17.1)	50 (1.4)	51 (1.4)	9 (0.3)
Antidopaminergics	1,377	257 (18.7)	369 (26.8)	117 (8.5)	7 (0.5)	19 (1.4)	17 (1.2)
Dopaminergics	710	113 (15.9)	158 (22.3)	77 (10.9)	13 (1.8)	8 (1.1)	4 (0.6)
Na channel blockers	629	107 (17.0)	115 (24.6)	52 (8.3)	9 (1.4)	10 (1.6)	3 (0.5)
Stimulants	379	73 (19.3)	114 (30.1)	42 (11.1)	10 (2.6)	44 (11.6)	2 (0.5)

Abbreviations: ADHD, attention deficit hyperactivity disorder; OCD, obsessive compulsive disorder.

patient sex and race may influence rates of oral medications: males and Asian patients were less likely and Black patients were more likely to be prescribed oral medications. Further, individuals with BSP and MeS from the southern U.S. were less likely to be prescribed oral dystonia medications. The sex and race findings possibly reflect gender and cultural differences in taking oral medications, while the regional differences may stem from the lower number of urban medical centers and/or a paucity of neurology specialists available to treat dystonia [42]. Indeed, a 2022 study reported that only 3.1% of neurologists in the U.S. had a practice in a rural county [43].

Finally, polypharmacy was common in our BSP and MeS population, with 38.3% being prescribed 3 or more classes of dystonia medications. One likely reason for this is oral medication across different medication classes are insufficiently effective in treating BSP and MeS [5, 44]. Combining different classes of medication is also recommended if symptom control is incomplete or a patient reaches an optimal dosage of another medication [13]. Another possibility includes the presence of neurologic and psychiatric co-morbidities that are being treated with similar medication classes used for dystonia [12, 23, 41, 45]. Similar to findings from a Dystonia Coalition study [23], our identified BSP and MeS patients frequently had co-occurring psychiatric diagnoses. For example, nearly 20% of our cohort carried an anxiety diagnosis. This is unlikely to account for the majority of individuals taking benzodiazepines, however, as 65.7% of patients receiving benzodiazepines in our cohort did not have a diagnosis of anxiety. This pattern carried across the other psychiatric comorbidities we assessed.

Our study has some strengths and limitations. TriNetX offers a large database of patients both in the US and globally, but most available data are from the U.S. similar to other medical database platforms, we are unable to confirm the BSP and MeS diagnoses, and it is possible to miss instances of a BSP or MeS diagnosis if not included in the patient's medical record or if the diagnosis was documented outside of the index window and therefore not included in our cohort. Additionally, while we aimed to evaluate only isolated idiopathic dystonia cases, it is possible some of the cases were acquired dystonia cases or cases that stemmed from another neurological disorder such as Parkinson's disease. We limited the chance of this by excluding patients whose records included a confounding diagnosis (Supplementary Table 1) and by exploring the medication history for patients across a 20-year period which allowed us to capture any prescriptions even prior to a formal diagnosis of BSP or MeS. Also unavailable in our study are data on clinical severity, which could have been explored as possible factor underlying lack of oral medication prescriptions and the rates of polypharmacy. TriNetX additionally does not attribute a diagnosis for the prescription of a given medication. Therefore, we are unable to confirm the reason for prescription is for BSP or MeS. For example, muscle relaxants and gabapentinoids may be prescribed for pain for other comorbid conditions and independent of the patient's diagnosis of BSP or MeS. Finally, data on BoNT injections, which is the primary treatment for BSP and MeS [46], are not captured by the TriNetX database. This is a limitation of study as a variety of prior studies have shown that most patients who have been diagnosed with BSP or MeS have tried treatment with BoNT injections and the majority (~65-75%) continue to receive these injections with good response for up to 15–20 years [25–28]. Future studies could benefit from the characterization of co-morbidities to better understand the prescription patterns that were observed in our study population.

Conclusion

Despite the lack of FDA-approved oral medications for BSP and MeS, many different types of treatments may be prescribed. While a handful of evidence-based reviews and small clinical trials have been done on some of the medications explored in our study in dystonia patients, to our knowledge no other work has explored a large cohort's prescription patterns in the BSP and

MeS patient population. Assuming many of the BSP and MeS patients were receiving BoNT injections as the standard of care, our findings provide support that oral medications are often used as adjunctive therapy in these patients. Our findings further support that a customized approach, as highlighted in a recently published current expert opinion [47], is likely needed to most effectively treat patients with BSP and MeS.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, as permitted by TriNetX policies.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Author contributions

RH, NM, CD, AN, MB, and BB contributed to the conception and design of the study. RH, NM, AN, and MB performed the statistical analysis. RH and BB wrote the first draft of the manuscript. RH, NM, CD, AN, MB, and BB critically reviewed and edited the subsequent drafts of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

BB: Has received research grant support from the Dystonia Coalition (receives the majority of its support through NIH grant U54 NS116025), Parkinson's Foundation, VCU School of Medicine, Administration for Community Living, Dystonia Medical Research Foundation, and Neurocrine Biosciences. He currently serves on the Medical and Scientific Advisory Council of the Dystonia Medical Research Foundation as well as the director of the Medical Advisory Board of the Benign Essential Blepharospasm Research Foundation and is a member of the National Spasmodic Torticollis Association. He has served as a consultant for the Dystonia Medical Research Foundation and has received honoraria from the International Parkinson and Movement Disorder Society.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontierspartnerships.org/articles/10.3389/dyst.2025.15368/full#supplementary-material

References

1. Defazio G, Jinnah HA, Berardelli A, Perlmutter JS, Berkmen GK, Berman BD, et al. Diagnostic criteria for blepharospasm: a multicenter international study. *Parkinsonism Relat Disord* (2021) 91:109–14. doi:10.1016/j.parkreldis.2021.09.004

2. Berman BD, Groth CL, Sillau SH, Pirio Richardson S, Norris SA, Junker J, et al. Risk of spread in adult-onset isolated focal dystonia: a prospective international cohort study. *J Neurol Neurosurg Psychiatry* (2020) 91(3):314–20. doi:10.1136/jnnp-2019-321794

3. Svetel M, Pekmezović T, Jović J, Ivanović N, Dragašević N, Marić J, et al. Spread of primary dystonia in relation to initially affected region. *J Neurol* (2007) 254(7): 879–83. doi:10.1007/s00415-006-0457-8

4. Weiss EM, Hershey T, Karimi M, Racette B, Tabbal SD, Mink JW, et al. Relative risk of spread of symptoms among the focal onset primary dystonias. *Mov Disord* (2006) 21(8):1175–81. doi:10.1002/mds.20919

5. Ma H, Qu J, Ye L, Shu Y, Blepharospasm QQ, Dystonia O, et al. Blepharospasm, oromandibular dystonia, and meige syndrome: clinical and genetic update. *Front Neurol* (2021) 12:630221. doi:10.3389/fneur.2021.630221

6. Zeppieri M, Ameer MA, Jahngir MU, Patel BC. Meige syndrome. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing (2025). Available online at: http://www.ncbi.nlm.nih.gov/books/NBK513358/ (Accessed May, 2025).

7. Duarte GS, Rodrigues FB, Marques RE, Castelão M, Ferreira J, Sampaio C, et al. Botulinum toxin type A therapy for blepharospasm. *Cochrane Database Syst Rev* (2020) 11(11). doi:10.1002/14651858.CD004900.pub3

8. Jinnah HA, Comella CL, Perlmutter J, Lungu C, Hallett MDystonia Coalition Investigators. Longitudinal studies of botulinum toxin in cervical dystonia: why do patients discontinue therapy? *Toxicon* (2018) 147:89–95. doi:10.1016/j.toxicon.2017.09.004

9. Yi M, Li J, Liu G, Ou Z, Liu Y, Li J, et al. Mental health and quality of life in patients with craniofacial movement disorders: a cross-sectional study. *Front Neurol* (2022) 21(13):938632. doi:10.3389/fneur.2022.938632

10. Alfradique-Dunham I, Jankovic J. Available treatment options for dystonia. *Expert Opin Orphan Drugs* (2017) 5(9):707–16. doi:10.1080/21678707.2017.1366309

11. Balint B, Bhatia KP. Dystonia: an update on phenomenology, classification, pathogenesis and treatment. *Curr Opin Neurol* (2014) 27(4):468–76. doi:10.1097/WCO.0000000000000114

12. Jankovic J. Medical treatment of dystonia. *Mov Disord* (2013) 28(7):1001–12. doi:10.1002/mds.25552

13. Termsarasab P, Thammongkolchai T, Frucht SJ. Medical treatment of dystonia. *J Clin Mov Disord* (2016) 3(1):19. doi:10.1186/s40734-016-0047-6

14. Bledsoe IO, Viser AC, San Luciano M. Treatment of dystonia: medications, neurotoxins, neuromodulation, and rehabilitation. *Neurotherapeutics* (2020) 17(4):1622–44. doi:10.1007/s13311-020-00944-0

15. Siniscalchi A, Gallelli L, De Sarro G. Use of antiepileptic drugs for hyperkinetic movement disorders. *Curr Neuropharmacol* (2010) 8(4):359–66. doi:10.2174/157015910793358187

16. Xian HL, Lin SC, Hu YF, Liu LY, Liu JB, Hong YC. Efficacy of carbamazepine combined with botulinum toxin a in the treatment of blepharospasm and hemifacial spasm. *Eye Sci* (2012) 27(4):178–81. doi:10.3969/j.issn.1000-4432.2012.04.005

17. Eftekhari K, Choe CH, Vagefi MR, Gausas RE, Eckstein LA. Oral methylphenidate for the treatment of refractory facial dystonias. *Ophthal Plast Reconstr Surg* (2015) 31(3):e65–6. doi:10.1097/IOP.0000000000000079

18. Pirio Richardson S, Wegele AR, Skipper B, Deligtisch A, Jinnah HA, et al.For the Dystonia Coalition Investigators Dystonia treatment: patterns of medication use in an international cohort. *Neurology* (2017) 88(6):543–50. doi:10.1212/WNL.0000000000003596

19. Heo RJ, Negida A, Wyman-Chick KA, Bateman JR, Rodriguez-Porcel F, Berman BD, et al. Patterns and predictors of cholinesterase inhibitor use in dementia with lewy bodies. *Alzheimers Dement N Y N* (2025) 11(3):e70136. doi:10.1002/trc2.70136

20. Sun Y, Tsai PJ, Chu CL, Huang WC, Bee YS. Epidemiology of benign essential blepharospasm: a nationwide population-based retrospective study in Taiwan. *PLOS ONE* (2018) 13 e0209558. doi:10.1371/journal.pone.0209558

21. Hamedani AG, Gold DR. Eyelid dysfunction in neurodegenerative, neurogenetic, and neurometabolic disease. *Front Neurol* (2017) 8:329. doi:10.3389/fneur.2017.00329

22. Zhu L, Meng H, Zhang W, Xie W, Sun H, Hou S. The pathogenesis of blepharospasm. *Front Neurol* (2024) 14:1336348. doi:10.3389/fneur.2023.1336348

23. Berman BD, Junker J, Shelton E, Sillau SH, Jinnah HA, Perlmutter JS, et al. Psychiatric associations of adult-onset focal dystonia phenotypes. *J Neurol Neurosurg Psychiatry* (2017) 88(7):595–602. doi:10.1136/jnnp-2016-315461

24. Defazio G, Gigante AF, Hallett M, Berardelli A, Perlmutter JS, Berman BD, et al. Motor and psychiatric features in idiopathic blepharospasm: a data-driven cluster analysis. *Parkinsonism Relat Disord* (2022) 104:94–8. doi:10.1016/j.parkreldis.2022.10.008

25. Dutton JJ, Buckley EG. Botulinum toxin in the management of blepharospasm. *Arch Neurol* (1986) 43(4):380–2. doi:10.1001/archneur.1986.00520040060020

26. Elston JS. Long-term results of treatment of idiopathic blepharospasm with botulinum toxin injections. *Br J Ophthalmol* (1987) 71(9):664–8. doi:10.1136/bjo.71.9.664

27. Lee J, Jansen A, Samadzadeh S, Kahlen U, Moll M, Ringelstein M, et al. Long-term adherence and response to botulinum toxin in different indications. *Ann Clin Transl Neurol* (2021) 8(1):15–28. doi:10.1002/acn3.51225

28. Streitová H, Bareš M. Long-term therapy of benign essential blepharospasm and facial hemispasm with botulinum toxin A: retrospective assessment of the clinical and quality of life impact in patients treated for more than 15 years. *Acta Neurol Belg* (2014) 114(4):285–91. doi:10.1007/s13760-014-0285-z

29. Jankovic J, Ford J. Blepharospasm and orofacial-cervical dystonia: clinical and pharmacological findings in 100 patients. *Ann Neurol* (1983) 13(4):402–11. doi:10.1002/ana.410130406

30. Ransmayr G, Kleedorfer B, Dierckx RA, Poewe W, Kemmler GW, Gerstenbrand F. Pharmacological study in meige's syndrome with predominant blepharospasm. *Clin Neuropharmacol* (1988) 11(1):68–76. doi:10.1097/00002826-198802000-00007

31. Hipola D, Mateo D, Giménez-Roldán S. Meige's syndrome: acute and chronic responses to clonazepan and anticholinergics. *Eur Neurol* (1984) 23(6):474–8. doi:10.1159/000115731

32. LeDoux MS. Meige syndrome: what's in a name? *Parkinsonism Relat Disord* (2009) 15(7):483–9. doi:10.1016/j.parkreldis.2009.04.006

33. Trihexyphenidyl. In: *Meyler's side effects of drugs*. Elsevier (2016). p. 174–5. Available online at: https://linkinghub.elsevier.com/retrieve/pii/B9780444537171015961 (Accessed: July 24, 2025).

34. Kamitsukasa I, Yamada T, Tokumaru Y, Hirayama K. Clinical features and factors related to the functional prognosis in Meige's syndrome. *Rinsho Shinkeigaku* (1995) 35(3):231–6.

35. Price KM, Ramey NA, Richard MJ, Woodward DJ, Woodward JA. Can methylphenidate objectively provide relief in patients with uncontrolled blepharospasm? A pilot study using surface electromyography. *Ophthal Plast Reconstr Surg* (2010) 26(5):353–6. doi:10.1097/IOP.0b013e3181cffa14

36. Jankovic J, Orman J. Blepharospasm: demographic and clinical survey of 250 patients. *Ann Ophthalmol* (1984) 16(4):371–6.

37. Thenganatt MA, Jankovic J. Treatment of dystonia. *Neurotherapeutics* (2014) 11(1):139–52. doi:10.1007/s13311-013-0231-4

38. Waln O, LeDoux MS. Blepharospasm plus cervical dystonia with predominant anterocollis: a distinctive subphenotype of segmental craniocervical dystonia? *Tremor Hyperkinetic Mov* (2011) 1(0):01. doi:10.5334/tohm.77

39. Liow NYK, Gimeno H, Lumsden DE, Marianczak J, Kaminska M, Tomlin S, et al. Gabapentin can significantly improve dystonia severity and quality of life in children. *Eur J Paediatr Neurol* (2016) 20(1):100–7. doi:10.1016/j.ejpn.2015.09.007

40. Hardoy MC, Hardoy MJ, Carta MG, Cabras PL. Gabapentin as a promising treatment for antipsychotic-induced movement disorders in schizoaffective and bipolar patients. *J Affect Disord* (1999) 54(3):315–7. doi:10.1016/s0165-0327(99)00085-3

41. Jinnah HA, Factor SA. Diagnosis and treatment of dystonia. *Neurol Clin* (2015) 33(1):77–100. doi:10.1016/j.ncl.2014.09.002

42. Pearson C, Hartzman A, Munevar D, Feeney M, Dolhun R, Todaro V, et al. Care access and utilization among medicare beneficiaries living with Parkinson's disease. *NPJ Park Dis* (2023) 9(1):108. doi:10.1038/s41531-023-00523-y

43. Owens M, Owens J, Whiting C. Geographic distribution of neurologists in rural areas (S28.008). *Neurology* (2022) 98(18_Suppl. ment):1975. doi:10.1212/WNL.98.18_supplement.1975

44. Hassell TJW, Charles D. Treatment of blepharospasm and oromandibular dystonia with botulinum toxins. *Toxins* (2020) 12(4):269. doi:10.3390/toxins12040269

45. Yang J, Zhang L, Hou Y, Wei Q, Ou R, Lin J, et al. Sex related differences in nonmotor symptoms of patients with idiopathic blepharospasm. *Sci Rep* (2021) 11(1):17856. doi:10.1038/s41598-021-97289-1

46. Dressler D, Adib Saberi F, Rosales RL. Botulinum toxin therapy of dystonia. *J Neural Transm Vienna Austria* (2021) 128(4):531–7. doi:10.1007/s00702-020-02266-z

47. Scorr LM, Jinnah HA. New trends in the treatment of blepharospasm: replacing the standardized approach with a personalized approach. *Expert Rev Neurother* (2025) 25:1075–83. doi:10.1080/14737175.2025.2532080