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ORIGINAL COMMUNICATION

Alcohol responsiveness in laryngeal dystonia: a survey study

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Abstract Laryngeal dystonia (LD) is a task-specific focal dystonia of unknown pathophysiology affecting speech production. We examined the demographics of anecdotally reported alcohol use and its effects on LD symptoms using an online survey based on Research Electronic Data Capture (REDCap^{TM}) and National Spasmodic Dysphonia Association's patient registry. From 641 participants, 531 were selected for data analysis, and 110 were excluded because of unconfirmed diagnosis. A total of 406 patients (76.5 %) had LD and 125 (23.5 %) had LD and voice tremor (LD/VT). The consumption of alcohol was reported by 374 LD (92.1 %) and 109 LD/VT (87.2 %) patients. Improvement of voice symptoms after alcohol ingestion was noted by 227 LD (55.9 % of all patients) and 73 LD/VT (58.4 %), which paralleled the improvement observed by patient's family and/or friends in 214 LD (57.2 %) and 69 LD/VT (63.3 %) patients. The benefits lasted 1–3 h in both groups with the maximum effect after 2 drinks in LD patients ($p = 0.002$), whereas LD/VT symptoms improved independent of the consumed amount ($p = 0.48$). Our data suggest that isolated dystonic symptoms, such as in LD, are responsive to alcohol intake and this responsiveness is not attributed to the presence of VT, which is known to have significant benefits from alcohol ingestion. Alcohol may modulate the pathophysiological mechanisms underlying abnormal neurotransmission of γ-aminobutyric acid (GABA) in dystonia and as such provide new avenues for novel therapeutic options in these patients.

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Introduction

Laryngeal dystonia (LD), or spasmodic dysphonia, is a task-specific focal dystonia affecting predominantly speaking and occasionally singing. Typically, LD develops in the fourth to fifth decade with either sudden or gradual symptom onset [30]. LD is a relatively rare disorder with the prevalence up to 5.9/100,000 in general population [3], which preferentially affects more women than men with the ratio of about 4:1 [7, 23, 30]. LD most often presents as an adductor type (ADLD), which is characterized by involuntary spasms in the adductor laryngeal muscles, leading to the forceful closure of vocal folds, breaks on vowels and strained, strangled quality of voice. Less common form of LD is the abductor type (ABLD), during which slowed vocal fold closure leads to breathy voice breaks, prolonged voiceless consonants, and excessive breathiness during speaking. Rarely, both types of LD occur in the same individual. About one-third of LD patients are known to develop action-induced voice tremor (VT), which further complicates the diagnosis and management of this disorder [7, 47]. The current gold standard treatment of LD is botulinum toxin (BoNT) injections into the laryngeal muscles [6, 30, 36]. However, BoNT injections are not beneficial for all forms of LD as it is estimated that 90 % of ADLD patients receive 90 % benefit and only 10 % of ABLD patients receive 70 % benefits, whereas co-occurring VT has an unpredictable response [10, 17, 30, 45]. In addition, BoNT injections are relatively expensive and must be typically repeated every 3–4 months throughout a patient's life, which may lead to both psychological and financial burden for a patient [4].

One of the contributing factors to limited therapeutic interventions in these patients is our lack of full understanding of LD clinical phenomenology, etiology and pathophysiology. To this end, an interesting clinical observation in some LD and almost all VT patients is marked improvement of their symptoms after alcohol ingestion. LD and VT are not unique in this regard as several other movement disorders, including essential tremor, myoclonus-dystonia, and posthypoxic myoclonus, are known to improve with alcohol intake, which sometimes leads to the misuse of alcohol to self-manage this range of disorders [22]. Despite the growing evidence of potential therapeutic effects of alcohol in dystonia [5, 9, 13, 15, 25, 34], our knowledge about its effects remains scarce. To characterize the demographics of alcohol use and symptom responsiveness in patients with isolated dystonia, we analyzed the responses to an online survey in a large population of LD patients. As a secondary aim, we compared our results in LD patients to the findings in LD/VT patients because VT has been already known to benefit from alcohol intake [17, 45]. Based on our prior clinical observations, we hypothesized that LD patients will have significant benefits of alcohol on their voice symptoms and these will be independent from improved symptoms of VT.

Methods

All participants were recruited through the National Spasmodic Dysphonia Association's (NSDA) registry via the email invitations to complete an online survey. The NSDA staff member, who contacted the potential participants, was requested to send the online survey invitations only to the individuals who identified themselves as patients with LD or LD/VT. The survey was administered using Research Electronic Data Capture (REDCap^{TM}) hosted at the Icahn School of Medicine at Mount Sinai [18] and was active for online completion for 3 weeks. REDCap^{TM} is a secure, web-based application designed to support data capture for research studies, providing: (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages, and (4) procedures for importing data from external sources. The survey included questions in lay English language pertaining to the use of alcohol and its effects on voice symptoms (Table 1). The questions were designed by one of the authors (SJF) based on similar questions asked in our clinic, then cross-checked and modified by another author (KS), and mock-completed and refined by the laboratory members without a prior knowledge of the survey questions before actual data collection. When patient survey data were downloaded from REDCap^{TM}, all responses were checked by two independent members of the laboratory (including DNK) and any missing values were followed up on and checked with the survey participants, whenever possible. All participants provided written online informed consent, which was approved by the Institutional Review Board of the Icahn School of Medicine at Mount Sinai.

Out of 2024 individuals who opened the NSDA email inviting to the survey participation, a total of 641 subjects (31.6 %) completed the online survey. Among these, 531 subjects (26.2 % of total) were included in further data analysis and 110 subjects (5.4 % of total) were excluded because of incomplete responses and the diagnosis not confirmed or associated with LD or LD/VT. The final participants were followed up to confirm that they were diagnosed with LD or LD/VT by an otolaryngologist, neurologist and/or a speech-language pathologist and that their diagnosis was documented using fiberoptic nasolaryngoscopy. Within-group effect of alcohol use on LD or LD/VT symptoms was assessed using a single proportion test or one-way Chi-square test of association, wherever appropriate, at a Bonferroni corrected $p \leq 0.0045$ to account for multiple comparisons (0.05/11 comparisons). As a secondary aim, we used two-way Chi-square test at a corrected $p \leq 0.0045$ to examine the differences of the alcohol effect between LD and LD/VT groups. All statistical analysis was performed using Systat12 (Systat Software, San Jose, CA, USA).

Results

Among 531 online survey participants, 406 patients (age: 57.3 ± 13.5 years old) were diagnosed with LD and 125 patients (age: 65.2 ± 12.2 years old) were diagnosed with LD/VT (Table 2). The majority of participants were females with the ratio of 3:1 in the LD group and 7:1 in the LD/VT group. The predominant subtype in each group was ADLD with 262 patients (64.5 %) in the LD group and 75 patients (60.0 %) in the LD/VT group. In addition, 10.6 % of LD patients and 15.2 % of LD/VT patients had at least one other family member affected with LD and/or other forms of dystonia. The majority of patients (83.0 % LD and 88.8 % LD/VT) received BoNT injections to manage their voice symptoms; however, only 55.5 % of these LD patients and 35.1 % of LD/VT patients were 'a lot' satisfied with this treatment (Table 2). Other treatment options included voice and speech therapy in 67.7 % of LD and 67.2 % of LD/VT patients; oral medications in 17.5 % of LD and 34.4 % of LD/VT patients; laryngeal surgery in 5.4 % of LD and 7.2 % of LD/VT patients, and deep brain stimulation (DBS) in 1 patient with LD/VT. The vast majority of patients (96.1 % LD and 94.4 % LD/VT)

Table 1 REDCap™ online survey questionnaire

Have you been diagnosed by an ear, nose and throat physician (ENT), speech-language pathologist or neurologist with (select all that apply)	Laryngeal dystonia, adductor type
	Laryngeal dystonia, abductor type
	Laryngeal dystonia, mixed type
	Voice tremor
	Muscle tension dysphonia
Have you ever received any of the following treatment (select all that apply)	Botulinum toxin injections
	Voice and speech therapy
	Had laryngeal surgery
	Had deep brain stimulation (DBS)
	Other medications
	None of the above
If you receive botulinum toxin injections, how much do your injections help?	A lot
	A little
	Not at all
How satisfied are you with your current treatments for your voice (including medications, therapy and injections)?	Very satisfied
	A little satisfied
	Not satisfied
How often do you drink alcohol?	Daily
	Weekly
	Occasionally
	Only on special occasions
	I do not drink alcohol
How much do you typically drink when you do drink alcohol? (1 drink = 1 glass of wine = 1 bottle of beer = 1 shot of hard alcohol)	1 drink
	2 drinks
	>2 drinks
Have you or a family member or friend noticed a change in your voice when you drink alcohol?	Yes
	No
What is the effect of alcohol on your voice?	My voice sounds better
	My voice sounds worse
	I do not notice any changes in my voice
If you voice sounds better, how much better does it get?	Slightly
	Mildly
	A lot
How much alcohol does it take to see the most benefit in your voice?	1 drink
	2 drinks
	>2 drinks
Do you notice that drinking more makes your voice better?	Yes
	No
How long does the effect alcohol last?	<1 h
	1–3 h
	>3 h
How well do you tolerate alcohol?	Well
	OK
	Poorly
Have you used alcohol to help you with your voice in a social or professional situation?	Yes, always
	Sometimes
	Never
If a medication were available that might help your voice, would you consider taking it?	Yes
	No
	Yes

Neurological problems (including but not limited to other types of dystonia, Parkinson's disease, Alzheimer's disease, brain tumor, stroke, etc.)	No
Psychiatric problems (including but not limited to major depression, bipolar disorder, schizophrenia, etc.)	Yes
	No
Any other major medical problems?	Yes
	No
Do you have any relatives with history of (select all that apply)?	Laryngeal dystonia
	Other primary dystonias (e.g., blepharospasm, cervical dystonia, hand dystonia, oromandibular dystonia)
	Tremor (e.g., voice, hand, head)
	Other movement disorders (e.g., Parkinson's disease)
	None of the above
What is your gender?	Male
	Female
How old are you?	

expressed the willingness to try a new medication if it were available (Table 4).

The use of alcohol was reported by the majority of patients who participated in the online survey, including 374 (92.1 %) of LD and 109 (87.2 %) of LD/VT patients, with a good tolerance (all $p \leq 0.0001$) (Table 3). In the survey dataset, the majority of LD patients (34 %) consumed alcohol occasionally, as compared to daily (25.4 %) and weekly (25.9 %) intake ($p \leq 0.0001$), while the pattern of consumption (i.e., daily, weekly, occasionally) did not significantly differ in LD/VT patients ($p = 0.031$). No differences in alcohol consumption ($\chi^2 = 0.036$, $p = 0.99$) and tolerance ($\chi^2 = 3.80$, $p = 0.15$) were found between the two groups; however, LD patients showed a tendency to more alcohol consumption (on average 2 drinks, 42.8 % of patients) compared to on average 1 drink by LD/VT (50.5 % patients) ($p = 0.026$) (Table 3). This pattern of alcohol consumption in LD and LD/VT patients was higher compared to 64 % of regular or infrequent drinkers in general adult population [1].

Improvement of LD symptoms following alcohol ingestion was noticed by 227 patients (55.9 % of all LD patients or 60.7 % of those who drank alcohol) ($p \leq 0.0001$), while 130 patients (32.0 % of all LD patients or 34.8 % of those who drank alcohol) had no changes, and 14 patients (3.4 % of all LD patients or 3.7 % of those who drank alcohol) had worsening of their voice symptoms. Three patients (0.8 %) were not sure about the effects of alcohol on the quality of their voice (Table 4). The amount of alcohol required to see the best response was on average 2 drinks in 43.5 % of LD patients ($p = 0.002$) with the duration of effect from 1 to 3 h ($p \leq 0.0001$). The degree of symptom improvement following the alcohol intake varied from slightly (25.2 % of LD patients) to mildly (30.4 %) to strong (43.5 %) with the majority of patients reporting noticeable symptom improvement following 2 drinks (43.5 %). While there is a possibility that patient's judgment of symptom severity might have been affected by alcohol consumption, this possibility, however, appears to be minimal considering that symptom improvement was also noticed by a family member and/or friends in 214 (57.2 %) LD patients ($p = 0.003$), which is comparable to patients' self-reports.

Responses to alcohol intake in the LD/VT group were reported by 73 patients (58.4 % of all LD/VT patients or 67 % of those who drank alcohol), who observed better quality of voice from slight (20.3 %) to mild (24.3 %) to strong (52.7 %) improvement lasting 1–3 h (55.4 %) (all $p \leq 0.001$) (Table 4). Furthermore, friends and relatives of 63.3 % of LD/VT patients noticed their voice symptom improvement ($p = 0.002$). However, in contrast to the LD group, LD/VT patients did not report a significant amount-dependent response, that is changes in voice symptoms were relatively equally seen following 1 drink (33.8 % patients), 2 drinks (36.5 % patients) or more than 2 drinks (25.7 % patients) ($p = 0.48$).

As means to improve the voice quality, a significant portion of patients in both groups (45.2 % LD and 53.2 % LD/VT) reported that they used alcohol at least sometimes in professional/social situations to self-manage their symptoms (all $p \leq 0.001$).

Discussion

Laryngeal dystonia, as the other forms of focal dystonia, is a multifactorial disorder of unclear pathophysiology, the current gold standard treatment of which is repeated botulinum toxin injections into the affected laryngeal muscles. Alcohol has been previously reported as a potent pharmacological agent alleviating the symptoms of other movement disorders, such as tremor, including VT [12, 17,

Table 2 General patient demographics

	LD	LD/VT	Total patients
	406 (100 %)	*125 (100 %)*	*531 (100 %)*
Gender			
Male	95 (23.4)	13 (10.4)	108 (20.3)
Female	282 (69.5)	93 (74.4)	375 (70.6)
No response	29 (7.1)	19 (15.2)	48 (9.0)
Age			
Mean ± st. dev.	57.3 ± 13.5	65.2 ± 12.2	59.0 ± 13.6
Subtype			
Adductor	262 (64.5)	75 (60.0)	337 (63.5)
Abductor	93 (22.9)	21 (16.8)	114 (21.5)
Mixed	51 (12.6)	29 (23.2)	80 (15.0)
Muscle tension dysphonia (MTD)			
Yes	19 (4.7)	21 (16.8)	40 (7.5)
No	387 (95.3)	104 (83.2)	491 (92.5)
Family history			
Yes	43 (10.6)	19 (15.2)	62 (11.7)
No	363 (89.4)	106 (84.8)	469 (88.3)
Neurological problems			
Yes	42 (10.3)	17 (13.6)	59 (11.1)
No	364 (89.7)	108 (86.4)	472 (88.9)
Psychiatric problems			
Yes	46 (11.3)	16 (12.8)	62 (11.7)
No	360 (88.7)	109 (87.2)	469 (88.3)
Other major medical problems			
Yes	64 (15.8)	23 (18.4)	87 (16.4)
No	342 (84.2)	102 (81.6)	444 (83.6)
Treatment types			
Botulinum toxin injections	337 (83.0)	111 (88.8)	448 (84.4)
Voice and speech therapy	275 (67.7)	84 (67.2)	359 (67.6)
Other medications	71 (17.5)	43 (34.4)	114 (21.5)
Laryngeal surgery	22 (5.4)	9 (7.2)	31 (5.8)
Deep brain stimulation (DBS)	0	1 (0.8)	1 (0.2)
Satisfaction with treatment			
Very satisfied	128 (31.5)	27 (21.6)	155 (29.2)
A little satisfied	126 (31.0)	51 (40.8)	177 (33.3)
Not satisfied	126 (31.0)	42 (33.6)	168 (31.6)
No response	26 (6.4)	5 (4.0)	31 (5.8)
	337 (100 %)	*111 (100 %)*	*448 (100 %)*
Satisfaction with botulinum toxin			
A lot	187 (55.5)	39 (35.1)	226 (50.4)
A little	101 (30.0)	48 (43.2)	149 (33.3)
Not at all	47 (13.9)	24 (21.6)	71 (15.8)
No response	2 (0.6)	0	2 (0.4)

LD laryngeal dystonia, *LD/VT* laryngeal dystonia and voice tremor, *st.dev.* standard deviation

24, 29, 45], and myoclonus-dystonia [21, 31, 37, 46]. Although systematic studies of alcohol effects in primary dystonia have not been, to date, reported, single cases of writer's cramp [27] and generalized dystonia [16] have been described to significantly benefit from alcohol consumption. In the current large study of 531 patients, we observed that over 55 % of patients with LD alone and over 58 % of patients with combined LD/VT reported

Table 3 Demographics of alcohol use

	LD	Within-group *p* value (CI)	LD/VT	Within-group *p* value (CI)	Between-group *p* value	Total patients
	406 (100 %)		*125 (100 %)*			*531 (100 %)*
Alcohol use						
Yes	374 (92.1)	<0.0001 (0.89–0.95)	109 (87.2)	<0.0001 (0.81–0.93)	0.09	483 (91.0)
No	32 (7.9)		16 (12.8)			48 (9.0)
	374 (100 %)		*109 (100 %)*			*483 (100 %)*
Daily use						
Daily	95 (25.4)	<0.0001	27 (24.8)	0.031	0.99	122 (25.3)
Weekly	97 (25.9)		28 (25.7)			125 (25.9)
Occasionally	127 (34.0)		38 (34.9)			165 (34.2)
Special occasions	55 (14.7)		16 (12.8)			71 (14.7)
Amount used						
1 drink	135 (36.1)	<0.0001	55 (50.5)	0.0002	0.026	190 (39.3)
2 drinks	160 (42.8)		34 (31.2)			194 (40.2)
>2 drinks	75 (20.1)		20 (18.3)			95 (19.7)
No response	4 (1.0)		0			4 (0.8)
Tolerance of alcohol						
Well	163 (43.6)	<0.0001	38 (34.9)	<0.0001	0.15	201 (41.6)
Ok	165 (44.1)		54 (49.5)			219 (45.3)
Poorly	37 (9.9)		16 (14.7)			53 (11.0)
No response	9 (2.4)		1 (0.9)			10 (2.1)

Values in parenthesis provide the percent of total population, which is depicted above in the corresponding italicized area

CI confidence interval, *LD* laryngeal dystonia, *LD/VT* laryngeal dystonia and voice tremor

significant positive effects of alcohol on their voice symptoms, such as voice breaks and tremor. Patients' self-reported improvement of voice symptoms following alcohol intake was substantiated by similar observations made by their friends and/or family members, which minimizes the possibility of false-positive subjective responses by patients, due, in part, to potentially reduced accuracy of patient's judgment secondary to alcohol consumption. Our survey data further showed that symptoms of isolated LD responded to alcohol intake and such responsiveness of patients with focal dystonia was not attributed to the presence of VT, which is known to improve following alcohol ingestion [17, 45]. In the majority of patients with LD alone, the symptoms were modulated in dose-dependent manner, i.e., positive effects were noticed following on average two drinks, whereas improvement of combined LD/VT symptoms appeared not to be contingent upon consumed amount of alcohol. Such an effect may be due, in part, to distinct influences of alcohol on pathophysiology of LD vs. LD/VT.

While mechanisms of alcohol action in isolated dystonias are yet to be elucidated, its positive influences may be due to the direct modulation of GABAergic neurotransmission, which has been shown to be abnormal in dystonia [11, 14, 26, 32, 38]. Taking into account that brain abnormalities in LD are not limited to the basal ganglia but include, in addition, the sensorimotor cortex and cerebellum [2, 19, 40, 42–44], effects of alcohol on GABAergic transmission may also be exerted at multiple levels. Indeed, alcohol has been shown to potentiate GABA-mediated neurotransmission in the cortex of healthy subjects and patients with myoclonus-dystonia [35, 48], decrease cerebellar hyperactivity in patients with essential tremor [8], and directly elevate the dopamine level in the nucleus accumbens in the rat [28]. Thus, beneficial effects of alcohol on LD symptoms might be a result of complex modulations of different subsystems contributing to the pathophysiology of LD. Future studies need to examine this assumption in detail.

While the findings of this study provide the first insights into alcohol responsiveness of LD, the study limitations should be noted. First, 26.2 % survey inclusion rate might represent a potential bias by not accounting for patients who check their emails less frequently and who are less inclined to participate in online surveys. Next, the use of the online survey as a tool for collection of patient's information based on subjective self-reports may be viewed as another study limitation. On the other hand, the conduct of online surveys in rare disorders such as LD might prove in some instances to be important for capturing data in a

Table 4 Effects of alcohol on voice symptoms in LD and LD/VT

	LD	Within-group *p* value (CI)	LD/VT	Within-group *p* value (CI)	Between- group *p* value
	Total: 406 (100 %)		*Total: 125 (100 %)*		
	Total drinking LD: 374 (100 %)		*Total drinking LD/VT: 109 (100 %)*		
Response noticed by patient					
Better	227 (55.9/60.7)	<0.0001	73 (58.4/67.0)	<0.0001	0.09
Worse	14 (3.4/3.7)		0		
No change	130 (32.0/34.8)		35 (28.0/32.1)		
Unknown	3 (0.7/0.8)		1 (0.8/0.9)		
	*230 (100 %)**		*74 (100 %)**		
Degree of response					
Slightly	58 (25.2)	0.002	15 (20.3)	0.001	0.31
Mildly	70 (30.4)		18 (24.3)		
A lot	100 (43.5)		39 (52.7)		
Unknown	2 (0.9)		2 (2.7)		
Amount required to see a response					
1 drink	61 (26.5)	0.002	25 (33.8)	0.48	0.41
2 drinks	100 (43.5)		27 (36.5)		
>2 drinks	63 (27.4)		19 (25.7)		
Unknown	6 (2.6)		3 (4.1)		
Does drinking more make voice better					
Yes	159 (69.1)	<0.0001 (0.63–0.75)	48 (64.9)	0.003 (0.54–0.75)	0.59
No	65 (28.3)		23 (31.1)		
Unknown	6 (2.6)		3 (4.1)		
Duration of effect					
<1 h	24 (10.4)	<0.0001	13 (17.6)	<0.0001	0.09
1–3 h	159 (69.1)		41 (55.4)		
>3 h	43 (18.7)		18 (24.3)		
Unknown	4 (1.7)		2 (2.7)		
	*374 (100 %)***		*109 (100 %)***		
Response noticed by family					
Yes	214 (57.2)	0.003	69 (63.3)	0.002	0.17
No	157 (42.0)	(0.52–0.62)	37 (33.9)	(0.54–0.72)	
Unknown	3 (0.8)		3 (2.8)		
Use of alcohol to help with voice in social or professional situation					
Always	33 (8.8)	<0.0001	10 (9.2)	<0.0001	0.31
Sometimes	136 (36.4)		48 (44.0)		
Never	194 (51.9)		48 (44.0)		
Unknown	11 (2.9)		3 (2.8)		
	*406 (100 %)****		*125 (100 %)****		
If a medication were available, would you consider taking it?					
Yes	390 (96.1)		118 (94.4)		
No	4 (1.0)		6 (4.8)		
Unknown	12 (3.0)		1 (0.8)		

Values in parenthesis provide the percent of total population, which is depicted above in the corresponding italicized area

CI confidence interval, *LD* laryngeal dystonia, *LD/VT* laryngeal dystonia and voice tremor

* Data are pulled from the patients who responded "Better" and "Unknown" in the category "Response Noted by Patient"

** Data are pulled from the total of patients who reporting drinking alcohol

*** Data are pulled from the total of all patients

large patient population, which is typically unattainable within a short time frame if based on data from single clinical centers. Taking into account these limitations, our findings are in line with earlier epidemiological studies in LD, reflecting general demographics of surveyed patients. This includes the prevalence of LD in females, predominant ADLD subtype, the mean range of patients at around 60 years, and co-occurrence of VT in about one-third of LD patients [30, 33, 39, 47]. We also found that 11.7 % of all surveyed patients had one or more family members affected with LD or other forms of dystonia, which is similar to a previous report of 12 % [10]. Finally, we observed similar demographic characteristics in an independent group of 126 LD (age: 55.0 ± 12.7 years old) and 52 LD/VT (age: 59.9 ± 10.9 years old) patients who were seen in our clinic between 2009 and 2014 and underwent detailed examination of their voice symptoms for the participation in other studies. Specifically, these patients also had a female:male ratio of 3:1 in the LD group and 7:1 in the LD/VT group, predominant subtype of ADLD in 72.2 % of LD patients and 75 % of LD/VT patients, and a family history of dystonia in 18 % of all patients (unpublished data). Notably, these independent groups of patients reported similar levels of symptom improvement following alcohol consumption (54.8 % in LD and 50 % in LD/VT) as observed in the present study.

In conclusion, the findings of our survey point to alcohol as a possible novel therapeutic agent for LD. However, because continuous consumption of alcohol may lead to abuse and dependency, self-medication or the prescription of alcohol for treatment of this disorder will remain undesirable. Instead, novel drugs mimicking the alcohol effects and increasing GABAergic neurotransmission, such as sodium oxybate [41] and octanoic acid [20], may lend new therapeutic opportunities for treatment of LD both with and without VT.

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Conflicts of interest None.

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