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ORIGINAL REPORT

Long-Term Daytime Use of Sodium Oxybate in Laryngeal Dystonia: A Follow-Up Online Survey Study

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ABSTRACT

Background: Laryngeal dystonia (LD) is a task-specific focal dystonia marked by involuntary spasms in the laryngeal muscles during speech production. Sodium oxybate has recently been demonstrated as a new treatment option for alcohol-responsive (EtOH+) LD patients.

Objective: The objective of this study is to evaluate the long-term use of sodium oxybate for the treatment of LD.

Methods: A total of 149 LD patients were invited to complete the online survey study. Seventy-seven patients (mean age 65.2 ± 11.5 years, 54 females/23 males) completed 21 questions related to their disorder and the use of sodium oxybate.

Results: Six patients (7.8%) reported receiving a prescription of sodium oxybate for the treatment of their voice symptoms. Of these, three EtOH+ patients (50%) reported receiving 1–1.25 g of sodium oxybate on an as-needed basis, with an average of 79.3% ± 20.0% reduction in self-perceived voice symptoms following drug intake. Drug usage ranged from three times per day 5 days per week to three times per month over the span of 6 months–12 years. Patients reported experiencing mild side effects that lasted 1–2 h, including drowsiness, dizziness, or nausea. The remaining three patients reported not being able to fill their prescriptions due to medical insurance reimbursements.

Conclusions: Despite the limited sample size, this study demonstrates that the long-term daytime use of sodium oxybate for the treatment of voice symptoms is safe and effective for EtOH+ isolated focal LD patients. The study highlights medical insurance coverage as one of the limiting factors hindering LD patients from accessing this medication.

Level of Evidence: Level 4.

1 | Introduction

Laryngeal dystonia (LD) is a chronic and debilitating disorder that involves involuntary, uncontrolled spasms of the laryngeal muscles predominantly during speech production. Sodium oxybate has been recently identified as the first potent oral medication for the treatment of patients with alcohol-responsive (EtOH+) LD with and without dystonic tremor of voice (DTv). The safety and efficacy of sodium oxybate in these patients have been established in a phase II open-label single-dose clinical trial [1], followed by a phase IIb randomized double-blind placebo-controlled two-period crossover clinical trial [2]. These

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studies have shown that sodium oxybate provides statistically significant and clinically meaningful improvement of voice symptoms about 40–45 min after intake, with benefits typically lasting 3–3.5 h.

Sodium oxybate is the sodium salt of gamma-hydroxybutyrate (GHB), an endogenous metabolite of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) [3, 4]. It is the primary pharmacological agent approved by the U.S. Food and Drug Administration (FDA) to treat cataplexy and excessive daytime sleepiness in patients with narcolepsy aged 7 years and above [5]. Additionally, it is used off-label to treat fibromyalgia syndrome [6], alcohol use disorder [7], and different forms of alcohol-responsive movement disorders [8]. Long-term night-time administration of sodium oxybate has been studied in adult and pediatric patients with narcolepsy and cataplexy for up to 54 months [9–11] and in patients with fibromyalgia syndrome for up to 38 weeks [12]. Across these disorders and time frames, the safety and tolerability profile of sodium oxybate was reported to remain consistent with the known profile of the medication [5].

In this study, we conducted an electronic survey of patients with LD and LD/DTv who were included in the previous clinical trials of sodium oxybate [1, 2] to evaluate the self-reported long-term efficacy and tolerability of daytime drug intake in this patient population. We hypothesized that long-term daytime use of sodium oxybate in EtOH+ LD patients, both with and without DTv, would demonstrate consistent efficacy and safety over time, without drug tolerance and major side effects, similar to a single-dose daytime administration used in the clinical trials [1, 2].

2 | Methods

Study participants ($n = 149$) were recruited from previously published clinical trials that investigated the immediate efficacy and safety of sodium oxybate in LD and DTv patients [1, 2]. The diagnoses of LD and DTv were confirmed based on a detailed case history, a review of medical information from the referring physicians, perceptual voice and speech analysis, and neurological and laryngological evaluations, as described previously [1, 2].

All patients received an email invitation to complete the online survey, which was administered using Research Electronic Data Capture (REDCap), hosted at Mass General Brigham. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to standard statistical packages; and (4) procedures for data integration and interoperability with external sources. The survey included questions in lay English developed by the authors of this study and mock-completed and refined by the laboratory members before data collection.

The survey questions aimed to (1) identify patients who had received a prescription of sodium oxybate for the treatment of LD and DTv symptoms, and (2) assess the self-reported long-term daytime efficacy and safety of sodium oxybate in these patients. The survey included 21 questions (Table 1) and was active for online completion for 7 weeks (January 15, 2025–March 3, 2025). All survey entries were checked for completeness in the responses.

Written electronic informed consent was obtained from all patients before study participation. The study was approved by the Institutional Review Board of Mass General Brigham.

3 | Results

Among 149 patients invited to complete the study, 83 patients consented to participate in the survey. Eight consented patients did not complete the online study survey. Therefore, the final study cohort included 77 LD patients, 38 of whom were diagnosed with co-occurring DTv (mean age 65.2 ± 11.5 years, 54 females/23 males). The survey cohort included 20 patients (29.4%) from the phase II open-label single-dose clinical trial [1] and 66 patients (61.1%) from the phase IIb randomized double-blind placebo-controlled two-period crossover clinical trial [2], noting an overlap of 9 patients between the two studies. A larger loss to follow-up from the open-label study was expected, given that patient recruitment for this study concluded in 2016.

The final cohort included 43 EtOH+ and 34 alcohol-nonresponsive (EtOH−) patients (see detailed demographics in Table 2). Six patients (7.8%, 4 EtOH+ and 2 EtOH−), including one LD and five LD/DTv patients, reported receiving a prescription of sodium oxybate for the treatment of their voice symptoms after participating in the clinical trials [1, 2]. Of these, three EtOH+ patients (50%) reported taking 1–1.25 g of sodium oxybate on an as-needed basis for their voice symptoms (Table 3). Daytime use of sodium oxybate ranged from three times per day 5 days per week to three times per month. Patients reported using sodium oxybate for 6 months ($n = 1$), 7 years ($n = 1$), and 12 years ($n = 1$).

Using a 10-point visual analog scale (VAS, 0 = none, 10 = most severe/profound), patients reported an average of 79.3% ± 20.0% reduction in self-perceived voice symptoms following drug intake. Reported drug efficacy duration ranged from 1 to 2 h in two patients and up to 24 months in one patient.

All three patients reported experiencing some mild side effects that lasted 1–2 h, including drowsiness ($n = 2$), dizziness ($n = 2$), and nausea ($n = 1$). Additionally, one patient reported experiencing nausea at a higher dose of 1.5 g, after which their physician reduced the dose to 1.25 g. When asked whether the drug-related side effects affected their daily activities, two patients reported an insignificant impact. Among these, one patient currently continues to take sodium oxybate on an as-needed basis, and another patient reported wanting to continue the use of sodium oxybate for their LD symptoms but being unable to do so due to loss of insurance coverage. The third patient elected not to refill their prescription due to the minor side effects interfering with the timing of work-related responsibilities.

The remaining three patients (50%, one EtOH+, and two EtOH−) who received a prescription of sodium oxybate for the treatment

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TABLE 1 | Research Electronic Data Capture (REDCap) online survey questionnaire.

Today's date:	
First name:	
Last name:	
What form of spasmodic dysphonia/laryngeal dystonia have you been diagnosed with? (select all that apply)	Adductor form Abductor form Mixed form Voice tremor Muscle tension dysphonia I don't know Other (if so, specify)
Do you take any medications?	Yes (if so, list medications) No
What form of spasmodic dysphonia or laryngeal dystonia have you been diagnosed with?	Adductor form Abductor form Mixed form I don't know
Please slide the bar to indicate how much effort it is for you to talk without any treatment:	10-point VAS ranging from no effort (0) to constant effort (10)
Have you been prescribed sodium oxybate by your physician for the treatment of your voice symptoms after your study participation?	Yes (if so, name physician) No
Are you currently receiving sodium oxybate treatment?	Yes No (if so, explain why)
What is the dosage of sodium oxybate that you take for the treatment of your voice symptoms?	
Do you take sodium oxybate daily or as needed?	Daily As needed
How often do you take sodium oxybate for the treatment of your voice symptoms?	___ per day ___ per week ___ per month
How long have you been taking sodium oxybate for the treatment of your voice symptoms?	___ months ___ years
Please slide the bar to indicate how much effort it is for you to talk after taking sodium oxybate:	10-point VAS ranging from no effort (0) to constant effort (10)
For how long does your voice improve after the intake of sodium oxybate (in hours)?	
Do you experience side effects after the intake of sodium oxybate?	Yes No
What side effects do you experience?	Sleepiness Dizziness Nausea Other (if so, specify)
How long do the side effects last? (in minutes)	
Do the side effects interfere with your daily life activities?	Yes (if so, which activities are affected?) No
How do you accommodate for the side effects of sodium oxybate in your daily life?	
Any other comments or thoughts you would like us to know?	

Abbreviation: VAS, visual analog scale.

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TABLE 2 | Demographics of patients with laryngeal dystonia.

	EtOH+ ($n=43$)		EtOH− ($n=34$)	
	LD	**LD/DTv**	**LD**	**LD/DTv**
n (%)	21 (27.3)	22 (28.6)	18 (23.4)	16 (20.8)
Gender, *n* (%)				
Female	13 (16.9)	20 (26.0)	10 (13.0)	11 (14.3)
Male	8 (10.4)	2 (2.6)	8 (10.4)	5 (6.5)
Age (years) ± SD	63.5 ± 11.8	66.0 ± 11.3	63.1 ± 12.0	68.8 ± 10.9
Dystonia phenotype, *n* (%)				
Adductor type	13 (16.9)	10 (13.0)	10 (13.0)	9 (11.7)
Abductor type	8 (10.4)	9 (11.7)	8 (10.4)	6 (7.8)
Mixed adductor and abductor type	0 (0.0)	3 (3.9)	0 (0.0)	1 (1.3)
Family history of dystonia, *n* (%)	6 (7.8)	5 (6.5)	2 (2.6)	1 (1.3)
Age of onset (years) ± SD	41.1 ± 11.1	41.8 ± 16.3	46.1 ± 14.0	45.9 ± 16.5
Dystonia duration (years) ± SD	22.4 ± 13.0	24.3 ± 11.0	17.0 ± 8.4	22.9 ± 14.7

Abbreviations: DTv, dystonic tremor of voice; LD, laryngeal dystonia; SD, standard deviation.

TABLE 3 | Clinical profile of patients receiving sodium oxybate for routine treatment.

Subject	Diagnosis	EtOH response	Age of onset (years)	Dystonia duration (years)	Baseline symptoms	Post-drug symptoms (% change)	Duration of benefits	Years on SXB	Side effects
1	ABLD/DTv	EtOH+	52	17	9	2 (77.8%)	2 h	7	Yes
2	ADLD/DTv	EtOH+	36	15	10	0 (100%)	24 months	12	Yes
3	ABLD/DTv	EtOH+	14	39	5	2 (60%)	1–2 h	0.5	Yes

Note: Baseline and post-drug patient-perceived symptom severity was measured with a 10-point visual analog scale (VAS, 0 = none, 10 = most severe/profound).
Abbreviations: ABLD, abductor laryngeal dystonia; ADLD, adductor laryngeal dystonia; DTv, dystonic tremor of voice; EtOH, alcohol; EtOH+, alcohol-responsive; SXB, sodium oxybate.

of their LD symptoms reported not being able to fill their prescription due to medical insurance reimbursements.

4 | Discussion

This follow-up survey study found that the long-term use of sodium oxybate for the treatment of voice symptoms is effective in patients with isolated focal EtOH+ LD and DTv, with a stable safety profile of a daytime drug administration. We report stable self-reported efficacy with no drug tolerance for as long as 12 years, as well as mild and short-lived adverse effects, including drowsiness, dizziness, and nausea. Our results highlight the clinical benefits of using sodium oxybate on an as-needed basis for the treatment of dystonic voice symptoms, allowing patients the flexibility to manage their voice symptoms under the supervision of their treating physician.

The survey reports an average of 79.3% reduction of symptoms after drug intake, which is deemed significantly more effective than the previously reported averages of 33.5%–40.81% of symptom reduction. Notably, the double-blind study reported the drug efficacy range from 16.4% to 84.6%, suggesting that those included in the survey study were likely some of the most drug-responsive patients in the clinical trial. A strong drug response may have been a significant incentive for patients to seek a prescription.

While the previous studies found the benefits of 1.5 g sodium oxybate typically last 3.5 h, two out of three patients in this survey reported the treatment effects up to 2 h, likely due to the smaller dosage used. On the other hand, one patient reported voice symptom improvement for 24 months after a single dose. This atypical long-term efficacy of sodium oxybate has been previously reported [13] and should not be expected in the majority of patients. Taken together, further studies are warranted to clarify whether the long-term daytime use of sodium oxybate shortens the overall duration of drug effects or whether patients report peak effects of the drug without accounting for the gradual tapering of benefits.

Our results highlight several limiting factors that are hindering LD patients from accessing sodium oxybate. First, despite the drug being FDA-approved as the first line of treatment for sleep disorders, there is a perceived physician hesitancy in prescribing sodium oxybate, likely associated with the reports of illicit GHB

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use for nonmedical purposes. However, empirical research has consistently demonstrated that, contrary to recreational GHB, the rates of substance abuse, substance dependence, physical dependence, and diversion of pharmaceutical sodium oxybate at therapeutic doses taken at a prescribed dosing schedule have been extremely low since its introduction to the market in the United States in 2002 [14]. This can be attributed, in part, to the robust risk management program (REMS), which coordinates and dispenses the drug through a centralized pharmacy to ensure that prescribers and patients are educated on and understand the risks and safe use of the drug [15]. Second, the lack of medical insurance coverage appears to prevent patients from being able to access or afford the medication. Studies showing the high efficacy and safety of sodium oxybate in LD and DTv patients, along with its use at much lower doses (1–1.5 g) than in patients with narcolepsy (9 g and above), may eventually increase the success rate of insurance approvals, making the drug available to more eligible patients with dystonia.

The methodological limitations of this survey study must be acknowledged. An online questionnaire may have exposed the survey to a self-reporting bias. However, the replicability of the efficacy and safety observed in both immediate [1, 2] and long-term use suggests that the reported results may not exclusively be driven by self-perception or expectancy bias. Another limitation to consider is the sample size. Although this survey included a large cohort of LD and DTv patients, only a small percentage of patients received and filled the prescription for sodium oxybate. This finding again points to the current inaccessibility of sodium oxybate for dystonia patients, despite the fact that the vast majority of patients have previously expressed a willingness to be treated with a new medication if it were available [16].

In conclusion, despite the limited number of patients who were treated with sodium oxybate, this survey study demonstrates that the long-term daytime use of sodium oxybate is safe and effective in EtOH+ LD patients. This study also highlights the limiting factors hindering the advanced clinical care of these patients using this newly developed oral treatment.

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Conflicts of Interest

Kristina Simonyan receives funding from the National Institutes of Health (R01NS088160, R01NS124228, R01DC011805, R01DC012545, R01DC019353, P50DC01990), serves on the Scientific Advisory Board of the Tourette Association of America, and the Voice Foundation. The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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