Patient Experiences With Sodium Oxybate Therapy for Narcolepsy: A Social Listening Analysis

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INTRODUCTION

In this study, we used social listening (SL)¹ and a survey to address concerns in the narcolepsy community. Individuals with narcolepsy may experience increased socioeconomic burden and decreased quality of life. People with narcolepsy also are at increased risk for injury, with 30% to 50% of individuals living with narcolepsy experiencing accidents or injuries.² Sodium oxybate (SO), a twice-nightly therapy, has shown effectiveness for sleep issues associated with narcolepsy³; however, SO can present its own challenges for patients as a result of nighttime waking to take the required second dose, including dosing administration errors with immediate-release formulations taken <2.5 hours or >4 hours after the first dose.⁴ Treatment adherence for wakefulness-promoting agents in persons living with narcolepsy is poor, including for therapy with SO.⁵

METHODS

We developed a customized SL methodology for analyzing large amounts of social media data around particular diseases. Our analytics engine leverages natural language processing technology, such as a custom clinical entity recognition model, to construct a cooccurrence network of concepts and identify relationships between entities (e.g., substances, clinical findings). In addition, it employs a large language model to detect posts and comments discussing challenges taking a second dose of SO as well as posts/ comments that mention any type of injury or accident.

A Facebook group application was used to gather data from the private Facebook group.



Sodium oxybate changed my life for the better, but navigating the second dose is a struggle. I can't live my best life without consistent dosing.

> - Community member

DATA EXPLORATION RESULTS



TABLE 1. SODIUM OXYBATE AND INJURY CROSS-TABULATION

Mention

Second dose of SO

SO, but not second do

Does not mention SO

We used a G-test to examine whether there was an association between mentioning of injury and mentioning of SO (and dose) in posts/comments. The G-test results show a G-value of 34.47 and P < .00001 (significant at P < .05), indicating a statistically significant association. The probability of mentioning any injury or accidents in posts/comments is 5.90% for those mentioning a second dose of SO, compared with 3.28% for posts/comments mentioning SO (not mentioning second dose) and 2.93% for posts/comments not mentioning SO at all. However, the effect size, Cramér V, is 0.014, indicating the association is not strong.



FIGURE 1. CHALLENGES WITH SECOND DOSE

Challenges mentioned

A total of 4,275 of the subreddit users mentioned SO, with 398 users communicating challenges with taking a second dose of SO.

*Percentages reflect those from Reddit only, as user-level information is not available through Facebook.

EXPLORATION DATA SOURCES

Private Facebook Group and Subreddit r/Narcolepsy

> 226,046 **POSTS & COMMENTS EVALUATED**

AUGUST 2011 – OCTOBER 2022

DATE RANGE

		Post/Comment Mentions Any Type of Injury or Accident?		
	Count	Yes	Νο	Tota
	Actual	67	1,068	1,13
	Expected	33.82	1,101.18	
se	Actual	726	21,436	22,16
	Expected	660.31	21,501.69	
	Actual	5,942	196,807	202,74
	Expected	6,040.87	196,708.13	
	TOTAL	6,735	219,311	226,04

FIGURE 2. CO-OCCURRENCE NETWORK

The co-occurrence network (Figure 2) connected the second dose of SO with physical issues such as nausea, headaches, dizziness, and hunger, as well as mental health issues such as anxiety, panic, and depression.



SURVEY RESULTS

SURVEY DATA SOURCES

3 Private Facebook Groups and Discord Servers Patients: 85 Caregivers/Care Partners: 2

> Diagnoses Type 1 narcolepsy: 44 Type 2 narcolepsy: **39** Unsure: 2

Medications

Currently taking SO therapy: 64

Previously taken SO therapy: **45**

OCTOBER 2022 – NOVEMBER 2022 DATE RANGE

TABLE 2. FREQUENCY OF MISSING SECOND DOSE (n = 64)

FREQUENCY	%
A few times a week	17
Once a week	20
Once a month	28
Every 6 months	25
Once a year	5
Less than once a year	5

Of the survey participants, ~75% reported missing the second SO dose; effects included poor sleep quality, increased daytime sleepiness, mental health issues (especially depression), muscle spasms, work/school absences, and brain fog.

TABLE 3. BELIEF THAT SODIUM OXYBATE IS SAFER AS A SINGLE DOSE (N = 87)

RESPONSE	%
Strongly agree	46
Agree	30
Neither agree nor disagree	11
Disagree	6
Strongly disagree	7

When asked if a once-at-bedtime, premeasured SO dose would be safer, 76% of respondents agreed or strongly agreed.

CONCLUSIONS

Actively listening to the unmet needs of a community is an important step in understanding the efficacy of drugs, dosing regimens, and how patients report these effects on quality of life to find solutions to reduce clinical and socioeconomic burdens. In this study, the SL analysis identified concepts and issues from conversations associated with SO. The survey revealed that a missed or delayed second dose of SO was connected to decreased daily functioning, quality of life, and physical health. Although the association of the second dose of SO with injury was not strong through SL, taking a second dose is still an issue for people with narcolepsy when asked. Clinicians should ask their patients about potential issues with second dosing even if patients do not spontaneously offer that information. The engine revealed other significant connections that should be investigated in further studies.

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Taking the second dose late (>4 hours after the first) was reported by 59% of patients; effects of late dosing included grogginess, headache, and oversleeping, leading to school/work tardiness and missed responsibilities. Too-frequent dosing (<2.5 hours after the first dose) was another issue reported by 21% of those surveyed, with 39% of those reporting that this happens at least once a month. Injuries occurring at the time of waking to take the second dose (e.g., falls, stitches, concussions) were reported by 32%.

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Abstract

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Narcolepsy is a disorder of hypersomnolence with intermittent periods of sleep, hallucinations, and sleep paralysis. Social listening (SL) analyzes real-world data on social media to provide information on disease symptoms and impacts to inform clinicians about a community's unmet needs. This research used SL with a proprietary artificial intelligence (AI) engine, which leverages natural language processing (NLP) to understand experiences of people living with narcolepsy treated with sodium oxybate (SO), a twice-nightly medication. Using the proprietary AI engine to analyze text-based conversations, we evaluated 25,018 posts/comments from 15,280 participants which occurred from August 2011 to October 2022 from the subreddit r/Narcolepsy and a private Facebook group. Using a clinical entity recognition tagger, leveraging medicine ontology, conversations were filtered by mentions of (1) second dosage (e.g., second dose, 2nd) and (2) sodium oxybate (e.g., Xyrem, SO) to build a co-occurrence network for conversations discussing second doses of SO. Surveys and interviews were used to document patient SO experiences (Facebook, Discord channels, other networked contacts). Of 4,275 subreddit users who mentioned SO, 398 (9.3%) communicated challenges with taking a second SO dose. The co-occurrence network revealed that second SO dose was co-mentioned with physical (e.g., nausea, headache) and mental (e.g., anxiety, depression, eating disorder) conditions. Of survey participants (N = 87completed: patients, n = 85; caregivers, n = 2), 75% reported missing the second SO dose; effects included poor sleep quality, increased daytime sleepiness, mental health issues (especially depression), muscle spasms, work/school absences, and brain fog. Injuries resulting from waking to take the second dose (e.g., falls, stitches, concussions) were reported by 32%. Taking the second dose late (>4 hours after) was reported by 59% of patients. Effects of late dosing included grogginess, headache,

and oversleeping, leading to school/work tardiness and missed responsibilities. When asked if a once-at-bedtime, premeasured SO dose would be safer, 76% of respondents agreed/strongly agreed. The second nightly SO dose is associated with sleep-related issues for people with narcolepsy and their caregivers. Both the SL analysis and survey revealed that a missed/delayed second dose of SO decreased daily functioning, quality of life, and physical health.

Calculations for Table 1

Expected value in cross-tabulations

Cross-tabulations are commonly used in statistical analyses to explore relationships between categorical variables and to perform hypothesis tests, such as the χ^2 test or G-test, to determine whether there is a significant association between variables.

In a cross-tabulation, the rows represent the categories of 1 variable, whereas the columns represent the categories of another variable. The actual value in the cell displays the count of observations that fall into the corresponding categories of both variables.

The expected value for each cell is calculated based on the assumption of independence between the 2 categorical variables. To find the expected value for a specific cell, we multiply the corresponding row total by the column total and then divide the result by the grand total (i.e., the total number of observations).

Mathematically, the expected value (E) for a cell in row i and column j can be calculated as follows:

E(i, j) = (row_total_i × column_total_j) / grand_total

For the cross-tabulation table shown above, the actual value the cell in row 1 column 1 is 67, meaning there are 67 posts/comments that mentioned both injury and second dose of SO; the expected value is then calculated as $1,135 \times 6,735 / 226,046 = 33.82$. Similarly, for the cell in row 1, column 2, there are 1,068 posts/comments that mentioned second dose of SO but no injury; the expected value for this cell is calculated as $1,135 \times 219,311 / 226,046 = 1,101.18$.

After calculating the expected values, we can compute the χ^2 test statistic or the G-test statistic by comparing the observed and expected values for each cell in the contingency table.

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We conducted both χ^2 and G-tests in this study. Both turned out to be significant, but we report the G-test in the poster because it is considered more accurate with large sample sizes.

G-test

The test hypothesis is:

 H_0 : Mentioning of injury is not associated with mentioning of SO and its dose. H_1 : Mentioning of injury is associated with mentioning of SO and its dose.

The G-test results showed a G-value of 34.47 and P < .00001 (significant at P < .05). The G-value is calculated using the formula below:

 $G = 2 \times \sum [actual_value \times ln(actual_value / expected_value)]$

In a comparison of the probability of injury mentions across different categories, 5.90% of posts/comments mentioning a second dose of SO mentioned injury, whereas 3.28% of posts/comments that mentioned SO (without specifying the second dose) mentioned injury, and 2.93% of posts/comments not mentioning SO at all mentioned injury.

These percentages help us understand the proportion of injury mentions in each category (i.e., second dose of SO, SO but not second dose, and not mentioning SO). They provide insight into whether the mention of a second dose of SO is associated with a higher likelihood of mentioning injury in the posts/comments.

These percentages are calculated by dividing the number of posts/comments mentioning injury in each category by the total number of posts/comments in that category. This gives us the proportion of posts/comments mentioning injury for each category. Below is how these percentages are calculated:

- 5.90% (probability that a post/comment mentioning second dose of SO mentions injury):
 - Number of posts/comments mentioning injury and a second dose of SO: 67
 - Total number of posts/comments mentioning a second dose of SO: 1,135
 - Calculation: (67 / 1,135) × 100 = 5.90%

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- 3.28% (probability that a post/comment mentioning SO [no second dose] mentions injury):
 - Number of posts/comments mentioning injury and SO (not specifying the second dose): 726

- Total number of posts/comments mentioning SO (not specifying the second dose): 22,162
- Calculation: (726 / 22,162) × 100 = 3.28%
- 2.93% (probability that a post/comment that does not mention SO mentions injury):
 - Number of posts/comments mentioning injury without mentioning SO: 5,942
 - Total number of posts/comments not mentioning SO: 202,749
 - Calculation: (5,942 / 202,749) × 100 = 2.93%

Further, it is essential to consider the effect size, which tells us the strength of the association. In this case, Cramér V is 0.014, suggesting a weak association between the mention of SO (and dose) and injury mentions. In conclusion, although there is a statistically significant association between a second dose of SO and injury mentions in posts/comments, the effect size indicates that this association is weak.

Disclosures

Matthew Horsnell, Enming Zhang, Rachelle Cook, Lauren Dougherty, Wei Li, and E. Robert Wassman are employees of and own stock options with TREND Community; their clients are pharmaceutical and biotechnology companies including, but not limited to, Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. Allison Foley Shenk and Frederik Ascencion have no conflicts of interest to disclose. Anne Marie Morse is a consultant for Harmony Biosciences and Jazz Pharmaceuticals; has served on advisory boards and speakers bureaus for Jazz Pharmaceuticals; has received grant funding from the National Institutes of Health/National Institute of Mental Health; has served as an advisor for Epilog, Neura Health, and the American Sleep Apnea Association; and was a REST-ON site principal investigator for Avadel Pharmaceuticals. Luis E. Ortiz has served on an advisory board for Avadel Pharmaceuticals. Christopher DeFelice and Maria Picone are owners of and own stock options with TREND Community; their clients are pharmaceutical and biotechnology companies including, but not limited to, Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel.

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