Therapeutic Laryngoscopy During Exercise: A Novel Non-Surgical Therapy for Refractory EILO

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Summary. Background: Exercise-induced laryngeal obstruction (EILO) may affect as many as 6% of the adolescent population, with some patients experiencing symptoms refractory to conservative interventions. Objectives: This report describes therapeutic laryngoscopy during exercise, a novel, non-surgical intervention that harnesses real-time laryngoscopy video as biofeedback to control laryngeal aperture during high-intensity exercise. Additionally, we quantitate patient-reported perceptions of procedure safety, tolerability, learning value, and effectiveness. Methods: Clinical EILO patients with symptoms refractory to conventional respiratory retraining and other therapies were referred for the procedure which features laryngoscopy video as biofeedback during serial physician-guided 1-min exercise sprints. We quantify perceptions of procedure safety, tolerability, learning value, and effectiveness through questionnaires offered to all patients as well as observers of the procedure. Results: Forty-one patients and 37 parent observers were approached for feedback; 88% of patients and 95% of observers consented to participation. Patients and observers reported perceptions of safety and tolerability (81% and 86%, respectively), learning value (78% and 91%, respectively), and effectiveness (58% and 80%, respectively) with patient age predicting some responses. Seventy-five percent of patients noted that "Since the procedure, my breathing during exercise has improved," and 85% of this group noted that therapeutic laryngoscopy during exercise was "the most important therapy leading to my breathing improvement." The procedure also provided insight into the psychological experience of patients, a domain not clinically apparent prior to the procedure. Conclusions: Our data support further study of therapeutic laryngoscopy during exercise as a possible intervention for patients with refractory EILO. **Pediatr Pulmonol.**

Key words: therapeutic laryngoscopy during exercise; continuous laryngoscopy during exercise; exercise-induced laryngeal obstruction; vocal cord dysfunction; exertional dyspnea.

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INTRODUCTION

Exercise-induced laryngeal obstruction (EILO) is a condition in which the glottic and supraglottic structures cause upper airway obstruction during exercise. EILO was recently identified as the preferred terminology to describe the clinical entity formerly known as vocal cord dysfunction and paradoxical vocal fold motion by an international and multispecialty panel of experts.[1] First formally described in the 1980s, it is thought to affect approximately 6% of the adolescent population.[2–4] EILO is important for its impact on exercise performance, comfort, and enjoyment. Although several hypotheses regarding its mechanism have been proposed, the precise contributions of the cerebral cortex, peripheral nervous system, laryngeal epithelium, laryngeal connective tissue, and associated conditions are not fully understood.[5] Therapies for EILO that have been promoted include medical intervention (with anticholinergic agents as well as treatment of associated conditions),[6] surgical interventions (targeted at minimizing supraglottic obstruction),[7] and behavioral interventions (including respiratory retraining, voice therapy, biofeedback, hypnosis, and cognitive behavioral therapy).[4,8]

Although medical and behavioral therapy have been reported to be widely successful,[6,9] there are reports of patients that do not respond to conservative nonsurgical therapy.[7,10] Due to the hesitancy of patients and practitioners to intervene surgically in the context of an absence of data from randomized controlled trials regarding surgery, there is a need to develop additional nonsurgical therapeutic modalities for this condition.

For this reason, we designed an intervention that we call therapeutic laryngoscopy during exercise (TLE). This is a procedure in which a patient uses real-time laryngoscopy footage as visual biofeedback in an attempt to learn techniques that could maximize laryngeal aperture during high-intensity exercise, similar to a concept described by Panchasara.[11]

This initial report will describe the procedure and rationale behind selection of specific procedural variables. Additionally, we ask three questions: Among patients that underwent the procedure and family members that observed the procedure, (i) is TLE perceived to be safe and tolerable, (ii) is it valuable from the perspective of learning, and (iii) is it perceived to be clinically effective? In order to answer these questions, we invited all patients, many of whom were competitive athletes, and observers of TLE to provide survey feedback on these topics. We hypothesized that, among patients and observers, the procedure would be perceived to be safe, tolerable, valuable from a learning perspective, and effective against the primary problem.

METHODS

Therapeutic Laryngoscopy During Exercise Overview

We designed the TLE procedure in hopes of harnessing the power of visual biofeedback to improve motor learning, a technique that has been frequently employed in the competitive sporting world for decades.[12] Nearly 30 years ago, visual laryngoscopic biofeedback was used for patients with inducible laryngeal obstruction caused by stimuli other than exercise.[13]

After placement and mounting of a flexible laryngoscope in a manner previously described, we ask patients to perform several high-intensity sprints while simultaneously observing real-time laryngoscopy footage.[14,15] (Fig. 1, Video 1) The clinician is present to provide specific instructions regarding maneuvers hypothesized to maximize laryngeal aperture throughout the respiratory cycle.

Exercise Protocol and Rationale

In general, our clinical patients perform between eight and ten 60-sec cycle ergometry sprints on a 4-min interval at a work rate between 110% and 120% of their previously established peak work capacity. Treadmill sessions for selected runners are performed in some cases. High work rates are necessary to trigger EILO repeatedly,[16] thus allowing several independent opportunities to work on prevention, minimization, and resolution of symptoms. This is a challenging exercise stimulus, but high-intensity interval training is familiar to most competitive athletes. Work rates and intervals can be altered in order to optimize the learning benefit of the procedure, a practice that is necessary at times because respiratory distress can undermine learning.

Teaching Protocol and Rationale

The interval sprint model also allows for a significant amount of rest, which can be harnessed for teaching,

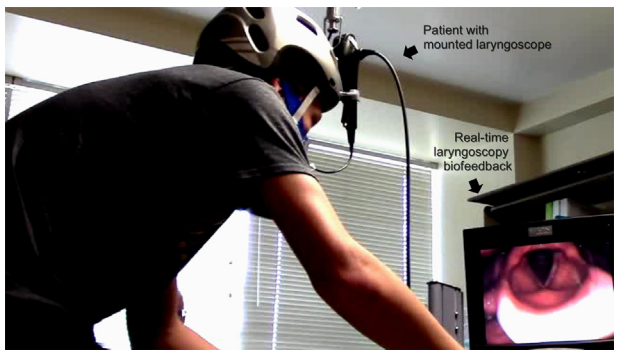

Fig. 1. Therapeutic laryngoscopy during exercise apparatus configuration.

reflection, and preparation for the next exercise sprint. In general, over a 1-hr session, we try to focus on one or two specific breathing strategies. The prolonged sessions allow providers to incrementally teach specific techniques over several intervals. Additionally, the strenuous exercise and repeated respiratory distress often provoke emotional responses. While our teaching initially focused on motor techniques designed to maximize laryngeal aperture during inhalation, the teaching plan has expanded to include attention to performance psychology domains that may be relevant to the overall clinical picture.

Target Population

Patients who underwent the TLE procedure were referred, in general, for EILO that was incompletely responsive to previously attempted therapies. Specific interventions attempted prior to TLE varied across patients, but included respiratory retraining and voice therapy by speech-language pathologists in the majority of cases, as well as general psychological evaluation and intervention, performance psychology evaluation and intervention, respiratory biofeedback, and hypnosis.

Participant Selection

The Institutional Review Board at National Jewish Health approved this study in which all patients who previously underwent TLE at our institution were approached with the opportunity to evaluate the TLE procedure. Observers of the procedure who were present during informed consent conversations as well as observers of the procedure that received invitations from patients to provide feedback also had the opportunity to complete a similar evaluation.

Evaluation of Perceived Safety, Tolerability, Learning Value, and Efficacy

Consenting patients and procedure observers were asked to complete a brief questionnaire (see online supplemental material). Questionnaire items were not prospectively validated. Participants were asked to evaluate statements about their sense of safety and tolerability of the procedure, the educational aspects of the procedure, and their clinical improvement during and after the procedure. Subjects responded to each statement on a five point Likert scale ranging from 0 to 4, with 0 indicating *strong disagreement* and 4 indicating *strong agreement* with a statement, respectively. Individuals were characterized as perceiving safety and tolerability of the procedure if they did not *disagree* or *strongly disagree* with any of the statements pertaining to these areas. Individuals were characterized as perceiving educational benefit in the procedure if they *agreed* or *strongly agreed* with all statements pertaining to education. Individuals were characterized as perceiving clinical benefit if they *agreed* or *strongly agreed* with all statements pertaining to immediate and longer-term respiratory outcomes. Characterization of observer data was similar in concept and categorized in terms of relevance to safety and tolerability, educational benefit, and clinical benefit. Specific observer questionnaire items varied slightly and were fewer in number as we felt it was misleading for observers to evaluate some individual items.

Data Analysis

Descriptive statistics were used to characterize questionnaire responses from both patients and observers. Logistic regression was used to model success in each of the three categories (safety and tolerability, educational benefit, clinical benefit). Backwards selection with a p-to-stay of 0.1 was used to develop parsimonious models. The following potential predictors were included in the backwards selection: age (years), age group (14 and under vs. over 14 years old), gender, athletic level (varsity and higher vs. junior varsity and lower), number of procedures (1 vs. more than 1), and timing of the procedure (early patients are defined as those who received the procedure before one half of procedures on patients in this report were complete). Agreement between patient responses and corresponding observer responses was analyzed (see online supplementary material for details). All specific comparisons were retrospective in nature and not adjusted for multiple comparisons as the nature of this report is descriptive. Analyses were performed in R version 3.2.3 with the *Stats* package.[17]

RESULTS

Patient and Observer Population

All 41 patients who had undergone the TLE procedure ordered for clinical reasons were approached with the opportunity to participate. Procedure dates varied from February, 2014 to January, 2016. Three of these potential candidates did not return three attempts to contact via phone and one attempt via email. One declined to participate. One agreed to participate but did not complete the questionnaire. Thirty-six patients (88%) completed the questionnaire after providing written informed consent (and assent when applicable). The respondent patient population was young and predominantly Caucasian female, and most competed at a high school varsity or collegiate level. (Table 1) Twenty-two of the responding patients completed one TLE procedure, 13 completed two, and a single patient completed the procedure five times.

Additionally, 37 observers either self-identified or were identified by patients as willing to complete the questionnaire. Of these observers, 35 (95%) associated

TABLE 1— Demographics of Participant Respondents

Age (years, SD)	17 (±3.5)
Gender (female, %)	28 (78%)
Race and ethnicity	
Causasian non-Hispanic (n, %)	33 (92%)
Causasian Hispanic (n, %)	3 (8%)
African-American (n, %)	0 (0%)
Asian (n, %)	0 (0%)
Athletic level	
Recreational (n, %)	1 (3%)
Competitive below junior varsity level (n, %)	6 (17%)
Junior varsity (n, %)	1 (3%)
Varsity (n, %)	19 (53%)
Collegiate (n, %)	8 (22%)
Professional (n, %)	1 (3%)

with 29 specific patients, completed the questionnaire after providing written informed consent. All responding observers were parents of patients.

Patient Perceptions of Safety, Tolerability, Learning Value, and Efficacy

Overall, the majority of patients reported that the procedure was safe and tolerable, provided learning benefit, and provided clinical benefit in their specific case. (Table 2) More specifically, the majority (81%) of patients did not disagree that (i) they felt safe, (ii) the laryngoscope was tolerable, and (iii) the exercise regimen was tolerable. Additionally, the majority (78%) of patients agreed or strongly agreed that (i) the time devoted to learning was appropriate and (ii) they learned specifically about relevant anatomy, relevant emotional responses during exercise, and a new breathing strategy with ample practice time. In terms of clinical benefit, more than half of the patients (58%) agreed or strongly agreed that (i) they were able to control their breathing during the session, (ii) breathing during exercise had improved since the TLE, and (iii) they would recommend TLE to similar patients. Seventy-five percent of patients agreed or strongly agreed with the single questionnaire item "Since the procedure, my breathing during exercise has improved." Of those patients, 85% agreed or strongly agreed that TLE was "the most important therapy leading to my breathing improvement." A summary of responses to individual items is provided in the online supplemental material.

Predictors of Patient Perceptions

The odds of perceiving safety and tolerability were age-related, with patients in the age group of 15 years and above more likely to perceive safety and tolerability than younger patients (odds ratio [OR] 33.8, 95% confidence interval [CI] 3.8, 298.5, $P = 0.002$). The odds of perceiving educational benefit were also affected by age, with patients aged 15 and above more likely to perceive educational benefit than younger patients (OR 8.3, CI 1.3, 52.1, $P = 0.02$). While no statistically significant associations occurred between any of the predictors and the patient's perception of clinical benefit, patients that had more than one procedure tended to have higher odds of reporting benefit compared to patients that had only one procedure (OR 4.4, CI 0.96, 20.3, $P = 0.057$).

TABLE 2— Patient Perceived Procedural Success Regarding Safety and Tolerability, Educational Value, and Effectiveness

Group	n	Safe and tolerable (%)	Educational benefit (%)	Clinical benefit (%)
Overall	36	81	78	58
Age				
14 years and younger	7	29	43	43
Greater than 14	29	93	86	62
Gender				
Male	8	88	75	50
Female	28	79	79	61
Athletic level				
Junior varsity and below	8	63	75	38
Varsity and above	28	86	79	64
Number of procedures				
1	22	77	68	46
Greater than 1	14	86	93	79
Procedure timing				
Earliest patients	19	79	79	53
Later patients	17	82	77	65

Observer Perceptions of Safety, Tolerability, Learning Value, and Efficacy

As with patients, the majority of observers perceived TLE to be safe and tolerable (86%), provide educational benefit (91%), and provide clinical benefit (80%). (Table 3) Using logistic regression to model and identify potential predictors of observer responses in the three domains above, patient age was relevant, modeled as a continuous variable. For each 1-year increase in patient age, the odds of an observer reporting that the procedure was physically safe and comfortable for the participant increased by 1.54 times (OR 1.5, CI 1.1, 2.1, $P = 0.006$). Similarly, for each 1-year increase in patient age, the odds of an observer reporting that there was sufficient time spent on learning increased 1.68 times (OR 1.7, CI 1.1, 2.5, $P = 0.01$). The odds of an observer reporting the procedure clinically benefiting the participant increased for each 1-year increase in a participant's age (OR 1.8, CI

TABLE 3— Observer Perceived Procedural Success Regarding Safety and Tolerability, Educational Value, and Effectiveness

Group	n	Safe and tolerable (%)	Educational benefit (%)	Clinical benefit (%)
Overall	35	86	91	80
Age				
14 years and younger	9	67	89	56
Greater than 14	26	92	92	89
Gender				
Male	10	80	80	70
Female	25	88	96	84
Athletic level				
Junior varsity and below	9	78	89	67
Varsity and above	23	87	91	87
Number of procedures				
1	17	77	94	77
Greater than 1	18	94	89	83
Procedure timing				
Earliest patients	16	73	87	80
Later patients	21	95	95	80

1.05, 3.1, $P = 0.031$). No statistically significant differences occurred between patient and observer reports on similar items.

DISCUSSION

This is the first report of TLE, a novel, non-surgical intervention for patients with refractory EILO. The procedure was initially designed to harness visual biofeedback of real-time laryngoscopy videos during exercise in order to optimize learning of respiratory retraining techniques. We present a series of patients who underwent TLE for EILO that was refractory to respiratory retraining, voice therapy, and treatment of perceived disease contributors. Both patients and observers of the procedure generally reported that the procedure was safe and tolerable, provided learning benefit, and provided clinical benefit. Patient age was an important predictor of perceived safety, tolerability, and educational benefit; increasing age was accompanied by higher reports of comfort and perceptions of education with the procedure. While not definitive in this study, the perception of clinical benefit appears to increase with the number of procedures.

Clinical and Scientific Implications

We believe that TLE is safe, well-tolerated in competitive teens above the age of 14, and worthy of further study due to this initial perception of effectiveness. While clearly not a first line therapy at this time, it is a consideration in patients with symptoms refractory to conventional non-surgical interventions. It is unlikely that TLE can be performed at all centers due to challenges in the mechanics of data acquisition and expertise in translating the video data ultimately into clinical benefit.

Visual-Mechanical Considerations

The TLE procedure offers a unique, real-time opportunity to visualize and refine motor movements that are difficult to conceptualize. Based on our clinical experience and observations, TLE patients are able to receive immediate feedback on their attempts to translate verbal instructions into improved laryngeal aperture. Patients are also able to correlate the sensation of optimal and suboptimal airflow with visualized differences in laryngeal aperture. The procedure also produces immediate and aggregate feedback for the clinician in the form of visualization of common motor translations of specific instructions. The procedure may be considered a form of biofeedback for the clinician that enhances teaching effectiveness. Our anecdotal experience suggests that there is not a single respiratory retraining technique or voice therapy technique that universally provides EILO symptom relief. We did not systematically treat patients differentially based on the level of upper airway obstruction-glottic versus supraglottic.

Visual-Cognitive Behavioral Considerations

Independent of the interaction between visual biofeedback and fine motor movements, an unexpected benefit of this procedure has been our recognition of the importance of the interaction between visual biofeedback and cognitive-behavioral factors within the patient. The procedure, which features prolonged intense exercise, provides a window into the adaptive and maladaptive behavioral responses of patients during exercise that is not apparent in a simple clinic setting. In many ways (although not initially designed for this purpose), the procedure also comprises a psychological intervention that increases the patient's sense of control over a condition frequently experienced as tauntingly unpredictable and uncontrollable. We list a subset of these observations (Table 4) representing domains in which very few pulmonologists, otolaryngologists, allergists, and speech-language pathologists receive formal training, but they provide an opportunity for intervention in the correct therapeutic setting. Future formalized assessment of these observations will help to increase understanding of the TLE, its psychological correlates, and the relative contributions of specific components of the procedure.

The inclusion of observers also introduces a cognitive-behavioral variable which must be appreciated by clinicians.

TABLE 4— Psychological Responses Noted in Therapeutic Laryngoscopy During Exercise Sessions

Fear of symptoms.
Unawareness of ability to control symptoms and laryngeal aperture.
Expectations of inability to control symptoms and laryngeal aperture.
Focus on immediate discomfort precludes focus on task.
Frustration with partially-maintained success.
Overconfidence after partially-maintained success.
Loss of focus upon exercise termination.
Fear of interaction with specific rivals.

In our laboratory, we allow parent observers, in part to generate a level of trust and understanding among caregivers. This decision has led to observations that interactions between patients and parents may be of clinical relevance in this condition. For this reason, we felt that observer perceptions were worthy of quantification and feel that assessment of interactions between patients and parents or coaches is important in future research.

Procedural Benchmarks

We feel it is critical to establish specific benchmarks during the procedure in order to optimize its learning value (Table 5). Patients must first be oriented to the visual stimulus and obtain a basic understanding of the anatomy. As the procedure progresses, we feel that specific short-term goal setting with respect to respiratory retraining techniques is important, regardless of the specific respiratory retraining technique attempted. It is critical over the first few sprints to establish a degree of fatigue that will increase the likelihood of EILO episodes. Later in the procedure, as EILO is more likely to occur, patients and providers independently assess the observed and perceived benefit of specific techniques. Independent of mechanical concerns, if maladaptive behavioral responses are observed over the course of the procedure, we feel that is critical to identify them and replace them with more adaptive responses. Finally, it is important to establish a sensory or auditory surrogate for the visual image which can be used for patient self-assessment in the field.

Procedural Concerns

We have learned several lessons that may help optimize utilization of this procedure moving forward. In certain instances, patients struggled with procedure tolerance, willingness to trigger respiratory distress, and understanding of visual data. Specific complaints included pain related to the laryngoscope, nausea and vomiting, lightheadedness, and general fatigue. One procedure was stopped due to vomiting in a patient recovering from infectious enteritis. Two procedures were terminated due to the discomfort and fatigue in young adolescent females. One procedure was terminated due to an episode of severe respiratory and emotional distress, the resolution of which was felt to be more important than the potential learning opportunity provided by the procedure. From our experience of these cases as well as some similar, minor episodes, patient selection is critical. Our data and anecdotal experience lead us to recommend considering this procedure only for patients of appropriate age that are highly motivated, independent of persuasion from parents and providers, and experientially aware of the expected exercise intensity. Good rapport with the providers is important.

A second small group of patients that did not initially benefit from TLE seemed somewhat unconvinced of the EILO diagnosis prior to TLE. In these cases, we find that it is critical to spend the necessary time to establish understanding and acceptance of the EILO diagnosis with information that supports the diagnosis as well as the reasons that patients refute the diagnosis.

TABLE 5— Procedural Benchmarks

Orientation to apparatus and anatomy.
Establishment of short-term goals.
Establishment of fatigue and mild to moderate respiratory distress.
Assessment of effect of respiratory retraining on laryngeal aperture.
Identification and correction of maladaptive behavioral responses.
Establishment of sensory or auditory surrogate for use in the field.

Analysis Limitations

The major limitation of this report is its lack of a widely-used outcome metric. While two metrics exist including one validated in adolescents with exertional symptoms,[9,18,19] we do not feel that either adequately captures disease severity or impact in highly competitive athletes. For this reason, we cannot compare the clinical effectiveness of this procedure versus placebo or this procedure versus other interventions at this time. The purpose of this initial descriptive report is to highlight basic procedural qualities rather than definitively quantify clinical efficacy. Other limitations may include responder bias, and variation in the timing between TLE and the questionnaire assessment.

CONCLUSIONS

We present TLE, a novel non-surgical therapy for EILO that has demonstrated perceived preliminary safety, tolerability, learning benefit, and effectiveness. TLE is worthy of study as a new intervention for patients with EILO that do not respond to conventional conservative therapy.

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AUTHORS' CONTRIBUTIONS

J. Tod Olin was responsible for the study inception, study design, data acquisition, data processing, and data interpretation. He wrote the first draft of the manuscript and compiled all author revisions. Emily Deardorff, Elizabeth Fan, Kristina Johnston, and Valerie Keever were each responsible for study design, interpretation of results, and manuscript revision. Camille Moore was responsible for the analysis design and implementation as well as manuscript revision. Bruce Bender was responsible for interpretation of results and manuscript revision.

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