A novel device combining acoustic vibration with oscillating expiratory pressure for the treatment of nasal congestion

Zachary M. Soler, MD, MSc, Shaun A. Nguyen, MD, Craig Salvador, BS, Thomas Lackland, BS, Vincent M. Desiato, DO, Kristina Storck, MSPH and Rodney J. Schlosser, MD

Background: **Chronic nasal congestion affects 20% of the population with significant impact on quality of life. This study investigated the simultaneous administration of nasal acoustic vibration and oscillating expiratory pressure for the treatment of nasal congestion.**

Methods: **Patients with chronic nasal congestion but without fixed anatomic obstruction participated in a prospective clinical study applying simultaneous acoustic vibrations and positive expiratory pressure to the nasal cavity twice daily over 5 weeks. Safety was assessed by rhinoscopy and patient questionnaires. Efficacy was assessed using peak nasal inspiratory flow (PNIF), visual analogue scale (VAS) of nasal symptoms, Total Nasal Symptom Score (TNSS), Nasal Obstruction and Septoplasty Effectiveness (NOSE) score, and the 22-item Sino-Nasal Outcome Test (SNOT-22).**

Results: **Forty patients (mean age 39 years, 65% female) completed the study with no adverse effects. At the 2 week follow-up, PNIF improved by 25.0 L/min (31% increase from baseline, $p < 0.001$). At the 5 week follow-up, nasal congestion VAS improved from mean ± SD of 5.8 ± 2.4 to 2.6 ± 2.3, TNSS improved from 7.2 ± 3.5 to 3.5 ± 3.1, NOSE improved from 50.4 ± 19.9 to 23.3 ± 17.2, and SNOT-22 improved from 31.7 ± 20.3 to 14.2 ± 12.7, all $p < 0.001$. Eighty percent of patients would use the device again and 87.5% would recommend to others.**

Conclusion: **Simultaneous administration of acoustic vibration and oscillating expiratory pressure appears to be a safe treatment for chronic nasal congestion. Results from this initial study are promising with regard to efficacy but will require further study.**

Key Words:
rhinitis; therapeutics; patient reported outcome measure; acoustic vibration; expiratory pressure

How to Cite this Article:
Soler ZM, Nguyen SA, Salvador C, et al. A novel device combining acoustic vibration with oscillating expiratory pressure for the treatment of nasal congestion. *Int Forum Allergy Rhinol*. 2020;10:610–618.

Chronic nasal congestion impacts roughly 20% of the worldwide population and presents most commonly in the form of chronic rhinitis.[1] The majority of patients with chronic rhinitis suffer from allergic rhinitis, characterized by an inflammatory reaction to specific airborne allergens. However, nonallergic rhinitis and mixed allergic/nonallergic rhinitis are common as well, often with considerable overlap in patient symptoms between conditions. Although generally non–life threatening, patients with nasal congestion report significant reductions in

Division of Rhinology and Sinus Surgery, Department of Otolaryngology - Head and Neck Surgery, Medical University of South Carolina, Charleston, SC

*Correspondence to: Zachary M. Soler, MD, MSc, Medical University of South Carolina, 135 Rutledge Ave, Charleston, SC, United States 29425; e-mail: solerz@musc.edu

Funding source for the study: Healthy Humming, LLC.
Potential conflict of interest: Z.M.S. and R.J.S. served as paid consultants for the design of this study. Z.M.S. has served as a consultant for Olympus, Novartis, Regeneron, and Optinose, which are not affiliated with this manuscript. R.J.S. has served as a consultant for Olympus, Styker, Optinose, and Sanofi, which are not affiliated with this study. The sponsor had no role in study design, data analysis, or manuscript preparation.
Public clinical trial registration: http://clinicaltrials.gov/show/NCT03906968. SinuSonic Study for Adults With Nasal Congestion.

Received: 18 November 2019; Revised: 19 January 2020; Accepted: 21 January 2020
DOI: 10.1002/alr.22537
View this article online at wileyonlinelibrary.com.

quality of life (QOL) on measures related to physical, mental, and social functioning.[1] These QOL disruptions are thought to be related to altered sleep pattern, fatigue, and poor concentration.

A number of pharmacologic options exist to treat nasal congestion. These include decongestants, antihistamines, and topical steroid nasal sprays and account for a sizable portion of the $2 billion direct costs of nasal congestion.[1] Despite availability of pharmacologic options, the "Allergies in Americas" survey found that many patients are not satisfied with available options. Some patients are concerned with side effects, some with costs, and others with lack of efficacy.[2] In fact, a pronounced difference in opinion was noted, with patients being much more pessimistic about available options compared with medical providers. This led a recent review to suggest that nasal congestion remains prevalent and highly problematic across the United States, with many patients failing to perceive adequate symptom relief with currently available therapies.[1]

With these concepts in mind, a novel device was developed to simultaneously apply acoustic vibration and oscillating positive expiratory pressure (PEP) to the nasal cavity in order to treat nasal congestion. Utilization of oscillating PEP has successfully been applied to the lower airway for a number of chronic conditions such as cystic fibrosis and bronchiectasis.[3,4] Incorporation of acoustic vibration is based on reports demonstrating that human humming results in up to a 15-fold increase in exhaled nasal nitric oxide, a molecule known to stimulate mucociliary movement.[5] A nonpharmacologic and nonsurgical option for the treatment of nasal congestion would be an important addition to the armamentarium available to the millions of patients worldwide who suffer with nasal congestion. This prospective outcomes study was designed to assess the safety and efficacy of simultaneous administration of nasal acoustic vibration and oscillating expiratory pressure for the treatment of nasal congestion.

Subjects and methods

Subjects with persistent bothersome nasal congestion were recruited from the community around the Medical University of South Carolina (MUSC) into a Phase I/II clinical trial. Inclusion criteria required adults ≥18 years of age with a complaint of nasal congestion present ≥2 weeks and a qualifying nasal congestion score >5 on a 10-point visual analogue scale (VAS). Exclusion criteria included fixed structural cause of nasal congestion (moderate or severe septal deviation, moderate or severe nasal valve collapse, Grade 3-4 polyps), recent upper respiratory illness, topical decongestant use in last week, current nasal crusting or ulceration on rhinoscopy, history of severe nose bleeding within last 3 months, use of anticoagulation (acetylsalicylic acid allowed), known pregnancy, allergic sensitivity to silicone or any other component of device, inability to read and understand English, and inability to perform treatment due to underlying medical condition. All subjects provided written informed consent in accordance with the MUSC Institutional Review Board (#83883) and the study was registered publicly (www.clinicaltrials.gov: ID# NCT03906968).

All subjects were evaluated at baseline by an otolaryngology provider who performed rhinoscopy to screen for exclusion criteria and assess the subject's medical history, in order to determine medical comorbidities. Those patients with prior positive allergen-specific immunoglobulin E (IgE) testing (ie, skin or blood) were considered to have allergic rhinitis. Chronic rhinosinusitis was classified based on American Academy of Otolaryngology–Head and Neck Surgery diagnostic criteria.[6] Those patients with chronic rhinitis but without prior positive testing were considered to have nonallergic rhinitis. Patients were queried regarding duration of nasal congestion, demographics, current smoking, and current daily use of medications for nasal congestion (nasal steroid sprays, nasal antihistamines, oral decongestants, oral antihistamines, mucolytics, and leukotriene modifiers).

Baseline assessments

Baseline peak nasal inspiratory flow (PNIF) was performed on each subject. A clinical research coordinator trained each patient to perform PNIF. This included an initial training run that was not counted. Three runs were then performed and averaged together and recorded in liters/minute (L/minute) airflow. Mean clinically important difference (MCID) of PNIF has been reported as an absolute change of 20 L/minute or as a relative change of 20% over baseline.[7]

Baseline patient-reported outcome metrics were then assessed for each subject. The Total Nasal Symptom Score (TNSS; range, 0-3) assesses 4 items including nasal congestion/obstruction, runny nose/secretions, nasal itching, and sneezing over a 1-week recall period. On the TNSS, a score of 0 indicates no symptoms, 1 indicates mild symptoms that are easily tolerated, 2 represents symptoms that are bothersome but tolerable, and 3 is reserved for severe symptoms that are hard to tolerate and interfere with daily activity. The TNSS is calculated by adding the score for each of the symptoms for a total ranging from 0 to 12. MCID of the TNSS has been reported as 0.28 points using anchor-based methods in allergic rhinitis.[8] Subjects also rated the impact of nasal congestion using the Nasal Obstruction and Septoplasty Effectiveness (NOSE) scale. The NOSE scale is a validated questionnaire that consists of 5 questions related to nasal congestion over a 1-month recall period. Each item is rated as follows: 0 = not a problem, 1 = very mild problem, 2 = moderate problem, 3 = fairly bad problem, 4 = severe problem. The total score is multiplied by 5 and can range from 0 to 100, 0 being the best and 100 being the worst. MCID of NOSE instrument has been reported as 24 points.[9,10] Sinonasal impacts were assessed using the 22-item Sino-Nasal Outcome Test (SNOT-22), which uses a 2-week recall period. The SNOT-22 contains 22 questions each scored 0 to 5 (total score range, 0-110), with higher scores representing worse sinonasal QOL; the SNOT-22

FIGURE 1. SinuSonic® device.

has an MCID of 8.9 points.[11] Last, subjects were asked to rate nasal symptom scores using a 10-point VAS, including individual symptoms and a global assessment of their overall sinonasal problem, with higher scores representing greater symptom burden. Prior reports using the distribution method (1/2 baseline standard deviation [SD] report MCID of 1.3 for VAS nasal congestion.[7]

Intervention

Subjects self-administered simultaneous nasal acoustic vibration and oscillating expiratory pressure using the SinuSonic device for 3 minutes (Healthy Humming LLC, Columbia, SC) according to the manufacturer's instructions (Fig. 1). The SinuSonic device consists of a disposable medical grade silicone nosepiece mounted to a resin body. The device is equipped with a flutter valve located at the top of the device that creates self-guided oscillating expiratory resistance. Acoustic vibration is emitted via a single circuit board speaker at the base of the device at approximately 128 Hz. Subjects were instructed to inhale normally and then gently exhale through the nosepiece in order to activate the flutter valve for 3 minutes per session.

Timeline

An immediate posttreatment assessment was performed 5 minutes after completion of the initial treatment session. Subjects were then instructed to perform twice daily treatment sessions (morning and night) at home using the SinuSonic device for 3 minutes each. Subjects returned after 2 weeks for an intermediate posttreatment assessment. Subjects continued twice-daily treatments in the home setting for 3 additional weeks. A final assessment was performed at 5 weeks via electronic survey using the Research Electronic Data Capture (RedCAP) secure web application.

Posttreatment assessments

At the immediate (5 minute) posttreatment assessment, PNIF was repeated on each subject. Similar to baseline, the first run was thrown away and the next 3 runs were averaged together. Subjects were again asked to rate nasal symptom scores using a 10-point VAS scale, including individual symptoms and a global assessment of their overall sinonasal problem, with higher scores representing greater symptom burden. TNSS, SNOT-22, and NOSE questionnaires were not performed at 5 minutes due to their longer recall periods. Subjects also rated pain and any bleeding associated with device usage.

At the intermediate (2 week) post-treatment assessment, PNIF was repeated on each subject. Once again, 3 runs were averaged together after throwing away the first. Patients then completed the TNSS, NOSE, and SNOT-22 instruments. As before, subjects repeated VAS scores and safety assessments. Subjects were additionally queried regarding willingness to use again and recommend to family/friends. Anterior rhinoscopy was repeated by an otolaryngology provider, assessing for ulceration and crusting.

At the final posttreatment assessment, subjects again completed the TNSS, NOSE, and SNOT-22 instruments. As before, subjects repeated VAS scores, safety assessments, and questions regarding willingness to use again and recommend to family/friends. Because these instruments were collected electronically and not at a clinic visit, PNIF was not performed at 5 weeks.

Analytic plan

Statistical analysis was conducted using SPSS Version 25 (IBM Corp., Armonk, NY). Descriptive statistics such as means, SDs, counts, and percentages were generated in order to present the baseline characteristics of the study population. Histograms of baseline and follow-up variables were visually assessed to determine normality. Paired *t* tests for normally distributed variables or Wilcoxon signed rank tests for non-normally distributed variables were performed to evaluate differences between baseline and follow-up measures. The amount of change between baseline and follow-up variables of interest was calculated and measured against previously reported MCID thresholds when available or by using one-half of the baseline SD if not previously reported. A value of $p \leq 0.05$ was considered statistically significant throughout.

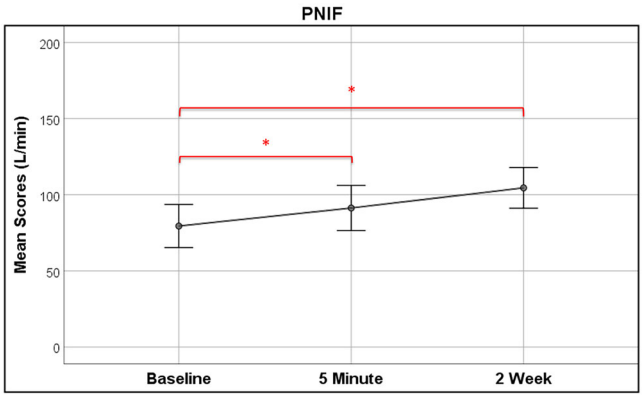

FIGURE 2. Mean PNIF over time. Minimal clinically important difference = 20.0. * = statistically significant. PNIF = peak nasal inspiratory flow.

Results

A total of 40 subjects were enrolled with an average age of 39.1 years (range, 20-72 years). Women accounted for 65% of the cohort, with a racial makeup which mirrors that of the United States overall (Table 1). Seventy percent of subjects reported >3 years' duration of nasal symptoms, with 87.5% reporting at least 1 year. The majority of patients were classified with allergic rhinitis (n = 26; 60%) or nonallergic rhinitis (n = 11; 27.5%). Based on rhinoscopy, just over one-half the subjects had mild septal deviation (57.5%) and 20% had mild dynamic nasal valve collapse with inspiration. Current medication usage is detailed in Table 1. Of note, about one-half of subjects were on daily oral antihistamines and one-third were using nasal steroid sprays.

Immediate (5-minute) assessment

After initial treatment with SinuSonic for 3 minutes, average ± SD PNIF scores increased from 79.5 ± 43.6 to 91.3 ± 45.8 ($p = 0.002$), a 15% relative increase compared to baseline (Table 2, Fig. 2). With regard to nasal stuffiness, there was a significant reduction in the VAS score for nasal congestion, improving from 5.8 ± 2.4 to 2.9 ± 2.5 ($p < 0.001$). Similar significant improvements were also seen for the immediate sensation of nasal drainage, sinonasal pressure, sense of smell, and overall sinonasal symptoms. Regarding safety, 95% of users reported no discomfort, with n = 2 (5%) reporting mild discomfort and none experiencing moderate or severe pain. No subjects experienced bleeding.

Intermediate (2-week) assessment

After 2 weeks of twice daily treatments with SinuSonic, average PNIF scores increased from 79.5 ± 43.6 to 104.5 ± 41.3 ($p < 0.001$), a 31% relative increase compared to baseline (Table 3, Fig. 2). With regard to patient reported metrics, the TNSS improved from 7.2 ± 3.5 to 4.1 ± 3.2 ($p < 0.001$), the NOSE scale improved from 50.4 ± 19.9 to 31.4 ± 19.7 ($p < 0.001$), and the SNOT-22 improved from 31.7 ± 20.3 to 15.0 ± 12.9 ($p < 0.001$) (Fig. 3).

TABLE 1. Baseline characteristics of the study cohort (N = 40)

Characteristic	Value
Age (years), mean (range)	39.1 (20–72)
Demographics	
Sex, n (%)	
Male	14 (35)
Female	26 (65)
Race, n (%)	
American Indian or Alaska Native	1 (2.5)
Asian	5 (12.5)
Black or African American	6 (15)
Native Hawaiian or Other Pacific Islander	0
White	26 (65)
Other	3 (7.5)
Ethnicity n (%)	
Hispanic/Latino	2 (5)
Non-Hispanic/Latino	38 (95)
Comorbidities, n (%)	
Allergic rhinitis	24 (60)
Non-allergic rhinitis	11 (27.5)
Chronic rhinosinusitis	1 (2.5)
Chronic rhinosinusitis with polyps	1 (2.5)
Other	3 (7.5)
Current medication usage, n (%)	
Nasal steroid spray	13 (32.5)
Nasal antihistamine spray	3 (7.5)
Oral antihistamine	18 (45)
Oral decongestant	4 (10)
Mucolytic	3 (7.5)
Leukotriene modifier	2 (5)
Disease duration, n (%)	
<3 months	2 (5)
3–6 months	2 (5)
6–12 months	1 (2.5)
1–3 years	7 (17.5)
>3 years	28 (70)
Rhinoscopic findings, n (%)	
Septal deviation	
None	17 (42.5)

(*Continued*)

TABLE 1. Continued

Characteristic	Value
Mild	23 (57.5)
Moderate	0
Severe	0
Valve collapse	
None	32 (80)
Mild	8 (20)
Moderate	0
Severe	0
Ulceration	
None	40 (100)
Mild	0
Moderate	0
Severe	0
Crusting	
None	40 (100)
Mild	0
Moderate	0
Severe	0

Similar improvements were seen for individual symptoms and global sinonasal symptoms on VAS scores (Table 3). Average improvement on these instruments approached or exceeded the reported MCID. Regarding safety, 90% of users reported no discomfort, with n = 4 (10%) reporting mild discomfort and none experiencing moderate or severe pain. No subjects experienced bleeding at any time. On anterior rhinoscopy, no subjects were found to have ulceration and 95% had no visible crusting, with n = 2 (5%) having mild visible anterior crusting.

Final (5-week) assessment

After 5 weeks of twice-daily treatments with SinuSonic, TNSS improved from 7.2 ± 3.5 at baseline to 3.5 ± 3.1 ($p < 0.001$) at study completion (Table 4, Fig. 3). Statistically significant improvements were also seen for the NOSE score (50.4 ± 19.9 to 23.3 ± 17.2; $p < 0.001$) and the SNOT-22 scale (31.7 ± 20.3 to 14.2 ± 12.7 ($p < 0.001$). Similar improvements were seen for individual symptoms and global sinonasal symptoms on VAS scores (Table 4). Average improvement on these instruments remained greater than the reported MCID and was essentially stable compared to the 2 week assessment (Table 5).

Regarding safety, 97.5% of subjects reported no pain or discomfort after 5 weeks of twice-daily treatments and there were no reported instances of bleeding at any time point. At study completion, 87.5% of subjects expressed willingness to recommend SinuSonic to friends/family and 80.0% expressed the desire to use again in the future (Table 6).

Discussion

Chronic nasal congestion impacts millions of Americans currently and will likely impact hundreds of millions of individuals worldwide with the rise of industrialization and estimated increases in prevalence of chronic rhinitis in developing countries.[2] At present, several classes of pharmacologic therapies have proven efficacy for nasal symptomology, most notably topical nasal steroids and antihistamines. However, not all patients achieve satisfactory improvement with available medication options.[2] This is evidenced by the fact that 33% of our cohort was using nasal steroids at baseline and 45% oral antihistamines. These medications are not curative and thus must be taken on a consistent basis, incurring repetitive costs over time. Topical steroid sprays and antihistamines are generally safe, but are not without side effects and potential complications. For steroid nasal sprays, this is most commonly in the form of nasal bleeding, with an absolute prevalence around 5% and a relative risk of 48%.[2] Decongestants are an even less attractive long-term option, with topical sprays inducing rhinitis medicamentosa with use beyond 5 days and oral formulations risking long-term cardiovascular impacts. For these reasons, a safe, nonpharmacologic treatment would be an attractive option for many patients with nasal congestion, either as an alternative to existing treatment options or as a complementary therapy.

This study provides important data on the safety and efficacy of simultaneous administration of nasal acoustic vibration and oscillating expiratory pressure as delivered through the SinuSonic device. After 5 weeks, no instances of bleeding were reported and 97.5% reported no discomfort. On rhinoscopy, no instances of ulceration were found at 2 weeks. This suggests that use of SinuSonic carries minimal risk in appropriately selected patients. Regarding efficacy, objective changes in PNIF were seen after immediate use and after 2 weeks of twice-daily treatments. Our subjects had a baseline PNIF of 79.5 L/minute, this compares with prior reports of normative PNIF that range from 104.6 to 174 in males and 80.8 to 128 in females.[12] Thus our patients appear to have significantly impaired baseline PNIF, which is consistent with their complaints of chronic nasal congestion and the focus of our study. When examining the improvements in PNIF with various treatments, prior reports use both absolute improvement and percentage of baseline improvement to gauge success. Our patients experienced an absolute improvement of 25 L/minute (31% improvement over baseline). This exceeds previously reported MCID for PNIF of 20 L/minute or 20% of baseline,[5] and 60% of our patients achieved MCID. Prior reports of decongestable airway obstruction report improvements in PNIF with topical vasoconstrictor spray of 35.8 L/minute (39.0% of baseline).[5] When examining the impact of surgery upon PNIF,

TABLE 2. Immediate (5 minutes) posttreatment assessments

Assessment	Baseline (mean ± SD)	5 Minutes (mean ± SD)	*p*
Objective assessment (N = 39)			
PNIF	79.5 ± 43.6	91.3 ± 45.8	0.002
Nasal symptom VAS (N = 40)			
Congestion	5.8 ± 2.4	2.9 ± 2.5	<0.001
Drainage	5.1 ± 3.3	2.3 ± 2.3	<0.001
Pressure	4.2 ± 3.0	2.0 ± 2.2	<0.001
Smell	3.0 ± 3.2	1.5 ± 2.5	<0.001
Global	5.5 ± 2.6	3.3 ± 2.5	<0.001

PNIF = peak nasal inspiratory flow; SD = standard deviation; VAS = visual analogue scale.

TABLE 3. Intermediate (2 weeks) posttreatment assessments

Assessment	Baseline	2 Weeks	*p*
Objective assessment, mean ± SD			
PNIF	79.5 ± 43.6	104.5 ± 41.3	<0.001
Patient-reported outcome measure, mean ± SD			
TNSS	7.2 ± 3.5	4.1 ± 3.2	<0.001
NOSE	50.4 ± 19.9	31.4 ± 19.7	<0.001
SNOT-22	31.7 ± 20.3	15.0 ± 12.9	<0.001
Nasal symptom VAS, mean ± SD			
Congestion	5.8 ± 2.4	2.3 ± 2.1	<0.001
Drainage	5.1 ± 3.3	2.3 ± 2.2	<0.001
Pressure	4.2 ± 3.0	1.4 ± 1.6	<0.001
Smell	3.0 ± 3.2	1.2 ± 2.1	<0.001
Global	5.5 ± 2.6	2.5 ± 2.1	<0.001
Rhinoscopy findings, n (%)			
Ulceration grade			
None	40 (100)	40 (100)	
Mild	0	0	
Moderate	0	0	
Severe	0	0	
Crusting grade			
None	40 (100)	38 (95)	
Mild	0	2 (5)	
Moderate	0	0	
Severe	0	0	

NOSE = Nasal Obstruction and Septoplasty Effectiveness; PNIF = peak nasal inspiratory flow; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test; TNSS = Total Nasal Symptom Score; VAS = visual analogue scale.

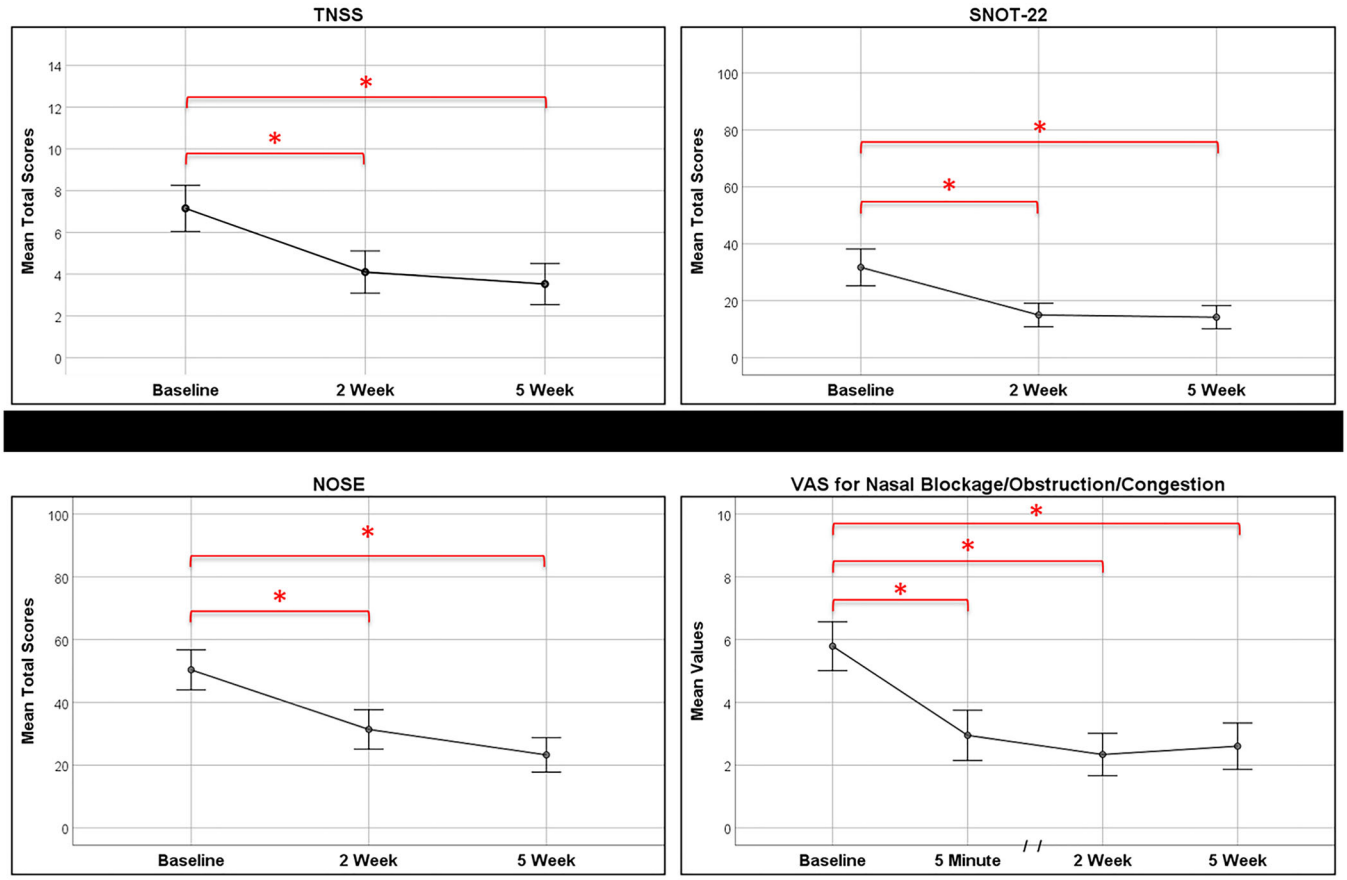

FIGURE 3. Mean patient-reported outcome measures over time. *Statistically significant. NOSE = Nasal Obstruction and Septoplasty Effectiveness score; SNOT-22 = 22 (item) Sino-Nasal Outcome Test; TNSS = Total Nasal Symptom Score; VAS = visual analogue scale.

TABLE 4. Final (5 weeks) posttreatment assessments

	Baseline (mean ± SD)	5 Week (mean ± SD)	*p*
Patient reported outcome measure			
TNSS	7.2 ± 3.5	3.5 ± 3.1	<0.001
NOSE	50.4 ± 19.9	23.3 ± 17.2	<0.001
SNOT-22	31.7 ± 20.3	14.2 ± 12.7	<0.001
Nasal symptom VAS			
Congestion	5.8 ± 2.4	2.6 ± 2.3	<0.001
Drainage	5.1 ± 3.3	2.5 ± 2.6	<0.001
Pressure	4.2 ± 3.0	1.5 ± 2.2	<0.001
Smell	3.0 ± 3.2	1.4 ± 2.2	0.001
Global	5.5 ± 2.6	2.4 ± 2.2	<0.001

NOSE = Nasal Obstruction and Septoplasty Effectiveness; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test; TNSS = Total Nasal Symptom Score; VAS = visual analogue scale.

improvements of 34.9 L/minute (33.5% of baseline) after septoplasty and turbinate reduction have been reported.[13] The relative improvement seen was therefore in the range of that reported for established interventions.

Although objective changes are important from a proof-of-concept standpoint, nasal symptoms are primarily a QOL problem and therefore patient-reported metrics are of paramount importance. The validated instruments used in this study examine different aspects of nasal

TABLE 5. Likelihood of achieving MCID

Assessment	Mean change from baseline (SD)	MCID threshold	Patients achieving ≥1 MCID (%)
Objective assessment (2 week)			
PNIF (L/minute)	+25.0	20.0	60.0
PROM assessment (5 weeks)			
TNSS	–3.7	0.28	80.0
NOSE	–27.1	24	62.5
SNOT-22	–17.5	8.9	70.0
Nasal symptom VAS (5 weeks)			
Congestion	–3.2	1.2	75.0
Drainage	–2.6	1.6	57.5
Pressure	–2.7	1.5	67.5
Smell	–1.6	1.6	40.0
Global	–3.1	1.3	75.0

MCID = minimum clinically important difference; NOSE = Nasal Obstruction and Septoplasty Effectiveness; PNIF = peak nasal inspiratory flow; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test; TNSS = Total Nasal Symptom Score; VAS = visual analogue scale.

TABLE 6. Safety and satisfaction data of the study cohort

Parameter	5 Minutes n (%)	2 Weeks n (%)	5 Weeks n (%)
Safety			
Pain			
None	38 (95)	36 (90)	39 (97.5)
Mild	2 (5)	4 (10)	1 (2.5)
Moderate	0	0	0
Severe	0	0	0
Bleeding			
No	40 (100)	40 (100)	40 (100)
Yes	0	0	0
Patient satisfaction			
Recommend			
No	n/a	4 (10)	5 (12.5)
Yes	n/a	36 (90)	35 (87.5)
Use again			
No	n/a	6 (15)	8 (20)
Yes	n/a	34 (85)	32 (80)

n/a = not applicable.

congestion. The TNSS is the most widely used instrument for clinical trials in patients with chronic rhinitis. The NOSE scale is validated for patients with nasal obstruction and is often utilized for trials investigating surgical treatment of nasal congestion. Finally, the SNOT-22 is typically used to assess outcomes in patients with chronic rhinosinusitis. Although each of these instruments typically examines different populations and interventions, this study found statistically significant improvements in all with MCID being achieved in 62% to 80% of patients. Taken together, changes in objective and patient-reported outcome metrics provide preliminary data for the use of

acoustic vibration and oscillating expiratory pressure in patients with nasal congestion.

Although this study suggests that the SinuSonic device is safe and efficacious, it is important to point out that the study methods excluded patients with moderate to severe fixed anatomic obstruction from septal deviation or dynamic valve collapse. One would not expect to observe similar efficacy in patients with notable septal deviation or valve collapse as the dominant underlying cause for their obstruction and these patients are often best treated with surgery. Similarly, the safety profile may not be the same, particularly with regard to severe caudal septal deviations or history of recent epistaxis. This underscores the importance of making treatment decisions in coordination with a medical provider.

As a Phase I/II clinical study, this study was focused on establishing safety and exploring the clinical efficacy of this device. Strengths of this study include assessment at various time points, inclusion of both objective and patient-reported outcome metrics, and use of validated questionnaires. However, it did not include a randomized control group for comparison. Therefore, impacts related to placebo effect or regression to the mean cannot be fully excluded. However, there are several aspects of study design that mitigate these risks. First, the vast majority of subjects had nasal congestion that persisted for greater than 1 year, with most reporting symptoms for greater than 3 years. None of these subjects were enrolled during an acute flare (ie, allergy flare or recent respiratory infection), where spontaneous improvement over 5 weeks would be expected. Additionally, many subjects were already on medical therapy and remained symptomatic. From a placebo standpoint, the inclusion of PNIF as an objective measure was important, demonstrating changes were not limited to just patient-reported metrics. Steps were additionally taken to mitigate any volitional influences, including a "throw-away" initial run for PNIF and averaging of 3 separate runs on each occasion. Last, the stability of patient-reported metrics between 2 weeks and 5 weeks suggests durability of response from a patient standpoint. Certainly, a blinded randomized clinical trial with a sham control is the ideal study design for Phase III device studies and could be considered in the future. However, blinding patients and administering a sham would be challenging considering patients can feel the acoustic vibration and oscillating expiratory pressure of an active device.

Although this study is an important step in demonstrating safety and proof-of-concept efficacy of SinuSonic, it is important to remember that each patient with nasal congestion is unique and may or may not be a good candidate. Certainly those with moderate or severe fixed nasal obstruction from anatomic causes would not be expected to improve to a similar degree. For those with chronic rhinitis, particularly allergic rhinitis, comprehensive evaluation and treatment remains important, because adjuncts like aeroallergen avoidance, pharmacologic treatment, and/or immunotherapy are important considerations. We did not specifically assess other allergic symptoms, such as sneezing, ocular symptoms, or lower airway symptoms. Therefore, treatment decisions are ideally done in coordination with medical providers who can best determine whether a treatment like SinuSonic is appropriate, and whether it should be standalone or as a complement to other options. Last, this study was not designed to investigate mechanisms of action. There are numerous prior reports studying the effects of both acoustic energy and positive expiratory pressure in the upper and lower airway. Although nitric oxide is the most widely studied molecule in this regard, precise mechanisms remain an area for further study. Additional investigations into the optimal frequency of acoustic vibrations, duration of treatment needed, and other potential patient populations would be logical next steps.

Conclusion

Treatment of nasal congestion with acoustic vibration and oscillating expiratory pressure via the SinuSonic device was found to result in significant improvements in PNIF after 2 weeks of twice-daily treatments. Patient-reported outcomes were significantly improved after 5 weeks of use, including TNSS, NOSE, and SNOT-22 surveys. SinuSonic device was safe with no instances of bleeding and minimal discomfort. The majority of subjects were willing to use the device again and recommend to family/friends. Future studies should consider a control group to minimize risks related to placebo effect and regression to the mean, explore long-term efficacy, and investigate additional patient populations, such as those with chronic rhinosinusitis.

References

1. Stewart M, Ferguson B, Fromer L. Epidemiology and burden of nasal congestion. *Int J Gen Med*. 2010;3:37-45.
2. Meltzer EO, Blaiss MS, Naclerio RM, et al. Burden of allergic rhinitis: allergies in America, Latin America, and Asia-Pacific adult surveys. *Allergy Asthma Proc*. 2012;33(Suppl 1):S113-S141.
3. Lee AL, Burge AT, Holland AE. Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis. *Cochrane Database Syst Rev*. 2017;9:CD011699.
4. McIlwaine M, Button B, Nevitt SJ. Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis. *Cochrane Database Syst Rev*. 2019;2019(11):CD003147.
5. Maniscalco M, Pelaia G, Sofia M. Exhaled nasal nitric oxide during humming: potential clinical tool in sinonasal disease? *Biomark Med*. 2013;7:261-266.
6. Rosenfeld RM, Andes D, Bhattacharyya N, et al. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg*. 2007;137(3 Suppl):S1-S31.
7. Chin D, Marcells G, Malek J, et al. Nasal peak inspiratory flow (NPIF) as a diagnostic tool for differentiating decongestable from structural nasal obstruction. *Rhinology*. 2014;52:116-121.
8. Meltzer EO, Wallace D, Dykewicz M, Shneyer L. Minimal clinically important difference (MCID) in allergic rhinitis: Agency for Healthcare Research and Quality or anchor-based thresholds? *J Allergy Clin Immunol Pract*. 2016;4:682-688.e6.
9. Stewart MG, Witsell DL, Smith TL, Weaver EM, Yueh B, Hannley MT. Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. *Otolaryngol Head Neck Surg*. 2004;130:157-163.
10. Kandathil CK, Saltychev M, Abdelwahab M, Spataro EA, Moubayed SP, Most SP. Minimal clinically important difference of the standardized cosmesis and health nasal outcomes survey. *Aesthet Surg J*. 2019;39:837-840.
11. Rudmik L, Hopkins C, Peters A, Smith TL, Schlosser RJ, Soler ZM. Patient-reported outcome measures for adult chronic rhinosinusitis: a systematic review and quality assessment. *J Allergy Clin Immunol*. 2015;136:1532-1540.e2.
12. Ottaviano G, Fokkens WJ. Measurements of nasal airflow and patency: a critical review with emphasis on the use of peak nasal inspiratory flow in daily practice. *Allergy*. 2016;71:162-174.
13. Balikci HH, Gurdal MM. Use of peak nasal inspiratory flowmetry and nasal decongestant to evaluate outcome of septoplasty with radiofrequency coblation of the inferior turbinate. *Rhinology*. 2014;52:112-115.