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Main Article

Therapeutic ultrasound as treatment for chronic rhinosinusitis: preliminary observations

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Abstract

Background: Bacterial biofilms have been implicated in the pathogenesis of chronic rhinosinusitis. In the laboratory setting, ultrasound is effective in disrupting such biofilms; however, few clinical studies have evaluated the role of therapeutic ultrasound in chronic rhinosinusitis.

Objective: This study was performed to investigate the short-term effectiveness of therapeutic ultrasound as a treatment modality for chronic rhinosinusitis.

Methods: Twenty-two patients with a positive history of chronic rhinosinusitis, according to the criteria set out by the Rhinosinusitis Task Force, together with a previous computed tomography scan compatible with a diagnosis of chronic rhinosinusitis, and who had failed previous, aggressive medical management, were treated with therapeutic pulsed ultrasound at 1 MHz two to three days per week for six sessions. Patients completed an assessment of individual sinus symptom severity and the 20-Item Sino-Nasal Outcome Test questionnaire before treatment, prior to session four and after completion of session six.

Results: Two patients were unable to complete the study protocol. After completion of session six, 18 patients had experienced improvement in symptoms, while two patients noted a worsening of symptoms. Median percentage improvement of the total overall symptom score was 16.7 per cent (Wilcoxon signed rank, $p < 0.001$). The 20-Item Sino-Nasal Outcome Test score improved by 34.1 per cent (Wilcoxon signed rank, $p < 0.0001$).

Conclusion: This study demonstrated a significant improvement in chronic rhinosinusitis symptoms after a six-session course of pulsed ultrasound therapy. Treatment with ultrasound alone or combined with antibiotics may provide a strategy to target biofilms on the sinus mucosa. Therapeutic ultrasound warrants further investigation as a potential treatment modality for chronic rhinosinusitis.

Key words: Sinusitis; Ultrasound Therapy; Bacterial Biofilms

Introduction

The pathophysiology of chronic rhinosinusitis remains unclear. Over the years, numerous factors have been suggested.[1] Recently, bacterial biofilms have been implicated in chronic rhinosinusitis pathogenesis.[2–5] Such biofilms could explain some of the paradoxes associated with chronic rhinosinusitis. Many chronic rhinosinusitis patients are refractory to antibiotic therapy, bacteriology culture swabs from such patients frequently grow no bacteria, and positive bacteriology swabs often do not correlate with clinical findings.[5] As antibiotics are largely ineffective in the treatment of bacterial biofilms, alternative therapeutic strategies are being explored.[6–8]

In the laboratory setting, low frequency, high intensity ultrasound is known to enhance the killing of bacteria in biofilm form. Ultrasound also appears to improve antibiotic efficacy; however, the exact mechanism or mechanisms by which this occurs remain unknown. Ultrasound is thought to increase antibiotic effectiveness by increasing the rate of antibiotic delivery to bacteria, the permeability of the cell membrane, and the metabolic activity and growth of the bacteria.[6]

While therapeutic ultrasound has been advocated as a clinical treatment for chronic rhinosinusitis, critical evaluation of this therapeutic modality has been minimal.[9] In the medical physical therapy literature, the two case series and one single-blinded study which have been published indicated that therapeutic ultrasound may have a role in chronic rhinosinusitis treatment.[10–12] The potential role of biofilms in chronic rhinosinusitis, and laboratory observations demonstrating that ultrasound has a role in breaking down biofilms, suggest that the role of therapeutic ultrasound in the treatment of chronic rhinosinusitis deserves critical reassessment.[6]

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The aim of this study was to evaluate the effectiveness and safety of low intensity, pulsed ultrasound as a treatment for chronic rhinosinusitis in patients attending an otolaryngology clinic.

Methods

Patients presenting to the Counties-Manukau District Health Board department of otolaryngology between January and March 2009 who met study criteria were invited to participate in the study.

The diagnosis of chronic rhinosinusitis was made according to the criteria published by the Rhinosinusitis Task Force and endorsed by the American Academy of Otolaryngology.[1] To be included, patients had to have failed aggressive medical management, including a previous course of prednisone combined with a prolonged course of appropriate antibiotic therapy.

Patients younger than 18 years of age, or those unable to provide informed consent, were excluded. Patients with pacemakers, artificial heart valves, or prostheses in the brain, face or orbit were also excluded.

The study was approved by the Northern Y regional ethics committee.

Patients were asked to evaluate their individual sinus symptom severity, as well as to complete a global assessment of sinonasal symptom severity and the 20-Item Sino-Nasal Outcome Test questionnaire, before treatment, prior to the fourth treatment session and after the sixth session.[1,13]

Global sinonasal symptom severity was assessed using a 6-cm visual analogue scale marked one to seven at 1-cm intervals, with word anchors. One represented no, or only occasional, symptomatic episodes; three represented mild, easily tolerated symptoms; five represented moderately bothersome, difficult to tolerate symptoms interfering with activities of daily living; and seven represented very severe symptoms preventing the patient from functioning most of the time. Patients were asked to make a mark on the scale indicating how much their nasal and sinus symptoms had troubled them over the last 24 hours. Twelve parameters were assessed – nasal obstruction, anterior nasal drip, posterior nasal drip, facial pain or pressure, headache, fatigue, hyposmia, ear pain or pressure, cough, halitosis, dental pain, and fever, giving a maximum score of 84.

The 20-Item Sino-Nasal Outcome Test questionnaire asked patients to indicate, on a scale from zero to five, the overall amount of disturbance or bother they experienced as a result of 'nasal and sinus problems'. Twenty parameters were assessed: need to blow nose, sneezing, coryza, cough, postnasal discharge, thick nasal discharge, ear fullness, dizziness, ear pain, facial pressure or pain, difficulty falling asleep, waking at night, lack of a good night's sleep, waking tired, fatigue, reduced productivity, reduced concentration, frustration or restlessness or irritability, sadness, and embarrassment. The maximum score was 100.

Flexible nasal endoscopy was also performed. Statistical analysis was performed using the Statistical Package for the Social Sciences version 15.0 software program (SPSS Inc, Chicago, Illinois, USA, version 15.0). As the distribution of results did not meet normal parameters, results were analysed as non-parametric data using the Wilcoxon signed rank test (Table II).

Patients were treated with therapeutic ultrasound two to three days per week, at intervals of at most every other day, for six sessions. Pulsed ultrasound at 1 MHz with a pulse duration of 1 ms, pulse interval of 9 ms, and pulse intensity of 1 and 0.5 W/cm^2 was applied to the maxillary and frontal sinuses, respectively. The treatment duration was 5 minutes for each maxillary sinus and 4 minutes for each frontal sinus. All treatments were applied by the same study researcher (DY) using the same machine. Ultrasound was applied using small, tight, circular motions of the soundhead probe. The surface area of the applicator was 1 cm^2.[9]

No other treatment was given.

Patients

Twenty-two patients were recruited to the study (Table I). Two patients failed to complete treatment due to inability to attend clinic sessions. Six patients had a history of previous nasal surgery.

Computed tomography (CT) scans performed prior to treatment were graded at baseline according to the Lund–McKay CT scoring system (Table I).[1,14]

Results and analysis

Twenty patients completed the study protocol. Of these, after session three, 17 reported an improvement in symptoms, one had no noticeable change and two reported worsening symptoms. After completion of session six, 18 patients reported an

TABLE I

BASELINE PATIENT DEMOGRAPHIC DATA

Parameter	Pts (*n* (%))
Gender	
Male	7 (35)
Female	13 (65)
Ethnicity	
European	12 (60)
Asian	5 (25)
Maori	2 (10)
Pacific Island	1 (5)
Age (median (range); yrs)	54 (18–78)
Symptom duration (median (range); yrs)	10 (1–64)
*Lund–McKay score** (median (range))	15 (6–23)
Co-morbidities	
Diabetes	3 (15)
Bronchiectasis	1 (5)
Polyposis	8 (40)
Previous surgery	
Antrostomy	3 (15)
Septoplasty	1 (5)
Endoscopic sinus surgery	2 (10)

Data represent patient numbers and percentages unless indicated otherwise. *Of a possible total of 24. Pts = patients; yrs = years

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TABLE II

PATIENTS' REPORTED SYMPTOM CHANGES

Symptom change	Pts (*n*)	
	After S3	After S6
Improvement	17	18
None	1	0
Deterioration	2	2

Pts = patients; S3 = session three; S6 = session six

improvement in symptoms while two patients noted worsening symptoms; these results were supported by both the global assessment of sinonasal symptom severity and the 20-Item Sino-Nasal Outcome Test (Table II). One of the patients whose symptoms deteriorated developed acute rhinosinusitis after session six and was treated with antibiotics. This was the only adverse event reported during the study.

Patients' global assessment of severity scores improved by 6.6 per cent after session three (interquartile range (25–75 per cent) 0–17.8 per cent; Wilcoxon test, $p < 0.005$). This value increased to a 16.7 per cent improvement after session six (interquartile range (25–75 per cent) 9.1–31.7 per cent; Wilcoxon test, $p < 0.001$).

The 20-Item Sino-Nasal Outcome Test score improved 24.0 per cent after session three (interquartile range (25–75 per cent) 6.6–46.4 per cent; Wilcoxon test, $p < 0.0001$). This value increased to 34.1 per cent improvement at session six (interquartile range (25–75 per cent) 12.2–62.5 per cent; Wilcoxon test, $p < 0.0001$) (Figure 1).

A statistically significant improvement in symptom score was noted for: sneezing ($p < 0.031$), coryza ($p < 0.023$), cough ($p < 0.027$), postnasal discharge ($p < 0.004$), thick nasal discharge ($p < 0.012$), ear pain ($p < 0.034$), facial pain ($p < 0.033$), lack of sleep ($p < 0.029$), waking tired ($p < 0.001$), fatigue ($p < 0.003$), reduced productivity ($p < 0.038$), reduced concentration ($p < 0.048$), frustration or restlessness or irritability ($p < 0.002$), sadness ($p < 0.004$), and embarrassment ($p < 0.020$) (Table III).

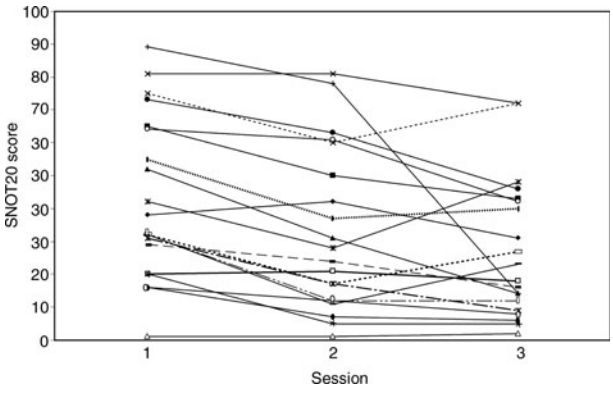

FIG. 1

Changes in patients' 20-item Sino-Nasal Outcome Test scores, comparing baseline, after session three and after session six.

TABLE III

20-ITEM SINO-NASAL OUTCOME TEST SCORES

Symptom	Median score		p^*
	Baseline	After S6	
Need to blow nose	3	2	0.088
Sneezing	2	1	0.031†
Coryza	2.5	1	0.023†
Cough	2	1	0.027†
Postnasal discharge	3	2	0.004‡
Thick nasal discharge	2	1	0.012†
Ear fullness	0.5	0	0.093
Dizziness	0	0	0.287
Ear pain	0	0	0.034†
Facial pressure or pain	2	1	0.033†
Difficulty falling asleep	2.5	1	0.111
Waking at night	3	1	0.069
Lack of a good night's sleep	4	1	0.029†
Waking tired	3.5	1.5	0.001‡
Fatigue	4.5	3	0.003‡
Reduced productivity	2.5	1	0.038†
Reduced concentration	2.5	1.5	0.048†
Frustration or restlessness or irritability	3	1	0.002‡
Sadness	1.5	0	0.004‡
Embarrassment	1	0	0.020†

*Wilcoxon test. †Statistical significance at $p<0.05$; ‡statistical significance at $p < 0.01$. S6 = session six

Using Spearman's rank correlation, there was no statistically significant association between patients' baseline Lund–McKay score, individual sinus symptom severity score or age, when compared with their global assessment of sinonasal symptom severity percentage improvement or their 20-Item Sino-Nasal Outcome Test percentage improvement.

Discussion

Therapeutic ultrasound has been used as a clinical treatment for chronic rhinosinusitis for decades; however, the results of such treatment have not been reported in the rhinology literature.[9] This study has demonstrated a significant improvement in chronic rhinosinusitis symptoms following a six-session course of pulsed ultrasound therapy, thus confirming the results of previous studies published in the musculoskeletal literature. Ansari *et al.* treated 57 chronic rhinosinusitis patients with pulsed ultrasound over 15 sessions.[10] Using a different reporting scale, the total improvement in symptoms was 81.3 per cent, with most sinus symptoms showing significant improvement. In a further case series, 30 chronic rhinosinusitis patients were treated with continuous ultrasound.[11] The severity of all symptoms showed significant improvement ($p < 0.05$), with a mean symptom improvement of 74.37 per cent. At one month, 72 per cent of patients reported ongoing benefit. In a single-blinded, randomised, placebo-controlled trial in which 10 patients received continuous ultrasound and 10 received mock-ultrasound, for 10 sessions, the mean percentage improvement in the ultrasound group (86.56 per cent) was significantly higher than that in the control group (37.14 per cent) ($p < 0.007$).[12]

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The major limitations of this study were its small size and lack of a control group, which limited its power and generalisability. Furthermore, given the relaxing nature of the intervention, together with the development of a strong therapeutic relationship between the patient and the ultrasound technician, there is likely to have been a significant placebo effect. This study was performed using ultrasound alone; the addition of appropriate antibiotics could have had a powerful synergistic effect. Nevertheless, this preliminary study indicates that the role of therapeutic ultrasound in the management of chronic rhinosinusitis deserves further investigation.

- **Bacterial biofilms have been implicated in the pathogenesis of chronic rhinosinusitis**
- **In the laboratory setting, ultrasound is effective in disrupting bacterial biofilms**
- **In this study, patients reported a significant symptomatic improvement in chronic rhinosinusitis symptoms after a six-session course of pulsed ultrasound therapy**
- **The use of ultrasound alone or combined with antibiotics may provide a strategy to target biofilms on sinus mucosa**

The mechanisms by which ultrasound may improve the symptoms of chronic rhinosinusitis remain uncertain.[6] Evidence can be extrapolated from *in vivo* studies. It is possible that vibrations produced by pulsed ultrasound have a mechanical effect, loosening secretions. This mechanical effect of ultrasound, termed acoustic streaming, has been demonstrated on a maxillary sinus bovine cadaveric model.[15] Anecdotally, patients reported increased nasal discharge early in the treatment programme. Ultrasonic treatment at sufficiently high levels is capable of killing bacteria. In this situation, such bacterial killing is usually attributed to unstable cavitation in or on the bacteria, or to the generation of peroxides which subsequently kill the bacteria.[16,17] At ultrasonic power levels sufficiently low to not kill bacteria, simultaneous application of ultrasound and gentamicin reduced the viability of sessile *Pseudomonas aeruginosa* bacteria in biofilms by several orders of magnitude. This synergistic effect of ultrasound and antibiotics has been termed the bioacoustical effect.[18] Low level ultrasound may cause biofilm bacteria to revert to a planktonic state in which they are more susceptible to antibiotics as well as to the body's innate and adaptive antibacterial defences. This is consistent with our clinical observation that two of our three patients with type II diabetes became symptomatically worse following treatment, with one patient developing acute rhinosinusitis after session six, requiring a course of antibiotics. The presence of type II diabetes was the only common factor between the two patients who failed to improve symptomatically. Type II diabetes is associated with deficiencies in innate cellular immunity.[19] Low intensity ultrasound has also been shown to increase bacterial growth.[20] If this is the potential mechanism of therapeutic ultrasound, then the addition of antimicrobial agents should lead to more significant clinical improvement. Indeed, one of the authors has observed this effect clinically (Figure 2).

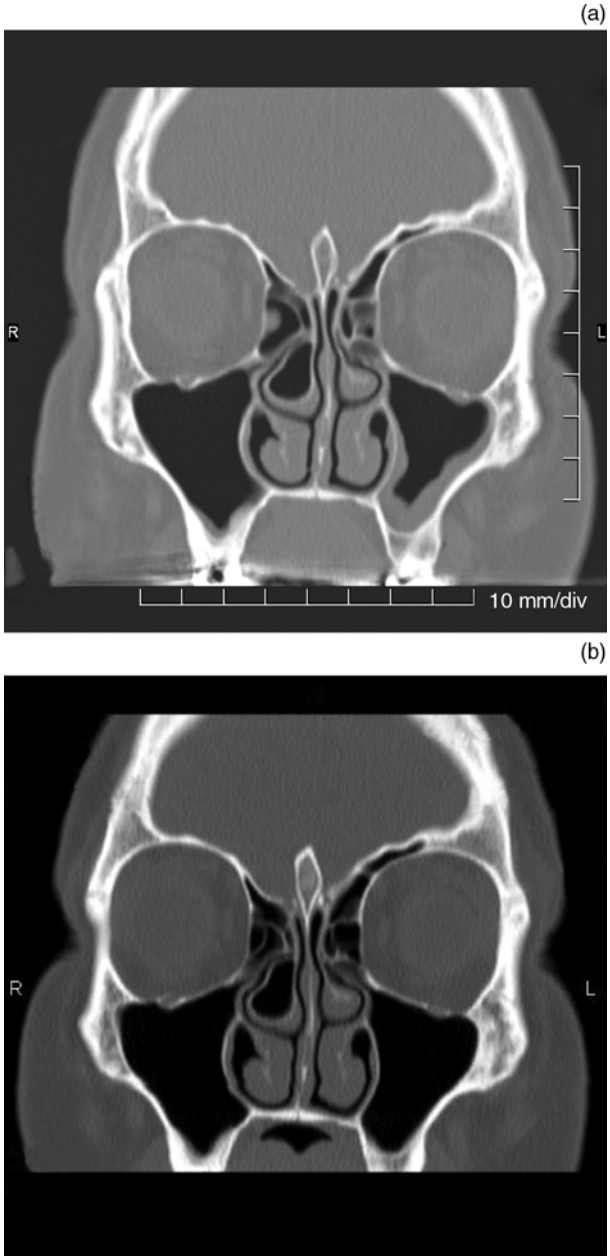

FIG. 2

(a) Pre- and (b) post-treatment computed tomography scans of a 50-year-old man with a nine-month history of left maxillary sinusitis refractory to aggressive medical treatment. He was treated with four sessions of ultrasound combined with ciprofloxacin 250 mg twice daily for two weeks, with complete clinical resolution of symptoms. He remained well six months later. L = left; R = right

A practical limitation of therapeutic ultrasound is the time commitment required. Patients must attend a minimum of six sessions lasting 20 minutes each. With busy work schedules, this was difficult for some patients. On the other hand, small, cheap

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ultrasound machines suitable for home use are readily available (e.g. the US-1000, 1 MHz Portable Home Ultrasound Machine; see http://www.ezuultrasound.com). The optimal frequency, intensity, treatment duration and number of sessions needed for the treatment of chronic rhinosinusitis by therapeutic ultrasound is yet to be determined; however, this treatment modality has potential as a safe, effective treatment for this condition.

Conclusions

This study suggests that therapeutic ultrasound is a well tolerated treatment which appears to significantly improve symptoms of chronic rhinosinusitis. Therapeutic ultrasound may offer a non-invasive medical intervention for the treatment of this condition. The combination of ultrasound with appropriate antibiotics may improve efficacy. Therapeutic ultrasound warrants further investigation as a treatment modality for chronic rhinosinusitis.

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