Reflexology for acute rhinosinusitis – Results from a blinded, early-phase comparative trial

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Highlights

•This methodology is feasible in investigating reflexology in acute rhinosinusitis

•The separation test is a valuable tool in assessing whether it is worthwhile to pursue research

•Further research is warranted using mean symptom score comparing baseline to day ten

•Further research is not warranted comparing baseline to day two

Abstract

Background

Reflexology is commonly used as an adjunct to conventional treatment by patients with respiratory tract infections. The effect of reflexology needs to be tested in a full-scale randomized controlled study. Small early-phase trials can give an indication on whether full-size clinical trials are warranted. The objective of this study is to determine whether the study design is feasible in a full-scale study of reflexology as an add-on to usual care compared to usual care alone in acute rhinosinusitis, and further if there is a statistical indication of an effect of reflexology warranting a full-scale study.

Methods

20 patients with symptoms compatible with acute rhinosinusitis, and an illness duration of 28 days or less were randomized to additional reflexology treatment along with usual medical care, or usual care alone. The patients scored how much each of 16 sinus-related symptoms bothered them in the past few days on a six-point scale (zero = no problem to five = severe problem). To determine if there is a statistical indication of an effect of reflexology warranting a full-scale study, the separation test was used.

Results

The methodology was considered feasible and could therefore be applied in a full-scale study of reflexology for acute rhinosinusitis. The mean reduction in symptom score from baseline to day two was 0.95 in the reflexology group and 0.78 in the control group. From baseline to day ten the mean reduction in symptom score was 2.12 in the reflexology group and 1.63 in the control group. A statistical indication of effect in a full-scale study in favor of reflexology was found from baseline to day ten but not from baseline to day two.

Conclusions

The research methodology in this study could be used in a full-scale study of reflexology in acute sinusitis. The results from the separation test indicates an effect warranting a full-scale study of reflexology regarding effects in acute sinusitis ten days after treatment.

Keywords

Rhinosinusitis; Reflexology; Early phase trial: Reduction in symptom; Separation-test

Abbreviations

CAM Complementary and Alternative Medicine, NAFKAM National Research Centre of Complementary and Alternative Medicine, UiT University of Tromsø, GP general practitioner, ENTEar Nose and Throat, SNOT-16 Sino Nasal Outcome Tests, 16 item QOL quality of life, VMC Vestskogen Medical Center, SD Standard Deviation, SDE Standard Deviation of Effect-Estimates

Background

Respiratory tract infections constitute approximately 17.7% of all General Practitioner (GP) consultations in Norway1. A total of 96.8% of patients with acute rhinosinusitis in five Swedish counties who consulted a GP left with a prescription for antibiotics2, while the prescription of antibiotics for acute rhinosinusitis in Norway was 75.9%3. This prescription practice stands in contrast to the low documented efficacy of antibiotics in clinically diagnosed rhinosinusitis4,5, and Norwegian6 and international guidelines7 of prescribing antibiotics only when they are needed.

Norwegian reflexologists report seeing patients with acute rhinosinusitis regularly, and often experience rapid clinical response in these patients, even though only a minor proportion of patients suffering from rhinosinusitis report use of reflexology8,9. Norwegians mostly use reflexology to treat long term illness and to improve wellbeing (82%)10.

In Norway reflexology is considered as Complementary and Alternative Medicine (CAM) and is mostly offered outside the national health care service. The treatment is fully paid for out of pocket and is usually administered as an adjunct to conventional health care. Treatment available within the national health care service in Norway is, on the other hand, mostly free of charge, only co-paid with a small fee.

Reflexology is a CAM modality employing manual pressure to specific areas of the body (usually the feet) which are thought to correspond to other organs with the intention to generate positive health effects. Reflexology is one of the most used CAM therapies in Norway, yearly used by 1.4% of the population. Most of the users (92%) find reflexology helpful for their complaint10.

In a survey of pattern of CAM use among adult out- and inpatients attending the Ear, Nose and Throat (ENT) department of the Aberdeen Royal Infirmary, Aberdeen, Scotland, 9% reported to have used reflexology. Of all herbal and non-herbal treatments reportedly used, only aromatherapy and homeopathy were more commonly reported than reflexology11.

A clinical trial from Wisconsin in the USA used reflexology as the control treatment when studying the effectiveness of decongestants. The results showed that reflexology was as effective as nasal irrigation12. However, the study was small and no larger randomized trials on the efficacy or effectiveness of reflexology on acute sinusitis have been identified where reflexology was the treatment primarily under study.

The methodological challenges in a large-scale study on the effect of reflexology needs to be explored, but results from these “small sample”-studies cannot be used for hypothesis testing due to very low statistical power. Small early-phase trials can, however, give an indication on whether full-size clinical trials are warranted. This decision is often made only by scientific and clinical judgment

but can better be determined using a separation test. With the use of this test, researchers can achieve information whether there is a statistical indication of an effect in a full-scale study13.

The objective of this study is to determine whether the study design is feasible in a full-scale study of reflexology as an add on to usual care compared to usual care alone in acute rhinosinusitis, and further, if there is a statistical indication of an effect of reflexology warranting a full-scale study.

Methods

The patients

All patients, 16 years of age and above with symptoms compatible with acute rhinosinusitis, and an illness duration of 28 days or less seeking urgent care in three towns in southern Norway between September 2017 and March 2018 were invited to participate in the study. Enrollment continued until 20 patients were included according to pre-study sample size calculation. A total of 24 patients were asked to participate before 20 patients signed the informed consent form and were treated according to the study protocol (response rate 83%).

Two or more of the following Berg and Carenfelt criteria14 symptoms or signs were required for inclusion: “Purulent nasal discharge with unilateral predominance, local pain with unilateral predominance, purulent nasal discharge bilaterally, or pus on inspection inside the nose”.

Patients who had known allergic reactions towards penicillin or amoxicillin, had a prior antibiotic treatment within four weeks, complications of sinusitis, comorbidity that may impaired their immune response, cystic fibrosis, who requires an antibiotic for a concurrent condition, who were pregnant or with cognitively impaired to a degree where they are unable to follow instructions, were excluded from the study.

Data collection

To measure the severity of the participant's symptoms, the Sino Nasal Outcome Tests 16 (SNOT-16), was used as the primary outcome measure. SNOT-16 is a validated disease-specific quality of life (QOL) instrument for use in acute rhino sinusitis measuring functional limitations, physical problems as well as emotional consequences15.

Considering both severity and frequency, the participant scored how much each of 16 sinus-related symptoms bothered them in the past few days on a six-point scale (zero = no problem to five = severe problem).

All 20 patients (11 in intervention group and nine in control group) filled in the baseline questionnaire after being included in the study. When enrolled in the trial, the patient further filled-in and returned the follow-up questionnaire for measurements at day two and day ten in a preaddressed, prepaid envelopes.

Nineteen of the patients gave their responses in the postal questionnaire for day two and eighteen for day ten. All patients in the intervention group responded, while eight and seven in the control group gave their responses at day two and day ten, respectively. When single item responses were missing at day ten (not the whole questionnaire), last value from the items missing at day two were carried forward to day ten. The two participant who gave no response on day two and/or day ten were excluded from the analyses (Fig. 1).

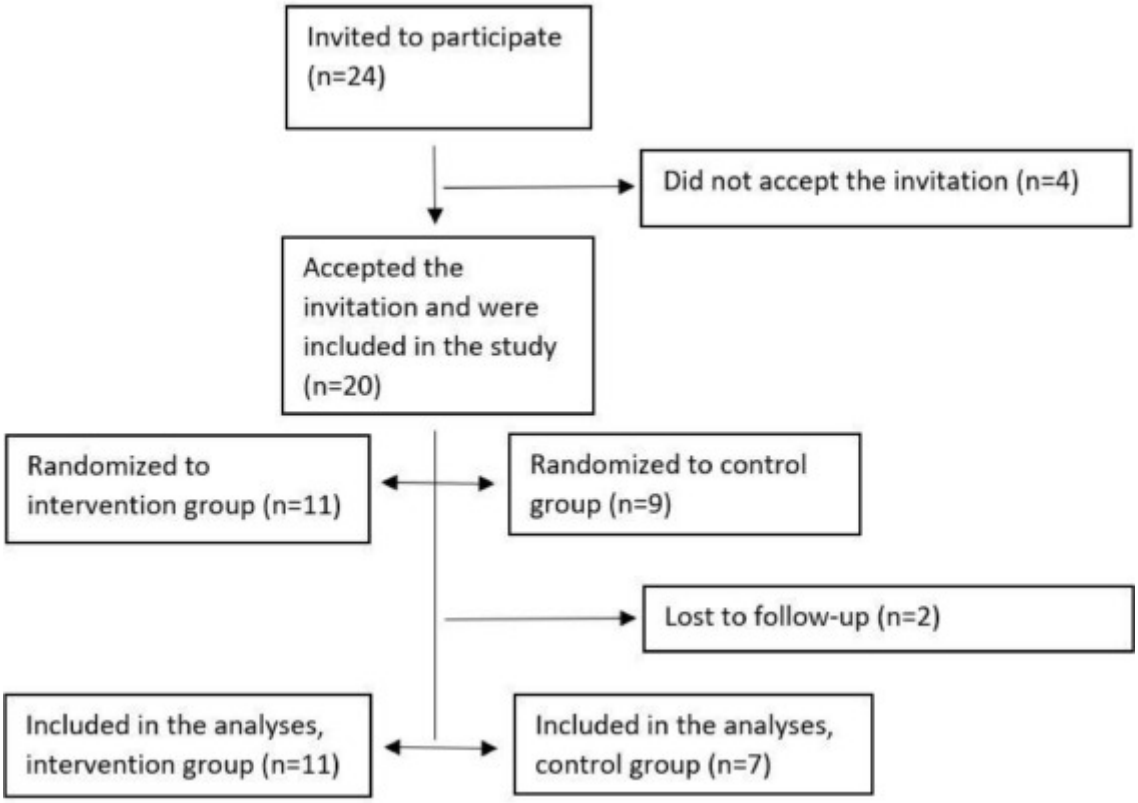

Fig. 1. Flow chart of the participants

Treatment plan

Enrollment to the study took place at Vestskogen Medical Center (VMC), a primary/family healthcare practice located next to the city of Tønsberg in the south-eastern part of Norway. Patients were invited to the study by advertisement in local newspapers, handouts at the pharmacies in the area, and using social media (Facebook).

Patients responded to the invitation and made their first inquiry to the staff at the primary care facility at VMC. The staff was oriented about the study procedures and trained before start of the study. All included patients had an ordinary visit with the study physician and received conventional treatment in a primary healthcare setting.

Patients were thereafter randomized to additional reflexology treatment along with usual medical care, or usual care alone. Allocation was performed by a random number generator at the University hospital of North Norway. The allocation was kept concealed until the data were analyzed, leading to blinding of the evaluator when computing and analyzing the patient-reported data. Patients were not blinded regarding their treatment allocation, and the study physician and the reflexologists were not blinded to group allocation, as further blinding of the patient and/or the therapist was not found appropriate in this early phase study.

Throughout the ten-day study period all participants were advised to follow the treatment plan given by the physician at the primary care facility. This might include a delayed prescription for antibiotics if the condition of the patient had not improved after a maximum of ten days after debut of their sinusitis-symptoms.

The study assistant at VMC followed up each patient at day two and ten, inquiring regarding compliance and completeness of prescribed treatment. The patients were also asked whether he/she had used any other kind of medication, antibiotics, visited another doctor and/or received any other treatment.

The reflexology intervention

Two registered reflexologists, both with more than thirty years clinical experience gave the reflexology treatments. The diagnostic process and choice of treatment was validated in a pre-study Delphi-process among experienced reflexologists in Norway, ensuring a conform reflexology treatment approach. There was several meetings and gatherings involving both therapists, researchers and ***health*** personnel concerning the reflexology intervention in the protocol.

The distance from the doctor's office to the treatment center was about two kilometers. The first treatment was usually performed on the same day as the doctor's consultation. No patients had more than 20 km from their place of residence to the place of treatment, and no logistic problems were experienced for follow up. The patients were divided among the therapists according to the one who could receive them first. The distribution was six patients on one therapist and five on the other.

The first consultation involved the case history focusing on the patients' medical history, the use of medical drugs, identification of symptoms such as sensations, time and circumstances concerning aggravation/amelioration, localization, accompanying conditions. No other therapeutic advice was given, except to register changes in symptoms and possibly report this per telephone or at the next consultation.

The average number of treatments per patient throughout the intervention period was 3.1 with two as minimum and four as a maximum within a ten-day treatment period. On average, the second follow-up treatment was given at day three and a third treatment at day six. Five patients were given additional treatment after day 10.

As most of the patient had other chronic ailments, the intervention was after a thorough assessment carried out as a "holistic treatment" according to reflexology theories. This is interpreted as a stimulation of zones for the whole body to achieve flow through all vital immune functions and to other organ/part of the organism than the sinusitis, which possibly could indirectly influence or have indirect impact on the local condition.

Statistical analysis

The two primary statistical outcomes in this study are the between-group difference in mean difference in SNOT-16 value from baseline to day two, and from baseline to day ten. The separation test is based on calculations regarding the mean reduction in symptoms. Between-group difference were calculated from baseline to day two, and from baseline to day ten and compared between the intervention group (reflexology and usual care) and the control group (usual care). The results from the separation test is in this early-phase comparative trial used to investigate an indication of an effect in a full-scale study16.

Results

Feasibility of the study protocol

The study showed challenges in the recruiting process and willingness among patients to adhere to a study where a complementary therapist needed to be visited in addition to their general practitioner.

On the other hand, patients that were randomized to reflexology as an add-on to conventional care expressed great satisfaction by being part of the study and receiving complementary treatment. The logistics in the medical center was excellent and the study did not add substantial extra work to the doctors and the medical secretaries, or time spent for the patient. However, an increased focus on completeness of the recordings of symptoms would reduce the number of missing values.

The patients in the intervention group were referred to the reflexologist for complementary treatment the same day without any delay or obstacles for the daily schedule in the VMC. None of the patients who completed the study had difficulties in following the conventional treatment plan, experienced side-effects or had problems related to the participation in the study.

Two patients dropped out of the study during follow-up. One of these patients responded to the questionnaire at day two, but not at day ten, while the other patient did not respond to questionnaires neither at day two, nor day ten. Both patients who dropped out of the study were in the control group receiving usual care only.

Two patients, one in in each group, used antibiotics in accordance with the study protocol, since the condition of the patient had not improved after a maximum of ten days after debut of their sinusitis-symptoms.

Basic and disease-specific characteristics of the participants

More women (60%, n=12) than men (40%, n=8) were included in the study with a mean age was 45.5 years (Table 1). The most severe symptoms reported were pain/pressure in the forehead/face (mean score of 3.9 on a five-pout scale) followed by awake at night (3.8), lack of sleep (3.7), tired when waking up (3.6), reduced productivity (3.5), and nasal discharge (3.5) (Table 1). Pain in the ears (1.7) and dizziness (1.9) were the symptoms troubling the participants the least (Table 1).

Table 1. Baseline characteristics of the participants.

Empty Cell	**Total**	**Intervention group (*n*=11)**	**Control group (*n*=9)**
Gender, % (n)			
Men	40.0 (8)	45.5 (5)	33.3 (3)
Women	60.0 (12)	54.5 (6)	66.7 (6)
Age, mean (SD)	45.5 (11.75)	43.5 (14.13)	47.9 (8.16)
Symptoms, mean (SD)			
Facial pain/pressure	3.9 (1.02)	4.3 (0.65)	3.4 (1.24)
Wake up in night	3.8 (1.08)	3.8 (1.17)	3.8 (1.04)
Lack of a good night's sleep	3.7 (1.42)	3.6 (1.69)	3.8 (1.04)
Wake up tired	3.6 (1.12)	3.7 (1.27)	3.5 (0.93)
Thick nasal discharge	3.5 (1.12)	3.5 (1.44)	3.6 (0.52)
Reduced productivity	3.5 (0.99)	3.7 (0.95)	3.3 (1.04)
Need to blow nose	3.4 (0.90)	3.2 (0.98)	3.6 (0.74)

Empty Cell	Total	Intervention group (*n*=11)	Control group (*n*=9)
Fatigue	3.2 (1.12)	3.3 (1.25)	3.0 (1.00)
Ear fullness	2.8 (1.34)	2.6 (1.43)	3.1 (1.25)
Cough	2.8 (1.24)	2.5 (1.57)	3.2 (0.44)
Difficulty falling asleep (Insomnia)	2.7 (1.36)	2.6 (1.35)	2.9 (1.46)
Runny nose (Rhinorrhoea)	2.6 (1.30)	2.6 (1.57)	2.6 (0.92)
Post-nasal discharge	2.4 (1.34)	2.4 (1.35)	2.3 (1.41)
Sneezing	2.2 (1.32)	2.5 (1.44)	1.9 (1.13)
Dizziness	1.9 (1.41)	2.4 (1.43)	1.3 (1.16)
Ear pain (Otalgia)	1.7 (1.70)	1.8 (1.60)	1.5 (1.93)

Mean symptom score

Both the intervention group and the control group showed a reduction of symptoms during the ten-day follow-up period (Fig. 2).

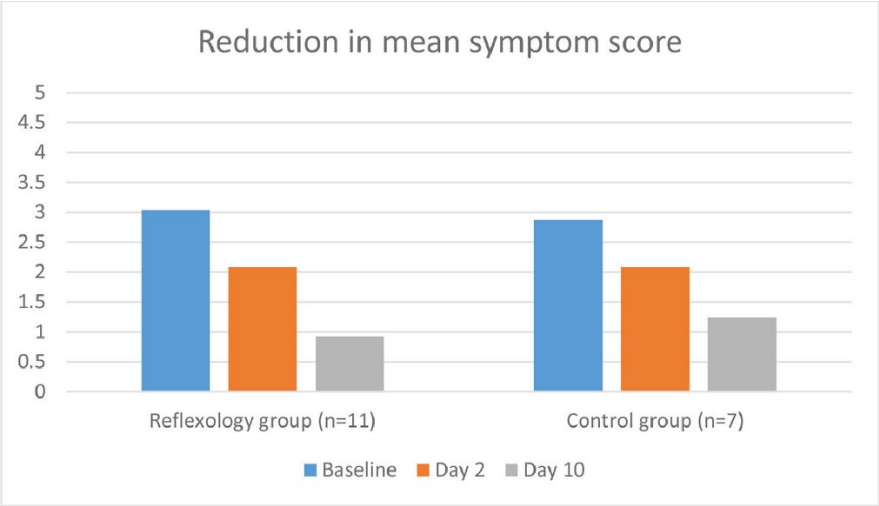

Fig. 2. Mean symptom score

The mean reduction in total symptom score from baseline to day two in the intervention group was 0.95, while the control group reported a reduction of 0.78. This represents a between-group difference of 0.17. The mean reduction in symptom score from baseline to day ten in the intervention group was 2.12, while the control group reported a reduction of 1.63. This represents a between-group difference of 0.49 (Table 2).

Table 2. Mean symptom score

Empty Cell	Reflexology group (*n*=11)	Control group (*n*=7)	Between-group difference
Mean symptom score (SD)			
Baseline (Day 0)	3.04 (0.70)	2.87 (0.57)	0.17

Empty Cell	**Reflexology group (*n*=11)**	**Control group (*n*=7)**	**Between-group difference**
Day 2	2.09 (0.63)	2.09 (0.83)	0.0
Day 10	0.92 (0.50)	1.24 (0.73)	-0.32
Reduction, baseline (day 0) to day 2	0.95 (0.73)	0.78 (0.58)	0.17
Reduction, baseline (day 0) to day 10	2.12 (0.88)	1.63 (0.49)	0.49

The separation test shows no statistical indication of an effect from baseline to day two of reflexology plus usual care compared to usual care alone in acute sinusitis regarding reduction of mean symptom score. From baseline to day ten, there is a statistical indication regarding reduction of mean symptom score in favour of reflexology in addition to usual care (Table 3).

Table 3. Indication of effect of the between-group difference in reflexology versus standard care for mean symptom score

Comparison of reflexology group and control group	**Difference in mean symptom score** [a]	**SDE**	**Δ/2** [b]	**Indication of effect** [c]
Baseline versus day 2 Reflexology vs conventional care	0.17	0,33	0,27	No
Baseline versus day 10 Reflexology vs. conventional care	0.49	0.32	0.28	Yes, In favour of reflexology

Abbreviation: SDE, Standard deviation of effect estimates

a Difference between the intervention group and conventional care-group in mean change in score (table 2)

b Δ is defined as 1,74 X SDE 16 degrees of freedom)

c If the difference in score is less than Δ/2 (in the direction favorable to reflexology), further research is not recommended. If the difference in score is greater than Δ/2 (in the direction favorable to reflexology), further research is recommended.

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Discussion

The methodology in this study is shown to be feasible in a large-scale study in reflexology in acute rhinosinusitis with an extra focus of reducing dropouts in the control group and reduce the number of missing responses to single questions in the questionnaire. It is a concern that two out of nine patients (22.2%) in the control group were lost to follow up. This underscores the challenge of keeping patients in control groups in exploratory studies17.

In this study, it appears (by calculating day 0 mean values on n=9 from Table 1) that those participants who did not complete the study had more severe symptoms than average, which can affect interpretation of results. Future strategies for helping to alleviate that problem could include offering reflexology treatments after the 10-day measurement point for individuals in the control group to keep them in the study.

The number of patients included in the study (n=20) could have been enlarged as a precaution to loss to follow-up. This is particularly important in a full-scale study design. A potential drop-out rate of at least 20% need to be considered when determining power for a larger full-scale rigorous study.

Even though Norwegian reflexologists experience rapid/early clinical response in rhinosinusitis patients when treated with reflexology, this study shows no statistical indication of effect in reduction of symptoms in favour of reflexology in addition to usual care compared to usual care alone from baseline to day two where both groups experienced a similar reduction. There was, however, a statistical indication regarding reduction of mean symptom score from baseline to day ten in favour of reflexology.

The patients in this study seem to have the same symptoms and signs as previously described in larger series among patients with clinically suspected acute rhinosinusitis18,19. Previous studies have shown that individual signs and symptoms are of limited value for the exact and correct diagnosis of acute bacterial rhinosinusitis20. However, due to the limitations of the methodology, our study cannot contribute to the debate regarding accuracy of symptoms or clinical decision rules.

Separation test has been used in small sized early phase trials to assess whether it is worthwhile to pursue further large-scale research21,22. This is particularly important in CAM research where both budgetary and safety considerations argue for a small sample size. The standard statistical methods applied in most comparative trials leaves small trials subject to be criticized for being underpowered. The fundamental theory of hypothesis tests is employed in the separation test, by invoking a different inferential rationale16,23.

This study was conducted to investigate early effect of reflexology (day two) and late recover (day ten) from more bothersome long-lasting complaints. We find it interesting that further research is indicated using mean symptom score in the last phase of the study (baseline to day ten), while further research is not indicated regarding the early phase (baseline - day two). The diverging results in the separation test do not fully support performing a large clinical trial, at least not regarding short-term effects.

Based on our experience, we find it useful to include both an early response and late effect for further research in the field. Whether exactly day two and day ten is the optimal timepoint in the disease-course for evaluation of effect from reflexology, is not evidence based and is therefore a question for further consideration.

The progression of treatments should also be given attention in future study design. The treatment intervals were given particular attention in the pre-study Delphi process leading to the unified reflexological treatment plan. The conclusion was that optimal treatment-intervals following from day one would be day three – five – and ten. Number of treatments and treatment intervals is also an issue that needs to be seen in the light of patient compliance, as more visits to the therapist might be challenged when diseased with sinusitis. The average number of reflexology treatments in this study was 3.1, and might serve as a template for future studies, although careful consideration regarding treatment intervals and number of treatments is necessary.

Further research

This paper has reaffirmed the critical role of early phase CAM research and can possibly encourage CAM researchers to value and conduct early phase studies for their proper purposes. The use of the separation test in small scale, early phase studies is valuable in assessing whether it is worthwhile to pursue research. This is particularly important in CAM research where both budgetary and safety considerations argue for research with small sample size before going forward with a full hypothesis-testing trial.

Ethics approval and consent to participate

Approval of the study was received by the Regional Committee for Medical and Health Research Ethics (REK: 2017/445). The patients were informed about the study both through a pamphlet and verbally by a research assistant. Written informed consent was obtained from all participants. All participants were informed that there would be no disadvantage if they did not wish to participate, and that they could withdraw from the study at any time of the study.

Consent for publication

The manuscript does not contain sensitive data from any individual person. All participating patients has signed the informed consent for publication.

Availability of data and materials

The dataset this paper has been based on has not been deposited in any repository. All dataset and materials are available from the corresponding author upon reasonable request. The unified Delphi-based reflexological definition of diagnosis and treatment in acute rhinosinusitis is available upon request.

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Authors' contributions

AJN, AEK, TS, JPL and VF conceived the study. AEK and VF performed the initial and final analyses. AJN and AEK drafted the initial version of the paper. CB, JPL and TV performed the clinical treatment in the study. All authors reviewed subsequent versions and read and approved the final manuscript.

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