Allergy & Rhinology
Volume 9: 1–5

DOI: 10.1177/2152656718800059
journals.sagepub.com/home/aar
SAGE

Effect of *Nigella sativa* Nasal Spray on the Treatment of Chronic Rhinosinusitis Without a Nasal Polyp

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Abstract

Background: Chronic rhinosinusitis (CRS) is a common inflammatory disease of nasal and paranasal sinuses, with many treatment methods available for the management of this disease. Recently, herbal medicines have shown a significant impact on inflammatory diseases such as CRS, and one of these herbal medicines is *Nigella sativa*. Therefore, the current study aimed to evaluate the effectiveness of *N. sativa* in patients with CRS without nasal polyp (CRSsNP).

Methods: In this randomized clinical trial, 65 patients with mild to moderate CRSsNP were enrolled based on the inclusion criteria. Patients were divided randomly into 2 parallel groups: intervention and placebo groups. Patients in the intervention group received 2 puffs/day of *N. sativa* nasal spray (1 g/day of *N. sativa*) and in the placebo group received 2 puffs/day of sodium chloride spray 0.65%.

Results: Thirty-one patients (19 men and 12 women) in the intervention group and 34 in the placebo group (18 men and 16 women) were evaluated. Lund–McKay, Lund Kennedy, and Sino-Nasal Outcome Test-22 scores were assessed for both groups after 8 weeks of treatments. These scores decreased significantly in both groups. However, these scores were significantly lower in the intervention group compared with the placebo group ($P < .0001$, for all).

Conclusion: The use of *N. sativa* nasal spray has symptom reliever effect with no adverse effects in patients with CRSsNP.

Keywords

Nigella sativa, nasal spray, rhinosinusitis, inflammation, symptoms

Introduction

Chronic rhinosinusitis (CRS) is an inflammatory disease of nasal and paranasal sinuses. The symptoms of CRS include, but not limited to nasal blockage or obstruction, nasal discharge, facial pain or pressure, loss of smell sensation, and cough. The presence of these symptoms mostly last at least for 12 weeks or more.[1] Based on recent studies, about 31 million patients with CRS are diagnosed each year, which indicates an increased incidence and prevalence among the general population in the United States.[2] CRS is diagnosed according to clinical symptoms, endoscopic, and radiologic findings such as computed tomography (CT); however, some studies suggest a diagnosis of CRS only based on clinical symptoms.[3,4] CRS is divided into 2 phenotypes according to nasal polyposis as chronic rhinosinusitis with and without nasal polyps (CRSwNP and CRSsNP).[1] Although there are different and conflicting lines of methods for the treatment of CRSwNP and CRSsNP, none of them have proved to be completely helpful due to various kinds of responses among patients. The patients with minimum degrees of CRSsNP or CRSwNP can be managed with medical therapies such as topical steroids for long-term therapies or oral steroids for short courses. Also, some patients with refractory CRSsNP or CRSwNP need combination surgical and medical therapies. Meanwhile, other adjuvant therapies are the topical usage of saline irrigations and antibiotics.[5–7] Topical steroids are in the form of spray and have shallow systemic

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side effects with little penetration in middle meatus.[8] Also, this mode of treatment can decrease postoperative adhesion, edema, discharge, and crusting.[9] It is noteworthy to mention that oral steroids also have multiple adverse effects including necrosis of the femoral head, mood changing, calcium demineralization, increasing blood glucose levels, and posterior cataract formation.[10] One other treatment method for the management of CRS is the usage of herbal medicines. Although there are few studies about the usage of herbal drugs on the treatment of CRS, these studies have indicated that about 32% of patients use herbal medicines as a complementary therapy.[11] One of these herbal remedies is *Nigella sativa*/Black Cumins or black seed. This plant belongs to the Ranunculaceae family and grows in Middle Eastern countries such as India and Pakistan.[12,13] In ancient medicine, this plant had been used to treat asthma, bronchitis, diabetes, eczema, and fever; and in modern medicine, the properties of this plant are attributed to the presence of thymoquinone in the plant. In addition, it has analgesic, anti-inflammatory, bronchodilatory, antibacterial, antibacterial, antiviral, antifungal, anticancer, and anticoagulant properties.[14,15] In this study, we hypothesize the effect of *N. sativa* nasal spray on the treatment of CRS; therefore, this study aimed to compare *N. sativa* nasal spray (1 g/day) and sodium chloride nasal spray 0.65% in the medical management of patients with CRSsNP.

Methods and Materials

Patients

In this randomized, double-blinded, controlled, clinical trial which was approved in the Isfahan University of Medical Sciences (No: 396324) and registered in the Iranian registry of clinical trial (No: IRCT2017082712782N17), 93 patients with CRS were referred to Amin Hospital, Isfahan, Iran. Sixty-five patients were selected for study based on the inclusion criteria. The patients were diagnosed according to the history of rhinosinusitis, clinical symptoms, endoscopic evaluation (based on Modified Lund Kennedy), and CT scan (based on Lund–McKay).[16] The study was conducted between 2015 and 2017. The inclusion criteria included the following: (1) patients with CRSsNP aged between 18 and 72 years, (2) $1 <$ Modified Lund Kennedy < 8 or $3 <$ Lund–McKay < 10, and (3) informed consent. Pregnant patients, nursing mothers, patients with any history of usage of topical or systemic antibiotics or corticosteroids until 1 month, patients with Samter's triad (combination of allergy, aspirin intolerance, and asthma) and with previous sinus surgery, and patients with serious side effects such as allergy to *N. sativa*, unwillingness to participate, and lost to follow-up prior to completing 8 months (telephone call was used to prevent loss of follow-up) were excluded from the study. At the onset of the study, demographic information such as age and gender of patients were recorded. Before interventions, patients were divided randomly into 2 parallel groups called investigation and placebo groups. The randomization was performed with OxMAR software (Charter College, Oxnard, CA) for concealment. Investigation group received 2 puffs/day of *N. sativa* nasal spray (2 puffs contained 1 g of *N. sativa*), and the placebo group had 2 puffs/day of sodium chloride nasal spray 0.65%. These administrations lasted for 8 weeks. Furthermore, tablets of cetirizine 10 mg/day and tablets of azithromycin 500 mg were administered for all patients (first day every 12 h and then 1 tablet per day for azithromycin) until 12 weeks.

The patients and physicians were blinded to the study protocol, and placebo drug was similar to intervention. Also, drugs and patients were coded, and even statistical analysis was blinded.

Study Assessment

Modified Lund–Kennedy, Lund–McKay, and Sino-Nasal Outcome Test-22 (SNOT-22) were calculated before and after interventions to evaluate the outcomes. Modified Lund–Kennedy scoring is an endoscopic evaluation which is scored from 0 to 12.[17] Lund–McKay scoring is a CT scan evaluation that is composed of 0 to 24. SNOT-22 is a questionnaire for outcome measurements that includes 22 questions and is scored from 0 to 110. Also, the olfactory recovery was determined as subjective by odors (this assessment was only used for patients with hyposmia or anosmia).

Statistics

The sample size was calculated according to sample size formula, and statistical power and significance level were considered as 80 and 5%, respectively. Also, the standard deviation (SD) of Lund–McKay score was 1.91, and the mean difference was 0.79,[18] so the sample size was calculated as 72. All data were analyzed with SPSS software version 24, while independent t test, χ^2 test, and Mann–Whitney test were used to compare the groups, and paired samples correlation was used to compare outcomes of scoring. Also, data were shown according to number or percent, and mean $\pm$ SD and $P < .05$ were considered a significant threshold.

Results

In this study, 31 patients (19 men and 12 women) with the mean age of 44.12 ± 13.03 years were enrolled in the intervention group, and 34 patients (18 men and

16 women) with the mean age of 45.50 ± 12.57 years were enrolled in the placebo group. There were no significant differences between 2 groups with regard to these factors ($P = .49$) and age ($P = .64$). Distribution of asthma, allergy, and smoking history is summarized in Table 1, and there were also no significant differences between 2 groups regarding these factors ($P = .71$ for asthma, $P = .77$ for allergy, and $P = .26$ for smoking history).

Before the intervention, there were no significant differences between both groups according to Lund–McKay ($P = .38$), Modified Lund Kennedy ($P = .05$), and SNOT-22 ($P = 0.21$) scores. After 8 weeks of interventions, Lund–McKay, Modified Lund Kennedy, and SNOT-22 scores in the intervention group were significantly lower than that of the placebo group ($P < .0001$, for all; other information are summarized in Table 2). According to paired samples correlation, it was shown that the changing of Lund–McKay, Modified Lund Kennedy, and SNOT-22 scores was significant in 2 groups after interventions ($P < .0001$, for all). Also, 8 patients in the intervention group had anosmia, and 5 of them improved after study (subjective improvement). We followed the patients until 8 weeks after intervention. During the investigation, 2 patients of the placebo group were excluded from the research (loss follow-up). Furthermore, no adverse effects were reported in both groups.

Table 1. Demographics and Clinical Information of Patients in Both Groups.

Characteristics	Intervention Group	Placebo Group	*P*
Number	31	34	–
Gender (M/F)	19/12	18/16	.49[a]
Age (mean ± SD), years	44.12 ± 13.03	45.50 ± 12.57	.64[b]
History of asthma	7 (22.6%)	9 (26.5%)	.71[a]
Allergy	19 (61.3%)	22 (64.7%)	.77[a]
Smoking history	8 (25.8%)	5 (14.7%)	.26[a]

[a]χ^2 test.
[b]Independent *t* test.

Discussion

Various aspects of *N. sativa* oil such as antimicrobial, antioxidant, antihistaminic, anti-inflammatory, and analgesic effects have been studied by Mahboubi, and it was concluded that as a common herbal remedy, *N. sativa* is useful for treating different diseases. It seems to be a safe oil as it does not remarkably changes vital organs and has few adverse effects.[19] Zaoui et al. also suggested a low toxicity level for *N. sativa* fixed oil in a study conducted on rats and mice. They evaluated the levels of LD50 and different paraclinical feedbacks.[20] In this study, we observed significantly decreased Lund–McKay, Modified Lund Kennedy, and SNOT-22 scores after interventions for both groups. Nevertheless, these scores were lower in the intervention group compared with the placebo group, meaning that 2 puffs/day of *N. sativa* (1 g/day) nasal sprays were more effective than 2 puffs/day of sodium chloride spray 0.65% for managing CRS. Also, some patients with anosmia were partially improved after using *N. sativa* nasal sprays.

This improvement may be due to neuroprotective and antioxidant effects of *N. sativa* on the olfactory epithelium.[21] However, it has not been studied for this effect, and so the implications are unknown. In a study performed by Cingi et al.[13] in which they evaluated the effects of thymoquinone on rat models with induced rhinosinusitis, it was concluded that thymoquinone has a bioactive agent in the treatment of rhinosinusitis, and also the histopathological effects of this plant are similar to an antibiotic. In another study by Nikakhlagh et al.,[22] the effects of *N. sativa* on the treatment of allergic rhinitis were evaluated. It is reported that *N. sativa* has antiallergic effects such as the reduction of nasal mucosal congestion, nasal itching, runny nose, sneezing attacks, turbinate hypertrophy, and mucosal pallor for 15 days. They also suggested *N. sativa* as an antiallergic drug for treating allergic rhinitis. In the study by Işik et al.,[23] *N. sativa* seeds improved immunologic responses in the allergic rhinitis via increasing polymorphonuclear leukocyte and CD8 counts, and the authors also suggested *N. sativa* seeds as an adjuvant therapy for these

Table 2. Lund–McKay, Modified Lund Kennedy, and SNOT-22 Scores in Before and After Intervention in Both Groups.

Variable		Intervention Group	Placebo Group	*P*[a]
Lund–McKay score (mean ± SD)	Before intervention	5.80 ± 1.62	6.14 ± 1.13	.38
	After 8 weeks	2.93 ± 1.15	4.81 ± 1.17	<.0001
Modified Lund Kennedy (mean ± SD)	Before intervention	3.64 ± 1.47	4.23 ± 1.12	.05
	After 8 weeks	1.54 ± 0.92	3.43 ± 1.16	<.0001
SNOT-22 score (mean ± SD)	Before intervention	27.25 ± 8.05	30.08 ± 6.92	.21
	After 8 weeks	14.87 ± 5.01	23.15 ± 5.01	<.0001

Abbreviations: SD, standard deviation; SNOT, sinonasal outcome test.
[a]Mann–Whitney test.

patients. In addition, it was also reported that topical black seed oil or *N. sativa* extract was effective with no adverse effects on the management of allergic rhinitis.[24] Also, topical *N. sativa* oil has effects on pain suppression in the elderly patients with knee osteoarthritis.[25] In 2006, a study was conducted on the effect of *N. sativa* on 20 patients with seasonal allergies. The results indicated that black seed (250 mg/day, for 15 days) significantly reduced respiratory symptoms and therefore could be used to treat seasonal allergic rhinitis.[26] In the study of Boskabady et al.,[27] it was suggested that *N. sativa* has antihistamine-like effects on asthmatic airways; however, the effects of *N. sativa* on measured pulmonary function tests were lower than theophylline. In a study by Koshak et al.[28] who evaluated the effects of black seed on 40 patients with asthma, it was concluded that black seed decreased respiratory symptoms and eosinophilia and improved pulmonary function tests. Yoruk et al.[29] also evaluated the effects of *N. sativa* on the treatment of rabbit models with induced bacterial rhinosinusitis and concluded that *N. sativa* increased superoxide dismutase and glutathione peroxidase activities and also reduced lipid peroxidation and myeloperoxidase activities in rabbit models with induced rhinosinusitis; therefore, *N. sativa* has an antioxidant effect on these experimental rabbits. In a study conducted by Oysu et al., it was concluded that intranasal *N. sativa* was a better alternative to sodium chloride solution for the management of elderly patients who suffered mucosal symptoms of the nasal cavity.[30] Although some symptoms did not differ in both treatment groups, it was shown that dryness, obstruction, and crusting improved significantly. Their subjects were participants older than 55 years while we enrolled subjects aged between 18 and 72 years. Also, while we included 65 participants and used a control group, they conducted a cross-over designed study on 42 patients. It should be noted that even though they did not design a double-blinded design, their results are similar to our study.

Conclusion

There is no evidence of causation only association with therapy which could be placebo. In this study, it would appear that *N. sativa* is effective at reducing symptom scores assessed by SNOT-22 and objective findings as determined by Lund–McKay and Modified Lund Kennedy scoring in patients suffering from CRS-related symptoms. Also, our study was the first intervention about the effects of *N. sativa* in CRSsNP, and we conclude that the usage of 2 puffs/day of *N. sativa* (1 g/day) nasal spray is effective with no adverse effects in patients with mild CRSsNP. Also, we suggest a comparison of the results of *N. sativa* and steroid nasal sprays in patients with CRSsNP.

Acknowledgments

We thank Dr. Keyvan Ghadimi for the many contributions that this study has given us.

Ethical Approval

This study was approved by our institutional review board.

Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

There are no human subjects in this article and informed consent is not applicable.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research and/or authorship of this article.

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