Evidence for Self-Medication
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Real-world data demonstrate added value of cineole over nasal spray monotherapy for rhinosinusitis

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The efficacy of 1,8-cineole in treating acute rhinosinusitis has been repeatedly demonstrated in randomised-controlled double-blind trials [1, 2]. Now, a non-interventional trial under everyday conditions has shown that significantly greater improvements in quality of life can be achieved when taking cineole capsules – on their own or combined with other drugs – than with monotherapy using decongestant nasal sprays [3].

Acute rhinosinusitis is usually the result of a viral cold, with a twelve-month prevalence of 6% to 15% [4]. Although the disease is typically self-limiting, the quality of life can be significantly impaired by the inflammatory disorder affecting the nose and sinuses [5]. Typical symptoms include a stuffy nose or nasal discharge, often accompanied by a pressure headache and a more or less pronounced loss of sense of smell [4]. In what is usually symptomatic treatment, decongestant nasal sprays are often used for short-term improvement of nasal breathing. In addition, drugs containing the active ingredient 1,8-cineole are used to treat the causes of symptoms such as increased mucus production and inflammation. The monoterpene is a major component of many plant essential oils and is chiefly extracted from eucalyptus [6]. The influence of 1,8-cineole on the quality of life of patients under everyday conditions has now been investigated in a non-interventional trial (registration number at ClinicalTrials.gov: NCT04703673) [3].

Trial design: Prospective patient survey under everyday conditions

The trial results are based on a prospective, non-interventional survey whose participants were recruited in German pharmacies [3]. The participants in question were adults with rhinosinusitis who visited a pharmacy because of their symptoms and received advice there on the various treatment options. Depending on the decision of the individual patients, the latter were assigned to one of two trial groups: Patients in group 1 (cineole group; n = 310) had opted for treatment with a cineole preparation (Sinolpan®), patients in group 2 for therapy with a nasally applied α-sympathomimetic (nasal spray group; n = 40). The treatment of both groups was carried out according to the recommendations of the respective drug manufacturer. Corresponding to everyday conditions with self-medication, additional concomitant medication was used in both groups by 54% (cineole group) and 48% (nasal spray group), mainly nasal spray by 44% of patients in the cineole group and other medicines by 48% in the nasal spray group. The data was collected using a validated rhinosinusitis quality of life questionnaire (RhinoQol) [7], which was completed before the first application and after the end of treatment, but after no more than 10 days.

Symptom frequency significantly reduced

Symptoms were recorded in terms of their frequency (from 0 "never" to 4 "always") and bothersomeness (from 0 "not bothersome" to 10 "very bothersome"), as well as in terms of the impact on everyday life (from 0 "never" to 4 "always"), for example through fatigue, disrupted sleep, or concentration problems. The mean frequency of all assessed symptoms decreased significantly during treatment with cineole capsules ($p < 0.001$; **Fig. 1**). The sum of all individual symptom frequencies (RhinoQol sum score) in the cineole group was 10.2 ± 3.7 before the start of treatment and decreased by 64.0% to 3.7 ± 3.1 after treatment (**Fig. 4**). By comparison, the frequency sum score in the nasal spray group decreased by 55.8% from 9.2 ± 2.9 to 4.1 ± 3.1 (**Fig. 4**).

Symptom burden significantly reduced

The mean bothersomeness of the symptoms "sinus headache/facial pain/facial pressure", "blocked or stuffy nose", and "post-nasal drip" (discharge of nasal secretions via the trachea) also

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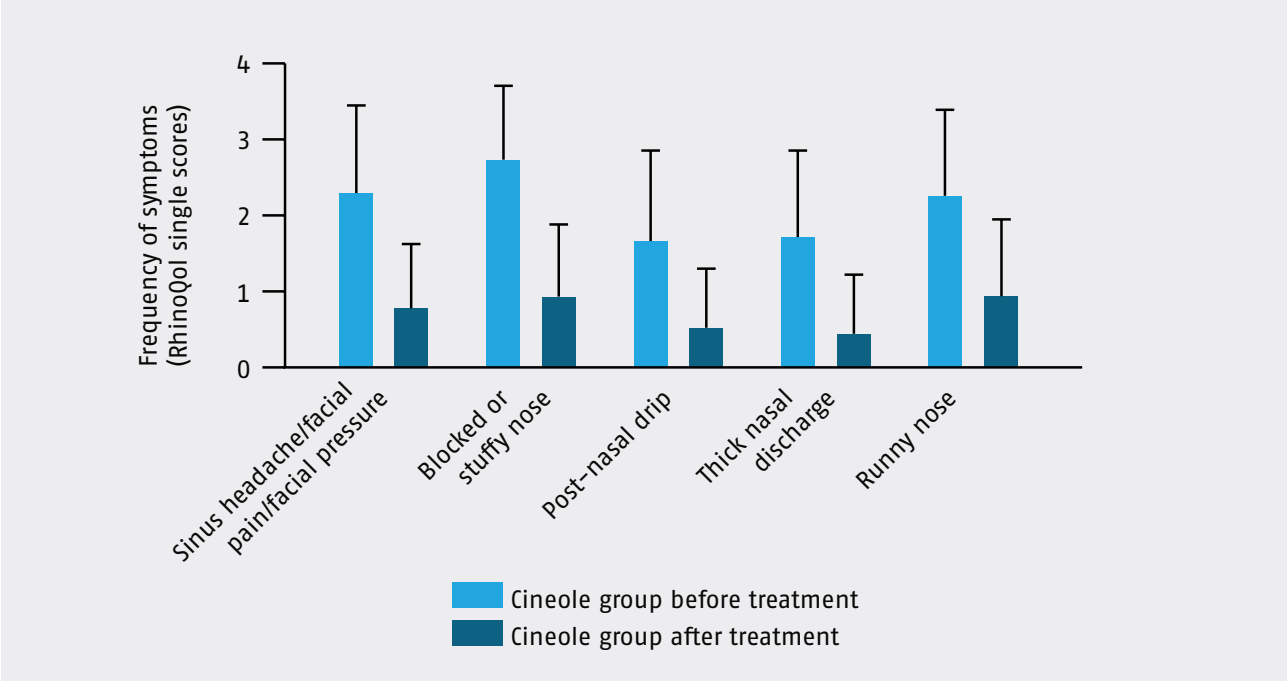

Fig. 1. Frequency of rhinosinusitis symptoms (RhinoQol single score 0–4) of the cineole group (n = 310) before and after treatment with cineole capsules (mean + standard deviation)

decreased significantly in the cineole group (each $p < 0.001$; **Fig. 2**). The RhinoQol sum score for bothersomeness of all symptoms mentioned decreased by 52.1% from 16.9 ± 6.9 to 8.1 ± 7.7 in the cineole group and by 39.4% from 13.7 ± 6.7 to 8.3 ± 6.5 in the nasal spray group, respectively (**Fig. 4**).

Everyday life less affected

The impact on everyday life from the disease symptoms also decreased significantly ($p<0.001$; **Fig. 3**). In the cineole group, the RhinoQol sum score decreased by 53.9% from 13.3 ± 6.8 to 6.1 ± 5.7, while the sum score in the nasal spray group decreased by 45.3% from 10.4 ± 7.0 to 5.7 ± 5.4 (**Fig. 4**).

Comparison of treatment with cineole and nasal spray therapy without cineole

Overall, there was a significantly greater improvement in the frequency and everyday impact of rhinosinusitis symptoms in the cineole group compared to the nasal spray group ($p = 0.037$ and $p = 0.028$; **Fig. 4**). Although there was no statistically significant difference between the two patient collectives when comparing the bothersomeness of symptoms, the cineole group tended to have better results ($p = 0.061$; **Fig. 4**). When assessing these results, it should be taken into account that participants in the cineole group were free to use concomitant medication at their own discretion, meaning that 50% of the cineole users used a decongestant nasal spray simultaneously. The comparison of both groups indicates that the use of a decongestant nasal spray can be usefully supplemented by additional intake of the cineole preparation Sinolpan®. While the nasal spray provides immediate local respiratory relief, cineole acts systemically against the causes of symptoms (inflammation and mucus). Finally, the use of decongestant nasal sprays is usually limited to a maximum of seven days due to the risk of a rebound phenomenon. Although it is important to note when using Sinolpan® that a doctor should be consulted if symptoms persist for

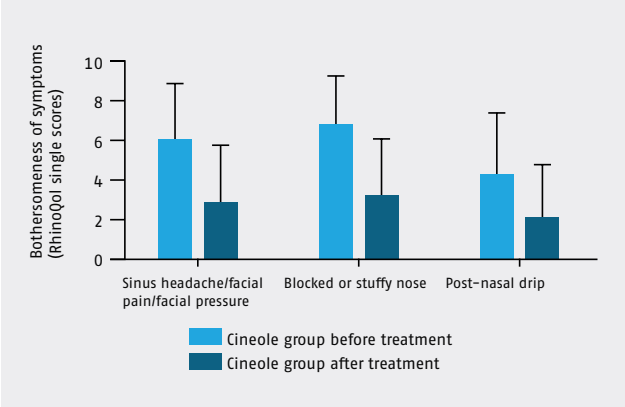

Fig. 2. Bothersomeness of rhinosinusitis symptoms (RhinoQol single score 0–10) of the cineole group (n = 310) before and after treatment with cineole capsules (mean + standard deviation)

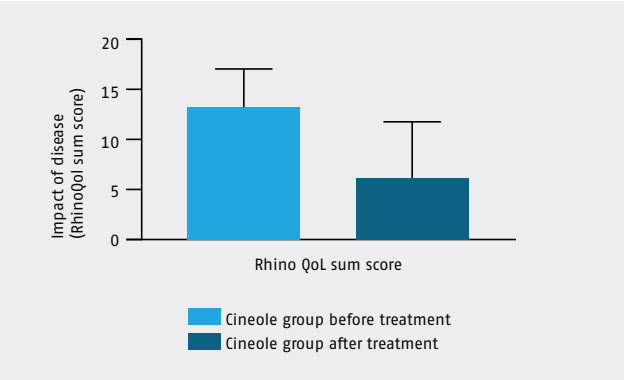

Fig. 3. Impact on everyday life from rhinosinusitis symptoms (RhinoQol sum score 0–36) of the cineole group (n = 310) before and after treatment with cineole capsules (mean + standard deviation)

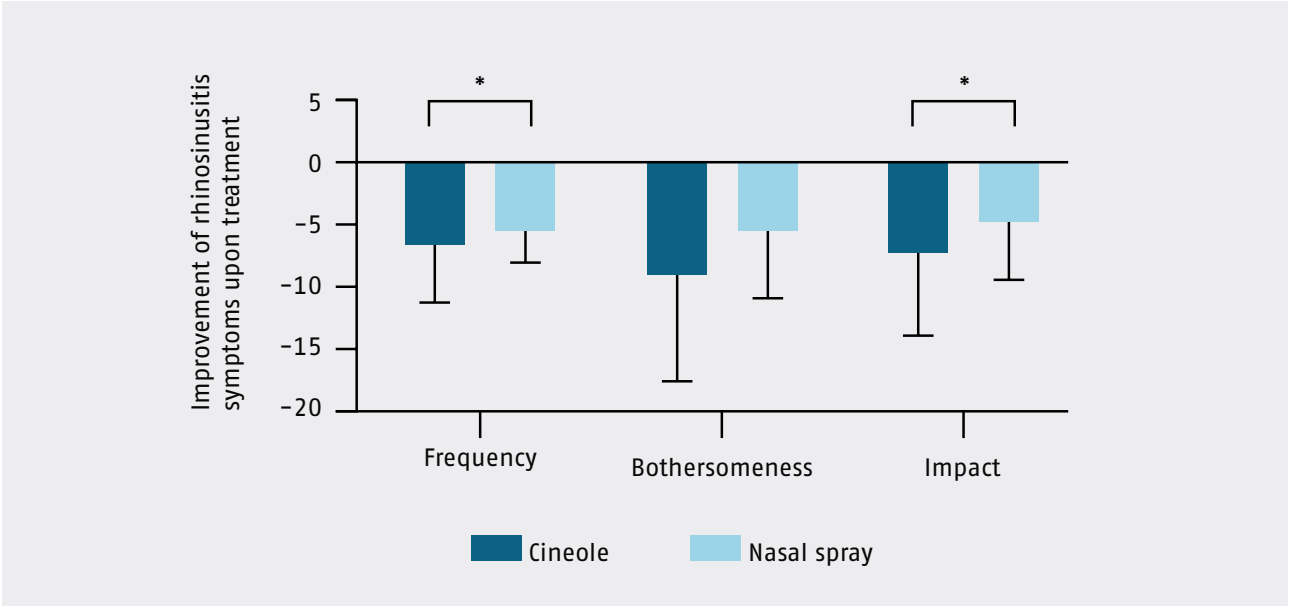

Fig. 4. Decrease in RhinoQol sum score for frequency, bothersomeness and impact on daily life from rhinosinusitis symptoms upon treatment with cineole capsules vs. nasal spray (mean + standard deviation; * $p < 0.05$)

longer than a week, in the case of shortness of breath, fever, purulent or bloody sputum, the medicine can also be used in principle as an additional treatment for chronic inflammatory respiratory diseases.

Patients benefit from cineole administration as an add-on or on its own

In principle, symptom improvements such as those observed in this real-world study can also be expected without pharmacotherapeutic intervention due to the self-limiting nature of acute rhinosinusitis. However, as early as 2004, Kehrl et al. [1] demonstrated in a placebo-controlled trial (n = 150) that the administration of 100 mg of cineole twice daily reduced the symptom sum score in acute rhinosinusitis after four (–55.8% vs. –21.7%; $p < 0.0001$) and seven days (–80.1% vs. –41.0%; $p < 0.0001$) significantly more than the placebo. While the accelerated symptom improvement from cineole has already been demonstrated under the rigorous conditions of a clinical trial, the current study proves that rhinosinusitis patients who come to the pharmacy with a request for a decongestant nasal spray also benefit from cineole therapy (on its own or in combination with the decongestant nasal spray). Not least because of the convincing tolerability (97.7% reported no side effects) and the positive evaluation of the efficacy (89.4% would recommend the therapy to others), cineole can be recommended as a useful addition in consultations on self-medication in the case of rhinosinusitis.

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