Original Article

The Efficacy and Adverse Effects of Ginger Extract for Treatment of Allergic Rhinitis Patients

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Background: Allergic rhinitis (AR) is a global health problem, and the prevalence of AR continues to increase worldwide. Ginger (Zingiber officinale Roscoe) is used widely as a spice throughout the world. Ginger extract has been reported to have high potential anti-allergic and anti-inflammatory activities.

Objective: To investigate the clinical efficacy and adverse events of ginger extract in treating AR.

Materials and Methods: A quasi-experiment study, 30 patients received ginger extract 500 mg per day for six weeks. All patients were followed up at the third week and the sixth week for the evaluation of the efficacy by using total nasal symptom score (TNSS), rhinoconjunctivitis quality of life questionnaire (RQLQ), and history taking for adverse events.

Results: Ginger extract can reduce nasal symptoms and improve quality of life after taking ginger extract for three weeks with no serious adverse events.

Conclusion: The ginger extract tends to treat the symptoms of AR.

Keywords: Ginger extract; Allergic rhinitis

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Allergic rhinitis (AR) is a global health problem. It is the most usual form of non-infectious rhinitis, affecting between 10% and 30% of all adults and as many as 40% of children. Epidemiological studies show that the prevalence of AR continues to increase worldwide. The World Health Organization has estimated that 400 million people in the world suffer from AR[1] and half of the global population will have had an allergic disease by 2050[2].

In Thailand, the incidence has increased 3 to 4-fold or 17.9% to 50.6%, within the last 40 years and continues to rise[3]. And 2,250 million Baht were spent for drug treatment[2]. AR affects social life, sleep, school, and work. The economic impact of AR is often underestimated because the disease does not have high direct costs. However, the indirect costs are substantial[4].

Therapies are available for AR, such as allergen avoidance, allergen immunotherapy, and pharmacotherapy, which include antihistamines, leukotriene-receptor antagonists, nasal decongestants, and corticosteroids[5]. Antihistamines are considered first-line treatment in the management of AR. The second-generation non-sedating antihistamines are particularly useful[5]. However, antihistamines have side effects, for example, drowsiness, fatigue, hair loss, and hepatitis. For Thailand, antihistamines are imported from abroad and therefore are expensive. This is an important reason to look for alternative treatments, especially herbs.

Ginger (Zingiber officinale Roscoe) is widely used as a spice throughout the world. In Thai traditional medicine, ginger has been used as a part of herbal remedies maintaining the balance of water element and wind element including cold, constipation, sleeplessness, relieving flatulence[6]. Besides that, ginger extracts have been reported to have a wide range of pharmacological properties and clinical trials have examined the clinical effectiveness of ginger for conditions such as motion sickness[7,8], nausea and vomiting[9], osteoarthritis[10-12], and

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diabetes mellitus[13]. However, there has been no clinical report of ginger extract relieving symptoms in patients with AR.

Ginger has been used for a long time and worldwide. There have been no reports of toxicity and serious side effects. It is also inexpensive. Thus, ginger should be studied and developed into a useful drug for the treatment of AR. The present study result would benefit both the patients and the country.

Materials and Methods

Study design

The present study was a quasi-experimental study pre and post-test, designed to investigate the efficacy and adverse effects of ginger extract for treatment of AR patients at Thammasat University Hospital, Pathum thani, Thailand. The study protocol and informed consent were approved by The Human Research Ethics Committee of Thammasat University (Medicine) registry number MTU-EC-TM-4-077/57.

Study population and protocol

Thirty patients from the Department of Ear Nose and Throat, Thammasat University Hospital aged between 18 and 70 were chosen. The patients had clinical histories of AR symptoms such as itching, nasal congestion, watery nasal discharge, runny nose, and sneezing, and were diagnosed by doctor with moderate AR, with a minimum total nasal symptom score (TNSS) scores of 7 points. Patients could stop taking antihistamine or intranasal steroids for one week before the trial and did not have history of heart disease, kidney disease, liver disease, epilepsy, high blood pressure, and severe asthma. Exclusion criteria included patients having taken anti-coagulant, anti-platelet aggregation, erythromycin, clarithromycin, ketoconazole, itraconazole, and fluconazole, or experienced serious side effects from ginger allergy. Pregnant and lactating women were also excluded.

Informed consents were obtained from the patients eligible for the study. All patients took two capsules of ginger extract two times daily for six weeks. The ginger extract was weighed and combined with necessary excipients and then filled into the gelatin capsules each containing 125 mg of the ginger extract, produced according to the good manufacturing practice (GMP) for traditional medicine. Ginger extract capsules were packed in aluminum foil that complied with the quality standards of the Thai Herbal Pharmacopeia, contamination testing, weight variation, and dissolution. In the present study, all patients were followed up at the third and sixth week for evaluating the efficacy, adverse events, safety, and patient compliance.

The clinical efficacy evaluation

The efficacy was evaluated by TNSS, and secondary efficacy variables were rhinoconjunctivitis quality of life questionnaire (RQLQ)

TNSS score(s), a subjective evaluation as a primary effective tool to measure the intensity symptoms of patients with AR[14], Overall assessment of nose symptoms used four aspects, runny nose, itchy nose, nasal congestion, and sneezing using a four-point scale with 0 for no symptoms to 3 for severe symptoms. The total possible score ranged from 0 for no symptoms to 12 for maximum symptom intensity[15]. Intraclass correlation coefficients confirmed the high internal consistency at each time point (Cronbach's α was 0.87 (95% CI 0.80 to 0.91)[16]. The RQLQ has 28 questions in seven domains, which are activity limitation, sleep problems, nose symptoms, eye symptoms, non-nose/eye symptoms, practical problems, and emotional function. There were three patient-specific questions in the activity domain that asked patients to choose three activities in which they were mostly limited by their rhinoconjunctivitis. Patients gave responses to each question on a 7-point scale with 0 for not impaired at all to 6 for severely impaired. The overall RQLQ score was the mean of all 28 responses and the individual domain scores were the means of the items in those domains. Test-retest reproducibility reported intraclass correlation coefficient at 0.86[17].

Statistical analysis

All statistical analyses were performed using the IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). The repeated measured analysis of variance (ANOVA) was used to analyze the changes in the mean values from baseline to the third week and the sixth week for each group, TNSS score, and total score of RQLQ. A p-value of less than 0.05 was statistical significance.

Results

Patient characteristics

The demographic, clinical, and other objective data were collected of each participant at the beginning of the intervention. The 30 volunteers consisted of 15 males and 15 females. Most of the participants had a normal body mass index and vital signs. Before taking ginger extract, the participants had moderate of nasal symptoms, and it moderately affected the quality of

Table 1. Baseline characteristics of participants

Data	Ginger extract (n=30)
Sex: female/male; n (%)	15/15 (50/50)
Age (years); mean±SD	35.42±12.73
BMI (kg/m^2); mean±SD	21.92±3.34
Total TNSS score; mean±SD	7.48±1.96
Total RQLQ score; mean±SD	2.98±0.99
Blood pressure (mmHg); mean±SD	
Systolic	117.05±9.60
Diastolic	75.95±9.49
Duration of allergic rhinitis (years); mean±SD	12.50±10.81
Frequency of symptoms; n (%)	
Less than 4 days a week	5 (16.67)
At least 4 consecutive weeks	1 (3.33)
More than 4 days per week	23 (76.67)
More than 4 consecutive weeks	1 (3.33)

BMI=body mass index; TNSS=total nasal symptom score; RQLQ=rhino-conjunctivitis quality of life questionnaire; SD=standard deviation

life. Moreover, the participants had an average of 12.50±10.81 years of AR disease, and 76.67% of participants had symptoms for more than four days per week. The results are shown in Table 1.

The clinical efficacy evaluation

The results showed that the ginger extract significantly decreased the TNSS scores. The four main symptoms were separately assessed as itching, runny nose, nasal congestion, and sneezing. The first three symptoms decreased in the third week. The sneezing symptom showed significant reduction in the sixth week (Table 2).

The overall quality of life was found to be moderately affected before taking treatment. After taking treatment, the participants had a better quality of life. The mean score decreased significantly from the third week and decreased continuously at the sixth week. It may be concluded that ginger extract could improve the quality of life (Table 3).

The adverse effects evaluation

From history taking, the most frequent side effect of the ginger extract was eructation (67.67%) and the second was dry mouth (13.33%) and dry throat (13.33%) as shown in Table 4.

Discussion

In good clinical studies, a preliminary measurement often uses the changes in symptoms and medication requirements. For the clinical outcomes of treatment for immune therapy, it assesses the

Table 2. The score of total nasal symptoms scores of ginger extract

Data	Treatment	Week 0; mean±SD	Week 3; mean±SD	Week 6; mean±SD
Total TNSS score	Ginger extract	7.48±1.96	4.30±2.47	3.42±2.80
	p-value		≤0.001†††	≤0.001†††
Runny nose	Ginger extract	2.00±0.82	1.19±0.82	0.89±0.78
	p-value		≤0.001†††	≤0.001†††
Itchy nose	Ginger extract	1.65±0.86	0.89±0.88	0.81±0.88
	p-value		≤0.001†††	≤0.001†††
Nasal congestion	Ginger extract	2.32±0.62	1.19±0.81	1.00±0.16
	p-value		≤0.001†††	≤0.001†††
Sneezing	Ginger extract	1.50±0.99	1.03±0.93	0.72±0.81
	p-value		0.52	0.002††

TNSS=total nasal symptom score; SD=standard deviation

Statistical analysis: repeated measured ANOVA, † Significant difference from day 0 within group (p≤0.05), †† Significant difference from day 0 within group (p≤0.01), ††† Significant difference from day 0 within group (p≤0.001)

Table 3. The score of quality of life of ginger extract

Data	Treatment	Week 0; mean±SD	Week 3; mean±SD	Week 6; mean±SD
Total RQLQ score	Ginger extract	2.98±0.99	1.88±0.96	1.34±0.95
	p-value		≤0.001†††	≤0.001†††
Activity limitation	Ginger extract	3.95±1.08	2.64±1.31	1.75±1.27
	p-value		≤0.001†††	≤0.001†††
Sleep problems	Ginger extract	3.00±1.46	1.87±1.32	1.13±1.23
	p-value		≤0.001†††	≤0.001†††
Non-nose/eye symptoms	Ginger extract	2.82±1.28	1.65±1.01	1.30±1.13
	p-value		≤0.001†††	≤0.001†††
Practical problems	Ginger extract	3.07±1.52	2.04±1.34	1.57±1.35
	p-value		0.002††	≤0.001†††
Nose symptoms	Ginger extract	3.48±1.20	2.28±1.30	1.67±1.36
	p-value		≤0.001†††	≤0.001†††
Eye symptoms	Ginger extract	2.39±1.44	1.47±1.44	1.05±1.16
	p-value		≤0.001†††	≤0.001†††
Emotion	Ginger extract	2.32±1.53	1.46±1.22	0.94±0.95
	p-value		≤0.001†††	≤0.001†††

RQLQ=rhinoconjunctivitis quality of life questionnaire; SD=standard deviation

Statistical analysis: repeated measured ANOVA, † Significant difference from day 0 within group (p≤0.05), †† Significant difference from day 0 within group (p≤0.01), ††† Significant difference from day 0 within group (p≤0.001)

severity of symptoms and medication requirements according to the regulations from the World Allergy Organization (WAO). Thus, the frequent evaluation of AR is TNSS. The TNSS is a subjective evaluation as a primary effective tool to measure the symptoms of AR patients[14]. The TNSS is a widely accepted and reliable tool to assess the efficacy of a drug for treating AR, and the decrease of the score indicates

Table 4. Side effects of ginger extract

Side effect	Ginger extract; n (%)
Eructation	20 (66.67)
Drowsiness	1 (3.33)
Dry mouth	4 (13.33)
Dry throat	4 (13.33)
Fatigue	1 (3.33)
Dizziness	1 (3.33)

Each symptom asks from thirty participants

an overall clinical improvement in the condition. The present study showed that AR patients treated with ginger extract could reduce total TNSS and four main symptoms. Symptoms of AR are primarily due to a combination of the allergic inflammatory response.

AR has been associated with significant impairments in quality of life, sleep, and work performance[4]. Assessment of quality of life has now become a standard of allergy clinical trials. Ginger extract reduced RQLQ scores in every aspect. These results indicated that ginger could improve their quality of life.

Ginger (Zingiber officinale Roscoe) is widely used as a spice throughout the world. In the previous research, the ethanolic extract of ginger and pure compounds 6-gingerol and 6-shogaol all showed good anti-allergic activity by inhibiting allergic reactions in rat basophilic leukemia (RBL-2H3)[18]. In an in vivo study, 6-gingerol, which is the marker of ginger, inhibited the expression of Th2 cytokine (IL-4, IL-10, and IL-13) and Th1 cytokine (IFN-γ) in OVA-sensitized spleen cells. In addition, 6-shogaol reduced the passive cutaneous anaphylaxis reaction compared to the control group. Furthermore, histamine release diminished significantly following the treatment of rat peritoneal mast cells (RPMCs)[19]. Moreover, in acute and subacute toxicity studies, single oral doses of crude ethanolic extract of ginger at all of the three levels, which are 1,000, 3,000, and 5,000 mg/kg body weight, did not cause mortality in any animal during the investigation period. Only stomach irritation was observed in all animals immediately after feeding with the extract[20]. Further, Rong et al reported that 2,000 mg/kg body weight of ginger ethanolic extract in chronic toxicity study did not cause mortality in any animal[21].

The side effect of ginger extract is eructation. The traditional ginger extract medicine is a carminative drug, and the present study confirms the finding of Micklefield et al who found ginger relieves flatulence and stimulates movement of gastro-duodenal tract during fasting and after eating[22]. Thus, after taking ginger extract, it can cause eructation.

Conclusion

The present study showed that ginger extract has demonstrated the effect of reducing AR symptoms. There was a good safety profile with mild GI side effects. Thus, the present study supports ginger extract capsule usage to treat patients with ARs. A long-term study and large scale are needed to completely evaluate the efficacy and safety of ginger extract. In addition, the follow up of recurrent symptoms of AR is important. Therefore, future studies should follow after the participants stopped the drug and the recurrent symptoms.

What is already known on this topic?

Antihistamines are considered the first-line treatment of AR. The second-generation non-sedating antihistamines are particularly useful, but antihistamines have side effects.

What this study adds?

The ginger extract has demonstrated the effect of reducing AR symptoms. There was a good safety profile with mostly mild GI side effects.

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Conflicts of interest

The author declares no conflict of interest.

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