Chapter 7

Therapeutic and Immunologic Effects of *Zingiber officiale* in Allergic Rhinitis

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1. Introduction

Allergic diseases are the most common problem in our community an d globally [1]. Allergic rhinitis is one of the most common allergic diseases in Iraq and probably in the world and nowadays it is increasing. It is with a chronic natural history and may appear at any age of life and subsequently converted into asthma [2] Up to now, there is no curative treatment for allergic rhinitis and most of the drugs that are used can only induce symptomatic relief and some of them have serious side effects and can cause withdrawal symptoms which lead the patients to continue treatment ending in more side effects [1]. There are marked increase in allergic diseases in developing countries as reported recently [3,4].

Allergic rhinitis with possibility of either under diagnosis in a countries with lower prevalence or difference in risk factors in these areas of the world [5]. In Iraq, the allergic diseases were increased with time including AR [6]. To date there were no curative treatment for AR, however, many pharmacotherapeutic treatment evaluated in different studies and suggested a variable clinical response [3]. Recently an interest was launched which is the evaluation of plant products in the treatment of allergic rhinitis [7].

Environmental control measures and allergen avoidance, pharmacological management, and immunotherapy are the main three approaches for treatment of allergic rhinitis [8-10]. However, most of these approaches are palliative and not curative and may be not cost effective due to the chronicity of the disease [11,12]. Although allergic rhinitis is not a life-threatening condition, various complications can occur and result in significant impairment in quality of life [11,12], eventually leading to increase medical cost and may be

converted into asthma [1]. Immunotherapy another option of treatment is reserved for patients with a less than adequate response to usual treatments and reported to be effective [13,14]. Although the effectiveness of SIT in the treatment of allergic rhinitis and allergic asthma has been proven, however its delayed time of action and adverse local and systemic side effects have limited its use as a treatment modality by majority of the patients [15-19].

Ginger is the rhizome of the plant *Zingiber officinal*, belong to Zingiberaceae plant family and it used as therapy in ancient medicine, spice or a tea [20]. Reported studies [21-26] suggest that ginger extract may exert its benefit as medicine through blocking of serotonin receptors, antioxidant activity, antiglycating mechanisms. In addition, ginger extract may be effective in treating nausea, vomiting and heart burn [27-31] and demonstrate antibacterial activity [32]. However, the extract should be not used during pregnancy because of it is mutagenic [28]. Furthermore, ginger may have analgesic, antipyretic, and antitumor activity [33-39].

Ginger adverse reactions that include some drugs interaction, increase of bile secretion, and induction of allergic reaction, may restrict its usage as medicine [40,41]. Since reported studies suggested the anti-inflammatory, suppressive effects on production of cytokines and reduction of IgE serum level [42-44], we conduct this study to evaluate the therapeutic effect of ginger in allergic rhinitis.

Aim of the study:

The aim of this study is to study the clinical and immunological efficacy of Zingiber officinale (Z.O) on the treatment of allergic rhinitis.

2. Materials and methods

2.1. Patients

A total of 79 patients allergic rhinitis were included in the study. Those patients were recruited from patients attending Aljumhory Teaching Hospital in Mosul and were selected on the basis that was with high total IgE serum levels. The study done during the period from November 2010 to October 2012. The patients were with age of > 10 years old. The patients divided into active and control group. The active group includes 42 patient and 37 patients were in control group. Each patients in active group received Zingiber officinale (Z.O) capsules, twice daily after meal. While each patient in control group received the same dose of sucrose powder capsules for 2 months, through which clinical follow up occurred completely in each monthly visit with recording the notes.

2.2. Diagnosis of asthma and allergic rhinitis

Allergic rhinitis diagnosis was performed according to previously reported guidelines [45].

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2.3. Skin prick test

The skin prick tests were performed for all patients and control and evaluated in accordance with European Academy of Allergy and Clinical [1]. Immunology subcommittee on allergy standardization and skin tests using standards allergen panel (Stallergen, France). The panel for skin test include: dust mite (Dermatophagoides farina, Dermatophagoides peteronyssinus), Aleternaria, Cladosprium, Penicillum mixture, Aspergillus mixture, Grasses mixture, Feather mixture, Dog hair, Horse hair, Cat fur, Fagacae, Oleaceae, Betulaceae, Plantain, Bermuda grass, Chenopodium and Mugworth. All tests were performed in the outpatient Asthma and Allergy Centre, Mosul by a physician using a commercial allergen extracts (Stallergen, France) and a lancet skin prick test device. A wheal diameter of 3 mm or more in excess of the negative control was considered as positive test result.

2.4. Determination of total serum IgE

ELISA was performed to estimate the total serum IgE level as a serological marker for treatment response monitoring [1]. Total serum IgE was determined by enzyme linked immunosorbant assay kit (Biomaghreb). Results were interpreted as allergy not probable if serum IgE was lower than 20 IU/ml, allergy is possible if IgE value is between 20 and 120 IU/ml and allergy is very probable if IgE is more than 120 IU/ml.

2.5. Treatment schedule and assessment

Z. officinale was given as capsules, one capsule twice daily after each meal. Each capsule contained about 0.5 gm (500 mg) of Z.O powder.

The control group received the same capsules but they were contained sucrose sugar powder, the treatment was given for 2 months. The results were recorded on the patient's questionnaire in each visit. The same routine physical examination & laboratory investigations as mentioned earlier were done in each visit & recorded with clinical evaluation which was done according to the following criteria and as reported previously[6]:

1. Clinical assessment (symptoms score); during each visit, the patients was examined clinically for vital signs & questioned about the improvement in his day & night symptoms (rhinorrhoea, nasal obstruction, paroxysm of sneezing, night snoring, chest tightness, wheezes, cough, shortness of breath, work & school attendance, skin wheals, itchy skin, swelling & the lip or eye lid, shortness on exertion.....etc).

2. Tolerability to the exacerbating factors: Many precipitating factors such as aeroallergens exposure, cold exposure, infection (sinusitis), drugs, exertion....etc. may precipitate the condition, so the response to the exacerbating factors were assessed in each visit.

2.6. Side effects

Side effects that were shown by the patients were recorded in all patients & for all allergies type.

2.7. Statistical analysis

SPSS version 19 analytic system: Paired Samples test; Independent Samples test & Descriptive Statistics were used to compare between active & placebo groups. Chi square also was used in this statistics of the research.

3. Results

3.1. Baseline estimation

A total of 79 patients were included, 51.9 % (41patients) male and 48.1% (38 patients) female. Those patients were classified according to their disease pattern into seasonal 39.2 % (31 patients) and perennial 60.7 % (48 patients), of the total 49.3 % (39 patients) had positive family history of atopic diseases while 50.6 % (40 patients) were with negative family history of atopic disease. They were subdivided into active (42 patients) and control group (37 patients) as show in Table 1.

Total number	**79**	
Gender	Male	41
	Female	38
Type	Seasonal	31
	Perennial	48
Family history	Positive	39
	Negative	40
Smoking	Positive	27
	Negative	52
Subgroups	Active	42
	Control	37

Table 1. Allergic rhinitis patients baseline information.

3.2. Frequency distribution of the patients according to the age

Table 2 shows the frequency distribution of patients according to their ages. It shows that the peak incidence age occurred within the age of 10-19 years which account for 30.3% (24 patients).

Age/year	**Number of patients**
10-19 years	24 (30.3%)
20-29 years	19 (24%)
30-39 years	16 (20.2%)
40- above	20 (25.3%)

Table 2. Frequency distribution of the patients according to the age

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3.3. Frequency distribution of the patients according to the duration of the disease

Table 3 shows the frequency distribution of the patients according to their duration of the disease. It shows that the peak incidence duration of the disease range between 1-5 years and this account for 64.5% (51patients).

Duration/ years	Number of patients
1-5 years	51 (64.5%)
6-10 years	14 (17.7%)
11-15 years	8 (10.1%)
16-20 years	1 (1.2%)
21- above years	5 (6.3%)

Table 3. Frequency distribution of the patients according to the duration of the disease

3.4. Relationship between family history of atopic disease and total IgE level in allergic rhinitis patients

The relationship between family history of atopic disease and total IgE level in allergic rhinitis patients is shown in Table 4. There was a significant relationship (p= 0.001) between family history of atopy and total IgE serum level.

Family history of atopy	Patients number	mean	Standard deviation	P value
Negative history	40	206.8	54.9	**0.001**
Positive history	39	335.2	223.2	

Independent Samples test

Table 4. Relationship between family history of atopic disease and total IgE level in allergic rhinitis patients

3.5. Relationship between smoking and total IgE level in allergic rhinitis patients

There was a non-significant relationship (p=0.124) between smoking and total IgE serum level in allergic rhinitis as shown in (Table 5).

Smoking	Patients number	Mean	Standard deviation	P value
Negative history	52	248.5	146.8	0.124
Positive history	27	311.9	211.6	

Independent Samples test

Table 5. Relationship between smoking and total IgE level in allergic rhinitis patients

3.6. Subgroups of allergic rhinitis patients

Table 6 shows the subgroups of allergic rhinitis patients : active group of allergic rhinitis included 42 patients (22 male, 20 female), (19 seasonal, 23 perennial), (21 positive family history of atopy while 21 with negative family history),(28 smoking cigarette while 14 not smoking cigarette). On the other hand, control group included 37(19 male,18 female), (12 seasonal,25 perennial), (18 had positive family history of atopy while 19 had not),(25 smoke cigarette, 12 not).

Group		Active	Control
Number		42	37
Sex	**Male**	22	19
	Female	20	18
Type	**Seasonal**	19	12
	Perennial	23	25
Family history	**Positive**	21	18
	negative	21	19
Smoke	**Positive**	28	25
	negative	14	12

Table 6. Subgroups of allergic rhinitis patients

3.7. Immunological effect (on total IgE level) after 2 months treatment

The effect of treatment on total IgE level is shown in Table 7 : It shows that the effect of *Z. officinale* is highly significant after the first month of treatment (p = 0.027) which also stayed significant after the second month treatment (p =0.002). While in case of placebo capsules, there is no significant decrease in the level of total IgE after first month (p= 0.112) nor after second month (p= 0.64).

Group	Month	Number of patients	Mean	Standard deviation	P value
Active	0	42	258.4	170.5	-------
	1	42	229.3	133.7	**0.027**
	2	42	175.7	85.5	**0.002**
Control	0	37	383.6	177.2	------
	1	37	256.1	157.8	0.112
	2	37	239.2	108.5	0.64

Table 7. Immunological Effect of treatment on Total IgE level in AR patients

3.8. Clinical effect after 2 months treatment

Clinical improvement after 2 months of treatment for both groups is seen in Table 8, from total, 78.5 %(33 patients) were improved in the active group after first month of treatment while 21.4

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%(9 patients) were improved from placebo treating group. There was a significant difference (p=0.010) between active and placebo treated groups. At the end of 2nd month, the result stayed significant (p=0.011) with 92.8 %(39 patients) were improved from active group corresponding to 35.1 %(13 patients) were improved from placebo treating group.

Months of Treatment	Subgroups	Improved patients Number	Not improved Patients Number	P value
Month 1	**Active**	33 (78.5%)	9 (21.4%)	**0.010**
	Control	10 (27 %)	27 (72.9 %)	
Month 2	**Active**	39 (92.8%)	3 (7.1%)	**0.011**
	Control	13 (35.1 %)	24 (64.8 %)	

Table 8. Clinical improvement in general condition in A.R patients after treatment

3.9. Effect on specific clinical features

The comparison between the improvement in specific nasal allergic symptoms in both subgroups(experimental and placebo) after 2 months of treatment is shown in Table 9. It shows that sinusitis had improved in 83.3% (35 patient) of experimental group while only 21.6% (8 patients) in control group demonstrate improvement and this difference was significant(p=0.002). Nasal itching had improved in 78.5% (33 patients) in experimental patients while it improved in 32.4 % (12 patients) in control group (p=0.027). While rhinorrhoea had improved in 69.0% (29 patients) in active group corresponding to 37.8 % (14 patients) in control group which is insignificant (p=0.126). Sneezing had decreased in 61.9% (26 patients) in experimental group while in control group it had improved in 24.3%(9 patients) with significant difference (p=0.033).

Clinical features	Active group improved patients	Control group patients improved	P value
Sinusitis	35 (83.3%)	8 (21.6%)	**0.002**
Nasal itching	33 (78.5%)	12 (32.4%)	**0.027**
Rhinorrhoea	29 (69.0%)	14 (37.8%)	0.126
Sneezing	26 (61.9%)	9 (24.3%)	**0.033**
Post nasal drainage	17 (40.4%)	5 (13.5%)	**0.042**
Conjunctivitis	11 (26.1%)	6 (16.2%)	0.385
Others	8 (19.0%)	4 (10.8%)	0.381

Chi square test

Table 9. Effect on specific clinical features after 2 months treatment

Post nasal drainage had decreased significantly (p=0.042) in 40.4% (17 patients) of active group while it had decreased in 13.5 % (5 patients) of control group. Conjunctivitis had decreased in 26.1% (11 patients) in experimental group but it had decreased in 16.2% (6 patients) in control group, but not with significant difference (p=0.381) result.

3.10. Medication score

Medication score of conventional therapy had been decreased in 71.4 % (30 patients) in active group and in 27.4 % (10 patients) in control in 1st month of treatment and the difference was significant (p=0.021). The significance degree became larger in the second month (p=0.004), which statistically measured the results of decreased conventional therapy use in active group which account for 88 % (37 patients) corresponding to 27 %(10 patients) in the placebo treating group.

Months of treatment	Subgroups	Patients with decreased medication	Patients not with decreased medications	P value
Month 1	Active	30 (71.4%)	12 (28.5%)	0.021
	Control	10 (27%)	27 (72.9%)	
Month 2	Active	37 (88%)	5 (11.9%)	0.004
	Control	10 (27%)	27 (72.9%)	

Chi square test

Table 10. Medication score

4. Discussion

Pharmacotherapy is still the corner stone in the management of allergic disease followed by immunotherapy. All therapeutic strategies have many side effects. Some of them may prove dangerous or even lethal, in addition, mostly there is no curative therapy [3,4]. One of the good substitutions is the use of herbal medicine and one of the ancient herb that was used medically for many diseases was *Zingiber officinale* [21,22]. This herb has been used for many diseases since no signs of serious adverse effects were known in antiquity.

Male were affected slightly more with AR than female. This result accords with other studies that showed no sex difference or slight male predominance [46]. About 54% of patients were less than 30 years old which means that the onset mainly started at the days of childhood

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adolescence. This goes in line with other studies [47] because allergy is a less common cause of rhinitis in elderly as compared with form of rhinitis like atrophic rhinitis [48].

Concerning duration of the disease, 64.5% of patients had duration less than 5 years. That means the allergic state in Iraq increased progressively in the last years especially after the last war in 2003 due to increased air pollutions. Our study demonstrated a significant association between family history and IgE serum level in allergic rhinitis patients. This finding is in accordance with well documented fact in allergic diseases [49-51].

The present study not shows a significant relationship between smoking and IgE serum level and this result is not agreed with that reported for Canada [52]. Z.O treatment showed a significant effect on total IgE level. This is not strange for Z.O because it has potent immunological effect in different studies [42-44]. Ginger extract seems to be with a wide range of therapeutic effects that include multiorgan [53] such as the immune response, metabolism, and gastrointestinal.

In the present study the patients showed excellent improvement in clinical symptoms and clinical response after 2 months treatment duration especially in patients as compared with control group. This may be due to the anti-mucous effect mainly, in addition to anti allergic effect that present in its contents. Ginger demonstrate effective therapeutic effects in the treatment of asthma and other respiratory diseases through its ability to loosen and expel phlegm from the sinuses and lungs [42].

In Japanese cedar pollinosis patients, and in the most sever cedar pollen scattering period, allergy symptoms (blowing the nose, itching eyes....etc) were significantly relieved in experimental group taking tea containing ginger extract for 13 weeks as compared with placebo group. Stuffy nose, sore throat medication score were significantly relieved. [54].

Medication score showed good decrease in conventional treatment of allergic rhinitis after 2 months uses of Z.O therapy as compared with control group. These results were a reflection and explanation of the improvement in clinical symptoms and augment the idea that says herbal treatment is benefit in medical fields.

In conclusion, *Zingiber officinale* is effective treatment for allergic rhinitis and significantly reduced serum total IgE after 4 weeks of treatment course.

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