The therapeutic effect of *Nigella sativa* seed oil in treatment of chronic urticaria

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Abstract

Urticaria is a common disease which affects an approximately 15-25% of the population at some point during their life time.

Chronic urticaria indicates the presence of hives for a protracted period (>6weeks). Antihistamines, steroids and immune suppressants are needed for the treatment of chronic urticaric.This study was designed to investigate the therapeutic effects of *Nigella sative* oil in the treatment of chronic urticaria. The results showed that 400 mg twice daily of *Nigella sativa* oil (in gelatin capsule) was significantly increase cure rate. It also significantly decreases $\log_{10}$ IgE and improves tolerability of patients to exacerbating factors.

The effects of Nigella sativa oil in urticaria could be attributed to inhibition of histamine release, blocking of histamine effects and inhibition of ecosanoides formation from arachidonic acid.

التأثير العلاجي لزيت بذور الحبه السوداء في علاج مرض الشري المزمن

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المستخلص

إن داء ألشري من الأمراض الشائعة حيث يصيب 15-25 % من الناس تقريبا في فترة ما من حياتهم. إن ألشري المزمن يشير إلى وجود حماق لفترة طويلة (أكثر من 6 أسابيع) وتستخدم مضادات الهستامين والسترويدات ومثبطات المناعة في علاج ألشري المزمن.

إن هذه الدراسة قد صممت لاستقصاء التأثيرات ألعلاجيه لزيت ألحبه السوداء في علاج ألشري المزمن . لقد أظهرت الدراسة إن أعطاء400 ملغم من زيت ألحبه السوداء مرتين يوميا (في محافظ جلاتينيه) أدى إلى زيادة ملموسة إحصائيا في نسبة الشفاء . كما أن هذا العلاج خفض لوغاريتم الاميونوكلوبيولين - أي بشكل ملموس إحصائيا ، وحسن من مقدرة المرضى على تحمل العوامل ألمهيجه للمرض.

ربما يعود تأثير زيت ألحبه السوداء في علاج ألشري إلى اثباطه لتحرر الهستامين وغلقه لمستقبلات الهستامين ومنعه تكون مركبات الايكوزنويد من حامض الاراكدونك.

Key Words: Chronic urticaria, Treatment , *Nigella sativa*

Introduction

Urticaria is an intensely pruritic rash with a central raised blanched wheal surrounded by erythematous flare that is generally circular, but can vary greatly in size and shape[1] . Urticaria is extremely common, it is estimated that approximately 15-25% of the population experiences an urticarial illness at some time of their life [2]. Acute urticaria is a self limited disorder typically caused by an allergic reaction to food, drugs or other allergens that last for a few days or as long as 6 weeks[1], while chronic urticaria indicates the presence of hives for a protracted period (> 6 weeks) . Chronic urticaria was predominantly affected adults and it was twice as common in women as in men [2]. The pathophysiology of urticaria correlates to many factors, which include, histamine, prostaglandin D2 , Leukotrine, C4, D4, substance P and bradykinin [3-8] .

The practical problem with management of chronic urticaria, that antihistamines have little or no effects on mediators other than histamine. However, they are effective for one third of patients with chronic urticaria. A number of other agents have been used including, mast cell' stabilizers, protease and leukotriene inhibitor, although the evidence of efficacy is not clear. Systemic corticosteroids are also widely prescribed for urticaria , but the evidence of benefit is still contestable.

This study was designed to investigate the therapeutic effects of *Nigella sativa* seed oil in the treatment of chronic urticaria depending on the previous studies which showed that this oil inhibited histamine release and ecosanoides formation.

Materials, Patients and Methods

This study is a prospective single blind clinical trial. It was conducted during the period from January to September 2002 . The total number of the patients included s122, with age ranged from 20-54 years, 55% (68 patients) were females and 45% (56 patients) were males. The study was performed in the outpatient clinic of Allergy center in Tikrit teaching hospital and Dermatology unit in Mosul general hospital. Full history and complete physical examination with clinical follow up in programmed visits were done for each patient. patients were divided randomly into two groups, the first group (98 patients) received *Nigella sativa* seed oil (in gelatin capsule) 400 mg twice daily for 6 weeks, while the second group (24 patients) received corn oil in the same dose and for the same period to serve as control . The efficacy of the treatment was evaluated after 3 and 6 weeks, the response was determined depending on the following criteria. Complete response, if the patient became free from symptoms all over the time. Partial response, if the patient, showed only mild symptoms intermittently, and these mild symptoms were subsided by oral antihistamines, taken on need . No need for continuous antihistamines and steroids. No response, if the patient showed no improvement during the period of treatment.

Results

All patients treated by *Nigella sativa* oil showed no response in the first two weeks of the treatment, however after the third week , 14 patients (14.2%) showed complete response, 42

patients (42.8%) showed partial response, while 42(42,8%) showed no response . In the control group, the clinical response was also improved, but the variation between Nigella sativa oil treated group and control group was highly significant ($p< 0.0001$). After 6 weeks of treatment, a complete response was recorded in 38 patients (38.7%) of *Nigella sativa* oil treated group, partial response was recorded in 32 patients (32.6%), and no clinical response was recorded in 28 patients (28.5%).The improvement in response was also recorded in the control group, but statistically, it was less than that recorded in Nigella sativa treated group ($p <0.0001$) (table 1). The $\log_{10}$ of IgE was significantly decreased in both groups after 6 weeks treatment, but the decline in *Nigella sativa* treated group was significantly ($p <0.0001$) more than that recorded in control group (table 2) .

An improvement was recorded in the tolerability to exacerbating factors (sun, heat, cold, dust, food, animal contact, and psychological factors) in *Nigella sativa* oil treated group after the third week of treatment. The percent of improvement ranged between 22.2 and 31.25%. However, the improvement in tolerability to exacerbating factors was further increased after six weeks treatment to reach 36.4 – 44.4%. No apparent improvement in tolerability to exacerbating factors in control group (table 3). The treatment is well tolerated and no side effects recorded during the period of treatment.

Discussion

Urticaria is a common disease, which affects an approximately 15-25% of the population at some point during their life time[1] . The pathophysiology of urticaria included local increase in permeability of capillaries as a result of activation of the cutaneous mast cells. Mast cell activation occurs as a result of the linkage of two adjacent subunits of high affinity IgE receptors($F_{CE}RI_a$) which caused releasing of histamine, proteases, PG D_2, LTC_4 and Cytokins including interleukin4 (IL_4) and (IL_8) and TNF-a. According to this pathophysiology, antihistamines are the drug of choice for the treatment of urticaria, in addition many other types of drugs were tried for this aim, like mast cell stabilizer, steroids, cyclosporine and other immune suppressants.

In this study *Nigella sativa* oil was used for the treatment of chronic urticaria depending on the promising result of Nigella sativa oil [10-16] in treatment of some allergic diseases.

Table1: The response of patients with chronic urticaria to 6 weeks treatment with *Nigella sativa* oil 400 mg twice daily

Response	Nigella sativa oil treated group (98 patients)		Control group (26 patients)	
	after 3 weeks	after 6 weeks	after 3 weeks	after 6 weeks
No clinical response	42(42.8%)	28(28.50%)	24(92.30%)	23(88.46%)
Partial response	42(42.80%)	32(32.60%)	2(7.60%)	2(7.60%)
Complete response	14(14.20%)	38(38.70%)	-	1(3.80%)
P- value of both partial and complete response in comparison with control	<0.0001	<0.0001	-	-

Table 2: The Log_{10} IgE level in blood of the patients with chronic urticaria before and after treatment with *Nigella sativa* oil 400mg twice daily for 6 weeks

	Nigella sativa oil treated group			Control group		
	Max.	Min.	Mean+ S.D	Max.	Min.	Mean + S.D
Before treatment	2.88	1.78	2.463 +0.315	2.61	1.82	2.286+0.272
After treatment	2.78	1.78	2.282 + 0.319	2.60	1.9	2.299 +0.24
P-value between the levels before and after treatment	P<0.0001*			P > 0.05		

*P<0.0001 in comparison between the decline of Log_{10} IgE after 6 weeks treatment between *Nigella sativa* oil treated group and control group

Table3: Improvement in tolerability to exacerbating factors in patient with chronic urticaria treated with *Nigella sativa* oil 400mg twice daily for 6 weeks.

Exacerbating factors	*Nigella sativa* oil treated group					Control group				
	Before Treatment	3w after treatment		6w after treatment		Before treatment	3w after treatment		6w after treatment	
	No.	No.	%	No.	%	No.	No.	%	No.	%
Sun	36	9	25.0	14	38.8	9	0	0	0	0
Heat	55	15	27.2	22	40.0	15	0	0	1	6.6
Cold	16	5	31.2	7	43.7	5	0	0	0	0
Dust	26	7	26.9	11	42.3	7	0	0	0	0
Food	49	15	30.6	18	36.7	13	0	0	0	0
Animals	9	2	22.2	4	44.4	3	0	0	0	0
Psychological factors	45	13	28.8	18	40.0	17	1	5.8	1	5.8
Most of the patients have more than one exacerbating factors.										

Our resultas showed that Nigella sativa oil is a good alternative therapy depended on cure rate appeared after 6 week treatment . It also decreases log_{10} of IgE significantly in the treated patients. Nigella sativa oil also improves the tolerability of the treated patients to exacerbating factors.

The efficacy of *Nigella sativa* oil in the treatment of chronic urticaria in this study could be attributed to its antihistaminic effects. Many authors found that carbonilic compounds of *Nigella sativa* oil such as thymoquinone and thymohydroquinone are capable for blocking bronchospasm induced by histamine [13-15], accordingly, *Nigella sativa* oil and thymoquinone (nigellone) were effectively used for treatment of allergic conditions, such as asthma and allergic rhinitis [10,11,13] .

In addition to the antihistaminic effected of nigellone, Chakravarty, also mentioned that nigellone inhibit releasing of histamine induced by antigen, compound 48:80 and calcium ionophore, because it blocks the influx of calcium to mast cell ,the step which is necessary for degranulation of histamine granules [12] .

On the other hand nigellone also contains flavonoides [17]. These compounds are efficiently inhibit production of prostaglandins and leukotrienes from arachidonic acid, because they block cyclooxygenase and lipoxigenase [18,19] . So the effects of *Nigella sativa* oil in the treatment of chronic urticaria could be attributed to its inhibitory effect on many mediators which play the main role in the pathophysiology of urticaria .

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